BOOKS BY
WILLIAM EMERSON RITTER

THE HIGHER USEFULNESS OF SCIENCE.

THE PROBABLE INFINITY OF NATURE AND LIFE.

THE UNITY OF THE ORGANISM, OR THE ORGANISMAL CONCEPTION OF LIFE. *Illustrated.*

THE UNITY OF THE ORGANIC SPECIES, WITH SPECIAL REFERENCE TO THE HUMAN SPECIES.

WAR, SCIENCE AND CIVILIZATION.

AN ORGANISMAL CONCEPTION OF CONSCIOUSNESS.

RICHARD G. BADGER, PUBLISHER, BOSTON

THE UNITY OF THE ORGANISM

OR

THE ORGANISMAL CONCEPTION OF LIFE

BY

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TWO VOLUMES
VOLUME ONE

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TO MY WIFE

MARY BENNETT RITTER

MY SEVEREST CRITIC AND

BEST HELPER

PREFACE

THE right of any book to live must be determined finally by what is on its pages. Nevertheless, when the author of a scientific book undertakes such a task as I have undertaken in this one, his natural and acquired fitness for carrying out his project ought to count in some measure toward the determination. An attempt to speak with some degree of originality and authority on subjects so remote from one another as are the chemistry of organisms, heredity, human consciousness, and the nature of knowledge, would be somewhat audacious even if made by an author of secure reputation as an investigator in one or more of these fields. When, however, the attempt is that of a complete stranger to all the fields, as thus judged, the attempt is no longer entitled to be called "somewhat audacious." It is audacious out and out, and if defensible at all is defensible in spite of its audacity. But the very nature of the task I have attempted seems to require me to contend that while it is audacious it is yet not impossible, and to point out something of my own qualifications for performing it.

Such professional fitness as I have rests primarily on my being a general zoologist in the proper sense; that is, a student of the phenomena of the animal world without exclusion of any aspect of that world from professional interest and some measure of professional attention. These facts of my vocation, and of my conception of the nature of that vocation are crucial for the quality not only of this book but all my general writings.

If once one becomes as deeply convinced as I am of both the fundamental unity and the fundamental diversity of all nature; if, in other words, he becomes convinced that the whole of nature is, indeed, and not in mere expression, a *system*, the conviction will carry with it the perception that all specialized natural knowledge is absolutely dependent for meaning on the relation it has to its appropriate larger body of knowledge. Either analytic knowledge or synthetic knowledge of nature would be wholly void of meaning were it to be completely wrenched from the other. Most men of science perhaps, and most philosophers probably, would admit that this is true as an abstract proposition. But what about its truth when brought to the test of particular cases?

The audacity of my enterprise really consists in my attempting to act according to this general truth in a particular case—the case, that is, of the phenomena of animal life. I have gone on the assumption that knowledge of animal chemistry, for example, at one extreme, and of human consciousness at the other, would be simple blanks as to meaning but for the relation of the two knowledges to each other and to still more general knowledge of animal life. Could we imagine a chimpanzee possessed of as much laboratory knowledge of organic chemistry as an Emil Fischer, that knowledge would be really meaningless were the creature's mind that of a chimpanzee in all other respects.

A systematic defense of a conception of zoology based on a general theory of natural knowledge such as this, can not, of course, be thought of in a preface. Indeed, such a conception can not be fully justified by any argument merely *for* it. The justification must be found largely in a worked-out application of the conception itself. In other words, the very fabric of this book must be the chief justification sought. All I can wish to do in a preface is to mention certain subsidiary ideas and principles that have been specially influential in determining the plans of my undertaking; and certain methods and disciplinary preparations and present conditions that have been specially useful in carrying them out.

Probably no one zoological item has influenced me more than the perception that the evolutionary interpretation of man does not mean that man's derivation from the lower animals made him something that is now not animal. It means that man is just as much an animal to-day as were his prehuman ancestors. The truth is exactly stated by saying that when the transformation took place by which man came into existence that transformation was from a lower to a higher stage of animal life. The actual problem, consequently, of man's nature is not as to what man is in *opposition* to animals, but as to the *kind*, or species of animal he is.

With the distinction here made once fully grasped comes the revelation that man is an object of zoological research and treatment no less certainly than is a horse, a fish, a lobster, or an amoeba. But since man's highest, that is his *psychical* or *spiritual* attributes are the ones most decisive of his *kind*, it is these attributes which make him particularly interesting, zoologically speaking—just as, for example, it is the attributes of a horse as *a horse*, and not as an animal generally that elicits our particular interest in the horse. Zoology rightly understood is preëminent among all the sciences as the science of particulars. This important truth seems to have been first appreciated by Aristotle; and the fact that one of the most fundamental differences between him and his teacher, Plato, concerned the doctrine of Particulars as opposed to that of Universals, is probably connected closely with Aristotle's great interest in and attention to zoology. I have not seen any reference to this surmise by writers on Aristotle and his philosophy, yet it appears to me highly significant.

From these perceptions relative to the nature of man and the science of animal life, it follows that when the zoological study of man is undertaken—when the general zoologist becomes for the time being an anthropological zoologist—all the best tested and most approved methods of that science are taxed to their uttermost, simply because of the great complexity of the species under examination. Now it is absolutely beyond question, I believe, that of the methods employed in the biological sciences, none are more important, especially for the study of man, than those of description and classification with their necessary accompaniment, comparison. The essay *The Place of Description, Definition and Classification in Philosophical Biology* in my little book, *The Higher Usefulness of Science,* treats of this subject somewhat at length. But that to which I attach much more importance is that almost everything contained in the present book, except the heart of Chapter 24, I regard as an embodiment of the fundamental principles of descriptive and classificatory biology as these principles are established by modern research.

It seems to me I am privileged to claim that no reader of this and other general writings of mine is in position to pass judgment on them, except, of course, as touching trustworthiness of observation and statement, and of dependability of authorities cited, without having considered conscientiously my position as to method. For instance, am I right or wrong in holding (see the above mentioned essay) that far the larger part of what is usually called explanation in dealing with the phenomena of nature is really partial or tentative or hypothetical description and classification? What justification and scope are there for my contention that the motto "neglect nothing," which has long done good service in taxonomic research based on morphology, must be extended to all departments of structural and functional biology? What grounding and applicability are there for my distinction between synoptic and analytic description, and synoptic and analytic classification? Not until one has come to see that questions of this sort are necessary consequences of progress in information about, and interpretation of living nature, is he able to appreciate fully what I mean by chemical and psychological zoology. Formal biochemistry and animal psychology, that is, the chemistry and the psychology of laboratories devoted to these subjects, are to my zoological eyes really quite incidental and partial and crude, albeit immensely important. Let one once feel the full weight of the inductive evidence favorable to the hypothesis that every organism whatever performs every jot and tittle of its activities through chemico-physical agencies, and he must at the same time feel the meagerness and crudity, comparatively speaking, of even the fullest and best laboratory knowledge of those agencies by which he himself, let us say, operates as he carries through and expresses in words an argument like that now occupying us.

The absolute trustworthiness of the main findings of laboratory biochemistry and its incalculably great importance, but at the same time its great imperfection as compared with natural biochemistry, are what especially impress me as I bring my best powers to bear on the deepest, most distinctive problems of anthropological zoology; problems, in other words, of the *human* animal.

Such an attitude toward biochemistry will, I hope, be recognized even by biochemists as calculated to induce at least a receptive frame of mind toward knowledge in this domain. It should be one important qualification for "reading up" in the domain. But certain it is that something more than a receptive mind is essential to enable one disciplined in one field of science to be a successful gleaner of ripened fruit in another field. It is not true that all the domains of natural knowledge, highly developed as they now are, are enough alike to make training in any one an adequate preparation for acquiring second hand knowledge in every other. At least a background of systematic instruction in a particular science is requisite to make a highly successful reader even in that science.

So far, then, as I am able to pass upon my own qualification for making such use as I have made of biochemistry, it is a question of whether I have a sufficient ground-work of formal training to make me a safe chooser among authorities and estimater of the significance of their results.

Although my chemical practice was limited to three years, one of these as a student assistant, so much did I live in the laboratories during that period, that even to-day the opening of a book or journal on chemistry seems to fill my nose with foul though pleasantly reminiscent odors and to encrust and stain my fingers with diverse corrosives—all of which may mean that I was more a musser in chemicals than a real student of chemistry. Nevertheless I verily believe the experience enabled me to be a more intelligent reader of chemical writings.

As for the science of mind, I am obliged to own that I have never spent a day in an experimental laboratory of either animal behavior or human psychology. But I own also that for this I am not regretful if such defect of training be an essential condition of escape from the narrowing of interest in and conception of "behavior" which has attended later work in this field. I do not believe, however, that this is the only way of such escape. Zoologists must realize before long, I am quite sure, that laboratory experimentation in animal behavior can be only a rather minor agent for the task of understanding the psychical life of the animal world as a whole.

This leads to the remark I wish to make about the discussion of psychic integration in the last chapters of this book. One of the most important things accomplished by that discussion is, I estimate, the calling attention to the tendency of instinctive activity to excessiveness over the actual needs served by the activity. Why has this truth (for there can be no question that it is a truth) not received more attention from modern behavior specialists? There are probably several reasons, but a particularly influential one seems to be the fact that the very purpose, and the method of experimentation involving the idea of control by the student are such as to encourage overlooking the phenomena, and to obscure their significance even if they are noticed.

Unorthodoxly enough from the standpoint of present school psychology, my entrance into this realm was from the side of the nature and the theory of knowledge. And so far as my explorations in the realm have gone, two men, Aristotle and the late Professor G. H. Howison have influenced me so vitally that I must say a few words on the subject.

For many years Aristotle was two distinct persons to me, so far as any real influence upon my thinking was concerned. On the one hand there was Aristotle the metaphysician to whom I had been formally introduced by Howison in a private outside-of-hours University course (which with great generosity he had given me), the medium of the introduction being the *De Anima*. On the other hand was Aristotle the zoologist, acquaintance with whom was at first picked up in the usual naturalist fashion, but which had later ripened into intimacy, as I like to characterize it, by our common interest in marine zoology, his good description of the anatomy of a tunicate being a special passport to my affection. It would hardly be an exaggeration to say that all my philosophizing in biology has aimed at fusing these two Aristotles into one. I do not mean that this has been my conscious and express aim. It has been so only instinctively, or intuitively, or "at heart," or by "working hypothesis," or by whatever expression one chooses for it. And here comes the part played by Professor Howison: As I take a bird's eye view now of what is set forth in this and other general writings of mine, and contemplate the whole in the light of the preface to Howison's book, *The Limits of Evolution*, and then look reflectively back over my thirty years of contact with him and his teachings, most of it incidental and fitful, but some of it rather close, a few influences of his, some positive and some negative, stand out sharply indeed. The positive influences I mention first. No other influence contributed so much to my belief in the power of reason; that is, in a substratum of truth to the idealistic philosophy. Again no other influence contributed more to my belief in persons—in the power of personality; that is, in a substratum of truth to the Howisonian philosophy of personal idealism.

A statement of the negative influence coming from the same source takes us back to Aristotle. In the preface to *The Limits of Evolution* Howison writes, referring to his own theory of Personal Idealism, "The character of the present theory, relatively to Aristotle, is to be found in its attempt to carry out the individualistic tendencies in Aristotelianism to a conclusion consistently coherent." This statement I could almost adopt word for word as a characterization of the purpose that has animated all my general thinking and writing. Yet how profoundly does the outcome of my efforts differ from that resulting from Professor Howison's efforts! And here is the kernel of my present remarks: In commending to me the *De Anima* of Aristotle and generously undertaking to guide me through it, as a response to my appeal for help toward clarifying my mind concerning the deeper, the philosophical meaning of biological evolution, my greatly learned and much esteemed teacher had a purpose, I am now quite sure, that is impossible of realization. That purpose was to show that Aristotle failed in his effort to recognize a "real world" through combining "ideal form" with "real matter," because for him a real world was more fundamentally a sense-experienceable world than is actually the case. As I labored through the

De Anima I recall that I was disturbed by the rather cavalier fashion in which we disposed of those portions of the work which treat of reproduction, nutrition and growth, and especially the portions dealing with the senses. At the stage of scientific development I was then in, I knew little or nothing of Aristotle's biological writings, and Howison referred to them only in the most cursory way, if indeed he mentioned them at all. Certain it is he did nothing to arouse my interest in them, or to indicate that he regarded them as specially significant in connection with such important views of Aristotle's as those on the relation of Body and Soul. The question which now seems to me indispensable for grasping the essense of the Aristotelian psychology and philosophy that, namely, of why Aristotle was so greatly interested in zoology, and devoted so much time to its study, never came up during the course, I am quite sure. In science and philosophy as in everything else, the character of one's interests is a surer index to his general views and attitude than is anything he can express verbally. There may be ambiguity and error in Aristotle's theory of "synthetic Entelechy." This theory may, probably does, "beset," as Howison remarks, "all individual existence both behind and before," thereby implying some theoretical derogation from the real nature of personality. But over against this error and ambiguity stands indubitable proof of Aristotle's practical faith in the Particular, the Individual, that proof being the vast labor he expended in learning and interpreting the life of the animal world. The chief philosophic significance of Aristotle's zoological works is not in any information or theories they contain but in the fact that he produced them at all, since, as mentioned above, zoology is preeminent as the science of particulars, and his doctrine of Particulars as opposed to Universals was very close to the heart of his whole philosophic system.

This prepares for my final remark about the influence upon my thinking of Professor Howison and the idealistic philosophy generally. That philosophic Idealism, no matter of what variety, contains elements that are fundamentally erroneous seems to me to be proved more conclusively by its inadequacy for understanding the world in its entirety than by any particular errors of fact or reasoning which it can be shown to contain. Were all men philosophical idealists, there would be no natural science, merely because in the domain of learning men will not choose as their primary life work what they fully believe to be of secondary importance.

Fallaciousness or inconclusiveness of argument never deterred me half as much from embracing Professor Howison's teachings in their entirety as did his usually dignified but always-present presumption of professional self-superiority over all his colleagues who did not come under the, to him, sacred ægis of Philosophy. The reason why sincere humility and the spirit of democracy are alien to all forms of idealistic philosophy becomes clear once one attains a world view which truly strives to include, but makes no pretense of having already included, the whole world wholly in that view.

There remains the pleasant though difficult task of mentioning the few among my numberless obligations which are so personal and weighty that to leave them unacknowledged would be to brand me as ungrateful, more conspicuously than I can endure.

First as to those persons and conditions which, during the last ten years, have relieved me from the routine duties of a University teacher, and also from most of the exactions customarily attaching to an administrative post even in an institution of scientific research, and have given me a status the central purpose of which is scientific work. Whatever be the quality and final significance of my life-work, could these, I ask myself, have reached as high a level as they have reached had I not come into my present position? Almost certainly not, must be the answer. And beyond a doubt the raising of the question involves principles of organization for scientific research that lift it high above mere personal concern.

No faith of mine is greater because none is rooted more deeply in my scientific philosophy, than that in the ultimate triumph of popular, that is of democratic principles in all aspects of civilization. Indeed the *facts*—not the *theories*—of organic unity and integration which have dominated all my later work are the foundation of this faith. Whether my particular hypotheses and theories of organismalism succeed or fail, there still are the raw data on which they rest. These can not fail. If success does not crown my efforts in handling the data it will crown those of others who shall come after me. And when the principles for which I contend shall have worked themselves more fully into the fabric of civilization, the organizational, the administrative, and the scientific policies aimed at in the Scripps Institution for Biological Research of the University of California will be recognized as fundamentally sound. I will be specific here to the extent of mentioning the policy of providing a special business management for such institutions.

Although my indebtedness to my professional co-workers and official associates of the Zoological Department and the Museum of Vertebrate Zoology at Berkeley, Professors C. A. Kofoid, S. J. Holmes, and Dr. Joseph Grinnell, is indicated by special references in the body of this book, I should be sorry to have these references taken to indicate the full extent of my obligation to them, or to indicate that these are the only members of those departments to whom I am indebted.

It would be a source of keen regret to me, too, should my single short reference to two of my biological associates on the staff of the Scripps Institution, Mr. E. L. Michael and Dr. C. O. Esterly, be taken as the full measure of what I owe to them. I hope that my reference to their work, brief though it is, will be recognized as indicative of the high importance I attach to what they have done and are doing.

But what about my indebtedness to professional associates here in the home group of whose work no mention is made in my text? How subtle and far-reaching and innumerable are the influences which bear upon one from his daily co-workers! For example, by what unit of measurement could be gauged the effects on my treatment of heredity, which have come from my perpetual contact with the work of Dr. F. B. Sumner and Mr. H. H. Collins? But these men would probably resent the ascription to them of responsibility for my main conclusions in this field. Again, not many "environmental factors" have been more determinative of my present feelings (I hardly dare call them views) relative to various problems in geo-physics, and relative to quantitative methods in natural science, than have Dr. G. F. McEwen and his oceanographic work. Yet I hesitate even to mention this fact lest some one be led thereby to hold Dr. McEwen accountable for crudities, actual or implied, I may manifest in these domains.

Nor are my indebtednesses confined to the narrow circle of my immediately professional and official co-workers. Indeed I am keenly conscious of great debts beyond this circle. These are so numerous and on the whole so general as to make specification impossible, but I cannot pass by without mentioning my debt to my long-time and much-cherished friend, Professor G. M. Stratton, for the commentaries on the chapters on psychic integration made by him while this portion of the book was in an advanced though still formative stage.

For aid in structurel labor, as it may be called, my dependence upon Mr. Frank E. A. Thone, my secretary and scientific assistant, has been varied and intimate, and of a quality for which money can only partly pay.

To Dr. Christine Essenberg, librarian and member of the scientific staff of the Scripps Institution, I am indebted for help on the index and glossary.

And finally, what can I say about the part played in the creation of this and my other works by her to whom this volume is dedicated? The extent to which her life is involved with mine in these works only we two can know; but the wording of my dedication indicates something of the character of that involvement.

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CRITIQUE OF THE ELEMENTALIST CONCEPTION OF THE ORGANISM

A. Composition of the Living Individual

THE UNITY OF THE ORGANISM

Chapter I

INTRODUCTORY

Historic Background

EVERY biologist is familiar with the phrase "the organism as a whole." It occurs over and over again, particularly in later years, in written and spoken discussion touching a wide range of subjects; and the essential idea, expressed in different terms, is still more common. To attempt an exhaustive list of instances of the use of the phrase or its equivalents would be profitless, but enough must be said both at the outset and at various places along the way to furnish a secure historic foundation for the enterprise we are undertaking.

In its earliest infancy the science of living beings presented two theories apparently diametrically and irreconcilably opposed to each other. Stating the case in familiar terminology, according to the one the organism is explained by the substances or elements of which it is composed, while according to the other the substances or elements are explained by the organism. * Since it will be necessary to refer frequently throughout our discussion to these two

* The word "explain" calls so loudly to be itself "explained" when used in this offhand way that one reluctantly lets it go unheeded even temporarily, but it must be passed now with this sole remark: whatever meaning may be attached to it in one of the above propositions, exactly the same meaning must it have in the other.

standpoints or theories, a short designation for each is desirable. Historically viewed they might be spoken of as the Aristotelian and the Lucretian. But far more satisfactory because descriptive in a luminous way, are the terms "organismal theory," or if one may be permitted to coin a word, "organismalism," for the Aristotelian; and "elemental theory," or "elementalism" for the Lucretian.

The essence of the idea is set forth with admirable clearness in the early pages of that protogenal book on zoology, *On the Parts of Animals*, by Aristotle. "But if man and animals and their several parts are natural phenomena, then the natural philosopher must take into consideration not merely the ultimate substances of which they are made, but also flesh, bone, blood, and all other homogeneous parts; not only these, but also the heterogeneous parts, such as face, hand, foot, and so on. For to say what are the ultimate substances out of which an animal is formed . . . is no more sufficient than would be a similar account in the case of a couch or the like. For we should not be content with saying that the couch was made of bronze or wood or whatever it might be, but should try to describe its design or mode of composition in preference to the material. . . . For a couch is such and such a form embodied in this or that matter, or such and such a matter with this or that form. . . . It is plain, then, that the teaching of the old physiologists is inadequate, and that the true method is to state what are the definitive characters that distinguish the animal as a whole; to explain what it is, both in substance and in form, and to deal after the same fashion with its several organs." [1]

Not only is the idea itself piquantly stated, but as no one will fail to notice, the antithetic idea with which it has had to contend perpetually from that day to this is also unmistakably indicated. Another cardinal point will not be missed: not only does Aristotle sketch these two antithetic ideas with a firm hand, but he leaves no room for doubt as to which side of the ages-long controversy he is on. He is always on the side of the organism as against its substance.

Were we permitted to take this statement by Aristotle out of its setting in his general doctrine of living beings it would very well present, as far as it goes, the standpoint that will be maintained in the present treatise. However, when we come to follow him further and find what his distinction is between substance and form, and to see how the latter is related to the soul and becomes involved in the problems of purpose and necessity, we have to recognize that in reality the passage comes a long way from meaning what we should mean by the same words. Wherein the difference lies will appear as our enterprise develops.

The earliest defender of the opposite idea whom we shall notice was Lucretius. Although this poet-naturalist professed to be a follower of Empedocles and Epicurus, his formulation of biological elementalism is so explicit and so readily accessible to modern readers that it will serve well the needs of this discussion. In the third book of *The Nature of Things* Lucretius gives his reasons for rejecting the Greek notion of the "mental sense" of man and animals as a Harmony—a something which arises as a vital product of the whole, and then defends at length the counter hypothesis, namely that the mind and soul, that is, life, is a definite, independent, though complex substance. I quote a few sentences from the theory which Lucretius is sure is right, using the translation by the Reverend J. S. Watson: "I shall now proceed to give you a demonstration, in plain words, of what substance this mind is, and of what it consists. In the first place, I say that it is extremely subtle, and is formed of very minute atoms." After illustrating the activity and pervasiveness of the soul throughout the body, the author continues: "It must therefore necessarily be the case, that the whole soul consists of extremely small seminal-atoms, connected and diffused throughout the veins, the viscera and the nerves." Then comes a discourse on the nature of the soul substance: "Nor yet is this nature or substance to be regarded by us as simple and uncompounded. For a certain subtle aura, mixed with heat, leaves dying persons; the heat moreover, carries air with it. . . . Nor yet are all these constituent parts, aura, heat, and air, sufficient to produce mental sense or power. A certain fourth nature or substance must therefore necessarily be added to these: this is wholly without a name; it is a substance, however, than which nothing exists more active or subtle, nor is anything more essentially composed of small and smooth elementary particles; and it is this substance which first distributes sensible motions through the members. . . . This fourth principle lies entirely hid, and remains in secret, within; nor is anything more deeply seated within the body; and it is itself, moreover, the soul of the whole soul." [2]

The further need our enterprise has to draw upon history as such permits us to leap across nearly eighteen centuries, for the next occurrences touching these theories which greatly concern us belong to the period of splendid achievement in the sciences of living beings from Linnaeus' *System of Nature* to Darwin's *Origin of Species.* The course of thinking and discovery during this period has been so interpreted as to appear to constitute a virtual proof of the correctness of the elementalist theory. It is said that in the Linnean era plants and animals were treated from the standpoint of the organism as a whole, and that later, under the chieftainship of Cuvier, "instead of the complete organism, the organs of which it is composed became the chief subject of analysis." Then, with Bichat leading, came the advance to the tissues; then before long the discovery was made that not the tissues but the cells are the real units of structure, Schleiden and Schwann being foremost in this forward step; and finally, with the demonstration, accomplished chiefly by Max Schultze, that one substance, protoplasm, is the common basis of life in plants and animals, real biology was attained. This interpretation declares that on the morphological side there was progress step by step "from the organism as a whole to organs, to tissues, to cells, and finally to protoplasm, the study of which in all its phases is the chief pursuit of biologists." [3]

This picture is undoubtedly true to a certain extent. Science surely began with observations on organisms whole and living, and only gradually did it take them to pieces to learn their parts and so to deepen understanding. But in so far as it gives the impression that the study of organic beings has moved along a direct course from the organism as a whole toward the ultimate elements or substances of which organisms are composed, and has become scientific just in so far as and no further than it has advanced in this direction, becoming genuine biology only when protoplasm is reached, it is not in accord with history or the nature of scientific knowledge. The introduction of the word *biology* into science by Treviranus and Lamarck in the very first years of the nineteenth century was deliberate and fully justified though it had no special reference to tissues or cells, much less to protoplasm. But the unfaithfulness of the above sketch to actual history which I wish to point out particularly, concerns the part played by the group of French biologists of which Cuvier is the best known member.

It would hardly be possible to miss more completely the significance of these men than to conceive Cuvier as making the "organs of which the organism is composed" the chief subject of study "instead of the completed organism." The distinctive feature about the school was not the idea of the organs as such, but as parts of the whole. The ensemble, the principles of co-existence, or correlation, of subordination of organs and "characters," are what stand out most prominently in the writings of these men, so far as general conceptions are concerned. Cuvier, as above indicated, is regarded as the central figure of the group, but this comes more from the vast extent of his achievements and from his general masterfulness than from his originality and depth of insight. The leading idea was not due to him, as he fully recognized, but to the Jussieus, uncle and nephew. Concerning their *Genera Plantarium,* Cuvier said in his *History of the Natural Sciences*: "This work produced a veritable revolution in botany, for only since its publication have plants been studied according to the relations which they exhibit and according to the totality of their organization." These botanists, we are told, conceived the organs and parts to be correlated with one another, i.e., dependent on each other and united to form the totality of their organization. Cuvier made this principle his own by adoption, and applied it with great vigor and success in all his zoological and anatomical studies. His statements of it are numerous and varied in form, one of the fullest and clearest being in the "Discourse" with which the *Researches on Fossil Fishes* is introduced: "Every organized being forms a whole, a system unique and closed, of which the parts mutually correspond and concur in the same definitive action through a reciprocal reaction. No part may change without the others changing also; and consequently each of them, taken separately, serves as an index and an exposition of the others." [4]

While Cuvier made much of this principle, his shortcomings in understanding and applying it are obvious and far-reaching. He used it primarily in the interest of classification, and classification seems to have been the first goal of his scientific endeavor. But it being as little possible for a Cuvier as for any other thoughtful biologist really to go no further than to glean and marshall facts, it was exactly this principle that became his speculative stronghold, and then his speculative undoing. He made it the basis of his conception of types, and the Type became with him a sort of Platonic Idea, an eternal, more or less subjective entity. It was in the hands of Geoffroy Saint-Hilaire, Cuvier's early collaborator and later antagonist, that the principle received its best development. Working out a Theory of Analogies in his *Philosophical Anatomy*, he considers several possible explanations of analogies but rejects all but three, these being: (1) the relative position, the mutual dependence of organs; (2) the elective affinities among the organs, defined to mean that "the materials of the organs survive in some fashion the organs themselves, and, when the latter cease to exist, the analogy nevertheless does not cease"; and (3) the balance of organs, the meaning of which is that "an organ, normal or pathologic, never acquires an unusual prosperity, without a related organ, or one in the same system, suffering for it." [5]

Saint-Hilaire's application of these principles to the interpretation of rudimentary organs and to teretological growths show well the thorough-going objectivity of his conception; and his *Principles of Philosophical Zoology* (1830) are only accentuated examples of the fact that the organism as a whole, as he looked upon it, was the organism as composed of all its parts, and further, that he was a genuine biologist if ever there was one, in spite of the fact that if he ever saw any protoplasm there is no evidence that it played any considerable part in his thinking. This whole group of the late eighteenth and early nineteenth century biologists must be taken not only as upholders of the organismal theory, but as having greatly advanced its definition and application.*

* Were it our purpose in this chapter to present an exhaustive critical study of the presence and growth of organismal conceptions in biology it would be necessary to examine somewhere, probably at this point, the ideas of the *organicists,* a group of embryologists and physiologists who

As we glanced at the organismal and elemental theories when they opposed each other in the infancy of biology, we must look at them still opposing each other in this era of what we may call the adolescence of the science. The organismal side we have already spoken of in our glance at the work of the French biologists of the early nineteenth century. As an elementalist of this period I choose Theodor Schwann. In his *Microscopical Researches into the Accordance in the Structure and the Growth of Animals and Plants*, published in 1839, he said: "We may, then, form the two following ideas of the cause of organic phenomena, such as growth, etc. First, that the cause resides in the totality of the organism. By the combination of the molecules into a synthetic whole, such as the organism is in every stage of its development, a power is engendered, which enables such an organism to take up fresh material from without, and appropriate it either to the formation of new elementary parts, or to the growth of those already present. Here therefore the cause of the growth of the elementary parts resides in the totality of the organism.

"The other mode of explanation is that growth does not ensue from a power resident in the entire organism, but that each separate elementary part is possessed of an independent power, an independent life, so to speak: in other words, the molecules in each separate elementary part are so combined as to set free a power by which it is capable of attracting new molecules and thus increasing, and the whole organism subsists only by means of the reciprocal action of the single elementary parts. So that here the sin-

worked during the first two-thirds of the nineteenth century. Delage (L'Hérédité, p. 750) mentions C. E. Von Baer, Claude Bernard, M. Bichât, W. His and E. Pflüger as representative of this group. The philosophical importance of the ideas held by these investigators has been emphasized by L. J. Henderson (The Order of Nature). But there is, as I believe, a vein of subjectivistic metaphysics implicit in their conceptions which throws them somewhat out of the main organismal current.

gle elementary parts only exert an active influence on nutrition, and the totality of the organism may indeed be a condition, but is not in this view a cause." [6]

It is hardly necessary to say that Schwann himself adopted the view last presented, and that cells were, as he believed, the "elementary parts" mentioned in his statement. Under other heads we shall find it necessary to speak with some fullness of Schwann's doctrinal views and mode of reasoning. Our needs in this purely historical reference will be satisfied by calling attention to the fact that he states the elementalist theory in general terms only, that is, in terms of "elementary parts" and "molecules." This fact shows his conception of the problem in the large. His contention that cells are the elements sought must be understood to be an hypothesis secondary only to his broader conceptions. The recognition of this two-fold aspect of Schwann's teaching I deem of prime importance, for it shows clearly that his theory of cells as the ultimate elements of living beings was not a conclusion arrived at by purely inductive processes, but rather as an interpretation of cells in accordance with an ancient idea well known to him and adopted by him. So the very great significance of Schwann's work must be looked upon in two distinct lights: first, in that of a generalization of unqualified validity and of the highest importance, concerning the proximate composition of plants and animals, that is, their cellular composition; and second, in that of furnishing what seemed so solid a foundation for the ages-old elementalist theory of living beings as to secure to it well-nigh complete domination of biological thought for a generation. I think it is not going too far to say that through the influence of the cell theory as promulgated by Schwann, following as it did close upon the foundation of histology by Bichat, the organismal conception lay almost wholly dormant during the fifty years from 1840 to 1890.

This reference to Schwann as an elementalist being primarily in the interest of our historic background, a critical examination of his position would be out of place. But it is desirable to call attention to one important logical, or perhaps more properly psychological, implication of his standpoint. The elemental theory applied to organisms which, as we have just seen, he stated so well and adopted in his interpretation of the cellular composition of organisms, is in reality not so much of a theory of organic phenomena themselves as of knowledge of those phenomena. In other words, Schwann started out in his investigations not, in the first instance, with a theory of *organisms*, but with a theory of *knowledge of organisms*. The great importance of this mode of approach to biological problems will be brought out more fully later. Enough is it to remark here that so much has the theory of scientific knowledge applied in Schwann's position grown in definiteness and influence with time, that to-day many biological elementalists hold unquestioningly the view that the sum and substance of scientific knowledge of organic beings is a knowledge of the elements of which these beings are composed. According to the theory of biology held by these biologists, the business, and the only legitimate business, of the science is to reduce organisms to as few and as simple elements as possible; and in its extreme form the aim is exactly what it was with the very earliest elementalists, namely to reach finally one or a very few ultimate elements. To explain organisms is, according to this theory of knowledge, to reduce them to their elements, and it is nothing else.

Since 1890 the organismal view has exhibited a rather vigorous reanimation. Details as to how this has come about and as to what the renewed manifestations of life consist in cannot be entered into now. However, one highly significant circumstance must be noted: the rehabilitation has had little or nothing to do with the form assumed by the theory in the hands of the French biologists considered above. It has on the contrary arisen in a sense *de novo*, and in consequence of a growing recognition of the inadequacy of elementalism as bodied forth in the cell theory applied to the development of individual organisms. So while we listen now to voices that have been raised against the attempt to explain ontogenesis as a cellular phenomenon merely, it must be borne in mind that we are doing so not for the purpose of examining the cell doctrine in general, but only to fix attention on the historical fact that the elementalist standpoint as manifested in this aspect of the cell theory finds itself face to face once again with its old opponent, the organismal standpoint. The cell theory as such will demand a chapter for itself, when its turn comes.

The case of the organismal theory is shown with special clearness in the writings of three American biologists, C. O. Whitman, E. B. Wilson and F. R. Lillie. Whitman, as is well known, was primarily an embryologist, his best researches having been on the development of leeches and bony fishes, and his observations in this field were the starting point for his views on the relation existing between cells and the organism. In his essay, *The Inadequacy of the Cell-Theory of Development*, he says: "Comparative embryology reminds us at every turn that the organism dominates cell-formation, using for the same purpose one, several, or many cells, massing its material and directing its movements and shaping its organs, as if cells did not exist, or as if they existed only in complete subordination to its will, if I may so speak." [7] And he ends the essay *The Seat of Formative and Regenerative Energy*, with this: "The fact that physiological unity is not broken by cell-boundaries is confirmed in so many ways that it must be accepted as one of the fundamental truths of biology." [8] The reader should not fail to notice that while in both these essays Whitman's arguments were against the hegemony of cells, in the one case he was looking at the organism primarily from the morphological standpoint while in the other he viewed it more from the physiological side.

In the mere matter of extent and deliberateness of reliance upon the principle of organic wholeness, nothing in recent biological literature with which I am acquainted is more impressive than what one finds in *The Cell in Development and Inheritance*, by E. B. Wilson. The organism as a whole or some obvious substitute therefor is appealed to on no less than seventeen pages of this book, these appeals being scattered all through from the beginning to the end of the volume. So far as such views of this distinguished cytologist have been embodied in a single sentence, the following in his essay, *The Mosaic Theory of Development* seem to contain them: "The only real unity is that of the entire organism, and as long as its cells remain in continuity they are to be regarded, not as morphological individuals, but as specialized centers of action into which the living body resolves itself, and by means of which the physiological division of labor is effected." [9]

The most recent and in several ways the most significant presentation of the organismal theory in relation to cells comes from another embryologist, F. R. Lillie. It is worth noting that this time the chief grounds of the presentation are experimental embryology, whereas with Whitman they are embryology unaided by experiment. In 1906 Doctor Lillie published an unusually interesting research on the development of a species of worm, *Chaetopterus pergamentaceus.* The kernel of the results was a confirmation and extension of previous observations by himself and several other investigators that under certain conditions the embryo of some species of annelid worms may progress some distance on the developmental course before cellular or even nuclear multiplication takes place. The author's summary of facts may be given in his own words: "In general the following statement may be made concerning the differentiation of the uninucleated eggs. (1) Organs are never formed, but only such structural elements as may occur in single cells of the trochophore. (2) Organs may, however, be simulated by the aggregation of the characteristic matter of the organ, for instance in the case of the yellow endoplasm, which simulates the gut of the trochophore, or the row of large vacuoles situated near the upper margin of the yellow endoplasm which simulates the row of vacuoles of the prototroch. (3) Structural elements appear in the same order of time as in the trochophore. (4) The distribution of the structural elements tends to resemble that of the trochophore. (5) The yellow endoplasm (yolk?) is used up, apparently for the maintenance of the metabolism in the ciliated unsegmented eggs precisely as in the larva." [10] The theoretical bearings of the observations are indicated by the following: "The possibility of a considerable amount of embryonal differentiation without either nuclear or cytoplasmic division may be considered established. This in itself is an important fact, for it disposes effectually of all theories of development that make the process of cell-division the primary factor of embryonal differentiation, whether in the form of Weismann's qualitative nuclear division, or Hertwig's cellular interaction theory. Further, the phenomenon establishes firmly, as I pointed out in 1901, the view that the role of cell-division in development is primarily a process of localization.[11]

Lillie presents his still broader interpretation in an exceedingly interesting section headed "Properties of the Whole (Principle of Unity)." From this I quote somewhat more at length than is essential for our immediate purpose of gaining a bird's-eye view of the field we are entering, since later we shall want to examine several of the items more closely. "The traditional view, held by many embryologists at the present day, is that the physiological unity arises in the course of embryonic development by the secondary adaptation of originally independent parts to one another. But this explanation has, in my opinion, become untenable, and must be replaced by the view that there are certain properties of the whole, constituting a principle of unity of organization, that are part of the original inheritance and thus continue through the cycles of the generations, and do not arise anew in each. Weismann places this principle of unity of organization in the architecture of the germ-plasm, but, as I cannot accept his view of vast complexity of the germ-plasm, neither can I accept this principle in the sense of Weismann." [12] . . . "If any radical conclusion from the immense amount of investigation of the elementary phenomena of development be justified this is: That the cells are subordinate to the organism, which produces them, and makes them large or small, of a slow or rapid rate of division, causes them to divide, now in this direction, now in that, and in all respects so disposes them that the latent being comes to full expression. . . . The organism is primary, not secondary; it is an individual, not by virtue of the coöperation of countless lesser individualities, but an individual that produces these lesser individualities. . . . The persistence of organization is a primary law of embryonic development." [13]

Without looking further into recent and contemporaneous literature, enough has been brought forward to show that the organismal standpoint has a solid footing in current biological theory. We should, however, be grievously amiss should we conclude that because the theory has captured one stronghold it has won the whole battle. As a matter of fact, the very men who have admitted the rights of the organism as against its cells in development are yet far from admitting those rights as a general proposition; that is, as against all the elements of whatever order that enter into its makeup. Thus Whitman says, "If the formative processes cannot be referred to cell-division, to what can they be referred? To cellular interaction? . . . The answer . . . will . . . as Wiesner has so well insisted, find a common basis for every grade of organization. It will find the secret of organization, growth, development, not in cell-division, but in those ultimate elements of living matter for which idiosomes seems to me an appropriate name." [14] This sentence, with those immediately following it, leaves no question that in 1893, when he wrote the essay in which it occurs, Whitman was at heart an elementalist as much as was Lucretius or Schwann or Weismann. The only real step he had taken in the direction of the organismal standpoint was that of seeing clearly that the cells could not be "ultimate units" of organization. Indeed there is considerable indication that so far as the general problem is concerned, the position he held in 1893 was somewhat backward from that which he held five years before, when he wrote *The Seat of Formative and Regenerative Energy*, for in that essay he said: "Let us now consider whether any rational basis can be found for the idea of a formative power as a resultant from, and an expression of, physiological unity. I am fully conscious that the subject is one of profound mystery, the solution of which appears to lie as far beyond our grasp to-day as at any time in the past. We draw nearer to the problem, but the effect is rather to enhance than to reduce its apparent magnitude. Every step in advance only brings us to a keener sense of the subtle and incomprehensible nature of the force or forces contemplated." [15]

The extent and nature of Wilson's faltering between the two standpoints, even as between the organism and its cells, in spite of his constant and earnest appeal to the the organism as the "only real unity" we shall consider in some detail when we deal with the cell-theory.

Lillie has, I believe, advanced farther toward the conception that will be defended in this work than either of the other biologists whose view we are now considering, even though he is far from admitting the organism to full standing in his conceptions. "Undoubtedly," he says, "it [the principle of unity] is capable of further analysis, and it must ultimately be derived from particular relations and properties of material particles";[16] and the conceptual form which the material particles, by virtue of their "particular relations and properties" assumes in Lillie's mind is the "formative stuffs" which, since the theory of such substances was first given definiteness and plausibility by Julius Sachs, have figured largely in speculative biology. "The theory of formative stuffs," Lillie writes, "does away with any 'determinant' hypothesis. 'Characters' are not due to 'unfolding' of the 'potencies' of 'determinants' but are results of morphogenic reactions between two or more formative stuffs. The 'character' need no more be preformed in the reagents (formative stuffs) in the case of a morphogenic than in the case of a chemical reaction." [17]

This interesting, and up to a certain point entirely acceptable, language of Lillie's will be examined more closely in another connection. Enough for now to say dogmatically that the author's "formative stuffs" is only another elementalist refuge and so no more satisfactory than is the cellular refuge which he himself abandons, or than are any of the innumerable other refuges to which innumerable other elementalists have fled.

The historic background for our enterprise will be completed when we have pointed out how it is faring with these two theories at present. This can be done with great brevity since what we find will be exactly what will most occupy us when we come to the substantive rather than the historic part of our task, when the superstructure rather than the foundation is at hand.

The organismal line of descent which our cursory survey has traced from the period of Aristotelian zoology, through that of French comparative anatomy of the late eighteenth and early nineteenth centuries, through what might with propriety be called the period of American embryology, now barely ended, holds its unmistakable course on into what we may speak of as a physiological period, in the midst of which we now are. It should be remarked that "physiological" as here used does not refer so much to physiology in the professional sense as to an approach to certain developmental phenomena of the organism from the functional side, since the biologists who are tending toward the organismal theory are not primarily physiologists but students of individual development.

The term most characteristic of this latest outcrop of organismalism is correlation, and what is distinctive about the present effort as contrasted with that which marked the idea of correlation held by the French anatomists is that now the correlatedness of parts in the organism is being looked at from the functional more than from the structural side; and that the necessity is felt more than it was in the earlier period, of finding a causal explanation of the correlations. "Equilibrium" is another term that is frequently used by the biologists whose thinking is of this cast, and the kinship of this to Saint-Hilaire's "balance" will not escape the reader's notice. This doctrine of physiological correlation is receiving its fullest elaboration at the hands of C. M. Child, though numerous investigators are contributing importantly to it. K. Goebel, E. Radl, W. Pfeffer, L. Jost, J. Nusbaum, E. Schultz, H. Rand, S. J. Holmes and C. Zeleny may be mentioned as biologists who have dealt more or less directly with the problem. Undoubtedly H. Driesch's "harmonious equipotential systems" ought to be mentioned in this connection, though this author's unqualified commitment to an extra-natural explanation of biological phenomena will hardly permit us to enroll him in the group of workers referred to.

The organismal standpoint escapes its ancient adversaries when it comes to expression as physiological correlation just as little as it has escaped when it has appeared under any of its earlier forms. Thus although correlation plays a large role in the writings of W. Roux, the founder of developmental mechanics, approach to the correlation-complex for him seems always to be from the direction of the elements in the complex and never from that of the complex itself; so it results that the organism as such has no standing in his conceptions on a par with that of the elements which constitute it. This fact comes out clearly from an examination of the various definitions bearing on the point given by Roux in his *Terminologie der Entwicklungsmechanik der Tiere und Pflanzen.* Thus as a definition of *organism* we find "*Organism* means a complex of organs; hence, of instruments." [18] Or for *living being* (regarded as a synonym for *organism*) we find: "*Living beings, bion,* pl. *bionten,* are natural bodies which distinguish themselves 'minimally' from inorganic natural bodies through a sum of definite elementary functions which directly or indirectly subserve self-preservation, as also through self-regulation in the exercise of all these functions; and thereby, in spite of 'self-alteration,' and through the same, and also in spite of the necessary complicated and soft structure, are very permanent." [19] Again, " 'Ganzbildung,' Holoplast, is a more or less fully developed, but fully formed structure, representing an entire organism, which has arisen out of a blastomere, or egg-fragment." [20]

From these as typical definitions it is seen that in no case is *organism* conceived and defined as having characters wholly its own, but, by implication, only those belonging to its parts. Indeed, a critical study of the speculative writings of Roux and his adherents will, I believe, convince any one that the most characteristic thing about developmental mechanics as a system of thinking on biological subjects is its effort to deal with organisms in terms of *parts of organisms;* otherwise expressed, that it is a systematic effort to avoid recognizing the organism in itself as a true objective entity. Because of the persistence, industry, enthusiasm, and withal great ability shown by Roux in applying elementalism to many aspects of living beings, his title to chieftainship of what the Germans call "Zersplitterungstheorien" can hardly be disputed, at least so far as this present era is concerned.

We shall have to deal with both the practical and theoretical sides of the Rouxian school under several other captions, but this much may be said now. Developmental mechanics has one great merit over any other form that elementalism has taken at any time in the history of biology, in that it gives ungrudging recognition to many orders of constituent parts of plants and animals. Organs and tissues of various grades and classes—cells, nuclei, chromosomes—in short all the *parts* of the organism, are accepted as real existences, only the organism itself being ruled out. In this respect Roux's elementalism is far more genuinely biological and scientific than is, for example, the purely chemical form of elementalism, that form which virtually denies reality not only to the organism as a whole but to all of its parts except what in its most general mode of expression it calls the "living substance."

Superior in some respects as the conceptions underlying developmental mechanics are to those underlying purely chemical elementalism, far more superior are they to that form of elementalism the citadel of whose biological faith is constructed from deepest foundation to highest pinnacle of "hypothetical living units," of which Spencer's physiological units, Darwin's pangens, and Weismann's determinants are the most famous examples. The reason why strictly metaphysical conceptions of this type all prove to be so noxious to scientific biology we shall point out later.

Finally, to bring our historical survey to the present hour, brief reference must be made to the form the controversy has assumed in its very latest stage. To show that the Mendelian-unit-character-factorial-chromosomal theory of heredity has become thoroughly permeated by the elementalistic philosophy will be one of the cardinal aims of some of our critical chapters. This philosophy more than the intrinsic importance of the objective discoveries is what has aroused the imagination and enthusiasm and stimulated the activity of geneticists, as the new school of investigators of sexual reproduction call themselves. Reference to this latest phase of biological elementalism cannot serve the future in any better way, I think, than by calling attention to the remarkable illustration furnished by these late developments of the narrowing power of elementalistic philosophy.

A calm and just judgment of what the strongest motive in philosophical biology is to-day, would be that it is a firm belief that the most important problems of the whole living world are centered in—what? Sex-cells? No, not even in entities thus large and complex; but in a few minute and relatively simple fractions or parts of these cells, the chromosomes!

Viewed broadly both as to historical development and factual content, we are warranted in being confident of the triumph of the organismal standpoint at a day not far distant, this confidence being warranted largely by the fact that it seems as though elementalism has run nearly its whole natural course. It has consumed all the material there is for it to live on, as one may say. It is now engaged in trying out the very last portion of the organism as the "seat" or ultimate explanation of life phenomena. This judgment of the situation becomes especially cogent if the broadly generic term "chemical substances" be put in the place of "hereditary substance" or "genes" which are imagined to make up largely or wholly the chromosomes.

A striking example of the rapid progress made by elementalism toward its own extinction through contracting itself to nothingness is furnished by the course of speculation about ultimate biological units from the period of Spencer and Darwin to the present moment. Spencer's physiological units were by no means restricted to the germ-cells but were held to permeate the whole organism. In this the doctrine had a strong organismal flavor. And Darwin's gemmules had an unmistakable organismal leaning in that they belonged to the organism as a whole at least as much as to the germ-cells. His conception was one of *pan* or universal genesis and not merely of genesis from germ-cells toward soma. In fact, the main object of his quest was an explanation of how body, or soma, may influence germ-cells.

After Darwin came the next long step toward elementalist *reductio ad absurdum* in Weismann's proposal to limit the efficient ultimates of organization, the determinants, to the germ-plasm whether this be in sex or other reproductive cells; that is, to so conceive the ultimate nature of the organism that there should be no reciprocal action between soma and germinal elements; that the whole movement, both individual and racial, in organic evolution should be a one-way movement, that way being from invisible germ to visible organism.

Finally, there has arrived the ultra-modern school, the geneticists, with those wonderfully efficient instruments of analysis, the factorial hypothesis of Mendelian inheritance, and the hypothesis that chromosomes are the "seat" of the "factors" of heredity. These two hypotheses coupled together and with the hypotheses that all evolution is by mutation, and that all mutations consist in the dropping out or losing of factors and characters, need only to be pushed hard enough and speculative biology will be carried to its apotheosis and objective biology to its extinguishment.

How far theorizing has gone on this road is indicated by the much noticed address by William Bateson, one of the foremost Mendelian geneticists, as president of the British Association for the Advancement of Science in 1914. In this address Bateson suggested, whether with full seriousness or not no one seems quite sure, the above mentioned hypotheses of the loss-of-characters method of origin of all organic species.

The chromosome theory having been elaborated into what it now is, the easy step, to the conception that the First, or Original Organism, as something close of kin to a chromosome, has already been taken by an able student, E. A. Minchin, the imaginary Primal Organism being called by him "Biococcus." This speculation we shall consider in our formal discussion of the chromosome theory of heredity.

To bring together these suggestions by Bateson and Minchin and elaborate them into a complete, well-rounded theory requires only a biologist, preferably a German, with the industry and learning and imaginative logic of a Weismann. This accomplished, the ultimate nature and the evolution of the whole past, present, and future organic world would be causally explained by referring it to a primordial chromatinic hierarchy which contained the determiners, or factors, of all later visible organisms, and from which these issued by the transformation of latent into actual organisms through the removal of factors which inhibit the actuation of other factors. But practicable as such a complete explanatory theory is, and harmonious as it could readily be made with certain far-reaching and widely favored conceptions in modern physics, it is very doubtful if the enterprise is ever carried out—at least for any other purpose than as an illustration of how elaborate and consistent and withal beautiful a structure can be erected by pure logic.

My main reason for believing the enterprise will never be carried through, seriously, is that the organismal standpoint has already advanced so far on secure observational and experimental and inductive foundations, that the scientific uselessness if not folly of such elementalistic systems will deter working biologists from spending their time on them.

The barest mention of some of the most important lines of organismal advance, just referred to, will fittingly close this historical sketch.

From the standpoint of biology in the narrowest sense, no researches are yielding more of organismal significance than are those on internal secretions or hormones, or "chemical messengers" as they have been called by Starling, one of the foremost investigators of these substances. Two chapters of the constructive part of this work are devoted to this subject.

Another province in which research is yielding results scarcely if at all secondary in significance to those coming from the biochemical realm just mentioned, is that on the integrating office of the nervous system. The fundamental and extensive work of Sherrington is of prime importance here. But a genuinely organismal aspect is recognized in the tropism theory of Jacques Loeb, which turns out to be almost as important for our general enterprise as the unifying character of the nervous system.

Finally, the realm of the indubitably psychic life of organisms, particularly of man, is found to contain much of the utmost usefulness to the organismal conception. Especially to be mentioned in this connection is the doctrine of Apperception as understood and worked out by Wundt, and its relation to the tropism theory, this relation having apparently been first pointed out by Royce. A discussion prominently involving this relation will conclude the constructive part of the volume.

Nature and Scope of the Undertaking

The foundation of our enterprise, so far as historic summary is concerned, being laid, we may now exhibit the plans, floor-plans and elevations, as architects say, of the superstructure; but the barest outlines will suffice. Leaving off figurative speaking, we must now state in bald outline the central aim of the undertaking. It is to show that while the two conceptions, the organismal and the elemental, contain much that is thoroughly irreconcilable, there is a great substratum of truth underlying both. Adhering to the mode of expression previously used in characterizing the two points of view, the central idea which we shall try to establish may be put as follows: *The organism in its totality is as essential to an explanation of its elements as its elements are to an explanation of the organism.* This formulation which has been in service with me for many years in university lectures and in verbal discussions with colleagues, is approached, somewhat remotely by several authors, earlier and later. Thus L. Rhumbler says at the conclusion of the article *Correlation*, in the *Handwörterbuch der Naturwissenschaften:* "One may assume perhaps that each function of an organ, etc., is bound correlatively to the functions of all other organs, even though perhaps many times in the slightest way and through means in part replaceable, so that by this the organism as a whole is influenced to a definite degree by each of its organs, and *vice versa* [that] through these numberless influences the so-called influence of the whole upon the parts in turn finds its explanation even though complicatedly and at present reaching only to some details."[21] We have here the Rouxian form of elementalism at which we have already glanced, but it seemed worth while to notice this particular expression of it since its advance toward organismalism as contrasted with chemical elementalism is well brought out.

We may preface a slight expansion of our dogmatic formula by asking the question, "How is it that the principle, embodied in such phrases as the 'Organism as a whole' so confidently used by eminent investigators, should be so distrusted by most biologists as to give it little influence on biological conceptions?" The proximate reply is that for most biologists the notion is too vague and general to be of high and permanent worth. One statement of this depreciatory estimate is that to take the organism in its entirety is to take it unanalyzed; and this, so such a view holds, is superficial and contrary to the whole purpose and spirit of modern research. To analyze complexes of natural phenomena, that is to reduce them to their elements is, according to this view, exactly what makes science science. Scientific knowledge in biology as in all other fields, *is* analytic knowledge; and conversely, analytic knowledge not only is science, but (at least so says full-fledged elementalism) is the whole of science. Our undertaking will require us to combat, incidentally but yet vigorously, this view. Stated positively, while assuming as science always does assume, the validity of analytic knowledge of nature, we shall contend that synthetic knowledge of nature is not only valid also, but that it is as foundational and essential a part of science as is analytic knowledge. Furthermore we shall touch briefly, but as we believe very fundamentally, the question of the nature of synthetic knowledge itself.

In accordance with this general statement of purpose, I hope to be able to clear the conception of the "organism" taken alive and whole, of the vagueness that has hitherto enveloped it and make it as clear, as serviceable, and as indispensable to science as are "foot" or "head" or "brain," or "eye" or "muscle" or "cell" or "ovum" or "nucleus" or "chromosome" or "nucleo-proteid" or "ptyalin" or any other fully accredited and unescapable biological entity. Let me state the case from a slightly different angle, attaching it to a quotation from E. B. Wilson given in our historic survey. This quotation is: "The only real unity is that of the entire organism." This I would modify thus: The entire organism is not the only real unity but it is a *real* unity, and represented by the highest animals, especially man, is the *supreme* unity.

Whatever warrantableness there may be in the prejudgment among biologists to the effect that the "organism as a whole" connotates "the organism unanalyzed" even if not unanalyzable, will I hope be met largely by the phrase "Organismal Integrity" of which I make much. Obviously, if one stops to reflect a little, "the organism as a whole" if taken strictly, could mean nothing less than the organism *and* all of its parts. The whole would not be the whole if some of its parts were omitted; so even from this standpoint one might contend that "the organism as a whole" must mean the organism taken wholly, that is, through and through, no part being neglected, and that consequently instead of connotating the organism unanalyzed, in reality it connotates just the opposite and thus indicates the only starting point for *complete* analysis of the organism. But "organismal integrity" not only carries all the other phrase implies so far as mere totality is concerned, but it does more in that *integrity* and its etymological kindred, point definitely not only to the parts, but to them as interdependent. The past participial form of the verb *integrate*, i.e., *integrated*, we shall find particularly serviceable, it being susceptible of use in the comparative degree. The greater or less extent of integratedness of organisms we shall need to speak much about as we proceed. Again such terms as *integration*, *integrally*, and *integrality* will, upon occasion, contribute to precision and flexibility of expression. The kinship, both as to terminology and conception, between what is foreshadowed in the justification of the phrase *organismal integrity* and Herbert Spencer's *Physiological In-*

tegration will not escape the notice of any reader acquainted with Spencer's ideas, particularly if he be at the same time acquainted with the conception as adopted by O. Hertwig and made the third law in his Theory of Biogenesis. Hertwig's elaboration of this law contains more probably that accords with my central thesis than does any other writing known to me.

A brief on the procedure which will be followed in developing our thesis may now be given.

Part I will be devoted to setting forth efforts that have been made in recent and present-day biology to deal with several great classes of the constituent parts or elements of organisms in accordance with the elementalist theory. If my basal proposition be true that the organism taken alive and whole is as essential to an explanation of its elements as its elements are to an explanation of the organism, then it would follow that all attempts to assign explanatory values to the elements in their relation to the whole organism, while at the same time denying either expressly or tacitly, similar values to the entire organism in its relations to the elements, must fail in large degree.

And here comes in sight a vitally important aspect of my general standpoint. Were the basal proposition just stated handed out as a postulate, that is, as a proposition the acceptance of which is demanded without proof, or were it even held to need no other proof than such as might be adduced by syllogistic reasoning alone, in the manner, for example, that both Aristotle and Lucretius mainly supported their views, our task would be comparatively simple. As an illustration of how easily organismalism could be demonstrated by this method, take the case of the relation of the organism to its cells. We should first point out in general terms what characters certain groups and classes of cells might be expected to show in accordance with the hypothesis that the larger structural and functional requirements of the organism influence its elements, and then search among the cells for examples of such influence. But this, the deductive mode of reasoning, is a complete antithesis to that on which we shall chiefly rely in this treatise, indeed to that on which biology always has chiefly relied so far as its progress has been healthy and vigorous and straight ahead.

Holding, consequently that the proposition must be inductively established if it is to be established at all, the heavy task devolves upon us of examining, as above indicated, a great range of the biological field to see how it fares with the two opposing hypotheses (and viewing the theories from the present stage of our enterprise, they should be considered as hypotheses in the strictest sense) when they are tested by a great number of fully authenticated observations. From this general statement it is apparent that the first division must be for the most part distinctively critical. That, however, it is not wholly of this character, I trust will be patent enough to the attentive reader.

Part II will consist of a systematic presentation of the fully established inductive evidence which, if fairly considered, compels, as I believe, the adoption of some such general view as that here defended and would be called, according to nomenclatorial precedent, *organismalism.*

On behalf of this unauthorized and rather bungling word, I make no plea. In fact, the use of it goes against the grain with me somewhat and I avoid it as far as possible. The sum and substance of the situation is, though, that the term seems to force itself upon me at times. It corners us, so to speak, and will not let us escape without taking it up and carrying it with us. But perhaps the possession of such power as this is just what entitles new words to live. If so, and should the idea prevail for which the word stands, the word will prevail too unless some one having special competency in fabricating words finds a better. Which of these alternatives may befall is immaterial. My only concern is for the idea. If that survives and flourishes I shall be satisfied, no matter under what name it becomes known.

1. Aristotle ('11) ....
2. Lucretius ....
3. Locy 139
4. Merz ....II, 240
5. Saint-Hilaire 214
6. Schwann & Schleiden.... 191
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18. Roux ('12) 287
19. Roux ('12) 241
20. Roux ('12) 163
21. Handwörterbuch ......II, 736

Chapter II

THE ORGANISM AND ITS MAJOR PARTS

Reflections on the Problem of Individuality in the living World

THERE has been a great deal of inconclusive discussion of late years, about the nature of the organic individual. Biologists holding the natural-history viewpoint have never had much difficulty in making up their minds as to what an individual is, but many experimenters, encountering problems presented by the parts of an individual and by individuals as parts of a society, have tended to dodge the issue—have attempted to find a solution to the puzzle of individuality by the rather naïve method of changing their definitions of it.

To get some clear-cut idea on this question, out of the welter of nebulous notions that prevail at present, is so important for our general discussion that we can afford to stop for a moment to consider it.

A homely and common illustration will serve as a starting-point. When a scientific dairyman is buying a milch cow or a bull, the deciding factor in the deal is usually what he calls the animal's "individual performance." That is, while various separate "points" are taken into consideration and pedigree lists are consulted, the final decision is based not so much on these as on the cow's record as a milk producer or the bull's as a sire of good calves. In the estimation of the purchaser, the animal stands or falls on its own merits as an individual.

While the individual plant does not appear quite so conspicuously in plant husbandry as does the individual in animal husbandry, it is still never a negligible, and is often an important element. This is especially true in horticulture, where individual performance is subject to much the kind of testing that is applied to the individual animal, namely that of seasonal repetition. In a well kept orchard, for example, the individual tree holds a prominent place.

To question the reality of the *individual* cow or apple tree would be, to a breeder or orchardist, equivalent to questioning the reality of any such animal at all as a cow, or any such plant as an apple tree. Yet a considerable number of zoologists and botanists have been thrown into a distracted state of mind as to the reality of the individual, especially among the lower orders of plants and animals. Botanists have been particularly subject to this malady, obviously because in none of the plants, not even the highest, are the individuals so thoroughly integrated as they are in most animals, particularly in the higher classes. And so, as we shall see presently, some speculative botanists have gone to the ridiculous extreme of asserting that there is no such thing as an individual plant.

What, exactly, is the matter with biological reasoning which lands men in such absurdities? For absurdities they surely are, even though given the habiliments of science. Test the matter this way: If I look at a tree and a man standing beside each other, there is, so far as this observation is concerned, not a shred of valid objection against applying the term "individual" to each. The one is an individual tree and the other an individual man, and the individuality of neither is a whit less certain or more certain than that of the other, as I now perceive the two.

But *as I now perceive the two* is exactly what we are here discussing. For anybody to contend that one of these beings—the man—is an individual, while the other—the tree

—is not, merely on the ground of what is learned by later study about the differences in makeup of the two, is literal nonsense. It is a virtual denial of the validity of obervational knowledge. Granted that science can not rest satisfied with "common-sense" knowledge, there is still no ground for repudiating *all* commonsense.

Attempting to ascertain what the trouble is with biologists who reason thus about individuality, one soon discovers that the botanist who deals with a tree thus unjustly quite ignores the obvious and unescapable fact that the raw material of all his botanical knowledge is individual plants taken one after another; that for trees there is an *each tree;* that each, as it actually stands before him, is *one,* not two or three or any other number; and that it is not in the least confusable with any other tree, no matter if several are connected together by their roots or in some other way. These confused-minded persons either ignore the patent facts of observation, or if their sophistication is refined, they deny the validity of the "mere perception" of an individual when that way of predicating individuality is measured against supposedly more fundamental principles of scientific knowledge-getting, as analysis is held to be.

This question of more and less fundamental principles of scientific procedure, especially those involved in analysis, is undoubtedly of great importance. But undoubtedly, too, it is a question of the nature of scientific knowledge rather than of the nature of plants and animals, so does not fall within the scope of such a treatise as the one now occupying us. The question before us is that of the nature of the individual organism.

As soon as we see the necessity of separating these two questions, and address ourselves to the strictly objective question, we perceive that the difficulties center around the fact that no individual plant or animal is simple in its constitution, but in almost all cases is exceedingly complex.

The kernel of the difficulty arising from the complex make-up lies in the fact, emphasized by recent investigations, especially those on regeneration, that in very many animals and plants, when the individual is artificially divided, parts of individuals have remarkable powers of independent life, even to the extent of reconstituting themselves into other individuals as perfect as the one that was divided. The reasoning from these facts is, essentially, that because a given individual may divide or be divided artificially into two or more parts, which may in turn develop into other individuals like the original, the original was therefore not a single individual. In other words, individuality is denied these organisms because of what parts of them can do *when severed from the whole.* The unity, the integrity of the individual is called in question, not on account of what it is *here and now,* but on account of what the parts may do *after they have been severed,* naturally or artificially, from the original unity.

No biologist, and especially no organismal biologist, would minimize the significance of the fact that the severed parts of many organisms possess such remarkable reconstitutive powers. The organismal biologist, I assert, is especially interested in the phenomena because they are to him unique and unanticipated evidence favorable to his general standpoint. What he denies is that the phenomena count a scintilla against the reality and essentiality of the individual. He points out that their importance, so far as the problem of individuality is concerned, is not that they show much about the *ultimate nature* of the individual's unity, but that they do show much about the *degree* of that unity.

The Individual Plant and Its Parts

The purposes of this chapter will be best served by devoting a section to examining a few efforts which have been made to interpret the organism in accordance with the theory which denies its individuality. Our first instance will be taken from botany. But before proceeding with this, it is desirable to point out that some of the most distinguished botanists, especially physiological botanists, have recognized the unity of the plant without stint or cavil.

We appeal to only one of the botanists of this class, Pfeffer. In *The Physiology of Plants,* he says: "The intimate correlation of the entire vital mechanism renders it probable that every excitation exercises some effect upon other manifestations of irritability, even though this effect may not always be directly perceptible."[1]

Again: "In the plant community the activity of every cell and of every organ is subservient to the common weal, and may, when necessary, be modified as already indicated so as to fulfill the changed requirements of the whole."[2]

It is true, I believe, that the mode of thought about plants illustrated by these quotations is characteristic of botanists in whom observation and speculation maintain a due balance; botanists with whom, in other words, speculation has not got the upper hand of observation.

It is highly significant that one of the most pronounced and, so far as I have discovered, earliest authors to speculate on the non-individuality of the plant was Schleiden, one of the fathers of the cell-theory. In his famous *Contribution to Phytogenesis* we read in a discussion of the individuality of plants: "In the strictest sense of the word, only the separate cell deserves to be called an individual."[3] Elaborating this notion, "The woody stem," he tells us, "cannot come under the idea of a plant." And further: "It necessarily pertains to the notion of a plant, that it produces foliaceous organs on its stem, yet there is no tree which produces leaves."[4] This last statement sounds, the author admits, rather paradoxical, but, he contended rightly enough, the mere circumstance of its sounding paradoxical does not prove it false. Since, as we have previously seen, Schleiden's brand of elementalism necessitated the sacrifice of the individuality of the plant to that of the cell, our critical examination of it belongs properly to our examination of the cell-theory. Here, consequently, we do no more than point out that Schleiden himself did not succeed in carrying through fully his simple denial of the plant's unity. The oneness of the young *developing* plant was an obstacle to his theory, even though he seems not to have been aware of the fact. "After the woody mass is formed, we miss," he says, "the influence of the law of formation, which until then had without exception directed the growth of the entire plant in all its parts."[5]

Schleiden seems to have felt no difficulty in his conception that the "law of formation" which "directed the growth of the entire plant in all its parts" could be accounted for by the "separate cell," the only individual "in a strict sense." His immunity from qualms on this score was due probably to the fact that, being an "ultimate problem" botanist instead of a naturalist really interested in plants, it did not occur to him that the question of how the cells could explain the fact that in one instance the "entire plant in all its parts" should be an apple tree, in another an oak tree, in a third an orange tree, and so on, might be considered a really important one by somebody.

We now pass to the examination of a single modern instance of the attempt to "explain away" the individuality of the plant. The principle made use of in this attempt is that of symbiosis, which is a sort of partnership between organisms of different species, so close in some cases as to be really organic. Although I do not know that the example I have chosen has had much recognition among botanists, it yet seems justifiable to use it since it is certainly typical, even though possibly somewhat extreme. It is taken from H. C. Davidson, an English botanist, his publication being entitled *The Nature of the Plant.* After illustrating the principle of symbiosis by referring particularly to the case of the mutually dependent combination existing between the flat-worm *Convoluta roscoffensis* and a green alga, recently well studied by Keeble and Gamble, Mr. Davidson goes on to argue that if a typical plant, a tree for example, be considered to be a like symbiotic complex, "much that has been dark in the vegetable world becomes clear."[6]

The members of the partnership in the plant so conceived would be the flowers, equivalent to the "hermaphrodites and males and females" occurring in the world of insects, and the buds equivalent to the underdeveloped females or neuters. Among the darknesses enveloping plant life which the author believes would be illumined by this theory he mentions that of the plant's individuality. In the light of the theory it becomes obvious, the author holds, that a "plant is not, as is generally supposed, an individual entity, but in reality a group or family of individuals, associated within a common protecting envelope, the bark, and upon a common root for the common good."[7] These "associated individuals" Mr. Davidson calls *plantagens* since, he says, "they cannot well be written about unless they have a name."

Another meritorious thing about the plantagen theory, its inventor believes, is that it removes the difficulties in the way of the germ-plasm theory of Weismann, presented by plants. The type of reasoning which has given rise to this rather ingenious speculation will receive due attention in various parts of this volume. I bring up the case here only as a specific instance of "certain general tendencies to erroneous reasoning" above referred to. There is always the inclination to ascribe more casually interpretative value to some of the parts of organisms in their relation to other parts and to the whole than actually belongs to them. In the present instance this effort is seen in the fact that both the asexually and sexually propagating elements of any given plant are treated as though they were distinct, ultimate data, whereas they certainly are not. The term "symbiosis" was introduced into biology exactly for the purpose of expressing the fact that individual organisms, usually of very distinct species, get together in an intimate relation wherein one or both members of the partnership gain some advantage, each at the same time preserving its unmistakable identity. There is certainly not the slightest evidence that the asexual and sexual parts of plants were originally independent of each other in this way.

Let us accept momentarily (since his speculation is dependent on our doing so) Mr. Davidson's contention that "germ-cell must develop from germ-cell, bud from bud, individual from individual." Even so, no biologist who is a genuine believer in organic evolution, that is, in the teaching that all organic kinds have descended from ancestors of different kinds, can allow that "much that has been dark in the vegetable world" is made any less dark by the assumption of such a fundamental independence of germ-cells and germ-buds and "individuals" until he is informed as to the ancestry, not only proximate but remote, of germ-cells and germ-buds and "individuals."

The kinship between these modern speculations about symbiosis and an ancient notion due, it seems, to Empedocles, comes to light at this stage of the discussion. What that notion is we shall see presently. Mr. Davidson's symbiosis theory of plants involves, he points out, his theory of plant-*agens*, which last theory involves, as he rightly says, the conception that "germ-cell must develop from germ-cell, bud from bud, individual from individual." But any ten-year-old farmer's son may know this statement is not true. Keeping the form though not the meaning of Davidson's expression, such a boy can assert that germ-cells develop not only from germ-cells but also from buds, and that buds develop not only from buds but also from germ-cells.

Following a killing frost in southern California a few years ago, thousands of lemon trees whose normal foliage had been destroyed put forth great numbers of new shoots on their trunks and largest branches. Such new shoots may occur anywhere and everywhere on the trunk and branches, and since they rarely arise, so long as there is no occasion for them because of the activities of the normal foliage, the term "adventitious"* is appropriately applied to them. So lemon-tree germ-cells and lemon-tree plantagens, or speaking in terms free from speculative sophistry, lemon-tree seeds and lemon-tree buds, are dependent for their origin upon lemon trees. In other words, the tree is as essential to a causal explanation of the seed and the bud as the seed and the bud are to a causal explanation of the tree.

Reproduction by adventitious buds among the higher plants is so important from the organismal standpoint that we must consider it a little further. One additional fact which the reader should appreciate is that the method is by no means an exceptional and insignificant thing in plant economy. It is a regular way many trees have of perpetuating themselves. An illustration of this even more striking than that of the lemon tree is furnished by the Coast Redwood of California (*Sequoia sempervirens*). A stump of this tree, even a stump that has passed through a severe

* The question of adventitious or cambium buds from lemon trees seems not to have received much attention from botanists. Judging from the distribution of the new growths in such an epidemic, as it might be called, of budding as that which takes place under conditions like those here mentioned, there is scarcely a doubt that very many of the new branches arise quite independently of previous bud germs; in other words, from some source not germinal until it becomes so under the special conditions. The only experimentation on bud production in the lemon with which I am acquainted has been carried on by Prof. H. S. Reed of the Citrus Experiment Station of the University of California, at Riverside. Doctor Reed has kindly shown me the results of his work and permitted me to make use of them in this connection. So far as these experiments go, it seems that while leafless pieces of branches kept under suitable conditions readily put out undoubted cambium buds, these produce roots only.

forest fire, will put out thousands of shoots. That these arise from the cambium I am assured by Dr. Percy Brandt, a botanist who has given special attention to the matter. Now I ask the reader to reflect on what is before us here. When the tree's life not merely as an individual but as a potential parent is destroyed, so far as all visible evidences are concerned, one of the general tissues of the stump, its cambium layer, proceeds forthwith to do what under the normal life-conditions of the tree it does not do, namely, produce new buds, each one a potential new redwood tree. The indubitable facts compel us to recognize that any part whatever of the cambium, at the base of the tree at least, is capable of being diverted from its normal function and made to do what it would not do except for the special conditions imposed. I say it is "made to do" these things rather than merely that it "does" them as though from its own inherent nature alone, simply because it does not do them unless they are subjected to the very particular conditions which are imposed, namely those of the destruction of the normal propagative parts of the tree.

Whether one has in mind the question of how the whole cambium, normally not reproductive, becomes endowed with reproductive power; or the negative side of the question, that of why it should not be reproductive under normal conditions, there is no way of reasoning adequately about the causes of the phenomena without bringing in the tree as a structural and functional whole. The redwood tree as a whole is essential to a causal explanation of the capacity of its cambium tissue. Efforts to escape such a recognition by resorting to conceptions like those of germplasm and plantagens is unmitigated sophistry.

The Individual Animal and Its Parts

So obvious is it that in the full-grown individual of any of the higher animals the organs and parts are in some measure an adaptation to one another and have some structural dependence upon and correlation with one another, that it would be superfluous to enumerate the facts and dilate on their significance. The subject constitutes no small part of the older comparative anatomy and physiology.

Almost as obvious is it, too, that the major parts of such animals are incapable of long-continued life when they are severed from the whole. But the great capacity for continuance in the living state possessed by certain parts of some classes of animals has attracted much attention, mostly because of the intrinsic physiological and morphological importance of the phenomena themselves rather than of any assumed support afforded by them to the doctrine of autonomy of the parts in a strictly elementalistic sense. But these and other facts of organ-independence have been used as a groundwork for certain elementalistic conceptions of the organism which, viewed in their historical setting, are of much broader interest. The historical setting to which I refer goes back to a speculation by that primal elementalist Empedocles, and may be called an organ-assembling theory. The modern relatives of this old theory may be called aggregational theories, and are typified by the conception that the normal individual plant or animal is an affair of symbiosis or secondary union of previously independent organisms. A concise statement of Empedocles' hypothesis is found in the *De Generatione Animalium* of Aristotle (Book I, 722^b, 20): "in the time of his 'Reign of Love' says he [Empedocles], 'many heads sprang up without necks,' and later on these isolated parts combined into animals."

Symbiosis, as illustrated by Davidson's speculation, means a partnership between individual organisms of different species so intimate as to make each member of the combination really dependent to some extent on the other. A considerable number of such cases are now known in both botany and zoology. Perhaps the most striking example is that of the partnership between an alga and a fungus to make a lichen. The kinship between such a speculation as that of Empedocles concerning the origin of the individual and the modern speculation which would have the individual arise symbiotically is unmistakable. The most important likeness between the two conceptions is the fact that both are fundamentally *non*-evolutional. The isolated heads, necks, legs and arms of the ancient Greek, like the germ-cells and germ-buds of the modern Englishman, are just *taken* because they are necessary for the particular speculation. The question of how heads and legs and of how *tree* germ-cells and germ-buds arose in the first instance is not raised, or if it were it could be answered in accordance with the basal principle involved, only by assuming another and another and another set of elements of the *same kind*, ad infinitum. In a word, the theory really contains no provision in a truly organic sense for transformation, which is the very essence of the conception of organic evolution. It should be noticed that the principles of Love and Hate appealed to by Empedocles and that of struggle and survival appealed to by neo-Darwinians are held to explain not the *origin* of the heads, legs, etc., or of the germ-cells and germ-buds, but the origin of actual animals and plants from the respective elements once the elements are at hand. In a word, expressing the limitations on this mode of theorizing in the familiar language of Darwinism proper (*not* neo-Darwinism), the natural selection hypothesis does not pretend to explain the origin of variations and variants, but assumes them. What we are bound to see if we look at the relevant facts squarely is that the doctrine of organic evolution involves the conception of ancestry as fundamentally as it does that of progeny. Observation finds organisms produced *by* parents no less indubitably and inevitably than it finds them giving origin *to* progeny, so that the effort constantly recurring in recent biology to find ultimate security in something or other to which the word *genesis* can be attached, but which can yet be conceived as not subject to transformation, is everywhere hostile in a fundamental sense to the descent theory.

The latest manifestation of this hostility is the *gene* or *factor* theory of the ultra-Mendelians among present-day geneticists. The gene as conceived in the genotype theory turns out on close inspection to be still another something-or-other, which though not itself transformable can explain transformation in something else, and which has been appealed to by generation after generation of elemental-minded theorizers about the origin of living beings, from the ancient Grecian period at least. Jennings, one of the ablest of the experimental geneticists, and one who has a genuine regard for the visible as contrasted with the invisible and hypothetical data of organic genesis, has lately pointed out the essentially non-evolutionary character of the genotype theory. "The whole conception," he rightly says, "is in its essential nature static; alteration does not fit into the scheme." [8] We shall have occasion to consider this new phase of the non-transformism in other connections. Our purpose in referring to it here is merely to point out where it belongs in the general scheme of genetic theorizing when this scheme is viewed historically. Biology at present needs few things more sorely than a system of reasoning which shall not beget in students the mental habit of allowing recondite concepts and postulates and strange words to cast every-day, familiar facts into outer darkness. One of the most obvious and indubitable facts about all organic development is *transformation.* The development of a chick from a hen's egg is accomplished not merely by a great increase in size, but by the profoundest sort of transformation, this being deployed, as one may say, through a long series of stages grading insensibly one into another. And so with every other ontogeny, animal ontogeny especially.

The working out of these innumerable transformational stages constitutes the science of embryogenetics.

This transformational character of individual development, or ontogenesis, is even more startling, and in some ways confusing, in certain of the lower animals like the coral polyps, where secondary individuals are produced asexually but do not become wholly severed from the stock or colony. But each multiple animal, as these may be called, is a single germ-cell in the earliest stage of its life, and this alone is proof of a certain measure of individuality of the whole "colony" produced from the same egg. Indeed, some zoologists, Huxley for instance [9] have used this as the sole or chief criterion of organic individuality, and have defined the individual as all that arises from a single germ-cell. There can be no doubt about the validity and usefulness of this conception as one criterion of individuality, even though it does not constitute a basis for a complete definition. An exceedingly fertile field of zoological research is that of the varying degrees and exact character of functional as well as developmental integration in these metagenetically built-up, loose animal individualities. Much is already known on the subject, but very much is not known, and to extend knowledge in this field is one of the urgent needs of zoology. The subject received much more attention, relatively, two or three decades ago than it does now; so that few of the investigations on which he have to rely have had the benefit of the best technical methods. We may confidently anticipate that when the later technique of studies on neuro-muscular stimulus and response and on internal secretions are applied to metagenetic group-individuals, such as are found in many of the coelenterates and in some of the tunicates, much new light will be thrown on the interrelationship of the members and organs in these poorly unified individuals.

But—and the point is cardinal for us—no matter how much or what new knowledge we get as to the members and their relations to one another in these individuals, we are sure that that knowledge will not militate in the least against the *reality* of the individuals, nor against the fact that every individual has *some measure* of unity, of integratedness, structural, functional and developmental.

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8. Jennings ('17) 283
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Chapter III

THE ANIMAL ORGANISM AND ITS GERM-LAYERS

The Germ-layers, Their Rôle In Development, and the Germ-layer Theory

STRICT fidelity to the natural sequences of biological knowledge as viewed in this work would not permit us to introduce at this early stage of our discussion such a subject as that of germ-layers, or indeed any other purely developmental aspect of the organism, but would require us to deal more fully than we yet have with the completed organism. However, our general attitude having much of the pragmatic about it will be broadly tolerant in the matter of adapting methods to ends sought. This way of beginning is chosen for the two-fold reason that in this domain my own researches first came upon facts which contributed very largely to the ideas underlying this whole undertaking, and also that these and kindred facts constitute some of the most striking evidence we have of the ability of the organism to gain its developmental ends in unusual ways when the usual ways chance to be obstructed—evidence, in other words, of the domination of the organism as a totality over its parts.

From its very beginning with Wolff and von Baer, modern embryology has recognized that animal embryos pass through a stage in which the body consists of little more than uniform layers of cells, first one, then two, then three, and finally, in several classes of animals, four; these being disposed one inside the other and more or less regularly concentric. From these layers all the organs and tissues are developed by a great variety of unequal thickenings and foldings and concentrations and cellular differentiations. Details are not necessary for our purpose. As expressed by one standard textbook of embryology, these layers are as a rule "structural units of a higher order than the cells." "Primary organs of the animal body" is another term applied to them. The appropriateness of the descriptive term "germinal" applied to these layers is found in the fact that the tissues and organs are generated from them.

The passage of the embryos of so many different animals through this layered condition makes the phenomenon a law of animal ontogeny or individual development of wide applicability and this law, looked at from the standpoint of the full-layered stage, is found to reach in both directions, i.e., backward to the mode of origin of the layers from the single undivided egg-stage of the organism, and forward to the mode of origin of the tissues and organs from the layers. Because of the great measure of uniformity among many groups of animals which pervades the passage of the embyro from the egg-stage to the full-layered stage, embryologists have been able to recognize and so name several stages, the descriptions of which are in many cases very clear and precise. The best defined of these are the morula or cell-cluster stage, the blastula or one-layer stage, and the gastrula or two-layer stage.

On the other hand, looking from the full-layered stage toward the completed organism, a dominant uniformity in developmental procedure, i.e., a conspicuous law of ontogenesis, is seen in the part contributed by each layer to the completed animal. Since it is this aspect of the matter that particularly concerns us, we must go into a little more detail. As laid down in the standard text-books of embryology, three layers are recognized, namely the outermost, called the ectoderm; the middle, called the mesoderm (in many groups split into two, thus making a four-layered stage); and the innermost, called the endoderm. The derivatives of these layers, as typically stated, are: From the ectoderm, "The epidermis and its appendages, hairs, nails, epidermal glands, and the enamel of the teeth. The mucous membrane lining the mouth and the nasal cavities, as well as that lining the lower part of the rectum. The nervous system and the nervous elements of the sense-organs, together with the lens of the eye." From the endoderm: "The mucous membrane lining the digestive tract in general, together with the epithelium of the various glands associated with it, such as the liver and pancreas. The lining epithelium of the larynx, trachea, and lungs. The epithelium of the bladder and urethra." From the mesoderm: "The various connective tissues, including bone and the teeth (except the enamel). The muscles, both striated and non-striated. The circulatory system, including the blood itself and the lymphatic system. The lining membrane of the serous cavities of the body. The kidneys and ureters. The organs of reproduction." [1]

The summary here given is taken from *The Development of the Human Body*, by J. Playfair McMurrich, and consequently has special application to man; but it is a presentation of what is usually understood to be contained in the germ-layer theory applicable to all the metazoa with certain general modifications for the groups like the coelenterata which never advance to the three-layered condition. As thus treated the germ-layers are structures as indubitably as are bones or muscles or feet or hands or brains; and the now unquestioned fact that they are so alike in both structure and relations in so great a range of animals, and give rise with such constancy to the corresponding parts of the completed animals, has been and ever must be of great importance for the interpretation and comprehension of the vast complexity of animal structure. Says one of the foremost embryologists: "As our knowledge of the development from the germ-layers has grown, we have learned with ever-increasing certainty that each germ-layer has its specific rôle to play." [2]

Are Germ-layers Developmental Organs and Subservient to the Developmental Requirements of the Organism?

But after all this has been fully and gladly granted, there still remains much to be said concerning the deeper biological meaning of the germ-layers, and the different attitudes of mind which different biologists may assume, indeed do assume, toward these layers. What we have to offer on this subject will be from the standpoint of the difference between the elemental and the organismal ways of looking at biological phenomena generally. This difference may be brought out by asking, does the obviously very general rule of origin of the tissues and organs from the different layers hold with genuine universality, that is, in all animals in which the three (or four) layers occur, and under all circumstances of development in every animal? Or, putting essentially the same question, but modified so as to show more clearly its relevancy to the organismal and elemental standpoints: are the germ-layers, when looked at as "structural units" or elements "of a higher order than cells" so fundamentally independent of one another and of the organism as a whole that they always and under all conditions must give rise to just the tissues and parts typically arising from them, and nothing else? Or, shifting the point of view a little: has the organism, as such, needs and abilities so paramount that it is able to realize these needs by modifying to any extent the developmental course usual to the germ-layers?

A Negative Answer to the Question in the Last Section Expected of Elementalist Biology

Any one who perceives the essence of elementalism and so has seen that it perforce implies a denial of causal power of the whole organism over its parts in development will foresee what answer biology as strongly elementalist as the science has been in the recent period will be likely to give to these questions. It will not be satisfied with basing its expectation that an organ or tissue has arisen from a particular germ-layer solely on the fact that in all hitherto observed cases it has so arisen. The contention may be expected that the independence and autocracy of the layers are in no way subject to modification to meet the requirements of the organism as a unit: that in case of conflict between the needs of the organism as such and the proper powers of the layers, the organism must accommodate itself to the layers if any accommodating is to be done. As a matter of fact the germ-layer theory has been defended with great vigor in just this hard-and-fast way. Nerve tissue must arise from ectoderm if it comes into existence at all. Under no circumstances is it permissible to believe it to have arisen from either of the other layers. Muscle tissue must arise from mesoderm (or mesenchyme) or not at all; and so on, according to this way of viewing developmental phenomena. Numerous biologists say in substance that the entire teaching of embryology, anatomy, histology, and pathology, should be based on the doctrine of the germ-layers.

Evidence That Germ-Layers Are Thus Subservient to the Organism

This brings us to the facts previously alluded to as having played so considerable a part in generating the system of ideas set forth in this treatise. Put into a nutshell, the case is one in which the ontogeny or individual development being much out of the ordinary, several of the germ-layer relationships prevailing in ordinary ontogeny are profoundly modified, the end-results being the same as that resulting from an ordinary development. To be explicit on a single point, an instance is presented in which the nervous system arises not from the ectoderm in accordance with the general rule, but from the endoderm, this profound deviation from the typical being explicable, seemingly, from the generally different entogenetic course followed in blastogenesis. The case, well known to embryologists but insufficiently heeded, is one of bud propagation in some of the compound ascidians. I was not the first to observe the uniqueness in this form of development; but since in one of the instances studied by me the facts are probably clearer than in any other that has been examined, it will be best to present in the barest outline only, the evidence furnished by this one case. Full details are in my memoir.[3]

(*a*) *Evidence From Bud Propagation in Compound Ascidians*

We will confine our attention almost entirely to the one species, *Goodsiria dura* (according to the later classification *Metandrocarpa dura*), an abundant species on the coast of California. To understand the particular points with which we are concerned, it will be necessary to say a few words about bud formation and development in this group. The buds are not produced by "Stolons" as they are in most bud-propagating ascidians, but each blastozooid, as the bud-individuals are called, arises separately and directly from its parent zooid. It forms at the anterior end of the parent and in such a way as to be two-layered from the very first, the layers being ectoderm or outer layer, and endoderm or inner layer. The bud when first separated from the parent is exceedingly simple, being an almost perfect sphere. The layers are, at this stage, only a single cell thick and are quite uniform throughout. The endodermal layer, or "inner vesicle" as it is spoken of technically, is separated from the ectoderm or "outer vesicle" by a wide space all around. Because of these simple conditions the investigator is able to make out with great certainty most of the events in the transformation of the vesiculate stage into the completed organism. The first differentiating step noticeable in the inner vesicle consists of a somewhat elongated outpocketing of the wall of the dorsal side of the vesicle. What occurs later in connection with this outpocketing may be stated by quoting from the original paper: "Simultaneously with the closing off from the inner vesicle from before backward of the hypophyseal duct, the ganglion becomes differentiated in the same order from the cell mass that forms the last connection between the duct and the vesicle." The "ganglion" is, it should be stated, the beginning of the whole central nervous system of these animals. My observations being a confirmation and extension of those by other zoologists on other species, notably by the older zoologists Giard and Kowalevsky, and in the period of recent methods, by Hjort, there can be no question that the nervous system arises in some gemmiparously produced ascidians, from the inner germ-layer whereas in individuals of the same species produced from eggs, the nervous system arises as it does in the vast majority of animals from the outer germ-layer.

The only point that has been or can be made against this as an instance of complete transfer of the place of origin of the nervous system from one germ-layer to another, is that the "inner vesicle" of the bud is not in reality endoderm but ectoderm, this resulting from the manner of development in the parent of the layer from which the inner vesicle originates. There is considerable ground for this interpretation of the inner vesicle so far as Botryllus is concerned, but much ground against it for several other species. Even though the Irishism that the endoderm of the bud is not endoderm but ectoderm, that is, that the innerderm is really an outer-derm be accepted as true, the real issue so far as this discussion is concerned remains unaffected. Whatever the inner layer should be considered as judged by its *origin*, judged by its *developmental potency* its endodermal nature is beyond question, for nothing is more certain than that it gives rise to the main part of the alimentary system as, in accordance with the general rule, it ought to. The kernel of the matter is that here is a case in which both the digestive organ and the nervous system arise from the *same* germ-layer, which is contrary to the almost universal rule. What *that* layer should be called matters not, as we are now looking at the situation.

We can see, as intimated at the outset, the probable immediate cause of this fundamental modification of the ontogeny. Hjort was the first to dwell adequately on this aspect of the subject. But since my own conclusions were drawn before his memoir reached me and so were wholly independent of his, it will be permissible to present the explanation in my own way. This I will do in the original language slightly modified. The ectoderm of the ascidian bud, even at its very beginning, is part and parcel of the ectoderm of the parent, particularly in Goodsiria and Botryllus where, in the absence of a stolon, the budding region is enveloped in the cellulose tunic characteristic of all tunicata. This is equivalent to saying that the ectoderm of the bud is not, even at the very outset, an *embryonic structure* at all. It is, on the contrary, a *differentiated* organ whose function is, as in the parent, to secrete the cellulose matrix of the outer tunic. In the performance of this function, it would appear to be vigorously and consistently active, for the matrix is large in quantity and probably constantly renewed. This production may, as Hjort had well contended, be compared with the production of horn, or still better, of cartilage matrix by the cells appropriate to these substances. So the ectoderm has a well-established physiological rôle to play from the very earliest stage in the career of the bud. Quite otherwise is it with the endoderm. It is difficult to see how a structure could be more favorably circumstanced for retaining, so far as its physiological relation to the organism as a whole is concerned, an undifferentiated state than is the case with this one. It is wholly protected from contact with the external world by being enclosed in the ectodermic vesicle; furthermore, it has little or nothing to do with the preparation of its own nutriment, since it is constantly and completely bathed in the maternal blood. So why should not the production of structures which in embryogenesis belong to the ectoderm, be here transferred to the endoderm? And so it is.

This conclusion is the more justified when one considers how differently circumstanced are the two layers in the embryo. Here the incipient nervous system arises from the ectoderm while the layer is in a strictly embryonic stage and before the endoderm has freed itself from the rich store of yolk material which is passed on to it from the egg. We seem to have here an instance in nature where the later functional requirements of the organism as such have run counter to the way in which, through the operation of remoter hereditary influences alone, development would proceed; and the former have proved more powerful.

(*b*) *Evidence From Bud Propagation in Bryozoa*

Defiance of the germ-layer doctrine is by no means restricted to the gemmiparous ascidians. In bud propagation in bryozoa, a widely different group, departure from the rule is no less certain and fundamental. The developmental processes in these animals are somewhat more obscure at several crucial points than in the ascidians, and there has been proportionately more diversity of interpretation among investigators. Nearly all, however, from H. Nitsche who first pointed out the anomalies here presented, to the latest students in this field, Calvet and Römer, agree to the extent of recognizing that the layers of the buds in these animals do not conform to the germ-layer scheme that prevails so widely in ontogenesis starting from the egg.

A good summary of the view most commonly held by specialists in this field is given by Harmer.[4] "There is good reason for believing that in polyzoa the polypide-bud is developed entirely from ectoderm and mesoderm. This bud is a two-layered vesicle, attached to the inner side of the body-wall. Its inner layer is derived from the ectoderm, which at first projects into the body-cavity in the form of a solid knob surrounded by mesoderm-cells. A cavity appears in the inner, ectodermic mass, and the upper part of the vesicle so developed becomes excessively thin, forming the tentacle-sheath, which is always in the condition of retraction. The lower part becomes thicker; its inner layer gives rise to the lining of the alimentary canal, to the nervous system, and to the outer epithelium of the tentacles, which grow out into the tentacle sheath. The outer layer gives rise to the mesodermic structures, such as the muscles, connective tissue, and generative organs." Although this description may not give a very clear picture to readers unacquainted with the structure and development of the bryozoa, the point of central importance to this discussion is clear enough: The *outer* layer of the body wall gives rise to the inner layer of the bud, and from this layer is produced the lining of the alimentary canal, and the entire nervous system. No matter what the outer layer of the body-wall and its continuation as inner layer of the undifferentiated bud be called, the germ-layer doctrine is set at naught since *one* layer gives rise to both the digestive epithelium and the nerve ganglion.

As a matter of fact, this statement falls short of revealing the full measure of confusion as regards germ-layers which prevails in these animals, since one layer, the outer of the body-wall, contributes to every essential part of the polypide in some species. Thus Calvert shows that in *Bugula sabatieri* cells are set free into the body cavity from the outer layer at the time that the knob of cells of that layer, which is the foundation of the bud, makes its appearance, and these freed cells assemble to produce, in part at least, the layer on the surface of the knob usually called the mesoderm of the bud. And this observation Römer has confirmed "mit aller bestimmtheit" for another species, *Alcyonidium mytile.* It seems that the entire polypide may be formed from a single germ-layer, namely the ectoderm.

The reader should not fail to compare what is here set forth about bryozoan budding with what we learned about ascidian budding to the extent of noticing that whereas in the ascidian we found the inner layer (no matter whether called endoderm or by some other name) producing nearly the entire zooid; in the bryozoan the outer layer (no matter by what name called) produces in some cases, nearly the entire polypide.

If it be asked whether the principle invoked to explain why the ectoderm of the ascidian bud takes so small a part in producing the future animal (namely, that of greater functional specialization and activity of the ectoderm than of the endodorm at the place of origin of the bud,) be also available for explaining the reverse order in layer contribution to the bud-produced animal in the bryozoan, no very satisfactory answer is forthcoming from the information we now possess. Two facts may be adverted to, however, which suggest that the same principle is operative in the two cases. In the first place, it may be reasonably doubted whether the thin cuticular covering produced by the outer layer of the body wall in the bryozoan involves as great a degree of specialization either in nature of product or in extent of activity as does the far more voluminous "test" material produced by the ascidian ectoderm. In the second place, the so-called mesodermal layer of the bryozoan body-wall surely has no such direct and intimate connection with the parent polypides, i.e. the other members of the colony, as does the "cloison" or inner tube of the ascidian colony from which the inner vesicle of the bud is produced. We may consequently surmise that in the bryozoan as in the ascidian the layer that is most available because of being least fully occupied with activities pertaining to the parent organism is most largely drawn upon in bud propagation. A kind of balance between the functions of growth and maintenance on the one hand, and propagation on the other, is struck in each case although this implicates the germ-layers in opposite ways in two cases.

(*c*) *Evidence from the Regeneration of the Lens of the Amphibian Eye*

The supremacy of the organism over its germ-layer is shown in no way more strikingly than in facts brought to light in some of the researches of late years on animal regeneration. Perhaps the case at once the best established and most discussed is that of the way the extirpated lens of the eye is renewed in some amphibians. Referring to the parts enumerated above as arising from each of the three germ-layers in vertebrates, we note that the lens is assigned to the ectoderm. To be a little more explicit, this member originates from the outermost epithelial layer of the head of the embryo. Hardly any point in vertebrate embryology is easier to demonstrate than this. Experiments have proved, however, that when a new lens is produced in a full grown animal, to take the place of one that has been destroyed, this does not arise as did the original from the surface epithelium but from the edge of the iris, that is, from a part of the eye itself. The discoverer, Collucci, did not consider it to be out of accord with the germ-layer doctrine because the iris is the highly modified rim of the original optic cup, which is derived from the cerebral vesicle, which in its turn is derived from the ectoderm, so that in a round-about way the iris is an ectodermal product. The fact remains, nevertheless, that the mode of origination of the new lens is so radically different from that of the old that to regard it as sufficiently dealt with when attention is called to the fact that it conforms in a way to the germ-layer doctrine is an impressive illustration of the evil effects of subserviency to a theory—of the inhibiting effect of such a mental attitude upon interest and observation. Later investigators, notably G. Wolff, A. Fischel, and W. N. Lewis, have shown how much more there is to the phenomena of development and regeneration of the vertebrate eye than the single matter of reference of the several parts to their appropriate germ-layers. The work of these students carries the subject into other fields, particularly those of regeneration, and of formative stimulation.

The Germ-Layer Theory and the Germ-Plasm Theory

This discussion of the germ-layers will terminate with a section on the part played by the layers in producing the sex-cells where propagation is by the sexual method. This termination will also be the culmination in point of importance, since it will lead as well into the examination, to be continued in other sections and chapters, of the results and the general modes of reasoning of the Weismannian school of speculation about heredity.

The manner of involvement of the layers in the speculations of this school becomes apparent on a moment's reflection. As is widely known, Weismann and his adherents conceive a particular substance known as *germ-plasm* to which all the phenomena of heredity are due, this being fundamentally different from and independent of the great mass of substance called by them *somatoplasm* which makes up the bodies of organisms. Not only is this germ-plasm quite apart from the somatoplasm in a given individual plant or animal, but it passes along from parent to offspring, generation after generation, wholly uncontaminated, as one may say, by contact with the somatoplasm. This supposition of a propagative stream or string has been elaborated into what is known as the doctrine of the "continuity of the germ-plasm." A point fundamental to the doctrine is that not merely the germ-plasm *may* pass over in this way from parent to offspring, or that *some portion* of it always does thus pass, but that all the germ-plasm the offspring ever has comes from this source. Otherwise expressed, the doctrine is that germ-plasm is never produced anew in a strict sense.

Weismann is sufficiently explicit on this point. Not only does he assume that germ-plasm cannot be produced by the transformation of somatoplasm, but he holds it cannot be produced in any other way. Touching the more special case we read: "All these facts support the assumption that somatic idioplasm is never transformed into germ-plasm, and this conclusion forms the basis of the theory of the composition of the germ-plasm as propounded here." [5]

A fairly typical expression of the author's all-embracing denial of new germ-plasm is the following: "The offspring owes its origin to a peculiar substance of extremely complicated structure, viz.: the 'germ-plasm.' *This substance can never be formed anew; it can only grow, multiply, and be transmitted from one generation to another.*" [6] A form of expression much used by Weismann particularly in his later writings, which somewhat disguises though does not surrender the main point, is that of "primary constituents" of the germinal substance. Thus in his discussion of the germ-plasm doctrine in his last extensive work, *The Evolution Theory,* we find "I am forced to see in this fact alone [that of metamorphosis in ontogeny] an invalidation of all epigenetic theories of development, that is of all theories which assume a germ-substance without primary constituents, which can produce the complicated body solely by varying step by step under the influence of external influences, both extra- and intra-somatic."[7] *

The Exact Mode of Involvement of the Germ-plasm Theory in the Germ-Layer Theory

We return now to the immediate point, namely that of the way the germ-plasm doctrine involves the germ-layers.

* While this is not the place to point out in detail the far-reaching consequences of this assumed impossibility of new formation in organic evolution, much less to show the subtle fallacy which it involves, the general subject is so important and will loom up so greatly in our enterprise as a whole, that I would wish to get it well into the reader's attention even at this early stage of our progress.

Since it is the main office of the sex-cells to carry the supposed germ-plasm, and since germ-plasm cannot be distinguished from somatoplasm by direct observation, and since sex-cells are not present in the individual organism of most species up to and including the layered stage of its life, the question of exactly how and where the sex-cells arise will be seen to involve the question of which of the layers they arise in. The problem may be stated more explicitly as follows: Where is the germ-plasm between the time when the germ-cell which is the beginning of a new individual disappears through division, and the appearance of new germ-cells within that individual, as the first stage in the life of an individual of the next generation? Or, stating the question still more explicitly, by what means and by what route does the assumed pre-existent germ-plasm get from its original place in the sex-cell which produces a given individual to the sex-cell produced by that individual?

Weismann's Studies on the Origin of Germ-Cells in Hydroids

Our purpose restricts our examination of the question stated in this general form, to the particular question of where and how (relative to the germ-layer) the sex-cells arise in an individual. Since Weismann elaborated his solution of the problem largely on the basis of phenomena presented by the Hydromedusae, many of which phenomena were brought to light by his own researches, we shall give these animals the central place in our examination. In the first place, the fact should be clearly understood that Weismann has never contended that a direct observable continuity between the parent sex-cell and the sex-cells of the offspring occurs in this group of animals. On the contrary, he fully recognizes, as do all students of these animals who have occupied themselves with this particular point, that a wide gap separates the parental from the filial sex-cells.

The very earliest recognizable sex-cells occur in the one or the other of the two body layers; that is, in the ectoderm or the endoderm of the fully developed animal. Since Weismann's theory denies the possibility of the origin of the sex-cells, or at least the essential part of these, the germ-plasm, from somatoplasm, his theory of sex-cell production in such animals as the hydroids must contain two quite distinct parts: one as to the route by which the germ-plasm travels from parental to filial sex-cell, and the other as to the force or forces by which the journey is accomplished.

The first part of the theory starts from the indubitable facts that in those hydromedusæ having a free-swimming medusa, or jelly fish, the sex-cells are borne by this and not by the polyp; that these cells do not as a rule arise in the medusa itself, but somewhere in the colony of polyps, from which location they migrate (in some cases for considerable distances) to the buds which later develop into medusæ; and that in the majority of species which have been examined with reference to the point, the mature sex-cells are found in the ectoderm and not in the endoderm. On the basis of these facts Weismann thought out a very elaborate and ingenious theory by means of which through various assumptions about the evolutionary history of the hydromedusæ, he was able to make the facts seem not only to harmonize with, but to support positively the doctrine of the continuity of the germ-plasm. Into that part of the theory which concerns the phylogenetic relation of the medusoid to the polypoid forms of the group, we need not go further than to say that through his speculations on this point he was able to provide a *Marschroute* or germinal highway or germ track from the parent sex-cell to the filial sex-cell. The question of where this *Marschroute* runs, with reference to the germ-layers is what immediately concerns us.

According to the theory, the germ-plasm of the parental sex-cells passes first into certain cells of the ectoderm of the polyp-generation from which place those cells make their journey to the ectoderm of the medusa, usually to some portion of it connected with the manubrium or digestive part of the animal. But—and here we come to the real point of the present discussion—since sex-cells are found by actual observation in the endoderm, in several genera and species, the theory is that the *Marschroute* lies first in the ectoderm, then passes over into the endoderm and returns later to the final goal of the sex-cells in the manubrial ectoderm. The ectoderm therefore is the home by naturalization, so to say, of the germ-plasm in these animals; it is originally planted there from the parental egg and finally matured there. As will be seen from what has previously been said, the kernel of the theory is to account for the positions and movements of the sex-cells in accordance with the supposition that their most essential part, their germ-plasm, cannot be formed anew from somatoplasm of any sort either entodermal or ectodermal, but must come over in direct continuity from the germ-plasm of the parental egg. The reason why the theory is so insistent on ascribing the sex-cells to the ectoderm is that it supposes that originally in the evolutional history of the group, the germ-plasm destined for the next generation of sex-cells was lodged in the ectoderm, and that this predestined it to that layer for all time.

Inconclusiveness of Weismann's Results Shown by Goette and Others

We have now to inquire how it has fared in later research with the numerous subsidiary hypotheses which enter into this complex theory of germ-plasm behavior in these organisms. Alexander Goette has lately gone over almost the entire grounds covered by Weismann in the monograph already mentioned, and his results and general conclusions are interesting in the highest degree. It would be impossible, even were it desirable, to review the memoir exhaustively. As to the most general aspect of it, it will suffice to say that Goette takes issue with nearly every one of Weismann's most important conceptions. The hypothesis that the gonophores are in all cases degenerate medusæ; the hypothesis of *Marschroute* (of hard and fast germ tracks); the hypothesis of entirely independent activity of the sex-cells in migration supported by the suggestion that the cells migrate by virtue of a "homing instinct" something like that supposed by some naturalists to be possessed by migratory birds; and finally and most relevant to the present discussion, the hypothesis which denies the actual origin of the germ cells in the endoderm: all these hypotheses and others which could be mentioned, Goette holds to be either in positive opposition to the observed facts or not necessitated by them.

It would be contended on the Weismannian mode of theorizing that since the issue is mainly one of interpreting facts, and not of what the facts are, Goette's views are entitled to no more weight than are Weismann's, and so do not constitute a disproof of the hypotheses in question. As this contention comes very near to the center of Weissmann's logical procedure, we must look at it attentively. Assuming that Weismann and Goette are equally endowed by nature and by training as observational biologists (and I have no doubt the great majority of unbiased zoologists who know the work of the two men would allow this), it must be granted that Goette as pitted against Weismann does not constitute a disproof of the latter's hypotheses. But does this admission leave these hypotheses just where they were before Goette's attack upon them? By no means. We may state the case this way: Weismann observes a long series of facts concerning the structure and development of a particular group of animals, and on the basis of these and in the interest of a theory of still more general scope, and of previous formulations, sets up a number of hypotheses. That these are fully proved is not contended even by Weismann himself: they are only given a good degree of plausibility or probability. Then comes another investigator of equal competency who goes over essentially the same ground and reaches essentially the same factual results, but who does not believe the hypotheses propounded by the first investigator are supported by the facts. What can a third person legitimately see in the total situation other than that whatever probability was given the hypotheses by the one investigator has been taken away from them by the other investigator? So far as we have yet gone with our examination we are, I think, compelled to recognize that as regards interpretation of structure and reproduction in the hydromedusæ, Goette's work leaves the matter just where it was before Weismann propounded his hypothesis. But we have not concluded the inspection; we have only considered Goette's work in its refutational or destructive aspect. Whatever of positive results both as to observation and hypothesis he has to set over against Weismann's must now be briefly considered. And here we return to the matter in hand in this section, that, namely, of the relation of the sex-cells to the germ-layers.

Goette believes he has proved incontestably that the sex-cells do *arise in the endoderm* in some species, so that Weismann's assertion that in this group they always arise in the ectoderm is wrong. But of far greater importance, Goette shows that not only the endodermal but also the ectodermal origin of the sex-cells is such as *not to give the least warrant for the hypothesis that any part of the cell* (the supposed germplasm being of course aimed at) *does not arise by transformation of the material of the layer in which they first appear*. And in this it seems to me he has made his case. His description accompanied by numerous drawings of the sex-cells in *Corydendrium parasiticum*, may be instanced as a particularly clear case of the genuine transformation of endoderm cells into sex-cells. To be still more explicit, in his figure (115 plate V,) is shown a sex-cell so slightly different from the neighboring endoderm cells, and so related to the surrounding cells, that no one would hesitate to conclude that it had very recently arisen by division of one of the endoderm cells unless influenced by considerations other than the evidence actually before his eyes. Exactly the same conditions, he says, are observable in *Clava*, *Sertularia*, and *Sertularella;* and he then remarks: "From these observations it becomes unfair to assume that in other cases where germ cells are found in the endoderm that they have wandered from the ectoderm. Proof of this must be absolute." [8] The full force of this remark is seen only when it is taken in connection with Weismann's own statements about the sex-cells of *Corydendrium parasiticum.* He saw here no less positively than did Goette, very young stages of the cells in the endoderm; but since, he says, he could not find the absolutely first stages "the possibility of the ectodermal origin of the sex-cells is not excluded." [9] In other words, the absence of absolute proof of the endodermal origin of the cells is used to support the *a priori* conclusion that they arise in the ectoderm! So far as the observational evidence in this specific case goes, it strongly supports, as Weismann himself grants, the conclusion that the reproductive cells arise in the endoderm, but since the evidence falls a little short of finality it may be cast aside wholly in favor of purely theoretical grounds for supposing the origin to be elsewhere! Against this method of reasoning Goette strongly protests, and every biologist who genuinely believes that speculative proof must yield to observational proof when the two come into conflict, will say amen. And when once one sees the extent to which Weismann's whole system rests upon this method, and sees at the same time how widely influential the system is, he will recognize that it is hardly possible to overestimate the importance of correcting the method and neutralising the evil it has wrought.

Weismann's Erroneous Conclusions Concerning the Origin of Sex-Cells in Hydroids as an Example of the Effect on the Observing Powers of the Germ-Plasm Type of Speculation.

A striking example of the effect of this system of speculation on the observing and reasoning faculties is afforded by Weismann's way of viewing the part played by the germ-layers in bud propagation in young animals. We might have presented the case when we were dealing with budding in ascidians and bryozoans, but as it implicates germ-cells and germ-plasm more intimately than we were prepared for at that time we speak of it here.

As pointed out above, Weismann's general interpretation of the sex-cells in the hydromedusæ led him to conceive that the germ-plasm is lodged in the ectoderm in these animals. This being so, he naturally concluded that his imaginary bound ("*gebunden*"), or unalterable, or accessory germ-plasm set aside for bud propagation ("blastogenic germ-plasm") must also be confined to the ectoderm. But according to the various researches, both endoderm and ectoderm participate, as a rule, in giving origin to the bud. What was to be done about this? Notice carefully what, according to the system, would be a sufficient confirmation of the theoretical view that buds really arise solely from the ectoderm: To find one or a few instances in which the buds do either certainly or probably begin in that layer, to assume this to be the phylogenetically primitive condition, and then to point out that in cases in which the two layers undoubtedly enter into the bud in the earliest stage, the "possibility is not excluded" that latent invisible germ-plasm is present in the ectoderm, becomes active at the place where a bud is to form, migrates into the endoderm, and so explains the participation of the endoderm in bud production.

Goette's conclusions as to the actual endodermal origin of sex-cells in the hydroids are not unsupported by other workers. Thus Tichomiroff holds that the sperm cells of *Eudendrium aurentium* arise in this layer, and C. W. Hargitt, who has devoted much time to the question, is unqualified in his statements. He writes in a summary presentation of his results: "It may be said that while in *Eudendrium ramosum* and *E. tenue* the ova arise strictly in the endoderm, and never at any time find their way into the ectoderm, in the species *racemosum* and *dispar* these products are found abundantly in both tissues."[10] So the observations seem conclusive that taking the group of hydromedusæ as a whole, the sex-cells arise in the ectoderm in some species and in the endoderm in other species, and that this origination is by a transformation of substance in both cases from what it was originally into that of the reproductive elements. Indeed the power of the propagative function of the organism to start indifferently with either ectodermal or endodermal material and reach the same end as seen in different genera of the hydromedusæ, seems in some cases to extend to different species of the same genus. "If one holds rigorously to the facts," writes Goette, "he must in spite of all hold to it as most probable that the *Keimstätte* in different species of *Eudendrium*, perhaps indeed in the same species, changes."[11]

Finally, and as a cap-sheaf to the arguments here presented in favor of the view that sex-cells do arise genuinely anew in each individual in the hydromedusæ, it remains to be shown that Weismann himself was really in accord with Goette on this point when he wrote the monograph on the origin of the sex-cells; and that only later under the impulsion of his speculations about germ-plasm did he come to repudiate this view. On page 284 of the monograph we find the following: "After all this, there can be no doubt that the germ cells may reach their differentiation and separation from somatic cells only when the germ-layers have long since been formed, and it is impossible to accept as a general law the view of *Nussbaum* that sex cells are 'absolutely independent of the germ layers.' So far as we can now see, the sex-cells always arise in the hydroids from elements of one of the germ-layers and they are not merely inclusions in a germ-layer but are derivatives, are division products of it."[12] Stripped of all sophistry, how is it possible to avoid seeing that we have before us a clear case in which Weismann can defend his doctrine of heredity at one of its most critical points only by making purely speculative considerations supplant observational evidence which he himself produced at an earlier period in his career?

The conception of an "hereditary substance" distinct from a non-hereditary substance, by whatever name called, and continuous from parent to offspring is contrary to the observed facts of sexual reproduction in the hydromedusæ as established by Weismann himself and by other and later biologists of unquestioned competency and trustworthiness. To this conclusion we are forced by an examination of the available knowledge of the sex-cells in their relation to the germ-layers in this group of organisms.

The Strongly Organismal Implications of Goette's Conclusions on the Origin and Migration of Germ-Cells in Hydroids

With this conclusion we return to the examination of the constructive as contrasted with the destructive results of Goette's research. We have shown the most specific and immediate of these as viewed from the standpoint of this section on the organism and its germ-layers, that, namely, wherein he proves the actual origin of the sex-cells from the endoderm. The only other positive result which I will touch upon is that concerning the route and cause of migration of the sex-cells from their place of origin to their place of maturing. Goette denies that they have any single road which is the same for all species, as contended by Weismann. He affirms on the contrary, that at least four paths are demonstrable, namely, the gastric endoderm; the bases of the pouches of the radial canal; the spadix; and the ectoderm of the manubrium. The kernel of Goette's conclusion on this subject, as opposed to Weismann's is, as I understand, that the sex-cells arise widely scattered in the parts and tissues of the polypoid colony, and that the development of the gonads or sex glands consists in large part in the drawing together or concentration of these disseminated elements, in some cases into buds that are to become medusæ proper, and in other cases where the medusoid is wholly absent, into the gonophores or brood-sacs which are outgrowths on the polyps. The diversity of the place of origin precludes the possibility of any single "germ track."

Again Goette does not believe, as Weismann does, that the journeyings of the sex-cells are due wholly to their own independent activity, and considers the comparison of their movements with those of migratory birds, and the ascription to them of an innate instinct, to be entirely fanciful. He holds, on the contrary, that these cells are largely carried along passively by forces which originate in the surrounding tissues and structures. His observations on the cells of *Podocoryne* have, he says, been particularly convincing that the wanderings are largely passive, and that even where there is intrinsic movement this is indeterminate as to direction, so that the final goal of the cells is in every case determined chiefly by influences which lie outside the cells themselves.

What the outside force is which Goette conceives to produce and direct the movements, we will hear him state in his own words. It is "a result of the directive activity of the definite and always similar developmental processes, . . . therefore of those conditions which determine not only the form of a body part, or organ, but also the transportation and definitive emplacement of the separate particles. I retain for this the expression 'form-conditions' used by me several years ago."[13] Obviously this statement by Goette carries us far beyond the bounds of germ-layers or even of sex-cells and hereditary substance.

To the numerous biologists who would refuse to accept Goette's "directing activity of the developmental process" and his "Form-conditions" as an explanation of the migration of the sex-cells in the hydromedusæ, because they are vague and "unanalysed" conceptions, I put the question: Are Weismann's conceptions of a wholly independent power of movement possessed by the cells, and a determination of the route followed by them as an innate instinct of their ancestral home possessed by the cells, less vague and more satisfactory because of the results of such an "analysis"? Let it be granted for a moment that the cells perform their journeys by activities wholly their own, that they are competent both to travel and to reach the end proper to them. What then about the *elements* which enter into *their* make-up, for surely no one would contend for a moment that they are without elements? Shall we conceive that in moving they do so by making use of their elements or parts in such fashion as may be necessary to enable them to accomplish their journeys? Or shall we deny to the cells *as such* the power of using their parts, but conceive that the parts are the real seat of power—that in reality they move the cells instead of being moved by the cells? If we accept the latter alternative, as in consistency with the elementalist standpoint we should have to, we shall be committed to either a never-ending though ever-vanishing series of biological elements, or to *ultimate chemical* elements endowed with homing instincts and the rest. Surely if either of these sub-alternatives be accepted the analysis which goes no farther than that of ascribing to the sex-cells power and instinct sufficient to enable them to do what they do, would have gone but a short way on its course and ought not to make any pretence of being a complete explanation of the phenomena. On the other hand, if we conceive that the sex-cells *move* through the agency of their elements and are not merely *moved* by means of these elements, why not as well allow that the developing organism as such may move its cells to meet its needs? As a purely logical matter there would be no more hesitancy in admitting that the *organism* moves its parts than in contending that the *cell* moves its parts, for the difficulty of conceiving how the thing is done is no greater in the one case than in the other. The only reason why the conception that the cells migrate wholly by their own powers seems less vague, that is more analyzed, than the conception that the cells are moved by the growing organism, is that in the first case a whole set of inevitable collateral phenomena, that is those pertaining to the *parts* of the cells themselves, is unconsciously excluded from the view. In other words, the satisfaction felt by analysis of this sort is an entirely spurious and illegitimate satisfaction begotten of the fact that the analysis is false. It is a process of searching for the factors involved in the complex of phenomena under contemplation, but *ignoring* all excepting a few of these factors. And this criticism of Weismann's attempt to explain fully the migration of the sex-cells holds for the attempt to explain on elementalist principles any biological phenomena whatever.

I remarked above that as a "purely logical matter" there is no more ground for refusing to believe the organism directs the movements of the sex-cells than for refusing to believe the cells direct their own movements. It will not do to let this remark go even in a tentative discussion of this vastly important subject. If it is merely a question of equality of claim upon belief as between the two conceptions so far as logic is concerned, what is to determine the choice? Why not accept the elemental as well as the organismal way of interpreting the case if logically its claims be equal to that of the latter? Because, I answer with emphasis, the observational evidence is stronger in favor of the organismal interpretation. That is the sole legitimate ground on which to rest the decision. Assuming, as we do, that Weismann and Goette are equally competent and trustworthy investigators, and basing the decision for the present on their results alone, we are bound to recognize that Goette has brought forward much more observational evidence that the migration of the sex-cells is largely though not wholly passive than Weismann has that it is wholly active.

Remarks on the Relation of Germ-Cells to Germ-Layers and to the Organism Generally

Before taking leave of the concrete objects, germ-layers and germ-cells, I speak of one aspect of the general results of our examination which may escape the reader unless his attention is specially directed to the matter. In all those animals in which the sex-cells do not appear until the layered stage of the embryo is reached, and in which these cells arise by a genuine transformation of cells of the layer, as they do in hydromedusæ, the layers are germinal in a very fundamental sense, for it is in them that the transformations begin which issue in the completed tissues and organs of all sorts, the *sexual tissues and organs with the rest.* Viewed in this light the germ-layers have, on the whole, gained rather than lost in importance and interest, for while we are led to deny the rigorous specificity to each particular layer as to what may or may not arise from it that often constituted a part of the germ-layer theory, it is a great gain to have perceived clearly that it is in the layered stage of the individual's life in many species that the next generation of individuals takes its rise. However, it does not by any means follow that because the sex-cells are born, as one might say, at this early time in the life of the parent, they are fully exempt from parental influence during all the period intervening between the layered stage of the parent and its stage of sexual maturity, that is, of final separation and extrusion of the sex-cells.

It seems to me the fact that the sex-cells of even some vertebrates are found at an early stage of embryonal life embedded in one or another of the germ-layers at points far removed from where the definitive germ glands will later appear, may signify just such influence. In other words, it may be the meaning of the "precocious segregation," as it is called, of germ-cells ought to be taken along with their wide dissemination in the embryo, and interpreted as speaking against and not for the fundamental isolation of the germ-plasm.

The distribution of sex-cells in the early embryos of vertebrates has been studied by several zoologists, among them being C. H. Eigenmann and B. M. Allen. Allen's investigations are specially important because of their wide comparative scope. In *The Origin of the Sex-Cells of Amia and Lepidosteus* he gives a set of useful diagrammatical comparative drawings showing the mode of origin of the sex-cells from the endoderm of a reptile (*Chrysomys*), an amphibian (Frog), and two fishes (*Amia* and *Lepidosteus*), but reaffirms in his discussion the result that the cells arise in the mesoderm in the tailed amphibians.

The Relation of Ideas and Observations as Exemplified in the Discussions of This Chapter

I would have this discussion stand as one example of the general method of interpretation which underlies our whole undertaking: while interpretation of biological phenomena is wholly impossible without ideas, some of which take the form of hypotheses and theories, equally true is it that hypothesis and theory are wholly dependent upon observation for validity. To this every biologist in whatever field of research and of whatever manner of thinking, would assent. But I go farther and assert that no hypothesis is proved, nor can be elevated to the rank of a general theory or doctrine until it is brought into accord with *all* relevant and fully verified observational knowledge. To this no elementalist assents in practice even though he may in words. Measured by this standard our final constructive discussion will reveal the fact that such conceptions as those of Weismann's germ-plasm and DeVries' pangens are not legitimate scientific theories at all. They are not because they can be maintained only by positively refusing to admit as evidence many of the demonstrable relevant observational facts.

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Chapter IV

THE ORGANISM AND ITS CHEMISTRY

Standpoint of the Discussion that of the Evolutionary Naturalist

PHYSIOLOGISTS and biochemists are not forced into contact with questions of organic evolution to any such extent as are botanists and zoologists. Occupied as they are in any particular investigation with relatively restricted aspects of one or a few organisms, such matters as geographic distribution, geologic succession, abundance and variety of individuals and species, adaptation, and so on, come to their attention very little or not at all. But these are exactly the problems with which the naturalist is occupied, and they are at the same time the very building stones of the evolution theory. This difference in interests and occupations doubtless accounts for the fact that the great evolutionists of history have been, without exception, naturalists primarily. The three names that stand out with mountain like conspicuousness among those who in modern times have made the idea of evolution a household possession, Lamarck, Darwin, and Wallace, sufficiently illustrate the point. These men were each botanist and zoologist in almost equal degree and in the strictest sense. Their work began out of doors with the vast riches of living plants and animals, and the impetus from this source dominated all they did.

In the highly subdivided and specialized biological realm of to-day, those who are trained in either botany or zoology or in both, are perforce the ones who think most in terms of the doctrine of evolution, and whose undertakings are most guided and fashioned by evolutionary conceptions: How and where and under what influences did these organisms, these organs and tissues have their beginnings and undergo development? So it happens that when a zoologist, for example, is confronted with the vast array of chemical compounds which his co-workers in the chemical laboratories have made known, he is bound to extend to them his usual string of queries. No matter how much information he is given about the molecular construction, the solubility, the reactions, the methods of laboratory production, of organic compounds, he can be in no wise satisfied until he has been told something about their original source, their way of getting into existence, not only in the individual organisms but also in the race. Many physiologists on the other hand, and also it must be confessed, a considerable number of modern botanists and zoologists, are very little concerned with such questions. In fact it seems as though the evolution doctrine had not made the slightest impression on many biologists animated by the chemico-physiological spirit, so far as concerns their attitude toward their special problems. These students appear to "take" the substances they deal with as things without beginnings, as eternally existent, or as coming into being "by free grace," in some such way as pre-Darwinian naturalists "took" their species. We had occasion to refer at some length to a similar un-evolutionary character of elementalist biology in a preceding chapter.

The question of how far such an attitude is due to the fact that physics is preëminently *not* an evolutionary science is one of great interest, both practical and theoretical. The very basal conception of modern physics, that of Matter and Energy as the only real things (as in the quotation from Watson: ". . . in the physical universe there are only two classes of things; to these the names *Matter* and *Energy* are given."), or at least as the most real of all things in nature, seems to carry with it an element of hostility to evolution, to the conception of origination by transformation and growth. But this is no place to deal with the vast problems thus intimated; sufficient to have mentioned the matter for the sake of a background for the discussion now before us. Our standpoint in this chapter on the organism and its chemical substances is to be that of the evolutionary naturalist. We are to push our studies of the structure and function (the morphology and physiology) of organisms into chemical foundations, and are then to inquire concerning the mode and place of origin of the foundational substances, and also concerning the adaptation of these to the needs of the organism. In other words, we are to look upon the chemical elements and compounds entering into the make up of organisms in the same way that we look upon the cells, tissues, and organs which enter into their composition. In fidelity to the best traditions and practices of natural history for the last century at least, the evolutional and adaptational aspects of our inquiry will presuppose much careful description, definition, comparison and classification of these substances.

Touching the descriptions presupposed, the following qualifying considerations should always be kept in mind: The naturalist is entirely unable to "go behind the returns" of the chemist in estimating the accuracy and fulness of the descriptions. He must accept what is furnished him from the chemical laboratories, exercising no critical judgment beyond that always requisite in the choice of authorities where one is obliged to go into fields not his own for facts. From this consideration very little actual description of organic chemical substances will be given in our discussion. We shall in general restrict ourselves to substances the existence and main attributes of which seem to be no longer in question among chemists themselves.

The second and more fundamental qualifying consideration is that, knowing as he does something of the methods by which the chemist gets at the chemical substances of organisms in order to describe them, the naturalist is unable to suppose the compounds and processes described by his chemical coworkers to be anything better than more or less distant approaches to the substances that actually exist, and the processes that actually go on in the organism as the naturalist is primarily concerned with it; that is, as living normally. The naturalist accepts not only without hesitation but with eagerness and gratitude the chemist's report on what he *is able to get out of the organism.* That these reports come near setting forth what the organism *actually is*, the naturalist is bound to recognize cannot be the case.

This reservation the naturalist feels the more justified in making by noticing that there are physiologists of unquestioned standing who hold views which amount really to the same thing. Thus the distinction between living and dead albumen (*Eiweiss*), first sharply drawn by Pflüger (*Ueber die physiologische Verbrennung in den lebendigen Organismen*, Archiv für die gesamten Physiologie, Bd. 10, 1875) and since recognized by other investigators hardly less eminent is manifestly of the same import. (See, for example, Max Verworn, p. 596, Allegemeine Physiologie, sechste Aufl.)

The Organism as a Chemical Laboratory

Immediately the fertilized egg begins to develop, chemical substances are produced within it. Among the higher animals the hen's egg has been the most studied in this as in many other aspects. "Neither nucleo-proteins nor pentoses are present in the fresh egg, and purine bases are present only in very small amounts. The fact that during development these substances rapidly increase in amount indicates therefore that a synthesis of nucleo-protein from the reserve material of the egg (proteins and phosphorized fats) takes place during development."[1] This statement by Marshall on the authority of Kossel and of Mendel and Leavenworth, may be taken as typifying a wide range of present-day knowledge of the synthesizing power of the growing embryo.

Because of its inaccessibility the mammalian ovum has been but little studied chemically. However from what is known of the chemistry of the eggs and embryos of other animals, particularly of the chick, we are entirely warranted in asserting that a full grown man, for example, contains an enormous number of chemical substances which are not present in the egg from which he developed. The chondrin of cartilage, the paraglobulin of blood serum, the haemoglobin of red blood corpuscles, the myosin of striated muscles, the various enzymes of the digestive glands, the neurokeratin and protagon of the central nervous system, and innumerable other compounds more or less specific for particular organs and tissues, come into existence in the course of development. And this production of new substances continues, with many organisms at least, up to the very end of the developmental series, even to the end of the lives of the organisms. This is well illustrated by the more or less distinctive oils, essences, acids, etc. occurring in ripe fruit. And few facts bring home more forcibly the subtlety and intricacy of the organism as a producer of chemical substances than do odors and flavors of flowers and fruits. The products of the organism's operations as a manufacturing chemist are seen to be of two rather sharply distinguishable sorts when the total chemical make-up of the developed organism is compared with the total make-up of the germ-cells. First there is a considerable number of substances common to adult and germ. Thus both tail and head of the spermatozoa of various fishes were shown by the well known researches of Miescher and Kossel to contain lecithin and cholestrin, both substances occurring also in a large number of adult tissues, as the blood, brain and nerves. The nucleic acid of the spermatozoa is said by Cramer to be very similar to that of the somatic cells and "probably identical with the nucleic acid prepared from the thymus."[2] But more interesting than the substances of identical structure which may be extracted from both germ and adult are the series of mixtures of phosphorized fats more complex than lecithin, which are present in the yolk of various eggs, some portions of which disappear as development progresses, seemingly being consumed as a part of the energy of development.[3] Other portions are transformed (?) substances of the same general nature in the tissues.[4]

So far then as concerns substances that are identical in germ-cells and cells of the mature organism, development consists merely or primarily in increasing their quantity. Such substances may consequently be looked upon as an actual realization of the doctrine of preformation which formerly played so great a rôle in speculative embryology. But the number of substances remaining exactly the same from the earliest to the latest stages of development is very small in comparison with the number wholly or partly new in the later stages. So that from the chemical standpoint development is for the most part strictly epigenetic; that is, it is a process not merely of increasing the mass, the quantity, of what previously existed, but as well of coming into existence of new kinds of substance. It is a qualitative as well as a quantitative process. The living, growing organism is creative in the strictest sense and that on a vast scale. "The lout," writes Oliver Wendell Holmes, "who lies stretched on the tavern bench, with just mental activity enough to keep his pipe from going out, is the unconscious tenant of a laboratory where such combinations are constantly being made as never Wöhler or Berthelot could put together: where such fabrics are woven, such colors dyed, such a commerce carried on with the elements and forces of the outer universe, that the industries of all the factories and trading establishments in the world are mere indolence and awkwardness and unproductiveness compared with the miraculous activities of which his lazy bulk is the unheeding center." [5]

The scientist cannot afford to let the literary quality of this paragraph obscure the truth it expresses. The accomplishments of organic chemistry in producing substances in the laboratory which it was formerly supposed could be produced only by the living organism, have been so brilliant as to obscure somewhat the significance of the fact that these artificial products are imitations: Nature made them before man did, and for the ends they originally answered they are still produced only as they formerly were, by the organism itself.

The fact that the chemist is able to produce what the organism produces in no way derogates from the significance of the fact that the organism does produce them. One can hardly see the import of the point here made until he reflects on the difference between the chemist's ability to produce in his laboratory compounds which are the same as the discarded end-products of the living organism's operations, or which can be extracted from the dead body of the organism, and the elaboration of substances which constitute the essential parts of the organism while it is still living and working. The problem can be put in concrete form by noting that the chemist produces certain substances *in his laboratory* by the activities of his brain and hands, and certain other substances *in his body* by the activities of his digestive organs, glands, muscles, brain and so on; and then asking how far those produced by the first means can be the same as those produced by the second. May the operations of the first kind be fully substituted for those of the second kind? May the brain and the hands with the appropriate laboratory apparatus ever be able to do the actual work of the liver for example, or the blood, or the testes or the ovary? The views prevailing to-day among physiologists and biochemists would favor an affirmative answer to these questions. In order to maintain some show of modesty the contention would be that while the chemist is not yet able to make these substances, there is no reason for supposing he will not be later. At any rate, so the view is, except for practical manipulative difficulties the substitutions might be made.

And it should be pointed out that thinking of the organism as a chemical laboratory, as suggested above, is not a mere literary fancy somewhat tinctured with science. By modifying the conception to the extent of making cells and tissues instead of an individual man the laboratory, it has figured considerably in recent biochemistry. According to Bayliss,[6] Hofmeister definitely formulated the idea in 1901, so far as the cell is concerned, and it "is rapidly gaining ground."

About the clearest statement of it I have come upon was made in 1913 by F. G. Hopkins. This biochemist illustrates the synthesizing activities of the organism by several specific examples, the last of which concerns nicotinic acid. When this "is fed to animals, it is excreted as trigonellin, a known vegetable base. This conversion involves methylation, and is of striking character as an instance of the artificially induced production of a plant alkaloid in the animal body." [7] * At the conclusion of the illustrations Hopkins says: "The known facts have, one feels, an academic character in the view of the physiologist and even in that of the pharmacologist, to whom we owe most of our knowledge about them. But, in my opinion, the chemical response of the tissues to the chemical stimulus of foreign

* Looking upon the production here instanced as "artificially induced" is worth noticing, since it clearly suggests that the conception of the organism as "chemical laboratory" implies not only the laboratory but the chemist who works in it.

substances of simple constitution is of profound biological significance. Apart from its biological bearings as the simplest type of immunity reaction, it throws vivid light, and its further study must throw fresh light, on the potentialities of the tissue laboratories." [8]

Different Organisms as Different Chemical Laboratories

But this glance in the exclusively descriptive way, at the chemical foundations of the organism in the various stages of its life, in no wise satisfies the modern natural history standpoint. As indicated in the remarks introductory to this chapter, that standpoint is comparative as essentially as it is descriptive. The moment this methodological plank in the natural historian's platform is reached, the insufficiency is seen of the conclusion that some individual organisms are manufacturing chemists or even that all are. Taken thus the result is altogether too general. The most cursory observation leads to the recognition that if every organism be a producer of chemical substances, not all organisms can be producers of the same substances, and that the extent and nature of the diversity of products would be interesting and important from both scientific and practical considerations. Now the comparative method in zoology has its roots in the every day knowledge that animals and plants are to some extent different from one another. Applying this method consistently and with sufficient rigor for the present inquiry, the problem formulates itself as follows: How far do the readily observable resemblances and differences between organisms reach down into their chemical make-up? Does the present state of advancement of biochemistry warrant the supposition that for every well-established similarity and for every well-established difference between organisms, both as to individuals and species and as to structure and function, there is a corresponding chemical similarity and difference?

(*a*) *Different Odors and Flavors of Animals and Plants as Distinguishable by Man*

The attempt to answer these questions should be prefaced by calling attention to the fact that experience is very familiar with a group of phenomena that bears directly on the problem even though not much definite chemical knowledge of these phenomena has yet been acquired. I refer to the odors and flavors so wide-spread in the organic world. Everybody knows that the odor of the cow is different from that of the sheep, and that that of the pig is different from both. Equally familiar is the fact that the flavor of the meat of these three animals is different. Apples are different from pears in both smell and taste, as are peaches from apricots. No one with normal senses of smell and taste would ever mistake potatoes for turnips even though he did not touch or see them. We might go on indefinitely mentioning differences of this sort in both the animal and plant worlds. That these differences have a chemical basis is certain. As is well known, the odors of living animals are to a large extent dependent upon the secretions of various glands of the skin, some of these being sweat-glands and others glands of more specialized character. But the urine and feces contribute much to animal odors, a large number of more or less well known chemical substances being implicated; and the flavors of meat are known to be connected to some extent with the bile.

These facts of common experience and of fragmentary chemical experience lead naturally to more specific questions in two widely different directions. In the first place we wish to know how far the odor differences, so sharply characteristic of animal and plant groups widely separated from one another in classification, hold as between groups less and less separated; and second, we inquire whether the chemical differences which reveal themselves by differences in smell and taste, are the only or even the chief chemical differences between the organisms concerned. Taking the first question first, we may make it more specific by asking if there is any evidence as to whether or not species of the same genus and varieties of the same species are known to differ from one another in smell, or their flesh in taste.

Special students of mammals and birds seem to have given less attention to odors as specific differences in these classes than the subject deserves. I find little beyond incidental reference to the matter in the literature consulted, and Dr. Joseph Grinnell, Director of the Museum of Vertebrate Zoology at the University of California, writes "I know of no naturalist who has attempted to make a general classificatory study of odors." Answering my question as to whether the different species of skunks and petrels are distinguishable by their odors, this experienced naturalist tells me he cannot smell any difference between two species of skunk, a *Spilogale* and a *Mephitis*, and that the species of the genus *Oceanodroma* (petrels) produce an odor which, "as far as my experience has gone, seems identical in all the species." But Dr. Grinnell says he can distinguish a weasel from a skunk by smell, not only in the volume as one might say, but in the quality of the odor. And the two genera *Mustila* and *Mephitis* to which these animals belong, are allowed by all mammologists to be rather close of kin.

As to petrels, Mr. L. M. Loomis, whose work on the water birds of the Pacific Coast of North America is widely and favorably known, writes: "The strong musky odor of the petrels renders their discovery in the rock piles easy. It is only necessary to insert the nose into likely crevices to find them. With little practice one may become very expert in this kind of hunting, readily determining whether it is an auklet or a petrel that has its residence in any particular cranny." The auklets and petrels are rather widely separated in the system of classification, being assigned to different orders. Nevertheless their similarity in food and other habits makes this difference in odor interesting.

The great variety not only as to form and secretion but as to position on the body, of the scent glands in the mammalia has an obvious bearing on the topic in hand. The abdominal glands of the shrew-mice, the hip glands of the mouse genus *Microtus;* the leg glands and foot glands and suborbital glands of the deer family; the anal glands of many orders; and the almost universal presence of glands whose secretions are odoriferous connected with the sexual organs, may be mentioned as illustrating the wide distribution of such structures in the body. And it is noteworthy that these may be present or absent in closely allied forms. Thus the Indian rhinoceros (*Rhinoceros indicus*) is said to have hoof glands while the Sumatran species (*Rh. Sumatrensis*) has none.[11]

The well known fact may also be recalled that scent glands are often distinctive of the sexes. The musk-deer (*Moschus moschiferus*) affords a particularly striking illustration of this, not merely as to the production of the perfume which makes this animal famous, but as to a glandular secretion of quite another sort. In the adult male there is a naked area around the root of the tail which is, as Darwin expresses it, "bedewed with an odoriferous fluid." This area is neither devoid of hair nor secretory in the female at any time in life, nor does it appear in the male until he is two years old. That the musk-gland of this species is a strictly masculine affair goes without saying when it is recalled that it is connected with the male sexual organs.

Ants are particularly instructive from this as from many other standpoints, the sense of smell in them being of far greater importance relatively to the other senses than in the higher orders. This has been established particularly by the admirable researches of Forel and Wasmann. Corresponding to the high development of the olfactory sense there is a great diversity of odoriferous substances produced by these animals. Something of the extent of this diversification is indicated by Wheeler, the foremost student of ants in this country, who remarks: "Even the degenerate human olfactories can detect the different species and in some cases even the different castes of ants (Eciton) by their odors."[12]

Among plants there are many examples of easily recognizable differences in smell and taste between species of the same genus and even between varieties of the same species. In some species of *Rhus*, for example *R. integrifolia*, the ripe fruit is covered with a thick, white, pasty exudate which is extremely sour, while the fruit of *R. laurina* has no trace of such a product. Since these species are both native of southern California and often occur together, they furnish an impressive instance of difference in chemical activity of two closely related plants. While referring to *Rhus*, the familiar fact that some of the species as *Rhus lobata* "Poison-oak" produce an exceedingly active poison while others do not, may be noted as a case of undoubted chemical difference between species that are close of kin. And this difference in the poison producing habit of plants is rather common and found in widely separated portions of the plant world. The cases of *Rhus* and *Solanum*, some species of which are poisonous and some are not, chosen from the higher plants, are paralleled by the genus *Amanita* (mushrooms) among lower plants. According to Charles McIlvaine, of the twenty-seven species of the genus, nine are edible, nine are known to be either deadly or are so closely allied to deadly species that it is unsafe to class them as other than poisonous; while about the others nothing is known in this regard.

Some tests on apples make it highly probable that the different kinds might be distinguished from one another to a high degree of nicety, by smelling them. This is the case with three varieties selected by chance and known locally as "wine-saps," "pippins," and "pearmains." In attempts to recognize them blindfolded the successes were considerably more numerous than the failures. This conjecture is clearly supported by the familiar fact that some groups of varieties, as for example the russets, are less odoriferous than other groups; and that other varieties as the "belle fleur" have a highly characteristic odor.

The suggestion that not only apples and fruits and flowers are distinguishable by their odors to a far greater extent than we are accustomed to suppose, is in keeping with the well known trade practices of tea-tasting, wine-tasting, tobacco sniffing and so on.

(*b*) *Differences in Animal Odors as Distinguished by Animals Themselves*

Even though the little effort that has been made by naturalists to distinguish species and varieties of animals and plants by smell does not warrant the assertion that differences of this degree of refinement do not exist, it yet would not be worth while to speculate on the possibility of their existence had we not evidence of their existence of quite a different sort from that furnished by the naturalist's nose. I refer to the evidence furnished by the noses of the animals themselves; evidence, in a word, of the extent to which animals recognize one another by smell. Although we have only a few thoroughgoing researches in which animals have been made to serve through their sense of smell as analytical chemists of one another, the few we have are exceedingly interesting. The case of ants which has received so much attention in recent years may be brought forward first in illustration of the point. "The multiplicity of odors," says Forel, "is enormous, and it is possible to demonstrate, as I have done for the ants, and von Buttel-Reepen for the bees, that these animals in distinguishing their different nest-mates and their enemies, betray nothing beyond the perception of extremely delicate and numerous gradations in the qualities of odors."[13] And continuing the statement quoted from above relative to the odors of ants recognizable by man, Wheeler says, "but these insects carry the discrimination much further. They not only differentiate the different odors peculiar to species, sex, caste, and individual, and the adventitious or 'incurred' odors of the nest and environment, but, according to Miss Fielde, they can detect 'progressive odors' due to change of physiological condition with the age of the individual."[12]

Miss Fielde's formulation of her hypothesis referred to by Wheeler is as follows: "1. *The Specific Odor*—The mother-ant transmits to her offspring the distinctive odor which is identical for ants of all ages and of both sexes within the species. 2. *Progressive Odor.*—Female ants, including queens and workers, have, beside their specific odor, an odor which may be termed progressive. Queens of different lineage have different progressive odors. In a queen this odor is either unchanging or changes very slowly, and it is similar to that of her newly hatched offspring. As worker-ants advance in age their progressive odor intensifies or changes to such a degree that they may be said to attain a new odor every two or three months."[14]

To Ernest Seton is due credit for the nearest approach that has been made to a scientific application of this method of discovering chemical differences between animals of the vertebrate orders. The theory of what he calls scent-language is founded on his study of carnivorous animals which hunt by smell.

Nor can we, while on this subject of odors as a means by which individual animals of the same group distinguish one another, neglect the case of the human animal.

The well known fact that some at least of the races of mankind emit distinctive odors may be first alluded to.

> "The Lord He loves the nigger well,
> He knows His nigger by the smell,"

is the way the negroes of the West Indies are said to express their claim to distinction through this character. Anthropologists generally recognize that races are differentiated to some extent in this way. Thus Deniker,[9] while not certain that the claims made by such travelers as Erman and Huc, can be fully allowed that populations may be recognized by their odors, still affirms the constancy of difference between some races in this regard. He accepts the statement that peculiarities in the smell of negroes and Chinese cannot be fully obliterated even "with most scrupulous cleanliness." Nor has this author neglected to note the importance of distinguishing between odors that are "sui generis" as he says, and those due to odoriferous foods or other substances with which certain peoples are habitually associated.

Ludwig Hopf asserts, largely on the authority of Jäger, that "some people have the power of differentiating relatively insignificant odours of individuals as well as family odours, and even the peculiar scent attaching to the inhabitants of the same village (spezifische dörferrüche)."[10]

The Naturalist's Approach to Biochemical Problems

We now pass to the examination of the chemical nature of organisms as this has been determined by chemical researches proper. The first remark to be made under this head must be on the exceedingly detached and haphazard character of the knowledge in this realm when it is looked upon from the standpoint of the zoologist and the botanist. I hasten to explain my meaning of "detached and haphazard" and of being "looked upon from the standpoint of the zoologist and botanist" for the statement may sound deprecatory of biochemistry and its allied branches.

As to actual quantity of knowledge and also as to the complexity and reconditeness and exactness of much of that knowledge, the chemistry of organisms is an impressive and admiration-compelling science indeed. When, however, the naturalist plunges into the great archives and monographs and handbooks in which the knowledge is stored, that he may find what there is that will contribute to the deepening and broadening of his *systematic* information about and interpretation of the animal and plant worlds, he soon becomes aware that this knowledge has not been gathered with any reference to the initial and most elemental needs of his enterprise; that is, with reference to the necessities of describing and classifying the natural objects, the animals and plants with which he deals. What he finds is that the investigators who have produced the knowledge have been in the main impelled by their interest in *certain functions* as displayed by *the most familiar animals and plants,* man's own organ-activities being by far the most usual starting point. For example, some young physiologist, ambitious and energetic, becomes interested in a particular function, say the circulation of the blood or muscular contraction or digestion, wins a reputation by his studies, and being, as most investigators have ever been, a teacher in some institution of learning, draws assistants and students into the researches, and much new knowledge, with perhaps a whole system of theoretical views, is developed concerning this particular activity. And what has been the material on which the researches have been prosecuted? If blood and its physiological rôle stands at the center of his interest, blood first and foremost, is what he wants and must have for his studies. What animal within wide limits it comes from matters little. The very fact that a fluid is found in many animals so alike as to receive a single name, *blood,* accepted without question as applicable in all the cases, is a guarantee that it has more in common in all the cases than the attributes by which it is familiarly recognized. For instance the redness of the fluid in all vertebrates makes it almost certain that with the obviously common color there will be other common attributes not obvious to ordinary observation. And so it happens that our physiologist goes to the dog or the ox or the horse or the rabbit, or with a little more hesitancy, to the frog for his supply, these being as a rule the most convenient sources.

One cannot reflect too carefully on the difference between this mode of approach to the phenomena of organisms, and that peculiar to the natural historian. Consider a moment the difference as touching one thing, the blood, and as between only two animals, the dog and ox let us say. Notice first that whereas the physiologist's primary interest would be satisfied with what he might get from a study of the blood of either of these animals without reference to the other, not so with the naturalist. Just blood is what the physiologist is concerned with in this particular series of researches. Comparison is no essential part of his enterprise. All he does in this way is incidental, is secondary. Could he get all the dog's blood he needed to make out all that can be learned about that blood, he would never concern himself as a strict physiologist about the blood of any other animal. The physiologist so far as he holds himself to his calling, and accepts his calling as it has delimited itself in modern times, namely, as having for its field *one aspect* of organisms, i.e., their functions, can never consistently go outside of function except incidentally—except for such morphological facts as are essentially related in one way or another to function. To the physiologist blood is blood no matter whether from a dog or an ox.

To the zoologist, on the other hand, blood is never just blood. It is always blood *of a dog* or *of an ox*, or of some other animal, for the animal *as an animal*, the dog as a dog, the ox as an ox, is an avowed concern of his. So it comes about, as said in a former section, that the comparative method is fundamental to the naturalist. From this it directly follows that for him *differences* between organisms are no less basal than are *similarities*. As a zoologist in the strict sense he is no more concerned with the problem of wherein the bloods of the dog and the ox are alike than in that of wherein they are unlike. This is so because the dog and the ox being both animals, neither can be to him of any more significance or interest than the other, so that which makes the dog a dog is no more and no less significant than that which makes the ox an ox, and it matters not at all whether the differentiating attributes pertain to the feet or teeth or ears or stomach or blood. See then what this implies as regards the zoologist's attitude toward the chemical makeup of the dog and the ox. He wants to know everything about the chemistry *of the dog*, and also *of the ox*. It implies that the taxonomizing naturalist must be chemical-minded to some extent and also that the biochemist must be a taxonomic naturalist to some extent.

That the comparative method, so fundamental and indispensable to the naturalist, becomes no less so to the biochemist before his work is done, finds no better illustration than in this very problem of the chemistry of the blood. The effects of the bloods of different species of animals upon one another has now become a recognized and important branch of biochemistry. But here is a point the significance of which neither biologists nor chemists appear to have fully grasped: the discoveries in this field could not have been made by any other means than those by which they were made, that is, by actually mingling the bloods of different animals in the living animals. *Chemical discoveries of great importance are here dependent absolutely on one of the naturalist's most cherished methods, the comparative,* the chemist having, however, surpassed the naturalist in the refinement of the method. This coming of the chemist into the field of the taxonomist is of the utmost interest to the naturalist, since on the naturalist's principle of "neglect nothing" it is impossible for him to be satisfied until he knows the chemical as well as the anatomical and histological makeup of organisms.

Not organic-chemistry nor physiologic- nor bio-chemistry is what he wants, but homonine, bovine, canine, salmonine, quercine chemistry, and so on. Surely nothing less than this will satisfy him and probably this will not, for even it is only generic chemistry; it is not species chemistry, much less individual chemistry, and in all probability the time is not far distant when he will demand individual or personal chemistry.

From the standpoint of chemical practice this demand is almost overwhelming. Take a live dog or even a live shark to the best manned and best equipped chemical laboratory on earth and seriously propose that a complete chemical analysis be made, and what sort of an answer do you suppose you would get? Still more what will the answer be when you go on to say to the director of the laboratory that the analysis of this dog alone will not meet your needs, but that one other animal at least must be analyzed with equal care and completeness since your enterprise is as essentially comparative as it is descriptive and that really what you will finally call for will be an equally thorough analysis of every animal.

These reflections lead straight-away to the inquiry, first in a general way, as to how much may be found in the storehouses of chemical knowledge that is to the naturalist's purpose; and second, as to whether or not chemical researches of the sort needed by him have been undertaken to any extent. Or turning this into language in which the naturalist is wont to express himself, how far has biochemistry become *systematic* biochemistry? How far has it undertaken to contribute to the vast task of describing and classifying and interpreting the world of *living* beings? Or varying the form of the question a little, how far has *biotic* chemistry become *biologic* chemistry? How far has the chemistry of organisms become *biologically scientific* in the systematic sense?

Some Biochemical Results Viewed from the Naturalist's Standpoint

With a stronger desire to indicate a naturalist's appreciation than to observe historical or logical sequences in treatment, I speak first of the most important research which up to that time had been made in this direction. Reference is made to the monumental undertaking conceived and now well advanced by E. T. Reichert. The title to the installment so far published deserves special notice: "The Differentiation and Specificity of Corresponding Proteins and other Vital Substances in relation to Biological Classification and Organic Evolution; The Crystallography of Hemoglobins."

Highly significant from the standpoint of method no less than from that of accomplishment is the fact that in order to carry through this piece of work, Reichert was obliged to associate himself with a mineralogist, and that in his university colleague, A. P. Brown, he found a man both capable and willing to undertake the task.

(*a*) *Reichert and Brown's Results on Haemoglobin*

The discussion will be best served by seeing first the main factual results of the research. Afterward Reichert's mode of approach and interpretation of these results can be considered. Reichert has summed up in a short paragraph of the preface written by himself alone what was made out by the observations: "It has been conclusively shown not only that corresponding hemoglobins are not identical, but also that their peculiarities are of positive generic specificity, and even much more sensitive in their differentiations than the 'zoöprecipitin test.' Moreover it has been found that one can with some certainty predict by these peculiarities, without previous knowledge of the species from which the hemoglobins were derived, whether or not interbreeding is probable or possible, and also certain characteristics of habit, etc., as will be seen in the context. The question of inter-breeding has, for instance, seemed perfectly clear in the case of *Canidae* and *Muridae*, and no difficulty was experienced in forecasting similarities and dissimilarities of habit in *Sciuridae*, *Muridae*, *Felidae*, etc., not because hemoglobin is *per se* the determining factor, but because, according to this hypothesis it serves as an index (gross though it be, with our present knowledge) of those physico-chemical properties which serve directly or indirectly to differentiate genera, species, and individuals."[15] This investigation was extended to the blood of more than one hundred species of vertebrates and included representatives of all the classes of the phylum, though many more mammals than any of the other classes were studied. In several genera, as *Canis* and *Felis*, a number of species and varieties were included.

The crystallographic method was used almost exclusively in the investigation. Concerning the value of this method for recognizing chemical similarities and differences, the authors, trusting partly to such authorities as Groth, rest on the view that "Differences of chemical constitution are accompanied by differences of physical structure, and the crystallographic test of the differences of chemical constitution is recognized as the most delicate test of such differences."[16] In accordance with this the dictum, "Substances that show differences in crystallographic structure are different chemical substances" [17] is accepted.

As far as the conditions of the researches would permit, the crystals of oxyhemoglobin were made the standard of comparison. When several forms of this are obtained from the same blood "each form, A-oxyhemoglobin, B-oxyhemoglobin, etc., appears always in its own proper form and axial ratio when the blood of different individuals of the same species are examined. The same is true of the other hemoglobins—metoxyhemoglobin, reduced hemoglobin, methemoglobin; so that the hemoglobins of any species are definite substances for that species. But upon comparing the corresponding substances in different species of a genus it is generally found that they differ the one from the other to a greater or less degree; the differences being such that when complete crystallographic data are available, the different species can be distinguished by these differences in their hemoglobins. As these hemoglobins crystallize in isomorphous series, the differences between the angles of the crystals of the species of a genus are not, as a rule, great; but they are as great as is usually found to be the case with minerals or chemical salts that belong to an isomorphous group." [18] In illustration we may select the table for the species of cats studied, this being based on the crystals of *reduced hemoglobin.* The crystals belong to the orthorhombic system and are optically positive for all the species, so these items need not appear in the table.

Name of Species	*Axial ratio*	*Angle of unit prisms (normals)*	*Angle of macrodome normals*
Felis leo	0.9742:1:0.3707	88 30′	41 50′
F. tigris	0.9742:1:0.3838	88 30′	43 0′
F. bengalensis	0.9657:1:0.3667	88 0′	41 35′
F. pardalis	0.9489:1:0.3931	87 0′	45 0′
F. domestica	0.9656:1:0.3839	88 0′	43 20′
Lynx rufus	0.9869:1:0.3914	89 15′	42 46′
L. canadensis	0.9605:1:0.3944	87 42′	41 30′

As another example the table for the crystals of B-oxyhemoglobin from the baboons of the genus *Papio* is chosen. These all belong to the monoclinic system and all except those from the Guinea Baboon (*P. sphinx*) are optically positive.

Name of species	*Axial ratio*	*Angle B*	*Prism angle*
Yellow Baboon (*Papio babuin*)	1.6808:1:c′	72° 72′ 30″	118 30′
Guinea Baboon (*P. sphinx*)	1.8418:1:c′	70°	123 0′
Long-armed Baboon (*P. Langheldi*)	1.655 :1:c′	70° 30′	117 44′
Chacma (*P. porcarius*)	1.732 :1:c′	75°	120 0′
Anubis (*P. anubis*)	1.737 :1:c′	72° 30′	120° 11′

So far as one with little knowledge of crystallography may judge the numerous tables of which these two are samples, the copious illustrations many of which are from photographs, and the discussions, seem to justify fully the generalizations above quoted, with others to which no reference has been made. It would however be quite wrong to gain the impression that the very positive conclusions as to the specificity of hemoglobin crystals reached by these authors is in accord with all researches that have been made on the subject. Summing up their rather extensive review of studies previous to theirs, the authors say: "Equally expert observers working with blood of the same species have arrived at very different conclusions as to the specificity or non-specificity of hemoglobin crystals in relation to species, some claiming that the crystals are occasionally specific, others that they are always specific, and others that they are not specific because the same blood may yield crystals of very different forms and that the differences are probably accidental. Crystals of various colors and varying forms have been obtained from the same blood." [21]

A highly significant thing that comes from considering the results reached by those students who have opposed the idea of specificity of hemoglobin from different kinds of animals, is not that they claim that all hemoglobin crystals are alike, or even that only a few sorts can be demonstrated, but that the great number of kinds do not correspond in any definite way to different kinds of animals. And here comes the particular point made against these views by Reichert and Brown—and it is of great importance generally, and peculiarly interesting to the natural historian. They show that the reason why so many previous observers have failed to find a correspondence between kinds of crystals and kinds of animals, is that the crystals have not been *described with sufficient fulness and accuracy.* In a word the issue is, to the naturalist, the old and familiar one of *description, comparison* and *classification.* For example, the authors lay particular stress upon the insufficient attention hitherto given to the crystal forms of the different sub-species of hemoglobins, namely, oxyhemoglobin, reduced hemoglobin, metoxyhemoglobin, methemoglobin, etc. Again they point out the great inadequacy of earlier studies in the determinations of the axial relations and other physical attributes of the crystals. The upshot of their criticism of previous studies as seen in the light of their own, is that when a classification of hemoglobin crystals from the blood of many kinds of animals is based on *sufficiently thoroughgoing description,* that classification correlates itself with the kinds of animals from which the blood is taken.

(b) *The Precipitin Reaction Between Bloods of Different Animals*

If our comparative chemical knowledge of vertebrate blood were limited to the results of studies like this by Reichert and Brown, the presumption in the absence of very positive evidence to the contrary, would yet be strongly in favor of the hypothesis that the blood of each animal species is in some of its constituents unique to that species.

As is now widely known, this hypothesis is supported by another great mass of evidence from quite a different source, which though not as directly chemical as that just adduced, is still so clearly so in its implications that reference to it in this chapter is undoubtedly justifiable. What is in mind are the discoveries of recent years touching the compatibility and non-compatibility of the blood of one kind of animal for that of another kind; discoveries in other words, concerning the so-called "precipitin reaction" as between organisms of different kinds. Although this subject has attracted a good measure of attention, only a portion of its more fundamental significations has been much regarded. Its bearings on problems of affinity and racial descent, for example, have elicited their due of interest. But its contribution to light upon the opposite aspect of animal nature, namely, that of difference as well as of likeness between kinds, has not been appreciated in proportion to its merits. Once grasp the conception of each organic species, to say nothing of each individual, as something genuinely unique in the world in certain of its more obvious attributes, as a scheme of organization, shape, etc., and then extend this down into basal composition and process, so that the organism is seen in its rôle not merely of transformer and creator, but to some extent of *exclusive* transformer and creator of the elements of which it is constructed, and these and kindred discoveries fall into their right perspective of meaning and interest.

The underlying general principle of the precipitin reaction is that of the production within the organism of *anti-bodies* as a result of injecting into it certain foreign substances which, when the reaction occurs, are known as *anti-gens*, the *anti-gens* and *anti-bodies* usually reacting definitely and specifically upon each other. In one form of this reaction the antibody acting upon certain proteins, forms a precipitate, this precipitate carrying down both the antigen and the antibody. The point of special significance for us now is that the blood of a given species of animal has been found to act as an antigen when injected into the circulation of another species, and the extent of the reaction is in large measure dependent on the degree of affinity between the animal species to which the different bloods pertain.

A particularly instructive case worked out by Hamburger is given by Arrhenius. Serum from a rabbit was treated with serum from a sheep, the rabbit serum being in this way made to contain an antibody. The rabbit serum thus affected was then used for experimenting upon the serum of a normal sheep, a goat and an ox, with a view to testing quantitatively the action in the three cases. The same quantity of rabbit serum containing the antibody was used in each case, as was also the same quantity of equally diluted serum of the animals to be tested, and the amount of precipitate in each case was measured. The results given in terms of the antibody or precipitin, rather than in that of the precipitate are, in Arrhenius' words, as follows: "On injection of sheep-serum into rabbit blood we have obtained an antiserum containing per centimeter cube 300 equivalents of precipitin against sheep-serum, 212 equivalents of precipitin against goat-serum, and only 90 equivalents of precipitin against bullock-serum."[22] This result is obviously in agreement with the general zoological evidence that the goat and the sheep are somewhat closer of kin than the ox and the sheep or the ox and the goat.

Another inference of quite different import drawn from the experiments is not to be missed, namely, that the different amounts of precipitation in the three sera is not due merely to a quantitative difference in the precipitin contained in the rabbit serum, but that there are really three precipitins involved. This conclusion, Arrhenius points out, seems necessitated by the fact that a unit quantity (1 c. c.) of the normal serum from each of the three animals tested contains nearly the same number of equivalents of the precipitate.

In his well known work *Blood Immunity and Blood Relationship*, G. Nuttall has applied this principle more widely to the animal kingdom than any one else.

(*c*) *Comparative Chemistry of the Sperm of Different Species of Fishes*

Several biologists are impressed with the importance of knowledge in this field as bearing on philosophical natural history. No physiologist has so far as I am aware, ventured quite so far into the realm of prophecy with reference to it as has E. Abderhalden. He points out the possibility of increasing the number of attributes now recognized as distinguishing not only species but individuals through a systematic and concerted carrying out of researches already begun in this field, and foresees the time when biochemistry will play a leading rôle in problems of racial descent and taxonomic affinity.[23] The march of research in the decade since Abderhalden made these forecasts, has undoubtedly been toward a fulfillment of them, at least as touching biochemical distinctions between individuals. Thus C. Todd has very recently given a useful summary of what has been done up to the present hour on the comparative chemistry of the blood as revealed by the methods here being considered, and an account of an exceedingly interesting resarch of his own.

The chemico-zoological researches standing next in interest and importance to those on the blood are the well known ones inaugurated by Miescher and continued by Kossel and his students, on the spermatozoa of fish. Miescher discovered in the sperm of the salmon a group of protein substances called by him protamines, which are said not to have been found as yet elsewhere than in fish sperm.

There has been some question whether these are true proteids, but at any rate they seem to be relatively simple and definite in composition so that Kossel has regarded them as the foundation of the protein bodies. It has been possible to work out probable empirical formulae for them, and herein their natural history significance comes strikingly to view. The formula $C_{32}H_{54}N_{18}O_4$ was assigned by Miescher to the protamine of Salmon sperm, the substance being proved to contain the nucleic acid radical. The comparative studies of Kossel and his students extended to the sperm of the herring, mackerel, sturgeon, and perch, and brought out the fact that while the nucleic acid part of the molecule is the same for the different genera, the basic part is different in each, so a name is required for the protamine derived from each kind of fish. The names ***salmine, clupeine, scombrine, sturine, cyprinine, cyclopterine***, etc., proposed by Kossel have consequently come into general use. These differ in formulae. Thus Kossel gives clupine as $C_{30}H_{62}N_{14}O_9$ and sturine as $C_{36}H_{69}N_{19}O_7$. They also differ in the cleavage products yielded, histidine for example, being extracted from sturine and from none of the others, and tyrrosine from cyclopterine exclusively. All, on the other hand, yield arginine while lycine was found only in sturine and cyprinine, and so on.

(*d*) *Comparative Chemistry of Milk From Different Species*

The milk of several species of mammals has been extensively investigated mostly from physiological and dietetic standpoints, but the difference between the milks of different groups has come out with positiveness. It seems that on the whole the milks of carnivorous species are more alike, and those of herbivorous species are more alike, than those of either of these categories are like those of the other, but there are not enough observations to warrant laying this down as a law. As thorough a chemico-zoological investigation of milk as that made by Reichert and Brown of blood, ought to yield highly interesting results, for not only common knowledge, but technical knowledge as well, obtained in connection with the dairy industry recognizes that even as between different breeds of cows the milk differs in constitution. Jersey cows for example, produce milk containing a larger proportion of butter fat than do Ayrshires, and some at least of these breed-differences in milk cannot be explained on the basis of differences in food or other environmental factors, powerfully as these do undoubtedly influence milk.

Attention may be called to the extreme chemical sensitiveness of this fluid as a registering instrument. "Circumstances tending to cause discomfort usually lower the proportion of volatile acids present in the butter-fat, but the variation in the composition is very irregular, and appears to depend partly upon the nervous temperament of the cow." [24] And there is ample evidence that the character of the milk of women may be so changed by nervous and mental conditions as to become unfit for the nursing babe.[25]

(*e*) *Comparative Chemistry of Digestive Enzymes*

Another great field of chemico-zoological research has recently been opened up by studies on the enzymes of digestion. The investigations of this sort which we will notice have been specially prosecuted by the Swedish chemist, S. Hedin. The results are given in outline by A. Hardens and from this the following statement is, in the main, drawn.[26] The problem concerns rennet, the familiar milk clotting substance produced in the calf's stomach, and Hedin's results are not influenced so far as I can see, by the much debated question of whether or not pepsin and rennin are two entirely distinct bodies. It is shown that the mother-substance, the zymogen, of the clot-inducing substance is not simple but is a compound of the enzyme and an inhibitant for that enzyme. By proper treatment of the water extract of rennet with dilute acid, the enzyme is liberated and the inhibitant destroyed, while if the treatment be with dilute alkali the enzyme is destroyed and the inhibitant liberated. But if the solutions containing the two opposing substances are mixed, recombination takes place and the resulting solution has the attribute of the original water solution of rennet, namely, that of clot-production to a slight degree only.

To be specially noted is the fact that the inhibitant of a given rennet neutralized the enzyme of *that same* rennet. Now comes the thing of special importance from the standpoint of comparative zoology: When solutions of both enzymes and inhibitants are prepared from different species of animals (the calf, the pig, the guinea pig, and the pika, were used in the experiments), it turns out that the inhibitant from the rennet of one species does not inhibit the enzyme from the rennet of another species. And so it is concluded that "both the enzyme and the inhibitant are different for each animal, a fact of great interest and importance," to repeat Harden's words.

Special attention should be called to the circumstance that not only is this another method of differentiating species chemically, but that it is an exceedingly delicate method. This is particularly seen in the fact that the rennets of the species investigated were found capable of clotting cow's milk in spite of their being different in other respects as just shown, it being thus revealed that the fact that rennets from two different animals may act alike on cow's milk, does not prove them to be alike in all their attributes. No careful student of nature will ever neglect the principle involved in this. We may take this as an impressive reminder that the problems of the dependence and the independence of characters, so much to the front now in connection with the Mendelian mode of biological inheritance, extends down into the chemical reactions taking place within the organism.

(*f*) *Instances in General Biochemistry Where Interesting Facts of Comparative Chemistry are Incidentally Brought Out*

If now, taking our cue from these several distinct groups of positive evidence of a close correlation between attributes by which the naturalist ordinarily distinguishes individuals, varieties, species, genera, etc., and chemical attributes of these groups, we look through biochemical works which have no natural history intent so far as their authors are concerned, with the end in view of seeing to what extent they nevertheless contain incidental facts and statements which are in keeping with the results of the chemico-zoological researches just considered, we find an almost unlimited number of records of such import. We will notice a few of these, selecting them mainly with reference to the very wide range, both chemical and biological, from which they may be drawn.

One of these works has lately produced good experimental reasons for believing that trypsin of the liver of "the star fish" is considerably different from that derived from the same organ of the "large soft-shelled California Clam." So far as concerns the research here referred to, what species of starfish was used probably did not matter much, but to the zoologist bent on pushing as far as possible his knowledge of the differences between animals, the point is of genuine interest since the fragment of information thrown out might serve as the starting place for an important chemico-zoological study of the organs rather indiscriminately called liver occurring in many invertebrates. But even this additional knowledge, for we have much besides, favorable to the conception that trypsin can never be looked upon as just trypsin, but must be regarded as the trypsin *of* some particular species, or possibly variety, or even individual.

A. P. Mathews, more regardful of the source of his scientific blessings, that is, of the material on which he works, as well as of other essentials, is explicit and informs us that the eggs of the sea-urchin *Arbacea punctulata,* differ markedly in their physiological properties from those of the starfish *Asterias forbesii.* The differences in "physiological properties" noticed consist in the greater stability of the sea-urchin egg as manifest in its resistance to oxidation, low rate of respiration, and relative insensibility to stimuli inducing artificial parthenogenesis. These differences Mathews finds to be correlated with the possession by the sea-urchin egg of considerable quantities of the widespread substance cholesterol, and the absence either wholly or in part, of that substance in the starfish egg.

*The Coalescence of Natural History and Comparative Chemistry**

It seems then from all this that natural history and biochemistry are being inevitably drawn together by the very

* Since this chapter was written J. Loeb's *The Organism as a Whole* has been published. It is gratifying to find in this book evidence that the author is being carried, as it seems to me, unconsciously perhaps, toward the organismal and natural history standpoint. One piece of such evidence may be appropriately noticed at this point. It is that Loeb gives us a chapter with the title *The Chemical Basis of Genus and Species.* This seems to show that now, since specificity is coming down to a chemical basis, taxonomy is assuming a reality and significance in this author's mind which it did not have formerly. But attention should be called to the fact that knowledge of the chemical differentiation of taxonomic categories has not made their reality one whit more positive than it was before. *The chemist is following the naturalist and refining the latter's methods in certain particulars beyond anything he himself is capable of.* "In certain particulars," I say, because in certain other particulars the naturalist is still far in advance of the chemist. Thus the naturalist knows beyond a trace of uncertainty innumerable "specific differences" among plants and animals which the chemist, as a chemist, can not yet so much as touch. In fact, the lack of compre-

nature of the subject matter with which they are occupied. Descriptive zoology and botany are to become chemical in part, and the chemistry of organisms is to become zoological and botanical in part. Each science is to supplement, and reciprocally to be supplemented by the other far more essentially than has hitherto been the case. In one of its aspects biochemistry will become a branch of systematic zoology and botany, just as biology in one of its departments, is already a branch of chemistry. Although such a state of things is very far from full realization, that the movement is in this direction seems unmistakable. The conception that animals and plants as producers of chemical substances, and that each *kind* if not each *individual* is to some extent a producer of different substances is receiving new confirmation all the time.

When we pass from the primary task of identifying and describing the chemical substances produced by different animals and plants to that of gaining an insight into the *methods* by which these substances are produced; when, in other words, we pass from the problems of What to those of How, the vast complexity and uniqueness not only of the chemical operations of organisms as distinguished from non-organisms, but as well the uniqueness, within limits, of these operations come even more impressively into view. A

hensiveness and of refinement in some directions of the chemist's descriptions receives striking illustration in this very book "The Organism as a Whole." Restricting his consideration of the chemical bases of species to the evidence drawn from laboratory experimentation, Loeb writes: "Ford claims to have obtained proof that a glucoside contained in the poisonous mushroom *Amanita phalloides* can act as an antigen. But aside from this one fact we know that proteins and only proteins can act as antigens and are therefore the bearers of the specificity of living organisms." (p. 63). Exactly what is meant by "bearers of the specificity of organisms" no one knows, but if the assertion implies, as it seems to, that all such differences are due exclusively to proteins, it is contrary to a vast array of indubitable facts of natural history. Differential odors and flavors, for example, as dwelt upon above, are certainly not all, probably not usually, proteid in nature.

comprehensive discussion of the problems of how organisms, *all of them*, from the simplest unicellulars to the most complex multicellulars, accomplish the chemical transformations which they *do* accomplish, would require a broader knowledge of chemistry, both physico- and bio-chemistry than I suppose any professional chemist would pretend to have. It would be, then, wholly presumptuous for one who like myself is exceedingly meagerly possessed of first-hand chemical knowledge even to touch it. Nor do I intend to do this beyond the very simple extent of trying to present in schematized fashion the various ways in which organisms operate chemically, with the special end in view of presenting strikingly to both naturalists and chemists what is in store for them from the standpoint of research undertakings if the ideas set forth in this chapter are to be realized.

Provisional Enumeration of Chemico-naturalist Inquiries

A rough-and-ready enumeration and classification of the chemico-transformatory methods employed by organisms may be given as follows:

1. The methods by which green plants use the radiant energy of the sun in constructing their own substance, and doing it in such fashion as to store away the great quantities of this energy that is characteristic of them.

2. The methods by which plants utilize water and the inorganic elements of the soil to their needs.

3. The methods by which plants store up organic substances for future needs in seeds, bulbs, roots, etc., and make use of these supplies when the proper time comes.

4. The methods by which the organic foods of animals are reduced to a state in which they can be taken into the circulation.

5. The methods by which from the foods thus reduced the substances of and in the tissues characteristic of *particular*

species are built up; the methods, that is, of *particular* as contrasted with *general* assimilation.

6. The methods, oxidative and otherwise, by which the force liberated in muscular and other work is accomplished; that is, the methods of *particular* as contrasted with *general* work by organisms.

7. The methods by which the germinal elements of plants and animals, sex-cells, plant and animal buds, gemmae, bulbs, propagative cambium cells, etc., become so constituted as to be able to develop into other individuals like those from which they themselves originated.

8. The methods by which the chemical substances distinctive of organic varieties, species, etc., are originally produced, the *phylogeny,* in a word, of biochemical substances.

9. The methods by which acts of volition, memory, intellection, and emotion are accomplished.

Peculiar Importance to Natural History of the Application of Physical Chemistry to the Chemistry of Living Beings

The ascertainment of details of structure and process implied by this inventory obviously belongs to biochemistry alone. By himself, the naturalist is helpless in his longings for knowledge in these realms. But chemistry's initial answer to the naturalist's appeal is not very comforting, for if the particular chemist to whom the naturalist appeals is broadly experienced and learned, is thoroughly objective-minded, and quite frank, he assures the naturalist that his request is for light in one of the darkest places in the whole realm of chemical phenomena. Nevertheless, if plied closely, chemistry is found to have a certain amount of positive knowledge and certain well-supported conceptions which interest the naturalist of the organismal cast of mind very much—more, indeed, than they interest the chemist himself. This special interest of the naturalist in chemical facts and ideas is due to his seeing possibilities in them that the chemist sees but dimly if at all.

(*a*) *Individuation and Speciation of "Organic Matter" Fundamental Biologic Facts*

That some physiologists are not fully awake to the significance of certain of their possessions is shown, I think, by the following appraisement of plant productions that are used for drugs: "It is remarkable how great a variety of these active substances are formed by plants. It seems evident that they must be more or less accidental products of chemical change. A very small number would suffice for protection of the plant from being consumed by animals for food. Similar conclusions may be drawn from the occurrence of adrenaline and a substance related to digitalin in the 'paratoid' glands of a tropical toad, described by Abel. It is impossible to see what use to a toad a rise of blood pressure in the animal which attacks it would be."[29]

The naturalist must object to this view very strenuously. In the first place, he is bound to point out the unquestioned fact that these substances are subject to the law of heredity, one of the securest and most probably universal of all the laws thus far established by biology. Hence to pronounce the substances accidental is to commit what may justly be characterized as a scientific misdemeanor. Such a pronouncement is about as unsound in the general living realm as would be a declaration that the musical talent is an "accidental" product in the human realm. The really modern naturalist has outgrown the old practice of putting aside whatever he can not explain as accidental or abnormal.

But the naturalist must go on and point out that if the particular plant substances which have won the attention of chemists because of their toxic or medicinal properties may be regarded as accidental, then it would follow that an incalculably vast array of the phenomena of the living world taken as a whole would come under the same stigmatization. This would follow from the fact that the thoughtful naturalist is certain that the criterion of accidental (to wit, that of non-usefulness from the survival-of-the-fittest standpoint, invoked by Bayliss) is no more applicable to these particular substances than to myriads of structures and substances and activities of the most diverse sort presented by plants and animals. To illustrate, probably a majority of all organic odors, and all flavors so far as these are differentiable from odors, would have to be cast into the scientific discard of accidentals. In fact, I believe any open-minded taxonomist to-day will recognize that such a criterion of accidental would thus dispose of a majority, probably, of the attributes upon which he depends for distinguishing species, varieties, and races. And this brings up the exceedingly important question, is not such a physiological conception as that expressed by Bayliss due largely to the influence of the natural selection hypothesis, a conception which came straight from natural history? Bayliss's own words seem to constitute an affirmative answer to this query. But natural history is becoming convinced that while the numerous activities of organisms which Darwin grouped together and named the struggle for existence are of very great importance, they have very little originative power in a strict sense. This conviction is being forced upon natural history from two of its main fields of research, namely from that of taxonomy and that of genetics. The exact taxonomic studies of to-day, especially such of them as give due attention to the relation of the groups to their environment, are at one with studies on mutation and Mendelian heredity in denying to adaptation and natural selection the supreme rôle in evolution assumed by the Darwinian, and especially the neo-Darwinian hypothesis.

Natural history, then, is able with a strength peculiarly its own to deny physiology's right to set aside as accidental myriads of biological phenomena in the interest of inorganic hypothesizing about organic beings. Naturalists are in position to insist that physical and chemical conceptions as applied to organisms must be somehow so shaped that they will neither disregard nor minimize the importance of vast numbers of facts about the living world which natural history from her own peculiar labors knows to be facts.

So the naturalist pushes his quest among his biochemical confreres still more closely and broadly, for his general scientific sense and faith lead him to surmise that somewhere chemistry has something better than the accident hypothesis for dealing with the undeniable difficulties which the individual, varietal, specific and generic substances and activities present. Physiology almost certainly found the right starting point or base of operations for a broader, more adequate application of physics and chemistry to biology when it recognized (as indicated on a previous page) the fundamental difference between living and dead protoplasm. Once the full significance of this difference is recognized, biochemistry will be able to go ahead in its service of biology—and of human weal in general—unhampered by hypotheses that are really narrowing because too grasping.

Let me assure those biological readers whose scientific thinking has been more or less deranged by the dread bogy, Vitalism, that there is not the slightest real danger of running into Vitalism in the direction indicated. There is no such danger because what we are here concerned with does not raise the metaphysical problem of a Vital Force, or for that matter of any other "ultimate force." The strictly scientific problem before us is in deepest essence of the same nature as it is in its most obvious, most practical expression.

It is this: Are a man and a dead man, a horse and a dead horse, the same thing or are they different things? If the materialistic biologist and the vitalistic biologist will answer this question with an unfaltering "They are different things," and will give due attention to both the objective and the subjective grounds on which the answer is based, they will find that the words materialism and vitalism, to which they have clung so tenaciously, are emptied of any important significance as applied to their doctrines. Both vitalist and materialist will then become aware that the very nature of biochemistry, its nature in virtue of which it has a certain measure of independence, or self-sufficiency, is a peculiar revealer of both the necessity and the method of application of physical chemistry to biology.

So I bring this discussion of the organism and its chemical substances to a close with a brief natural-history statement of the probable rôle of physical chemistry in interpreting organic beings. First of all, we must insist that the obvious, the never-refuted, the universal fact that all living substance or protoplasm is individualized, shall not be ignored or cavalierly tossed aside. Nor can we permit its significance to be obscured by sophistical reasoning—by such reasoning as, for example, may be indulged in from the discovery that certain organs and cells may live for a long time and carry on their activities more or less normally, after being separated from the organism. What these important observations prove is that many living organs, tissues, and cells have wonderful tenacity of life, *once they have been brought into existence.* From this viewpoint the facts are of great interest, but they do not furnish a scintilla of evidence that organic substance or cells or organs are independent of individual organisms in the sense of being able to come into existence independently of individual organisms. Some physiologists talk about "organic matter" as though it had as little connection with organisms as has inorganic matter. "Living substance," unindividuated in a strict sense, has no better standing in the world of objective reality than have the ghosts and other apparitions with which the imagination of primitive men populates the world.

All the living substance that has existed on this earth or anywhere else has existed through and in and because of individual living beings. That this is a truism is no reason for treating it as though it were not true.

(*b*) *Indications That Variation and Individuation are Primarily Chemical, While Constancy and Uniformity are Primarily Physical*

Fixing attention, now, on organic matter as the matter of individual organisms, which individuals are subject to the laws of variation and heredity, and remembering that according to these laws no two individuals are exactly alike, and that every individual is derived from other individuals which it resembles because of being thus derived, see how in their very nature physics and chemistry are adapted to the needs of the natural historian in his efforts to interpret the "matter" of the organisms with which he is occupied. From being par excellence the science of transformation, of the production of what is absolutely different and absolutely new relative to that from which the products come, chemistry seems to the naturalist to be above all others the science which ought to illuminate the variational, the transformational, the productional side of "organic substance." On the other hand, from being par excellence the science of the general, the persistent, the non- and quasi-transformational side of natural objects, physics appeals to the naturalist as the science which ought to bring light into the darkness that envelops the repetitional, the like-begets-like, the heredity side of the same substance.

And since physics and chemistry have fused together as regards many phenomena in their own special fields to produce a single two-parted science, physical chemistry, natural history looks with much hopefulness to this new science for light on the "living matter" aspect of its problem. It is almost certain that the application of physical chemistry to the study of organisms has actually made a good start in the very quarter which, as indicated above, the naturalist would expect help from the new science.

As regards the *Cell*, biochemistry, prosecuted under the guidance of physical chemistry, is bringing out facts and formulating conceptions that are unmistakably organismal, it seems to me, in their trend. Deferring to the biochemist's predilection for the *cell* rather than for the *organism*, let us reflect on how the problem of the cell presents itself to the naturalist in one of its main aspects, that, namely, of its *existence* only, that is, its phenomena other than those connected with cell *reproduction* through division or otherwise. The basal problem thus arising is: what is the cell's constitution in virtue of which it is able so to transform the matter and the energy flowing through it as to enable it to carry out the various activities, contraction, secretion, conduction of stimuli and so on, peculiar to it, and at the same time maintain its identity as a space-occupying object; that is, maintain its individuality?

Place, now, alongside this formulation of the natural history problem of the cell's existence the following summary statement of what the cell is to a biochemist who sees physicochemically: "But it is clear that the living cell as we now know it is not a mass of matter composed of a congregation of like molecules, but a highly differentiated system; the cell, in the modern phraseology of physical chemistry, is a system of co-existing phases of different constitutions. Corresponding to the difference in their constitution, different chemical events may go on contemporaneously in the different phases, though every change in any phase affects the chemical and physico-chemical equilibrium of the whole system. Among these phases are to be reckoned not only the differentiated parts of the bioplasm strictly defined (if we can define it strictly) the macro- and micro-nuclei, nerve fibers, muscle fibers, etc., but the material which supports the cell structure, and what have been termed the metaplasmic constituents of the cell. These last comprise not only the fat droplets, glycogen, starch grains, aleurone grains, and the like, but other deposits not to be demonstrated histologically. They must be held, too—a point which has not been sufficiently insisted upon—to comprise the diverse substances of smaller molecular weight and greater solubility, which are present in the more fluid phases of the system, namely, the cell juices. It is important to remember that changes in any one of these constituent phases, including the metaplastic phases, must affect the equilibrium of the whole cell system, and because of this necessary equilibrium-relation it is difficult to say that any one of the constituent phases, such as we find *permanently* present in a living cell, even a metaplastic phase, is less essential than any other to the 'life' of the cell, at least when we view it from the point of view of metabolism." [30]

Or, again notice this: "For the dynamic chemical events which happen within the cell, these colloid complexes yield a special milieu, providing, as it were, special apparatus, and an organized laboratory."

Some of the particularly important features of the "colloid complexes" which make them a "special milieu," i.e., a special environment, of so remarkable a character are: The commingling in them of the solid and fluid, or "gel" and "sol" conditions of the colloids; the "surface effects" of colloidal particles as the free surface energy, the osmotic pressure, and perhaps the enzymic action, of such surfaces; the so-called *adsorptive* properties of solid colloids, that is, the power the substances have, dependent upon temperature, pressure, etc., to take up varying quantities of different substances, making them thus highly *selective;* and the ready transformation of the substances back and forth from the colloid to the crystalloid conditions to meet the needs of the living cell.*

Such expressions as those quoted from Hopkins (and others of similar purport could be quoted from other authors) it seems to me say merely this: The *physical* (in contradistinction to the *chemical*) constitution of the living cell is such as to enable it, as a complex unitary whole, to accomplish the *chemical* transformations of substance and energy which it is observed to accomplish. By its purely physical properties, its spacial and energy magnitudes and changes, the cell is primarily *quantitative,* while by its chemical properties, its transformation of substances and energies, it is primarily *qualitative.*

The *physical* principles implicated in organic phenomena make of the cell an "organized laboratory," in Hopkins' phrase, for bringing about "*dynamic chemical events,*" events, that is, which are qualitatively transformative.

So our appeal as naturalists to physical chemistry for help in interpreting the substances of which organisms are composed is carrying us toward some such conception as to their *individuation,* apart from which we are obliged to conclude organic substance never exists, as that individuation is dependent primarily on the *chemical* nature of the substance; while the *continued existence* of individuals and their genetic repetition is dependent primarily on the *physical* nature of the substance.

This, I say, is the direction in which the evidence thus far considered seems unmistakably to carry us. But we

* See especially The General Physical Chemistry of the Cells and Tissues, by W. Pauli, in *Physical Chemistry in the Service of Medicine,* translated by M. H. Fischer.

have not yet examined all the relevant evidence. For example, what we have seen up to now does not go beyond the *cell* in individuating the living substance. So a further stage of our discussion will have to deal with the nature of the cell and its place in the organic scheme.

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Chapter V

THE ORGANISM AND ITS PROTOPLASM

Protoplasm and Mystification

NOT many words belonging to purely technical and descriptive botany and zoology have become so much involved as has "protoplasm" in obscure speculation on the part of biologists themselves, and in more or less spurious regard by both biologists and generally intelligent persons. "The new Anthony studies the protean forms of life and at the end is ravished by the sight of protoplasm. 'O bliss,' he cries, and longs to be transformed into every species of energy, 'to be matter!' "

Though this is an undisguised bit of imaginative writing, it undoubtedly expresses a feeling toward "the physical basis of life" that in essence is no fiction. Many, perhaps most, educated persons know its meaning in some degree from personal experience. Whence this ravishment? Justification for approaching the protoplasm question from this direction is found in the belief that the validity of what is generally held to be strictly scientific observation and generalization is to some extent at stake.

Were Purkinje, Dujardin, von Mohl, Cohn, Schultze, and the other discoverers of protoplasm thrown into any such state of mind by what they saw? Not so far as any one knows. Yet I do not for an instant believe these observers were less sensitive to the deeper meanings of the phenomena of organic beings than have been other persons, scientific and non-scientific, who more recently have been affected much as St. Anthony was, on seeing or even hearing about protoplasm. Particularly may we believe Max Schultze, chief among the pioneers in this realm, was not thus defective, for we have explicit information that he was an artist as well as a scientist, and of a highly imaginative, sensitive nature.[1]

Responsibility for the Mystification of Protoplasm

Great as was Huxley's service in enlightening the rank and file of English-speaking people concerning matters biological, I believe what he did for protoplasm in this way by his renowned address, "On the Physical Basis of Life," he did partly at the cost of "making a Magic," as Kipling would say, of protoplasm.

A soberly scientific discussion of protoplasm cannot possibly ignore the fact that in the light of the extensive exact knowledge now in our possession, at least one excellent biologist has believed that it would be advantageous to give up the word "protoplasm" altogether, so far as technical biology is concerned,[2] because at the present time it promotes confusion rather than clearness of thought. And even those who do not hold so extreme a view about the value of the term, still admit that "on many sides the word is used in different ways." For Max Schultze, to whose writings the legitimate protoplasm doctrine probably owes more than to any other one of the pioneers, the word had connected with it a "quite definite conception." [3] Without taking grounds one way or the other on the question of whether it is or is not desirable to abandon the word, we will look at what came to pass both as concerns concrete knowledge and interpretation of the theory of protoplasm between 1861, when Schultze wrote the phrase just quoted, and 1912, when O. Hertwig last defended the right of the term to exist even though used in many different senses; for by so doing we shall come upon that which, to a large extent, has determined the present writer's attitude toward protoplasm.

To begin with, there can be no doubt that, historically considered, "protoplasm is a biological conception," as O. Hertwig insists.[4] Furthermore, equally certain is it that when so considered it is a term of *descriptive* biology pure and simple. The discoverers of protoplasm were engaged in the enterprise of *describing and comparing the minute structure* of animals and plants, no less avowedly than the discoverers of the capillaries of the blood system were engaged in the same enterprise. They were telling what they saw under their microscopes and were drawing conclusions from their observations. Even the titles of many of the foundational memoirs of the protoplasm theory show this.

On the plant side, Corti (1772) was describing what he saw in the interior of the living twigs of *Chara;* Meyen (1827) what he could see in the fresh leaves of water-celery (*Vallesnaria*); Robert Brown (1831) what the living hairs of the still higher plant *Tradescantia* revealed to him, and so on. Similarly from the account left by Rosel V. Rosenhof (1755) of the examination of his "Proteus animalcule" we know he had an amoeba under his microscope and was studying it as he had numerous other organisms, low and high, to find out how it was constituted. It was what seemed to Dujardin (1855) the resemblance of the soft, living material of the foraminifera examined by him, to the flesh of higher animals that made him propose the name *sarcode* for this material. Finally, to mention no others of the many whose observations contributed to the upbuilding of the science of microscopic anatomy, it was Max Schultze's examination of the minute structure of a great range of animals and animal tissues, from amoebae and the foraminiferae to the muscles and retinas of the higher vertebrates, that furnished the raw materials for his splendid inductions.

If we inquire how a strictly objective discovery concerning the structure of organic beings should have become enveloped in so much sentimental, half-mystical interest, one large element in the answer soon comes into view: it is due to Huxley's address. Undoubtedly what contributed most, historically, to the fame of this discourse was its popularization of the conception that life has, in deepest reality, a physical basis. Both its good fame and bad fame have rested largely on this.

I want to make it entirely clear that, important as this aspect of the matter is, there is another aspect very different from this and almost as important, with which alone we are concerned in this section. I refer to the conception, not definitely expressed by the phrase, but obviously implied in it as used both by Huxley and by nearly everybody since, that "all life is one," and that the "seat" of it is the single wonderful substance, protoplasm. Huxley's essay abounds in sentences and phrases expressive of this notion: "Beast and fowl, reptile and fish, mollusk, worm and polype, are all composed of structural units of the same character, namely, masses of protoplasm with a nucleus."[5] "With such qualifications as arise out of the last-mentioned fact [the chlorophyll function of green plants] it may be truly said that the acts of all living things are fundamentally one."[6] "Hence it appears to be a matter of no great moment what animal, or what plant, I lay under contribution for protoplasm [for food], and the fact speaks volumes for the general identity of that substance in all living beings."[7]

Conception of Animal Sarcode and Plant Protoplasm as "Identical Stuffs"

Since Huxley spoke (how far *because* he spoke it is impossible to say definitely) this notion has become a dogma, having all the objectionableness of all dogma in science. "Subsequently, Max Schultze and de Bary proved, after most careful investigation, that *the protoplasm and the sarcode of the lowest organisms are identical.*"[8] "However, Max Schultze in particular . . . produced incontrovertible evidence that the protoplasm of plants and animals and the sarcode of the lowest organisms are identical stuffs."[9] "As the culmination of a long period of work, Max Schultze, in 1861, placed the conception of the identity between animal sarcode and vegetable protoplasm upon an unassailable basis, and therefore he has received the title of 'the father of biology.'"[1] "Protoplasm, the physical basis of life, the living part of every living being, and essentially the same in its general properties and functions in all. . . ."[10]

These quotations, picked up at random, will perhaps suffice to illustrate the wide prevalence of the view. But though widely held, acquiescence to it is by no means universal and whole-hearted, judging from a considerable number of expressions that might be cited.

This not being the place to present in detail the facts and arguments which make the conception of the absolute identity of all protoplasm untenable, I shall do no more than put this question to those biologists who subscribe to the creed: In the light of what we now know about the reactions of the blood of animals of different genera and even species to one another, and about the chemical composition of the nitrogen-containing substances of tissues and elements in different groups of organisms, if the protoplasm of a dog, say, could be wholly removed, and that of a fish or even a tree could be substituted, would the dog continue to be the same dog, and none the worse for the change? No biologist untrammeled by speculative considerations will hesitate to answer this negatively, unless, indeed, it seems too ridiculous a question to deserve serious treatment. Yet if the "conception of the identity between animal sarcode and vegetable protoplasm" is warranted by what nature actually presents to us, the answer would certainly have to be diametrically the opposite; that is, it would have to be to the effect that a dog would be strictly himself and as well off with a tree's protoplasm as with his own sarcode.

But the particular point I want to bring out is that, taking the utterances of not merely the father but the fathers of modern biology at their maturest and best, one finds that not only did they *not* teach the identity of protoplasm in all living beings, but that what they did teach was something very different. Ferdinand Cohn, for example, said of the protoplasm which he saw escaping through the cell-wall of the alga studied by him, "if not identical" with animal sarcode, it "must be at any rate in the highest degree analogous" to it. [11]

Max Schultze's Actual Teachings as to Protoplasm and Sarcode

In 1861, after a great many trustworthy observations had been made in widely separated portions of the organic realm, of substances so closely resembling one another, came Max Schultze with the essay which gained for him the widely recognized title "the father of modern biology." Exactly what did Schultze aim at in this essay? He was primarily concerned with the nature of the cell and not of the protoplasm. The title chosen indicates this definitely enough: "Concerning muscle corpuscles and that which has been named a Cell." What he undertook was to dispose of the then prevalent doctrine that the cell-wall is the most essential part of the cell, by proving that the body itself, not the skin or membrane of the cell, is the really important thing; and partly by showing that even in cells having a distinct membrane, what is contained within it is similar to the bodies of non-membranous cells and is the really active, living part of the cell. His definition, "A cell is a little mass of protoplasm in the interior of which lies a nucleus" [12] epitomizes his results so far as concerns his understanding of the nature of the cell. But while Schultze's central aim in his essay was clearly to answer his own question, "Was is das Wichtigste an einer Zelle?" the nature of that which is the "Wichtigste" concerned him greatly although secondarily; and for the topic now occupying us, the author's conclusions under this head are of the utmost interest.

(a) *Cell Nucleus Distinct from Protoplasm But Both Nucleus and Protoplasm Essential to Life of Cell*

In the first place, it cannot be too strongly emphasized that Schultze did not consider the cell nucleus to be protoplasm in any sense: "To the conception of a cell there belong two kinds [of things] a nucleus and protoplasm, and both must be division products of corresponding parts of another cell. Both constituents are equally important. A disappearance of one, like that of the other, destroys the conception of the cell." [13]

This unqualified recognition of nucleus and protoplasm as "equally important" appears over and over again in the essay, so even from this point of view it is obvious that Schultze could not have subscribed to the conception that "protoplasm is the physical basis of life." For him protoplasm could be no more this basis than the nucleus, and the nucleus was not protoplasm. The expression which comes nearer than anything else in the essay to the Huxleyan notion reads: "The cell leads an exclusive (abgeschlossenes) life, as one may say, the bearer of which is again preëminently the protoplasm, but there falls to the nucleus also a rôle at least as significant although as yet not more definitely specifiable." [14]

This seeming ascription to the protoplasm of the place of first importance in the life of the cell in no way contradicts the conception of correlative essentiality of the nucleus.

But the most vital point at which the teachings of the essay are contravened by the dogma that protoplasm is *the* physical basis of life; that is, that "all life is one" and that its basis, protoplasm, is "essentially identical" in all living beings, involves quite another matter than that of the relation between nucleus and protoplasm. That what Schultze actually says comes far from implying such identity I shall now point out. The crucial part of his discussion of the relation between plant protoplasm and animal sarcode is introduced by a brief reference to his studies, previously published, on rhizopods. This reference he thinks important as a starting point for the comparison, in that the rhizopods furnish a solution to the "question of what in reality the unformed contractile substance of the Protozoa is." He remarks that Sarcode, brought into prominence by Dujardin, had become discredited because given too wide and indefinite an application. The term as used by Dujardin was intended to apply to a "contractile substance which can not be resolved into cells and which does not contain other contractile form-elements, as fibers and so on." [15] But, Schultze contends, a substance of this sort is exactly what we find the protoplasm of cells to be, and supports his contention by instancing the contents of many plant and animal cells, especially where, as in the cells of the hairs of *Tradescantia*, protoplasmic movements within the cell can be witnessed. Concerning the substance of these cells, he says there can hardly be a doubt that "we have to do here with a contractile substance in the same sense as it constitutes the body of many rhizopods." [16] Since, then, Schultze reasons, the term Sarcode was employed originally to designate a substance which is now brought into the same category as Protoplasm, "Sarcode" should be dropped.

(*b*) *Recognized Common Attributes But Not Identity of Protoplasm in All Organisms*

It is clear that Schultze's central purpose was to compare the contents of cells from widely different organisms for the purpose of showing that as concerns *some attributes* of these contents, that of contractility being foremost, the substances agree with one another. We shall do well to be attentive to the language in which this is expressed. As to the protoplasmic movements within the hairs of *Tradescantia* and in the bodies of many rhizopods there can be no doubt that we have to do with "contractile substance" "*in the same sense.*" For the point I wish to make I transfer the emphasis from where the author placed it, namely on "contractile substance," to "in the same sense." To affirm or even to imply (neither of which the author's words do) that the substances of two or more cells are the same in so far as they are contractile, is very different from saying that the substances are the "same" or "identical." And look closely at another sentence: "The proofs for the relationship of both substances have only multiplied by my own observations directed at this point." Note that a *relation* between at least two *substances*, not a *single substance*, nor yet two substances which are *identical*, is here talked about.

That there are other attributes than that of contractility in which these substances agree is made sufficiently clear, and it is on these attributes-in-common that the author bases his proposal to attach to the word "protoplasm" an "entirely definite conception," and have it displace the word "sarcode," to which, he says, no such conception has been attached. But that the attributes-in-common possessed by the protoplasm of different organisms comprehend *all* the attributes of protoplasm, Schultze neither says nor implies. On the contrary, several facts and arguments on which he lays no little emphasis ought, I believe, to be interpreted as meaning that he conceived protoplasm to be essentially different in different organisms as concerns some of its attributes. For example, after speaking of the differences he had observed in two species of rhizopods of the same genus, *Gromia oviformis* and *G. Dujardinia*, he says, "I bring this forward only in order to point out in indubitable cases of *naked protoplasm* differences again in movement, consistency, and tendency to fuse with like substances with which it comes into contact, upon which differences we come again in the naked cells of the tissues of higher animals." The immediate point Schultze was aiming to establish here was the individuality, in the sense of preservation of identity, of the protoplasmic mass which he was contending to be the essential thing in the cell, without the presence of a membrane or any sort of limiting outer layer to insure that individuality; so it is only secondarily that his argument touches upon the attributes of differentiation of the protoplasm itself as between different cells. Nevertheless his insistence in several connections on the differences, particularly in consistency and resistance of the protoplasm, surely bears strongly in this direction. I believe, then, enough has been said to show that the conception of protoplasm held by the "father of modern biology" gives no warrant for the Huxleyan and more recent conception of the essential identity of the protoplasm in all organic beings.

Ernst Brücke's Conception of the Cell as an Organism

Another essay recognized as constituting part of the classical literature of modern biology is Ernst Brücke's "Die Elementarorganismen." This essay is likewise particularly important for our enterprise, though in a considerably different way from the one just examined. Although Brücke's labors lay so largely in the same field with those of Schultze, and although he was familiar with his confrere's writings, significantly enough the theses he upheld in this essay led him to regard somewhat lightly Schultze's leading contention, namely, for the importance of the cell-contents, protoplasm and nucleus, as against the cell-membrane. That the cell should be regarded as an *organism* was, as is well known, what Brücke undertook to show, and his motive should be distinctly recognized. He was working in the interest of observational and descriptive histology and physiology. Nothing in this essay, at least, indicates that he was particularly interested in the broader implications of his main thesis, and there is much, as we shall presently see, to show that he was decidedly wary of "ultimate questions."

The very word "organism" implies organization, and organization implies some *thing* organized; something, that is, composed of parts a number of which, at least, are indispensable and correlated with one another. An organism, then, or an organized thing, and a thing of *ultimate simplicity*, are terms not only contradictory but are mutually annihilative of meaning. Brücke does not say this in just this language, but his whole argument is a setting forth of the idea in a concrete, particular case, namely that of the cell. After calling attention to the similarity of the cells to the organism in various attributes, as that of growth by ingestion of foreign material, movement, change of form, response to stimulation, and so on, and after reminding us further of the fact that organisms are composed of parts which we call organs and systems of the body, he says, "We can hardly think otherwise than that in the cell also the different activities proceed from differently constructed parts."[17]

Going further with this idea, he writes: "We naturally do not expect that the organs and systems repeat themselves as we find them in the human organism taken in its entirety. We know this is no more the case even in the lower animals.

We know that with reduction in dimensions nature changes the means by which the energies of the inorganic world are made serviceable in the organism. But with the exception of the differences conditioned by this fact, and with the exception of the less number of constituting parts, we have no right to hold one of these smaller organisms as less ingeniously constructed than one of another or greater dimensions, and this consciousness we ought to bring not only to the investigation of the smallest animals, but likewise to the investigation of plant and animal cells. We may always see in the cell a small animal body, and ought never to lose sight of the analogies which exist between it and the smallest animal forms." [17]

Characteristic Organization in All Cells

But it is in connection with the problem of the more detailed structure of all parts of the cell, membrane, nucleus, and cell-body alike, that this investigator's conclusions and attitude of mind are most fully revealed, his great point being that there must be far more of organization in the cell than microscopes reach. "What right have we to believe," he says, "that in our scheme we have exhausted the organization of the cell? Is it a ground for such an assumption that we can perceive no further details in the relatively giant retinal image given us by our present high magnifications? . . . Shall we conceal from ourselves the fact that many circumstances limit the field of our microscopical determination?" [18]

In view of the fact that later speculative biologists have appealed to Brücke's contention that there must be cell organization beyond that revealed by the microscopes, in support of their fancied "ultimate biological units," it should be emphatically pointed out that not only does Brücke's argument not give passive sanction to such hypotheses, but rightly interpreted it opposes them. He does indeed maintain that molecular structure as known to the chemist can not be the only kind which eludes observation. "These molecules," he says, are "not merely building stones placed one beside the other in a simple fashion, but are united together in an ingenious (*kunstreich*) living organization." [19]

And referring back to the paragraph quoted, in which the differences in structure between small and large organisms are dwelt upon, we find an unmistakable indication that the mode of conceiving, as one may say, which Brücke would hold, might be legitimately applied to the ultramicroscopic structure of organisms: "We may always see in the cell a small animal body and ought never to lose sight of the analogies which exist between it and the smallest animal forms." [20] That is, each living cell at any and every moment has organization *of its own* beyond what we can see with the microscope, the organization being analogous to that which exists in the smaller animals. No vagaries here about an organization in one cell (a germ cell) which *represents* the visible organization of some other cell-organism developed from that cell.

In another passage Brücke sounds a warning about theorizing in this domain of biology which, had it always been heeded, would have prevented much wandering about in a morass of speculation. "Desirable as it is," he says, "always to hold rigorously to immediate observation, equally necessary is it not to close the spiritual eye to that which is inaccessible to observation, so that we overprize the work of our microscopical determinations and with the help of final words (*Schlagwörter*)—*cell-membrane*, *cell-contents* and *cell-nucleus*, erect physiological doctrines which a future generation may refuse recognition." [21]

To be sure, the author was aiming in this at doctrinal perils considerably different from those of recent "representative biological units," but the essence of his warning is applicable in the one case as in the other. He would have no pseudo-scientific explanations, whether hidden behind "*Schlagwörter*" or entities of the pure imagination, given a semblance of objective reality by being connected with actual objects. One of the great merits of Brücke's attitude toward the problem of the constituents of the living beings which lie beyond the reach of direct observation should be specially pointed out, though this is not the place to speak of it in detail. From several of his statements, but particularly from that about the analogies between the cell and the smallest animals, we may infer that he had a genuine appreciation of the distinction there is between the conception that there must be some sort of organization beyond what the microscope reveals, and a conception of what the specific nature of that organization is in particular cases.

So a critical examination of Brücke's fundamental essay reveals the fact that though starting from a quite different standpoint from that of Max Schultze it contains as little as does Schultze's essay to support belief in the identity of protoplasm in all living things.

Results of Later Description and Classification of Cell Substances

The question still to be considered is whether or not the discoveries made since the pioneer era have furnished, by the actual study of protoplasm, more support for the belief in such identity. I do not believe any candidly critical student will maintain that they have. On the contrary I believe such a student will recognize that the indubitable tendency of the evidence is toward the opposite conclusion; namely, that the protoplasm not only of all organisms, but of many different parts of the same organism, is to some extent different.

That the observational knowledge of the substances constituting living organisms has been vastly increased since Schultze and Brücke wrote, hardly needs affirmation. This greatly augmented store of knowledge may well be regarded for a moment in the light of the circumstances referred to some pages back. One outcome of later work has been a serious questioning of the scientific desirability of longer retaining the word "protoplasm." To be sure, this question was not raised primarily because of interpretations of the substance of the cells of *different organisms*, but rather because of interpretations placed upon different substances in *the same cell.* Strasburger, who seems to have been the first to depart from Schultze's sharp distinction between the protoplasm of the cell and the nucleus, was led to this by determinations made largely by himself, which had accumulated during the two decades of research since Schultze wrote, that the nucleus is by no means the simple, homogeneous thing it appeared to the earlier investigators, but has itself an elaborate organization, portions of which resemble protoplasm in many respects.

Not without significance is the fact that beginning about the same time the custom has grown up of using the term *plasm* or *plasma* instead of protoplasm. It is not unusual to regard these words as exactly synonymous, and to suppose the only advantage in *plasma* is its brevity. Obviously the term is more non-committal in meaning than is *protoplasm*, the idea of a "*first* formed substance" being undoubtedly very different from that of merely a "*formed* substance." But Strasburger's proposal went further than merely to name the whole cell substance protoplasm. He proposed to replace it by *cytoplasm* for that part of the cell to which alone Schultze had applied the word *protoplasm*, and to call the portion in the nucleus *nucleoplasm.* This last, being a mongrel word, was soon replaced by *karyoplasm.*

In other words, the change in the scope and meaning of terms introduced the really more significant thing, namely, that of a definite effort toward a scientific classification of the constituents of the cell, this being based upon and necessitated by the fuller and exacter descriptions of the cell that had been reached.

This brings us to where we can formulate more closely the question now before us: Do the descriptions fully agreed upon at the present day, of the substances entering into the constitution of living beings, warrant the belief that a *single* substance, under whatever name, is *the* basis of life, and is identical for all organisms? No one should fail to notice the two parts of the question: (1) Is there a *single* substance which is the basis of the whole life of any one organism? (2) If this were answered affirmatively, would that substance be identical for all organisms?

(*a*) *Cytoplasm and Karyoplasm Differentiated Areas of a Common Basic Substance*

Several competent investigators in this department of biology have summarized both the observational and the interpretative knowledge now in our possession. A liberal appeal to these summaries will furnish a direct and sure answer to the first part of the question, and an indirect though hardly less sure answer to the second part. To begin with, I quote from Wilson, the first point to be brought out being that of the relation between the nucleus and the rest of the cell. "Careful study of the nucleus," he says, "during all its phases gives, however, reason to believe that its structural basis is similar to that of the cell-body; and that during the course of cell-division, when the nuclear membrane usually disappears, cytoplasm and karyoplasm come into direct continuity. Even in the resting cell there is good evidence that both the intranuclear and the extranuclear material may be structurally continuous with the nuclear membrane. . . . For these and other reasons *the terms 'nucleus' and 'cell-body' should probably be regarded as only topographical expressions denoting two differentiated areas in a common structural basis.* The terms *karyoplasm* and *cytoplasm* possess, however, a specific significance owing to the fact that there is on the whole a definite chemical contrast between the nuclear substance and that of the cell-body. . . .

"Both morphologically and physiologically the differentiation of the active cell-substance into nucleus and cell-body must be regarded as a fundamental character of the cell because of its universal . . . occurrence, and because there is reason to believe that it is in some manner an expression of the dual aspect of the fundamental process of metabolism, constructive and destructive, that lies at the basis of cell life." [22]

So far as I am able to make out, authorities are in essential agreement as concerns the directly observational part of this statement touching the relation between nucleus and cell-body. The general conclusion is that, keeping an eye on the actual structure of the cell and ignoring for the moment the system of naming applied to the different parts, Schultze and Strasburger were both right; Schultze in holding that there is something fundamental in the distinction between nucleus and cell-body, and Strasburger in holding that there is something fundamental in the kinship between the two. Interpretatively, therefore, the question resolves itself into one of naming and classifying what is observed, and there can be no doubt, as Wilson and a majority of recent authors have recognized, not only of the convenience but of the scientific soundness of using the term *plasm* for the living substance of the cell as a whole, and then designating the kindred but yet different kinds of plasm by the terms *karyoplasm* and *cytoplasm.*

(*b*) *Details of Cytoplasmic Structure*

Concerning the details of structure of these two main classes of cell material, Wilson writes: "As ordinarily seen under moderate powers of the microscope, protoplasm appears as a more or less vague granular substance which shows as a rule no definite structure. More precise examination under high powers, especially after treatment with suitable fixing and staining reagents, often reveals a highly complex structure in both nucleus and cytoplasm. Since the fundamental activities of protoplasm are everywhere of the same nature, investigators have naturally sought to discover a corresponding fundamental morphological organization common to all forms of protoplasm and underlying all its special modifications. Up to the present time, however, these attempts have not resulted in any consensus of opinion as to whether such a common organization exists. In many forms of protoplasm, both in life and after fixation by reagents, the basis of the structure is a more or less regular framework or *meshwork*, consisting of at least two substances. One of these forms the substance of the meshwork proper: the other, often called the *ground-substance*, (also cell-sap, enchylema, hyaloplasma, paramitome, interfilar substance, etc.), occupies the intervening spaces. To these two elements must be added minute, deeply-staining *granules* or 'microsomes' scattered along the branches of the meshwork, sometimes quite irregularly, sometimes with such regularity that the meshwork seems to be built of them. Besides the foregoing three elements, which we may provisionally regard as constituting the active substance, the protoplasm almost invariably contains various passive or metaplastic substance in the form of larger granules, drops of liquid, crystalloid bodies, and the like. These bodies, which usually lie in the spaces of the meshwork, are often difficult to distinguish from the microsomes lying in the meshwork proper—indeed, it is by no means certain that any adequate ground of distinction exists."[23]

(*c*) *Three Main Theories of the Structure of Protoplasm*

Wilson then sets forth in general terms the three leading interpretational views of the nature of what is here described; that is, the well-known reticular or filar theory, the alveolar theory, and the granular theory. It may not be superfluous to state briefly what each of these theories is. The reticular theory interprets what is seen in the protoplasm in its simplest form, as a network of actual fibers which branch and anastomose with one another so as to make, according to the familiar comparison, something like the network of a sponge, the spaces within the reticulum being filled by the fluid or semi-fluid portions of the protoplasm. This view holds that the granules, supposed by the older observers to be essential constituents of the protoplasm, are the angles where the threads join, the threads seen end-on, and in some cases true granules attached to the threads. The alveolar theory, proposed and defended with great detail of observation and argument by O. Bütschli, compares the protoplasm with foam rather than with a sponge. It contends that protoplasm consists of separate, closely crowded minute drops of a liquid alveolar substance suspended in a continuous interalveolar substance, likewise liquid, but of different nature. According to this interpretation what are taken by the reticular theory to be fibers are the walls of the alveoli, there being in reality no fibers present. The granular theory holds that granules of various sizes and nature are the fundamental constituents of protoplasm, the fluid and the semi-fluid parts, as also the fibers whenever present, being of secondary significance.

(*d*) "*No Universal Formula for Protoplasmic Structure*"

Finally, summing up his own conclusions regarding these three theories, Wilson says: "My own long-continued studies on various forms of protoplasm have likewise led to the conclusion that no universal formula for protoplasmic structure can be given. . . . It is impossible to resist the evidence that fibrillar and granular as well as alveolar structures are of wide occurrence; and while each may be characteristic of certain kinds of cells or of certain physiological conditions, none is common to all forms of protoplasm. If this position be well grounded, we must admit that the attempt to find in visible protoplasmic structure any adequate insight into its fundamental modes of physiological activity has thus far proved fruitless. We must rather seek the source of these activities in the ultramicroscopical organization, accepting the probability that apparently homogeneous protoplasm is a complex mixture of substances which may assume various forms of visible structure according to its modes of activity." [24]

And so we have this excellent authority's answer to the first part of the question above formulated: The knowledge we now possess derived from observational studies on the minute structure of organic beings does not warrant the belief that there is a single substance which is the basis of the whole life of any one organism.

But if the facts do not warrant such belief what possible ground is there for the doctrine of the identity of protoplasm in all organic beings? Were there no other evidence against it than this drawn from the microscopical morphology of organisms, here alone is sufficient evidence to banish the dogma completely and forever from scientific biology. But as we see in other sections of this treatise, particularly those on the organism and its chemical compounds, there are even more compelling evidences against the doctrine than those here passed in review.

Preliminary Remarks on the Bearing of Physical Chemistry on the Protoplasm Doctrine

The theory of protoplasm as *the* living substance, as though there were a single substance identical in all organisms and in all parts of the same organism, has passed into a new and peculiarly subtle stage during the last two or three decades. This has been one of the results of the application which was sure to be made of physical chemistry to biological phenomena.

An understanding of what is implied by this will be facilitated by reflecting on some of the most obvious differences between physics and chemistry, and on what physical chemistry as contrasted with chemistry pure and simple is; that is, chemistry as it was prior to the rise of physical chemistry. But since we are invading a perilous realm, one in which diverse and strenuously contested views prevail, we must confine ourselves to what is most obvious.

That that vast series of transformations of natural substances which occur when two or more of the substances come together under certain conditions, so profound that the new substance is wholly different from the originals, are real objective phenomena, and are the bases of the science of chemistry, no one will gainsay however unqualifiedly he may be committed to the theory that these phenomena belong to the domain of physics after all. The reality of the transformations, and hence the reality of the discrete, individuated bodies or substances, both those entering into the combinations and those arising from the combinations, is what especially concerns us. Whether the combinations and transformations are influenced by physical as contrasted with chemical forces, and what names and classifications shall be employed in dealing with the phenomena, are of very secondary importance to this discussion.

On the other hand, that there is an almost if not quite equally vast series of phenomena presented by natural bodies and substances which do not involve such combinations and transformations and which are the basis of the great science of modern physics, will also probably be accepted without cavil. But the point to be specially noticed is that since physics as thus indicated is primarily concerned with those attributes of bodies and substances which are common to very great numbers of them, and are not only common to them but while rendering the bodies subject to great *change*, do not make them subject to complete *transformation*, the discrete, the individuated bodies fall much into the background.

Physics is preëminently from its very nature an individual-ignoring science. Concentrated as its attention is, on the force of gravitation for example, or on the behavior of light, and finding these manifested almost everywhere regardless of how many kinds of bodies are concerned, it is not surprising that the habit should be formed by persons who devote themselves to studying these phenomena, of neglecting almost entirely the bodies themselves which have weight and emit and receive light. Then when this habitual tendency to neglect the bodies finds encouragement by well-reasoned hypotheses that the bodies are actually less important and real than certain essences or entities "behind" them, the ignoring of the bodies passes easily from the realm of habit to that of dogma, and such strange conceptions of the "Province of Physics" as the following arise: "If further we give the name *thing* to that with the objective existence of which we are acquainted by our senses, then it follows that in the physical universe there are only two classes of things; to these the names *Matter* and *Energy* are given." [25] That protoplasm, of just such a conceptual character as we are pointing out in this chapter does *not* exist, would obviously be acceptable to a physics holding such an unobjectified, denatured conception of nature as that just quoted. If there are "only two classes of things" in the universe, "Matter and Energy," it would follow that the myriads of individual organisms which according to our senses certainly *seem* to exist, are after all phantasms of some sort, and those departments of science which deal with the phantasmal individuals would have to concern themselves chiefly with "getting behind" the apparitions to the two real things, the Matter and the Energy.

But even those physiologists and biologists who adopt the physical-chemistry standpoint most unreservedly speak of the matter of which organisms are composed as "living" and so do not quite accept the restrictions upon them of such a conception of the "province of physics" as that formulated by physics itself in the quotation above given. They seem to insist by implication that "living matter" is a real thing, no less than are Matter and Energy. This is very significant from our standpoint and will be exceedingly important if finally physics, too, shall fully accept it. It will be thus important because if biology is driven, as this treatise holds it will be, to recognize that the individual organism, each and every one that exists or ever has existed, is as real a thing as are any of its parts or substances, by whatever criterion of reality science or philosophy can apply; and if physics goes with biology in this, then will objective science as a whole be committed to a doctrine of the universe vastly different from that which now dominates the physico-mathematical sciences. Put into the briefest, most concrete form possible, such a consummation would establish the so-called natural history, or descriptive, or "inexact" (sic?) sciences in a place at least as secure and exalted as that held through the centuries in western civilization by the mathematico-physical, the so-called exact sciences.

And we must not forget the important fact that physics itself as conceived by some of its eminent devotees, occupies no such all-inclusive, all-dominating and domineering place in the hierarchy of the sciences as that implied by the quotation given above. Thus: "Physics in the largest sense of the word is the *science of unorganized matter* and the phenomena which it manifests. These phenomena are called *physical phenomena.* All the other sciences which occupy themselves with matter, have to do with organized substance (the biological sciences)." [26]

The whole-hearted recognition by physics as thus conceived, of matter in two fundamentally different conditions, these giving rise to two coëqual realms of science, places no obstacles in the way of biology's bringing into clear view the significance of individuals as natural phenomena. That physical chemistry can be of enormous service in the interpretation of living beings if only it does not claim too much for itself, if it recognizes physiologico-, or better biochemistry, to be on a par with itself, we shall see to some extent in later chapters.

Experimental Evidence of the Specificity of Protoplasms

Up to this point the burden of the facts and arguments of this chapter has been in a sense negative. It has been in opposition, merely, to the generalization that protoplasm is one and the same thing in all organisms. Although relatively few researches in microscopic comparative morphology and embryology have been carried out with the avowed purpose of discovering in how far each organism or group of closely related organisms has its own fundamental substances, the few which have been made have yielded highly significant results and open the gate to an alluring realm for future exploration.

(*a*) *Greater Fusibility Between Closely Related Species, as in Tissue Mixtures and Grafts*

The morphological investigations which will, perhaps, be most crucial when carried far enough, are those on the fusibility of naked protoplasm from different organisms—from different individuals of the same and of different species.

The experiments of H. V. Wilson on the coalescence of dissociated cells of sponges and hydroids particularly, have blazed a seemingly very practicable manipulative path into the subject. Wilson cuts portions of the animals into small pieces, then squeezes these through bolting cloth. This operation separates the tissues into small groups of cells, and to some extent into completely isolated cells. These cells, kept under favorable conditions, soon assemble together into compact masses, and from the masses normal animals frequently develop. Although Wilson has thus far been chiefly occupied with showing that various animals are able within their own species to rehabilitate themselves under such conditions, he has not failed to raise the question of how far coalescence and normal development may take place when tissues of different species are mixed together. His experiments under this head are far less extensive than those on the commingling of cells from different individuals of the same species, but are nevertheless highly instructive. In his paper of 1907 his statement, "Unlike specific substances (protoplasms of quite different species) do not tend to fuse," [27] is perhaps a somewhat more unqualified denial of the fusibility of the protoplasms of different species; or stated affirmatively, a somewhat more unqualified assumption of the specificity of the protoplasms of each species than the observations presented by him in a later publication justify.

But if this much of restriction upon his conclusions may be necessary, there still remains evidence of the most convincing sort in his results of the specific nature of the protoplasm of different species. The only details he has so far given of his negative results are contained in his report on sponge culture to the Bureau of Fisheries. In this he describes experiments on intermingling the tissues of *Micro-*

ciona prolifera with those of *Lissodendoryx carolinensis,* and *M. prolifera* with *Stylotella heliophila.* In both cases the larger fragments were discarded, and only the cells and small cell masses experimented with. These were thoroughly mixed together in watch glasses by jets of water from a pipette. "The mixture was spread evenly over the bottom of the watch glass, and looked like a fine sediment." But the cells of each species could be readily distinguished, those of *Lissodendoryx* being greenish and those of *Microciona* being bright red (to speak of these two species). "Fusion began, and the bottom was soon covered, no longer with a continuous 'sediment' but with discrete small masses, some red, some green. . . . In general red mass fused with red mass, and green mass with green mass. Nevertheless fusion was also observed in some instances between red and green masses. . . . Such fusions, as the further history of the watch glass showed, must have been temporary or the combined masses soon died. For as fusion progressed and the masses increased in size, the distinction between red and green tissue became more evident." [28] The outcome was that, young sponges of pure *Microciona* were developed but none of *Lissodendoryx*, the development going no further than the early fusion stages. Likewise in the mixture of *Microciona* and *Stylotella* there was no fusion between the cells of the two species nor was there a full development of *Stylotella* sponges alone.

The point wherein these negative results are somewhat less conclusive than might be wished is that neither in *Lissodendoryx* nor *Stylotella* were full fledged young sponges produced from the dissociated tissues even when these were treated each species by itself. It may be said that a fusion of two species could not be expected if one of them is incapable of fusion and development alone. Nor is this objection fully met by the fact that in one of the species at least, *Lissodendoryx*, the early stages, that is the fusion stages, do occur. To make the case quite satisfactory failure to fuse ought to be shown between species both of which are able, and about equally able, to develop into typical animals of their own species.

But the evidence of specificity of the protoplasm of the different species indicated by the experiments is by no means restricted to the nonfusibility of the cells of the several animals. Quite as conclusive is difference in behavior of the various preparations. Although Wilson does not go into this particularly, his experiences show that the tissues of *Microciona* produce young sponges considerably more readily than do those of the other species when treated in exactly the same manner. As to the relative viability and developability of dissociated cells of *Lissodendoryx* and *Stylotella* the descriptions are not full enough to enable one to decide. A comparison of the species on the basis of quantitative determinations of both the extent of development and the conditions of the water under which the development takes place would probably settle this and would be highly instructive.

Another investigator, Karl Müller, reports that the dissociated cells of individuals of different species are able to fuse together but that the fusion masses "never regenerate to small sponges." No details are given under this head, but are promised in a later publication.

Obviously the fusibility or non-fusibility of isolated tissues as brought out by experiments of this kind are phenomena close of kin with those of the degree of compatibility of grafts in the ordinary sense with the "stock" upon which they are grafted. It was mentioned in another connection that we now have sufficient information about grafting in animals to show that much the same rules hold here as among plants.

Morgan reviews the work that has been done in animal grafting, and sums up the results on the congeniality between different kinds as follows: "The general statement may be made for both cases [grafting and fertilization] that closely related species combine more readily than those far apart, *i.e.*, the results are more successful for unions between closely 'related' forms than between distantly 'related' forms. Certain exceptions exist, however, in both directions." [29]

But while the fusibility or non-fusibility of the tissues of different animals as revealed by Wilson's methods are phenomena closely related to the compatibility or non-compatibility of scion and stock in plant grafting, the former would seem to be, so far as the methods can be employed, a considerably better test of the specificity of the protoplasms of different individuals and species. This is so because by comminuting the animals, as Wilson does, and then thoroughly mixing the elements, every part and kind of substance of the one may be supposed to be brought into contact with every part and kind of substance of the other, whereas in grafting only a relatively small portion of the scion can actually touch the stock, and generally speaking only in such manner that the corresponding kinds of substance *i.e.*, corresponding tissues, come together. From this it may well be, that there is really more specificity of substances in the ordinary graft than might at first thought be inferred from the perfection of the union. Actual fusion may occur only between *some* substances of each party to the union, and the general life and activities of the graft may be kept up through its ordinary metabolic processes, it, however, using as food to some extent, *substances received from its host*, instead of wholly from the outside world.

Indeed some such interpretation as this appears to be necessitated by the strict maintenance of type of both graft and host. From this standpoint a successfully grafted individual plant or animal might be defined as a partnership in which each partner while maintaining most of its own former individuality still supplies to the others certain essential food substances from its own body and activities essential to the other. The relation between the two organisms which are grafted together seems similar in important respects to the relation between two organisms living together symbiotically. In fact, a graft combination might be spoken of as an artificial symbiosis. On the whole, then, the morphologico-physiological study of the ability of organisms to fuse together bodily points unmistakably to the belief that different kinds of organisms must contain in their make-up certain fundamental substances that are different as well as certain others that are very much alike if not quite identical. In other words such studies furnish no warrant for the conception of a physical basis of life identical in all living beings.

(*b*) *Protoplasms, Not Protoplasm, Must Be the Form of the Protoplasmic Conception*

Studies of this kind show that if the term protoplasm is to have any scientific usefulness it must be used in the plural —*protoplasms*—and so must be subject to the practices and principles of biological description and classification in the same way that all other biological entities are, and the great and ever-increasing number of elements now known with more or less definiteness as entering into the makeup of living substance must, I believe, be looked at in this light by all departments of biology as well as by natural history. Protoplasms are the substances of which individual organisms are composed, so the protoplasms as well as the organisms must be individuated.

To set forth the facts and reasonings upon which such a conception of protoplasm must rest is one of the foremost objects of several of the discussions in this treatise. Those on the organism and its chemistry, and the organism and its cells, are especially dedicated to this end.

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Chapter VI

THE ORGANISM AND ITS CELLS

What the Cell-Theory Is, Viewed Historically and Substantively

(*a*) *Importance and General Character of the Theory*

THE cell-theory seems to some biologists second to the evolution theory alone in its importance to biological science. This may be too high an appraisement; but beyond question it is and ever will be one of the most influential generalizations yet reached by the science.

(*b*) *Various Forms of the Theory as Currently Held*

The views of the cell incident to our general standpoint necessitate a critical consideration of the theory. What, exactly, is included in it? Does it contain more than one crucial idea? If so are all equally well grounded in observation? Clearly it has differed considerably in both scope and specific meanings at different times and for different authors. The formulation of it by Theodor Schwann, generally regarded as its founder, undoubtedly left it open to a considerable range of interpretation. Schwann says, "The development of the proposition that there exists one general principle for the formation of all organic productions, and that this principle is the formation of cells as well as the conclusion which may be drawn from this proposition, may be comprised under the term cell-theory, using it in its more extended signification, while, in a more limited sense, by the theory of cells we understand whatever may be inferred from this proposition with respect to the powers from which these phenomena result." [1]

Two meanings, a broader and a narrower, are thus expressly indicated; and the permissive phrase "whatever may be inferred" attached to the more restricted one, points a way to diversification of interpreting it that was sure to be followed.

In view of the comprehensiveness of the theory as thus initially conceived, it is surprising to find Virchow, one of the earliest and most distinguished promoters of it, speaking of it as pertaining to the mode of origin of cells. "This description of the first development of cells out of free blastema, according to which the nucleus was regarded as preceding the formation of the cell, and playing the part of a real cell-former (cytoblast), is the one which is usually concisely designated by the name cell-theory (more accurately theory of free-cell-formation)." [2]

O. Hertwig's statement of the theory is as follows: "Plants and animals, so dissimilar in external appearance, agree in the foundation of their anatomical structure; for both are composed of similar elementary units mostly visible by the aid of the microscope only. According to an old theory, now abandoned, these units are called cells, so that the doctrine that animals and plants consist in a similar way of such smallest particles is designated the cell-theory." [3]

But Hertwig's treatment of the cell in his earlier volume *Die Zelle*, and in his later more comprehensive work, *Allgemeine Biologie*, (4th ed.), surely adds much to the theory that is not hinted at in this brief definition.

The characterization of the theory by E. B. Wilson more adequately expresses its scope as practically understood and used by many recent biologists, including Hertwig himself. "In its broader outlines," writes Wilson, "the nature of this organization is now accurately determined; and the 'cell-theory,' by which it is formulated, is, therefore, no longer of an inferential or hypothetical character, but a generalized statement of observed fact which may be outlined as follows":—[only the baldest essentials of the outline are here given]. (1) "In all higher forms of life, whether plants or animals, the body may be resolved into a vast host of minute structural units known as *cells*, out of which, directly or indirectly, every part is built." (2) "Essentially the cell is a minute mass of protoplasm," this substance being "universally recognized as the immediate substratum of all vital activity." (3) All the cells of each individual organism are descended by cell division from preceding cells and finally from one single cell, the fertilized egg-cell. (4) This fertilized egg-cell, which is the beginning of each individual organism, is produced by the fusion of two cells one of which comes from the mother, the other from the father of the individual in question, so that "the ultimate problems of sex, fertilization, inheritance, and development are shown to be *cell-problems*." [4]

The *tout ensemble* of meaning and of importance of the theory for Wilson are forced home in the very first sentence of his excellent book: "During the half-century that has elapsed since the enunciation of the cell-theory by Schleiden and Schwann, in 1838-39, it has become ever more clearly apparent that the key to all ultimate biological problems must, in last analysis, be sought in the cell." [5]

A concise formulation of the theory with the expansive meaning given it by Wilson is furnished by Locy in *Biology and its Makers*. "A statement of the cell-theory at the present time, then, must include these four conceptions: the cell as a unit of structure, the cell as a unit of physiological activity, the cell as embracing all hereditary qualities within its substance, and the cell in the historical development of the organism." [6]

This expanded form of the theory of cells, held implicitly rather than explicitly, has brought it to pass that many biologists seem to do most of their scientific thinking in terms of cells. The multiform activities of "cell-life," as a common expression has it, appear to be the final thought-goal of such biologists. But the theory is not by any means allowed so broad a scope by all biologists. This finds illustration in the article on the theory furnished to the *Dictionary of Philosophy and Psychology* by C. Lloyd Morgan and E. S. Goodrich. As understood by these authorities, the theory is, "The doctrine that all organisms are composed either of individual cells (unicellular organisms) or of a compound aggregate of cells (the higher plants and animals) with certain cell-products; and that every cell, no matter how differentiated in structure or function, is derived from a preceding cell." [7]

A few good authorities, for example, Driesch, even go so far in restricting the cell-theory to this aspect of it, and in standing so confidently on its factual nature as to deny that there really is now a cell-theory at all. The cellular composition of all organisms (the unicellulars of course excepted) is, he says, "a simple fact of observation, and I therefore cannot agree with the common habit of giving to this plain fact the title of cell-theory. There is nothing theoretical in it." [8] The examination of definitions has gone far enough to bring out several points of prime moment for our enterprise: The cell-theory has been in the past, and still is, understood quite differently by different biologists. In the narrower signification given it by such authorities as Morgan and Goodrich, it is held to the strict bounds of a generalization of observations on the minuter make-up of both adult and all developmental stages of plants and animals. Such observations, vast in range and number, have thus far found no exception to the rule that each plant and animal body can be resolved into very small units and products thereof, all the units in each organism being derived by division from preceding units. These units have so much in common both structurally and functionally that the same name may be applied to them all. The name fixed upon, though a bad misfit because of serious errors of observation and interpretation on the part of several early investigators, is *cell*.

When held down to these narrower limits, the theory contains no express reference to heredity; it makes no claim to "embracing all the hereditary qualities in its substance." Still less does it contain even by implication the notion that the "key to all ultimate biological problems must, in last analysis, be sought in the cell."

(*c*) *Statement of Theory Justified by Present State of Knowledge*

I may now state categorically my view of the cell-theory: If accepted in the broad signification given it by Wilson and many others, it must be recognized as consisting of two very distinct parts. First, there is the part which expresses in the generalization, no longer questioned by any one, the cellular constitution of all organisms and the origin of individual cells. And second, there is the vaguely hypothetical part about the cells "embracing in their substance all hereditary qualities," and for this and other reasons being the "key of all ultimate biological problems." If our discussion of "The organism and its cells" accomplishes its aims, it will remove the vagueness of this second part of the cell-theory, and in doing so, while questioning in no manner any established truth which it contains, will reveal the inadequacy of some of its central conceptions.

"The whole of an organism is as essential to the interpretation of its parts as the parts are to the interpretation of the whole." So runs the first of our fundamental propositions. Let us substitute "cells" for "parts" in this and examine it. The organism is as essential to the interpretation of its cells, as the cells are to the interpretation of the organism. A brief excursion into the history of the cell-theory is essential to the discussion.

It is well known that the early workmen on the cell-theory had quite erroneous notions of the nature of cells. The error has, unfortunately, left its conspicuous and ineradicable mark on biology in the term *cell*. This name was chosen from the circumstance that the first studies were made on grown plants where the cell-wall is the most easily observable part of the cell, so that the cells frequently appear like vesicles either quite empty or containing a clear fluid or semi-fluid. Cells were closed chambers the walls of which were the main thing, according to these pioneering views. For a long time the nature, structural and functional, of the contents of these chambers played only a subordinate part. Gradually, however, from widely scattered observations, partly on the simplest unicellular organisms, partly on the contents of certain simple plant cells, and partly on the tissues of higher animals, it dawned upon biologists that the material within the cell-wall is the main thing, and that this material is much the same in all cells, whether plant or animal, of low or high degree. The protoplasm of Purkinje and Von Mohl, the sarcode of Dujardin, the "cell sap" of Corti and Treviranus, and the "plant mucilage" of Schleiden, were all brought together because of their close resemblance and designated by a single name. On account of the seeming simplicity of this material and the undoubted dependence of life phenomena upon it, *protoplasm* is the designation now almost universally applied to it. To Max Schultze, writing in 1861, belongs the credit more than to any other one man, of comprehending the nature of cells as we now understand them, and the terminology in which Oscar Hertwig expresses Schultze's achievement is of prime significance. Although Schultze retained the name cell, naturalized in anatomy by Schleiden and

Schwann, he "defines it," Hertwig says, "as a bit of protoplasm endowed with life, in which lies a nucleus." [9]

Almost simultaneously with this insight by Schultze, Carl Brücke, contemplating cells from the standpoint of their complex structure as well as from that of their ensemble of life activities, advanced to the conception of the cell as an *organism*.

The language in which Brücke expresses himself on this point is of sufficient interest to warrant quoting: "We must ascribe to the living cell, in addition to the molecular structure of the organic compounds which it contains, still another and a differently constituted structure, and it is this which we designate as *organization*." [10] And in another connection he introduces the phrase, now firmly established in biology, elementary organism, as a designation for the cell.

One of the securest aspects of the cell-theory was reached only when the conception organism was applied to the cell. Both historically and logically, *the organism is made to do duty in interpreting the cell.* Whatever validity the conception *cell* has in the modern cell-theory, is due in large measure to whatever validity the conception *organism* has. But the conception organism was well established in biology long before the conception cell was; hence the justification of the statement that historically the organism interprets the cell. *Organism* as an idea is prior and contributary to *cell* as an idea. That logically also the cell is partly interpreted by the organism is seen in the fact that observers agree in ascribing to the cell the most distinctive attributes of the organism: namely those of metabolism, reproduction, response to stimuli, etc.

Our birds-eye view of the cell-theory enabled us to see that if it be held in the broad sense in which it is conceived by many but not by all biologists, it consists of two parts:—one a firmly established generalization of observed facts, the other a vaguely stated hypothesis. We further saw that the secure generalization has two quite distinct parts, the one stating that higher organisms are made up of cells, the other stating certain cardinal facts about the cell itself. But later examination fixed attention on the fact that the theory as now held regards the cell itself as an organism. In other words, the two essential components of that part of the theory which is solidly grounded interpret each other: By showing *how the organism is made up*, the cells interpret the organism; and by showing what the *cell is in its fundamental attributes*, the organism interprets the cell. The cell is a "key" to the nature of the organism, but not so in "last analysis" for, at least in equal measure, is the organism a "key" to the cell. Or, if the idea of heredity be introduced into the cell-theory, not more than half the truth is contained in the statement that the cell "embraces all hereditary qualities in its substance," for we have seen that one of the corner-stones of the modern conception of the cell, as laid down by Schultze and Brücke, is that the attributes of the organism belong to it also, not indeed merely hidden "in its substance," but patent and observable.

If we restrict attention to the germ-cells and apply to them the idea of hereditary qualities embraced in their substance, we are still bound, as consistent evolutionists, to ask how the germ-cells came by these qualities. No answer is forthcoming to this inquiry which does not essentially involve the fact that the germ-cells received the qualities from the parent organisms. The interpretative relation between the organism and its cells is one of strict reciprocality whether the germ-cells or soma-cells be regarded, even in the broad general terms of the cell-theory. The problem of the organism and its cells is the general form of the old special problem of the hen and the egg. Which came first, runs the familiar conundrum, the hen or the egg? Expressed in scientific terms, the question is, which interprets or explains the other, the parent organism or the germ-cells? If the cell-theory be taken in the broad sense above considered, the aspect of it which we are holding to be erroneously hypothetical, would answer that the germ-cells interpret the parents. According to our standpoint, on the other hand, this hypothesis is inadequate in that it tells at least no more than half the truth. The parents interpret the germ-cells quite as truly as the germ-cells interpret the parents. They follow each other in a casually related, regularly alternating series; and biology has no inductive ground for supposing that either term came first in any ultimate sense.

Certain Inadequacies of the Cell-Theory

Having now seen that, in the general development and formulation of the cell-theory, it is literally true that the organism has interpreted the cell as much as the cell has interpreted the organism, we must see something of how this works out in detail.

The impossibility of fully explaining an organism in terms of its constituent cells seems to have been felt earlier and more poignantly by students of the normal development of individuals than by any other class of biologists. De Bary's epigrammatic statement, already quoted, "The plant forms cells; the cell does not form plants (*Die Pflanze bildet Zellen, nicht die Zelle bildet Pflanzen*)" was induced primarily by observations of his own and others on developing plants. Here it is easily demonstrable that the form of the growing tip is often assumed before the mass divides up into cells. In other words, the formation of cells is certainly in these cases a secondary even though an essential phenomenon.[11]

(*a*) *As Tested by Embryonic Development*

On the side of animal development, C. O. Whitman was the first to produce arguments, both comprehensive and irrefutable, against the doctrine of cell hegemony, though Carl Rauber, Adam Sedgwick, O. Hertwig and a few others had already become more or less positive dissenters from the prevailing view. Whitman's studies on the initial embryonal stages of bony fishes appears to have strongly impressed upon him the subordination of the cells to the general needs of the developing fish. "That the forms assumed by the embryo in successive stages are not dependent on cell-division, may be demonstrated in almost any egg. Watch the expansion of the blastoderm in the pelagic teleost egg, the formation of the germ-ring, and especially the axial concentration of material, which is so beautifully illustrated in these eggs. Such developmental processes are, if I mistake not, clearly indicative of some sort of organization."[12] And approaching the problem from a slightly different angle, he says: "May we not go further, and say that an organism is an organism from the egg onward, quite independently of the number of cells present? In that case, continuity of organization would be the essential thing, while division into cell-territories might be a matter of quite secondary importance."[13]

It was the domination of cell division by forces other than those belonging to the cells taken independently that especially held his interest. "The more carefully we compare the cleavage in different eggs, the more clear it becomes that the test of organization in the egg does not lie in its mode of cleavage, but in subtile formative processes. The plastic forces heed no cell-boundaries, but mould the germ-mass regardless of the way it is cut up into cells."[14] And he clearly saw that to fly from cells to nuclei, there to seek final explanatory refuge, as Sedgwick particularly had proposed, was no more satisfactory than to stay with the cells.

"The essence of organization," he says, "can no more lie in the number of nuclei than in the number of cells. The structure which we see in a cell-mosaic is something superadded to organization, not itself the foundation of organization." Then follows this pregnant sentence: "Comparative embryology reminds us at every turn that the organism dominates cell formation, using for the same purpose one, several, or many cells, massing its material and directing its movements, and shaping its organs, as if cells did not exist, or as if they existed only in complete subordination to its will, if I may so speak." [15] After sketching the rise and fall of that puzzling structure in many vertebrate embryos known as Kupffer's vesicle, Whitman writes: "This remarkable reproduction of a form-phase that is to last only a few hours and then pass away without leaving a visible trace of its existence, cannot be explained as due to cell-formation nor as the result of *individual* action or interaction on the part of the cells. The embryonic mass acts rather as a *unit*, tending always to assume the form peculiar to the state of development reached by its essential 'architectonic elements,' (Brücke), elements that are no less real because, like the atom and molecule, they are too minute to be seen by the aid of our present microscopes. That cells as such do not participate in this formative act, is shown by the mode of development of the vesicle and by the absence of cells in its ventral and lateral wall." [16]

We have now examined Whitman's position far enough for our present point; that, namely, of showing the strength of his conviction that cells taken individually furnish no adequate explanation of the normally developing individual organism. The evidence he presents to this end never has been nor, I am persuaded, can ever be overpowered. On the other hand, any one who will study, as Whitman himself says, "more faithfully the living embryo during its formation" [17] will find abundance of further evidence to the same effect. So far—and this is a very long way—Whitman was crystal clear. Further than this he was unable to break away from the old elementalist form of reasoning.

The name of E. B. Wilson was coupled with that of Whitman in my general introductory remarks on the appearance in modern biology of the conception of the organism as a whole. We will now examine in some detail this authority's views concerning the cell in development. Discussing the so-called Mosaic theory of development in 1893 Wilson said, "I will here point out one all-important point which is definitely established by the work of Driesch and other experimentalists, and which is accepted by all opponents of the mosaic theory, namely, that the cell cannot be regarded as an isolated and independent unit. The only unity is that of the entire organism, and as long as its cells remain in continuity they are to be regarded not as morphological individuals, but as specialized centres of action into which the living body resolves itself, and by means of which the physiological division of labor is effected." [18]

After referring to Schwann's having drawn "the conclusion that the life of the organism is essentially a composite; that each cell has its independent life; and that the whole organism subsists only by means of the reciprocal action of the single elementary parts," Wilson says: "It is, however, becoming more and more clearly apparent that this conception expresses only a part of the truth, and that Schwann went too far in denying the influence of the organism upon the local activities of the cells. It would, of course, be absurd to maintain that the whole can consist of more than the sum of the parts. Yet, as far as growth and development are concerned, it has now been clearly demonstrated that only in a limited sense can the cells be regarded as co-operating units. They are rather local centres of a formative power pervading the growing mass as a whole, and the physiological autonomy of the individual cell falls into the background. Broadly viewed, therefore, the life of the multicellular organism is to be conceived as a whole, and the apparently composite character which it may exhibit is owing to a secondary distribution of its energies among local centres of action." [19]

Our only object in this section is to place before the reader as much as practicable of the views of biologists that the organism and not the cells of which it is composed is the main thing in development. It would consequently be out of place to go into a critical examination of this language. It will, however, be permissible by way of intimation of what will be involved in the discussion, to ask how the view that "the life of the multicellular organism is to be conceived as a whole," can be made to tally with the view expressed in the first sentence of *The Cell*, already quoted, that "the key to all ultimate biological problems must, in the last analysis, be sought in the cell." [5]

Wilson's authority is deservedly so great in all these matters that his utterances will be taken as one of the main centres around which our examination of the cell theory will hover. On this account, I quote somewhat more at length than would be essential to show merely his general position. In the chapter, "Cell-division and Development," he writes: "It remains to inquire more critically into the nature of the correlation between growth and cell-division. In the growing tissues, the direction of the division-planes in the individual cells evidently stands in a definite relation with the axes of growth in the body, as is especially clear in the case of rapidly elongating structures (apical buds, teloblasts, and the like), where the division-planes are predominantly transverse to the axis of elongation. Which of these is the primary factor, the direction of general growth or the direction of the division-planes? This question is a difficult one to answer, for the two phenomena are often too closely related to be disentangled. As far as the plants are concerned, however, it has been conclusively shown by Hofmeister, De Bary, and Sachs that the growth of the mass is the primary factor; for the characteristic mode of growth is often shown by the growing mass before it splits up into cells, and the form of cell-division adapts itself to that of the mass: 'Die Pflanze bildet Zellen, nicht die Zelle bildet Pflanzen.' Much of the recent work in normal and experimental embryology, as well as that on regeneration, indicates that the same is true, in principle, of animal growth. . . . Still more recently this view has been almost demonstrated through some remarkable experiments on regeneration, which show that definitely formed material, in some cases even the adult tissues, may be directly moulded into new structures." [20]

I go no farther here in the examination of Wilson's biological philosophy than to point out that, in spite of his clear perception, as indicated by these quotations, that the organism as a whole plays a determining part in the development of its constituent elements, his latest statements show that he is succeeding all too well in obeying the ancient injunction: "Let not thy right hand know what thy left hand doeth." Presumably his left hand still clings to the "whole mass as a moulding power of the parts." But his right hand seems now more confident than ever of finding the "key to all ultimate biological problems" in the cells, or maybe in the chromosomes.

In a lecture published in 1913, speaking of the interesting phenomenon of "criss-cross heredity" in the short and long-winged flies lately studied by Morgan, where the sons are like their mothers and the daughters are like their fathers, Wilson says: "This case, and many others of similar type, may be completely explained through our knowledge of the relation of the chromosomes to sex. . . . All the facts revealed by experiment are very simply and completely accounted for by the simple assumption that the x-chromosome is responsible not only for sex, but also for the short-winged character." [21] Our critical examination of this whole matter, when we come to it, will lead us to see that the essence of Wilson's criticism of Schwann relative to cells, quoted above, will now have to be applied to himself relative to chromosomes: "This conception expresses only part of the truth, and Schwann went too far in denying the influence of the totality of the organism upon the local activities of the cells," said Wilson in 1900. Now we shall have to say that Wilson goes too far in denying, by implication, the influence of the totality of the organism in determining sex; for the assumption that the x-chromosome is "responsible for sex," and that the facts are "simply and completely accounted for" by this assumption surely involves this implication.

Driesch's views touching the relation of the organism to its constituent elements generally are very important, and will have to be considered under several heads. We have already referred to his proposal to purge the cell-theory of all that is hypothetical in it. Continuing the previous quotation, we have this: " . . . attempts to conceive the organism as a mere aggregate of cells have proved to be wrong. It is *the whole* that uses the cells, . . . or that may not use them." [22] His much discussed theory of "equipotential morphogenic system" had its inception, as is well known, in his study of the blastomeres in early embryonic development. At present, I go no further than to point out that while it seems certain to Driesch that the "organism as a whole" is essentially implicated in some fashion in producing organic structure, it also seems certain to him that he knows nothing significant about the nature of that implication. He says: "So all we know about the proper stimuli of restrictions is far from resting on any valid grounds at all; let us not forget that we are here on the uncertain ground of what may be called the newest and most up-to-date branch of the physiology of form. No doubt there will be something discovered some day, and the idea of the 'whole' in organization will probably play some part in it. But in what manner that will happen we are quite unable to predict." [23]

I conclude this inventory of expressed recognitions by competent observers that the organism dominates its cells in embryogenesis, with two modes of formulating this recognition that are specially significant. They are expressions of the unity or oneness of the individual organism in *time;* and of its unity or oneness in *space.*

E. G. Conklin has expressed the first truth with commendable decisiveness and simplicity: "Furthermore, from its earliest to its latest stage an individual is one and the same organism; the egg of a frog is a frog in an early stage of development and the characteristics of the adult frog develop out of the egg, but are not transmitted through it by some 'bearers of heredity.'" [24] This proposition is so nearly self-evident that it would not need insisting upon but for its having been obscured by sophistical discussions of whether development is "predetermined" or "epigenetic." Huxley stated it in essence when he declared it to be "certain that the germ is not merely a body in which life is dormant or potential, but that it is itself simply a detached portion of the substance of a pre-existing living body."

Nägeli put it in still more concrete terms when he affirmed that the hen's egg differs from the frog's egg as much as the grown-up hen differs from the grown-up frog; that the species is no less certainly contained in the egg than in the adult. However this speculator befogged the truth with his fanciful idioplasm. The best expression of the spacial unity of the developing organism with which I am acquainted is that by F. R. Lillie: "The traditional view, held by many embryologists at the present day, is that the physiological unity arises in the course of embryonic development by the secondary adaptation of originally independent parts to one another. But this explanation has, in my opinion, become untenable, and must be replaced by the view that *there are certain properties of the whole, constituting a principle of unity of organization, that are part of the original inheritance, and thus continuous through the cycles of the generations and do not arise anew in each.*"[25]

For the present I do no more than remind the reader that the italics here are Lillie's, not mine; and that his clear and emphatically expressed conclusion does not rest alone on the experiments presented in the paper quoted from, but had been, in essentials, reached by him through earlier studies on normally developing animals.

Several of the few biologists who have taken a positive stand against the dogma of the all-sufficiency of the Cell in biology have deplored the well-nigh universal custom of early indoctrinating young students with that part of the cell-theory which I have characterized as vaguely hypothetical. Adam Sedgwick in particular concentrated his fire on this aspect of the matter. There can be no doubt that many if not most recent elementary text-books are unwitting sinners in this. On the outmost threshold of the temple of biological science, the student is made to feel, by the priests within, that the head should be bowed, the knee bent and the voice subdued when certain things, some difficultly visible, some wholly invisible, things situated deep in the interiors of the plants and the animals to be studied, are mentioned. Among these minute objects of adoration, the Cell holds a commanding place. "Every scientific animal and plant anatomy must, consequently, take its starting point in the doctrine of the Cell."[26] No matter how long a shelf of elementary text-books on botany and zoology one examines, he will rarely fail to find something akin to this explicit statement in R. Hertwig's excellent *Lehrbuch der Zoologie.*

According to this the anatomy of Vesalius, Wm. Harvey, John Hunter and George Cuvier, and others who lived and wrought before there was any cell-theory, are unscientific. But not quite all writers of guides for the young see the matter this way. B. Hatschek may be mentioned as one exception. In his *Lehrbuch* he writes: "If therefore we raise the question why one cell body undergoes this, another that transformation, we shall indicate as a chief cause the relation of the cells first of all to their neighbor cells, and then to the totality of the body." For the moment we will be satisfied with this recognition that in the relation of the cells to the totality of the body as well as to one another, resides a cause of differentiation of the cells in the completed organism, and will not be querulous over the statement that this relation stands "first of all" as a cause.

I believe enough has now been brought forward on the pros and cons of the cell-theory of development to establish two things: Those biologists who by reason of their own researches, either through unaided observation or through observation assisted by experiment, are most deserving of being heard on the subject are persuaded, first, that notwithstanding the fact that the developing and developed organism is wholly produced through the multiplication and differentiation of cells, these cells are not an adequate explanation of embryogeny; and, second, that the organism as a totality must enter as an essential element into any adequate explanation of the phenomenon.

(*b*) *As Tested by Isolated Cells and Tissues*

Before Lillie's contention that the traditional explanation of the developing embryo has "become untenable and must be replaced by the view that there are certain *properties of the whole, constituting a principle of unity of organization, that are part of the original inheritance*," can gain much influence on biological thinking, it will have to be examined from many directions.

What, on cursory view, looks more like confirmation of the theory of cells as wholly independent elements whose coöperation explains the organism, than any facts recently brought to light, are some of the results of recent researches on isolated tissues—"tissue cultures," as they are frequently called. The German phrase, *ueberlebende Gewebe,*—surviving tissues—for these is very apt.

Although the work of Alexis Carrel in this realm has attracted much interest and attention even on the part of the general public, it is recognized by biologists, including Dr. Carrel, that R. G. Harrison not only initiated the methods employed, but also reached highly important results by applying them. The specific purposes and results of Harrison's researches, and his general attitude toward problems of individual development, are of prime moment for our discussion. His central aim was to end the perennial debate over the mode of origin of nerve fibers in vertebrate embryos, and the persistence, technical skill, and cogency of reasoning with which he worked at the problem until he advanced its solution sharply beyond the point reached by any one else, are admirable.

According to the view attributed to Wilhelm His, the axis cylinders of the nerve fibers of the central nervous system are outgrowths of the ganglionic cells, their connection with the end organs being secondary. The other view, less generally held, originally advanced by the physiologist Victor Hensen, is that the fibers are differentiations within protoplasmic strands which have connected the central and peripheral cells from the very time when the cells themselves were formed, their character as nerve fibers being taken on only when, through the activities of the growing embryo, conducting paths are needed.

Harrison's earlier attempts to terminate the controversy by transplanting limb-buds, under various conditions, from one frog tadpole to another, had led him to believe strongly in the first mentioned view, though the methods of experimentation employed were not such as to make it possible for him to see the actual outgrowth of the fibers. He therefore tried to find a way of keeping sufficiently small isolated bits of the embryonal neural tube to enable him to observe the growths under the microscope if they actually occur.

A summary of his results stated in his own words is: "Pieces of undifferentiated embryonic tissue, when isolated under aseptic precautions in clotted lymph, will live for weeks and undergo at least the initial stages of normal histological differentiation: cells from the axial mesoderm give rise to striated muscle fibers; epidermal cells form a cuticular border; typical chromatophores and a mesenchyme-like tissue are formed from pieces containing portions of the neural tube and axial mesoderm; the walls of the neural tube and the primordia of the cranial ganglia give rise to long hyaline filaments closely resembling embryonic nerve fibers.

"Tissues grown in lymph function characteristically, as is seen in the movement of cilia and the contraction of muscle fibers when left in organic continuity with fragments of the neural tube." . . . "The experiments show that neuroblasts are competent to form primitive nerve fibers within a foreign unorganized medium simply by the amoeboid outgrowth of their protoplasm. By eliminating from the periphery all formed structures which have heretofore been supposed to transform themselves into nerve fibers and leaving only the neuroblasts in the field, it is demonstrated that the latter are the sole elements essential to the formation of nerves. The concepts of both Hensen and Held are rendered untenable." [27]

Thus a developmental point of capital importance which had been debated at length and with considerable spirit as long as investigation was conducted upon the organism in its entire state, was solved by separating from the rest a few cells and finding that when thus isolated they were able to develop much as they do normally within the organism. Surely no more conclusive proof that the cells of an organism have a large measure of independent life could be asked. Harrison epitomizes this aspect of his results in a very clear-cut paragraph: "The energy of outgrowth is immanent in the nerve cell, and the initial direction of outgrowth is already determined within the cell before the outgrowth actually begins. The formation of the fiber is therefore an act of self differentiation within Roux's definition." [28]

Do not such discoveries favor unquestionably the view that, in Wilson's way of saying it, "the key to all ultimate biological problems must, in last analysis, be sought in the cell?" Some authors, as for example Oppel, answer with a very positive *yes*, but I have found nothing in Harrison's writings to enable one to be sure what he would do were he to answer this question by choosing between an unqualified *yes* and an unqualified *no*.

However, discussing the general question of the relative trustworthiness and value of experimental studies of the sort devised by him, and those of the sort by which problems of histogenesis are ordinarily prosecuted, he has expressed views which bear strongly on the question, and which we present in his own language:

"Why, then, should we, in morphology, be still so dominated by the conception of the object as it occurs in nature, the organism as a whole, which to many seems to be a sort of fetish not to be touched lest it show its displeasure by leading the offender astray? There is no real ground for maintaining this attitude. On the contrary we should endeavor to extend our experimental analysis wherever possible, recognizing that through study of the abnormal, which consists merely of those combinations of conditions and effects that do not ordinarily occur in nature, we have the means of reaching an understanding of the normal, and that it is necessary to investigate the properties of the constituent parts of organisms before we can hope to understand them in their entirety. Because of our limited knowledge, we are for the present setting ourselves an impossible task if we expect to determine with certainty by means of a few experiments exactly the combination of factors involved in the normal ontogeny of any particular structure. In fact we can never 'explain' the processes of normal development with more than a certain degree of probability, until we succeed in synthesizing organisms from simple known constituents or construct working models that show all of the essential activities of organisms—achievements from which we still are very far removed. Syntheses may possibly be made, however, at different stages of the analysis with components of greater or less complexity. Thus it may be possible to extend the remarkable experiments of H. V. Wilson." [29]

The manifest worth and practicability of the manipulative methods introduced by Harrison assured their quick adoption by other workers, and already a considerable literature has come into being dealing with "surviving tissues." Owing, it seems, largely to the fact that Dr. Carrel has vigorously and skillfully applied the methods in the interest of surgery, he has attained wider distinction in connection with the researches than has any one else, though several other biologists and physicians have increased knowledge substantially by the new instrument of discovery.

The remarkable viability of tissues removed from their native setting in the organism and kept under artificial conditions is well brought out in a recent paper by A. H. Ebeling. This investigator made cultures of fragments of the heart of chick embryos seven to eighteen days old, a few of which lived and flourished nearly a year. "The experiments show," said Ebeling, "that connective tissue can be kept in a condition of active growth outside of the organism for more than eleven months, that its mass increases considerably, and its power of proliferation, after such long period, is more active than at the beginning of its life *in vitro.*"[30] In one culture, fragments of the heart pulsated after 104 days. The evidence is now conclusive that various tissues of numerous animals are able to live and grow and perform something of their characteristic activities for a long time after being separated in small fragments from the organism at various stages of its development.

Another striking attribute proved for the cells of young embryos is their mobility. Harrison dwells on the extensiveness and significance of this, and all the other investigators are impressed with it. The wandering about and the putting out of protoplasmic processes by cells of various sorts, notably by connective tissue and nerve cells, are mentioned by all writers. Burrows' account of the behavior of the growing nerve fibers is particularly full and well illustrated, and many of the facts are so significant that I quote at some length from his description: "Growth of the nerve cells is evident by filaments of various sizes. . . . The slender filaments are composed of a hyaline homogeneous protoplasm, while in the coarser bundles the homogeneous character is altered by the appearance of delicate, longitudinal striations. The latter bundles break up into many fine filamentous branches. . . . At the end of each of these growing filaments and branches is the characteristic thickened amoeboid swelling. . . . This is an oval or round swelling of the filament from which protrude many actively moving delicate pseudopodia. The growth of a fiber consists in the great prolongation and enlargement of one of these pseudopodia with a gradual moving outward of the end knob along the pseudopod. The growth may be so rapid that the end knob may entirely disappear, to reappear farther out along the new grown part. . . . During this time (48 to 72 hours) they may . . . reach a length of from one to two millimeters. . . . The activity of such fibers is noted at the amoeboid end and consists in a constant retraction and new formation of pseudopodia. All observations on the movement of the growing fiber suggest an active force within it causing its extension into the medium." [31]

Describing the activities still farther in connection with the degeneration of some of the nerves, the author continues: "The changes in the nerves are mainly at the end. Here there is periodic thickening, followed by a slow reduction in size until the entire nerve has retracted into the tissue in a manner similar to the retraction of the pseudopodia of an amoeba. These phenomena of extension and retraction may go on alternately in the same fiber. . . . The retraction is checked after a time and growth again proceeds in a different direction for a while when the process is again repeated." [32]

This primitive amoeboid activity of the cells is by far the most common and readily accomplishable. The testimony of all observers is at one on this point. But this activity is by no means the only kind. Contraction of muscle fibers was seen by Harrison, as mentioned in the quotation already given; a number of other investigators have confirmed and extended the observations. Burrows, for instance, has shown that muscle cells from the embryonic chick heart may contract rhythmically in cultures. He writes: "The muscular elements grow much less frequently and cellular outgrowths from them were observed in only about three per cent. of the experiments. The outgrowths take place from the myotomes and the heart, and appear in the form of short chains of striated cells. The striated cells contract rhythmically along with the portion of the heart from which they arise." [33]

Holmes has made the suggestive observation that although completely isolated, partly differentiated muscle cells of a newt may remain functionally active for eight months, "they had not changed their form, nor had they undergone any marked changes in structure." This result is the more interesting in that muscle cells of similar sort but contained in a piece of larva instead of being isolated, continued to differentiate.

A number of important questions touching the independent life of embryonal muscle cells are awaiting further study, but enough has been done to leave no doubt that, broadly speaking, they possess a considerable degree of such independence.

Not only are cells able to continue their physical activities, but in some cases they are also able to go on with their chemical activities, after being separated from the organism. The evidence is conclusive, then, that once formed, a number of kinds of tissue cells may survive for a long period after removal from the organism and may continue to perform more or less faithfully their wonted activities. Can new cells also be produced under the new and unusual conditions? Undoubtedly. While to a large extent the changes described by all observers in surviving fragments are due to the wandering out and wandering about of cells already in existence, cell multiplication has been clearly seen by too many good experimenters to leave any doubt on the main point. The large increase in mass of the fragments described by all those who have kept the same cultures alive and active for a long time would be conclusive even if cell-division itself had not been seen.

Carrel and Burrows were apparently the first to witness directly cell division. "A culture contains emigrated as well as proliferated cells. The proliferated elements consist of connective tissue and epithelial cells, the former predominating." [34] This is explicit though wanting in detail. But other observers have been sufficiently explicit. As long ago as 1906, H. Deeljen described with considerable particularity the division of the polynucleate leucocytes of human blood when kept under proper conditions in microscopic preparations. And more recently Oppel, applying the new methods, has described, figured, and discussed at length mitotic divisions of cells isolated from various tissues of the cat.

When we pass from the question of the independent life of individual cells to that of the independence of organs, or organized groups of cells, the prospect changes considerably. Harrison, in one of his earliest publications, says: "While the cell aggregates, which make up the different organs and organ complexes of the embryo do not undergo normal transformation in form, owing no doubt in part to the abnormal conditions of mechanical tension . . . the individual tissue elements do differentiate characteristically." [35] Without raising the question as to how "characteristically" the individual elements can differentiate while the cell aggregates "do not undergo normal transformation," the assertion that the aggregates *do not transform into organs* is sufficient for the point being made.

Carrel and Burrows have described "tubular formations" in cultures of both the kidney and the thyroid gland of the chick. The growth of kidney tubules is affirmed with special particularity. The authors write: "At several points, tubular formations were observed which extended themselves a considerable distance toward the middle of the plasma. Their ends were rounded, their lumina open, and their walls formed of cells which had the appearance of epithelial cells. These formations resembled renal tubules." [36]

The production of these structures is surely interesting, but more interesting is the question raised by the last sentence: are the formations actually renal tubules, or do they only resemble them? That *no organization of cells into normal organs takes place in these "cultures"* is attested by all who have pursued these investigations, so the statement by Carrel and Burrows that the formations resemble kidney tubules is to be taken as literally true, and to be understood to imply that the resemblance is not sufficiently close to make them indeed such tubules.

On the matter of organ production by tissues separated from the body, Burrows has given us a decisive statement. "Such growing cells," he says, "from an isolated piece of tissue have at no time shown evidence of grouping in a form comparable to organ formation in the body." [37]

Some experimenters appear to have clearly seen the importance of this limitation of power of the tissues, and on this account have taken rather strong grounds against calling the preparations "cultures." J. Jolly in particular has his eyes wide open toward the phenomena, though possibly some details of his criticisms are overwrought. He says, "In certain tissues *in vitro* it appears possible for cellular multiplication to continue for some time, that much is true; but between this last effort of certain cells and a 'culture'—a development continued and progressive—there is a gap, which may be filled up some day. For the present, it is an abuse of language to attach the name 'cultures' to the results obtained." [38] And the author thinks true development of kidney tubules is not proved by Carrel and Burrows.

Denial of development in a strict sense is made also by A. Dilger: "On the basis of this critique and of his own investigations, the author must emphatically deny that in the case of cultures of fragments of the mature organs of warm-blooded animals any genuine growth takes place in the sense of an organic formation. In this essential the author would adopt the view of Jolly, that the Carrel-Burrows experiment indeed demonstrates a survival and physiological functioning of tissue fragments, but has nothing to do with their growth." [39]

It may be unprofitable to spend time on the question of what name should be applied to these unique preparations, further than to insist that the name settled upon shall not give a false impression of their true nature. If they are to be called "cultures," then the word must be understood to have a somewhat different meaning from what it has in ordinary biological technology, where the production of true organisms is always contemplated. Indeed the distinction is at least partly recognized by Carrel and Burrows, for in one of their publications they say: "Since the tissues, in their development, must adapt themselves to the morphological plan of the organism, their growth must be constantly regulated by some unknown factor. This regulation may be caused by certain chemical compounds contained in the blood and the interstitial lymph. . . . Therefore, it may be assumed that the power of growth is kept under constant restraint, that every organ is compelled to follow the morphological plan of the organism, and normal plasma is far from being the optimal medium for the culture of normal cells." [40]

Now that we are learning so much about the part played by chemical messengers, or hormones, in normalizing growth (see Chapter 18, in Part II of this book), the conception that "every organ is compelled to follow the morphological plan of the organism" is gaining intelligibility.

This statement goes, by unmistakable inference at least, to the very heart of the matter. Even were it demonstrated that embryonal cells and organs are capable of developing into perfectly normal adult parts when isolated from the embryos, this would prove that these cells and organs are capable of independent life in an *ontogenic* sense only. It would not prove them so independent in a full sense, that is, in a *phylogenic* as well as an ontogenic sense.

The very fact that the adult organs into which they developed could be pronounced normal would mean that their development was, in Carrel and Burrows' language, "compelled to follow the morphological plan of the organism." In other words, the development would be guided by *heredity* just as certainly as though the parts had not been isolated.

And so we are able to see what is implied in Harrison's remark quoted above, "we can never 'explain' the processes of normal development with more than a reasonable degree of probability until we succeed in synthesizing organisms." If the condition thus placed on explanation of development is really necessary, such explanation will never be forthcoming, since to synthesize organisms would be to synthesize them endowed with their *hereditary* attributes and powers—in other words, with their *ancestral* attributes and powers. But in order to synthesize them with such attributes and powers it would be necessary to synthesize not only the organisms, but also *their ancestors*—a rather difficult task.

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Chapter VII

THE CELL-THEORY NOT SUFFICIENT FOR EXPLAINING THE ORGANISM

IN the preceding chapter the cell-theory was shown to be inadequate as a complete explanation of the organism when tested by studies of embryonic development and by experiments on isolated cells and tissues. We now proceed to consider other phases of the theory which still further show its limitations.

More General Inadequacy of the Cell-Theory

(*a*) *As Tested by the Regeneration and Restitution of Mutilated Organisms*

Few topics of research have a more instructive bearing on the hypothetical portion of the cell-doctrine than has that of regeneration, taking the word in its general meaning. Attention may be called first to the far greater inclination of investigators to neglect cells as such when studying the re-development of organisms that have been deprived of some of their parts than when dealing with their development from the germ.

Such problems as those of cleavage, of molecular behavior, and of cell-lineage, which stand out so conspicuously in most researches on ordinary embryonic development, particularly those concerning themselves primarily with early stages, are for the most part conspicuous by their absence in studies on the rehabilitation of mutilated organisms.

Undoubtedly one reason, perhaps the chief reason, for this is that regenerative processes so frequently involve considerable masses of more or less differentiated tissues rather than individual cells. A sort of mass action or mass performance takes place with little or no regard to the individualized activities of the constituent elements, whatever they may be, cells, nuclei, centrosomes, chromosomes or what not. The most palpable instances of this mass performance are afforded by those restorative processes in which cell division plays no part, or but a subordinate part. These processes are accomplished by the activity of cells already in existence, by the re-disposing of old cells, rather than by the production of new ones. Thus Rand describes how the "cells of the earthworm epidermis are seen to execute an extensive movement from their original position to an adjoining surface not previously occupied by epidermis." [1] This movement, Rand shows, is not a passive one due to pressure or pull by extraneous forces, but is inherent in the cells themselves, and "must be occasioned by an agency external to the cell, namely, by some factor of the conditions resulting from the injury." Rand looked carefully for dividing cells in the region of the wound but could find no indication whatever of these. To the mode of regeneration, "in which a part is transformed directly into a new organism, or part of an organism without proliferation at the cut-surface," Morgan has given the name *morphallaxis*, and sets it over against regeneration accomplished through proliferation, which he calls *epimorphosis*.[2] All investigators now recognize the importance of this distinction.

While cells occupy only a retired place in much of both the purely descriptive and the speculative writings on regeneration, it would be wrong to infer that the broader biological conceptions based on the facts of regeneration have really ignored the cell-theory to the extent that at first sight seems to be the case. As a matter of fact, it turns out that in many of the discussions of regeneration which on their face are little concerned about cells, there lies an abiding faith in the cell as the "key to all ultimate biological problems," those of regeneration with the rest. An illuminating instance of this came out some thirty years ago, before the period in which regeneration was the "firing line" for elementalist biology. I refer to Vöchting's attempt to explain a great range of phenomena in plants by the polarity of the plant's cells. This investigator's speculations were based quite as much on his observations on grafting as on regeneration, he having studied this subject along with regeneration and normal development for the purpose of gaining light on development in general and on still larger biological questions, rather than for ordinary horticultural purposes. In observing the result of grafting pieces of roots on branches and of branches on roots, of reversing the ends of grafted pieces, and of manipulating the grafts in several other ways, he was greatly impressed by the persistence with which the grafted pieces maintain their characters. The resemblance in several respects of these phenomena in organisms to those of the magnet led him to make the utmost possible of the resemblance.

Morgan's summary of Vöchting's speculation so far as this concerns the cells may be quoted: "The properties of the tissue-complex rest, in last analysis, on that of the cells; the properties of the whole being only the sum total of the properties of its elements, so that we may say that every living cell of the root is polarized, not only longitudinally, but also radially; each has a different apical and root pole, a different anterior and posterior pole, and also right and left polar relations." [3]

The conception of polarity in plants and animals, which has had a conspicuous place in later hypotheses of the production and regulation of form, has by no means been restricted to discussions in which cells have occupied the center of interest; so this is not the place to present it in all its aspects. For the setting forth of facts and opinions drawn from studies on regeneration, to see how these bear on the cell-doctrine, it is enough to say that these views of Vöchting seem not to have met with much favor among biologists even as a "working hypothesis." Morgan has shown conclusively the general objection to them, and the language in which he expresses himself is noteworthy: "Exception may be taken, I believe, to parts of Vöchting's conclusions, especially in the light of the recent experiments in grafting in animals. It is by no means to be granted without further demonstration that the properties of the whole organism are only the sum-total of the action of the individual cells. If, as seems to be the case, the cells are organically united into a whole, the properties of this whole may be very different from the sum of the properties of the individual cells, just as the properties of sugar are entirely different from the sum of the properties of carbon, hydrogen and oxygen." [3]

(*b*) *As Tested by the Principle of Aggregation*

By the "principle of aggregation" I mean the principle according to which, though a real unity of the organism is recognized, that unity is held to be secondary and not primary. This principle would be, as touching the cellular constitution of the organism, diametrically opposed to such a principle as that formulated by Lillie and quoted in the previous chapter, namely that there are properties of the organism which are "part of the original inheritance, and thus continuous through the cycles of the generations and do not arise anew in each."

Appeal to this principle in behalf of the cell-doctrine seems to go back to Schwann, but to have received its earliest full expression by Virchow and Haeckel in the "cell state" conception. More recently the discovery of that close copartnership between organisms of different species known as symbiosis has seemed to some biologists to furnish a type of secondary association which is both sufficiently unitary and sufficiently separatist, as regards the ultimate elements, to be available for the explanation of all biotic organization.

The influence of this aggregative conception of the organism cannot be said to have been very great, so our examination of it need not be extensive. We will here consider only the most plausible form of it, that namely which invokes the principle of symbiosis. S. J. Holmes has worked out a theory of this type more fully than any one else, so far as I know; so his paper, entitled *The Problem of Form Regulation*, will serve as the basis of our remarks.

After speaking of the organism as a self-regulating mechanism in which the whole is kept in functional equilibrium by the parts being "held in check" in some way, he writes: "If we suppose that the various cells constituting the body have each a different kind of metabolism, and that the products of each cell are in some way utilized by the neighboring cells, so that each derives an advantage from the particular association in which it occurs, we may understand, in a measure, how this check may be brought about. This supposed relation is realized in a simple scale by the cases of symbiosis that occur between plants and animals and between the algae and fungi of lichens. . . . There is reason to believe that the same fundamental principle which serves to explain the regulation of a simple symbiotic community of animal and plant cells will apply to highly developed organisms as well. We may regard the body of a highly complex organism as a sort of symbiotic community." [4]

Although Holmes nowhere says explicitly that cells are regarded as the vital units of his hypothetical organism, yet most of his discussion clearly implies this. Thus, he first considers the simple case of an organism consisting of "two kinds of cells"; then afterwards of one made of a "number of differentiated cells." From this the vital units assumed seem undoubtedly to be cells. It is significant, though, that at times in referring to the "balance," and "equilibrium," and "interdependence" so manifest in all living beings, he speaks of "parts," "elements" and so forth; that is, things which might be something other than cells: "By virtue of this dependence it is, to speak figuratively, to the interest of each part to play its normal role in the corporate life." And again, "The supposition that every higher organism is a symbiotic community on a vast scale composed of innumerable different elements." [5]

Indeed, taking the whole discussion together, it seems as though the term cell as sometimes used does not have the specific meaning attached to it in modern histology and cytology, but stands in a general way for anything, real or imaginary, within the organism to which some measure of independent life is ascribed. Thus, pointing out wherein his theory differs from Roux's *Struggle for Existence among the Parts* of an organism, he says: "The whole process of development . . . may occur, according to our theory, without the elimination of vital units of any kind, whether they be biophors, determinants, or individualities of a higher order, such as cells or organs. We have conceived the parts of an organism to be engaged in a struggle for existence, but, as the parts are mutually dependent, the struggle leads to an adjustment to a norm instead of the elimination of some parts and the survival of others." [6]

What are the "parts" here? Are they biophors, and so forth? Are some of them individualities of a higher order, as organs? Are all of them "vital units?" What relation do they hold to the "cells" talked about and diagrammatically figured, as constituting the hypothetical organism? Exactly how Holmes would answer these queries can not be made out from his discussion, yet from our standpoint they are fundamental questions. But it must be remarked that if Holmes uses "cells" in the ordinary sense, his speculation is distinctly a backward step from the conceptions presented by Roux in his *Struggle of the Parts*, who, so far as the constitution of the organism is concerned, frankly recognizes several orders of parts, and concerns himself very little or not at all with vital units. For instance, he discusses the struggle of the Molecules, of the Cells, of the Tissues, and of the Organs.

It seems worth while to call attention to this because while professedly adopting Roux's conceptions to a considerable extent, Holmes believes he has improved upon his forerunner in staking less than the latter does on the eliminative aspect of the struggle theory. In this I agree with Holmes, but must at the same time maintain, as above indicated, that in attempting to conceive the struggle in the terms of cells, regarding these as vital units in an ultimate sense, he falls considerably behind Roux in speculative soundness and very far behind him in the methodological usefulness of his speculation.

The objection to the aggregative conception of the organism, no matter under what form it presents itself, is so conclusive that little time need be taken in presenting it: *There is not an atom of evidence that is really in its favor.* Even the facts which at first sight seem most favorable to it, namely those of symbiosis on which Holmes chiefly relies, are found when considered a little more closely, to oppose it. No symbiotic combination known, even that between the alga and the fungus to make the lichen, ever occurs as *one* organism in the sense that any true organism is *one*. The symbiotic, or partnership organism, if organism it can justly be called at all, never begins its individual life as a *single reproductive* cell, either as a spore or as a zygote, i. e., a fertilized ovum, but each species has to reproduce *itself*, just as though the association did not occur. As a matter of fact, in nearly all known cases of symbiosis one of the members to the partnership actually enters the other and lives upon it at some stage of the game, so the "living together" is really a sort of parasitism. The taxonomic identity of the "consortia," as the partners are sometimes called, is lost. Concerning the most famous symbiosis known, that of the lichens, a class of plants which owes its very existence as a botanical group to the intimate association that has been contracted between plants of two other such groups, fungi and algae, we read, "Strictly speaking, both fungi and algae should be classified in their respective orders; but the lichens exhibit among themselves such an agreement in their structure and mode of life, and have been so evolved as consortia, that it is more convenient to treat them as a separate class. . . . From the symbiosis entered into by a lichen fungus with an alga, a dual organism results with a distinctive thallus, of which the form (influenced by the mode of nutrition of the independently assimilating alga) differs greatly from that of other non-symbiotic Eumycetes." [7]

As a purely imaginary construction one might, perhaps, picture an organism produced in this fashion which would not be "dual," as these authors express it, but monal, that is, *an* organism in the usual zoological and botanical sense. But since such an organism would be a work of the imagination, pure and simple, with all observational evidence weighing against its real existence, this particular form of the aggregational conception of the organism can not be held to have any scientific value, especially if the aggregants or consortia be imagined to be cells.

(*c*) *As tested by the Specificity and Metaplasy of Differentiated Cells*

The question now before us is, how far are cells which are wholly or largely differentiated into tissues bound, willy nilly, to continue to be just those tissues, and to produce as they proliferate, other tissues of exactly the same kind. Nothing concerning the minute structure of organic beings is better established than that in general tissue cells are "true to kind"; that is, once a muscle or nerve or gland cell, always a muscle or nerve or gland cell, not only in the particular cell's own existence but in its progeny also. Clearly this must be so. Were it not, the organism would really not be an organism at all; it would be a riot of cells differentiated and undifferentiated.

So obviously and widely true is this that some biologists have believed it deserves crystallization into a phrase comparable to *omne vivum ex vivo.* Accordingly we have Virchow's *omnis cellula e cellula* transformed by L. Bard into *omnis cellula e cellula ejusdem naturae.* But were this formulation rigidly true, and were the tissue elements absolutely unmodifiable in their individual lives, the adult organism, at least, would certainly be held in the grip, figuratively speaking, of its cells, and the fact might be taken as evidence of the weightiest kind in support of the theory that the cells are the key to all organic phenomena.

Much truth as there unquestionably is in this aphoristic statement, researches of later years have produced conclusive proof that it can stand only after receiving important modification.

Looking at the problem of the deviation of the cells of an organism from type in a broad way, though without presuming to make the classification and discussion exhaustive, we find that three rather well defined classes of such deviations have been observed. There are (1) cases in which tissues are induced to undergo radical and more or less permanent transformation by coming into close and long-continued contact with new or differently applied influences of the external world; (2) cases in which the replacement of lost parts of an organism is effected through either the direct transformation of tissue of one sort belonging to an intact part of the organism into other tissues of the newly added parts, or through the derivation of tissues of the renewed parts from tissues of another sort in the old parts by the latter's first returning to something like an embryonic condition; (3) cases of transformation of tissues in certain pathological growths.

Under the first head one of the oldest and most frequently cited examples is that of the transformation of the soft mucosa cells lining the vagina into pavement-like cells, when inversion of that organ occurs. A particularly clear and interesting example of cell transformation which may be properly ranged in the same class has recently been reported by Harms. This investigator transplanted pieces of the thumb pad of the sexually active male frog (*Rana fusca*) from one individual to another individual. After about two months he found that complete union of the grafted piece had been effected, and that the epithelial cells of the graft were in a normal condition. The glands, however, peculiar to the epidermis of these pads showed signs of retrogressive change. In the course of another month or so the glands had undergone complete transformation into a solid, wellnigh structureless mass, and the cells of the epithelium immediately surrounding them had reformed and rearranged themselves into well-defined encapsulating layers, constituting what Harms designates as a "metaplastically stratified epithelium." This case appears to be, as the author remarks, one which "shows all phases of tissue transformation in a way not open to objection." This case is considerably different from those previously cited in that the influences operative in bringing about the tissue changes are more intimately connected with the chemico-vital processes of the organism, and are less purely mechanical than in the other cases. Harms does not neglect this aspect of the matter, but a consideration of it would be out of place here.

Under the second head, one of the most striking and at the same time best authenticated instances of transformation of tissues accompanying the replacement of lost parts has been described by Nusbaum and Oxner. The results of their researches significant for our present needs are summarily stated in the translation which follows: "From what has been said above, we see that in the regeneration of the anterior part of *Lineus lacteus*, which has been robbed of the entire old alimentary canal, the formation of new tissues takes place heterogenetically in the highest measure; that is, it proceeds in such a way that the new tissues arise from an entirely strange old tissue from which they are never produced under normal conditions. We saw, that is to say, that the epithelium of the entire new alimentary tract, a tissue endodermal *par excellence*, is formed in regeneration by wander-cells which arise from the parenchyma and connective tissue, therefore from a material originally wholly mesodermal." [8] The elaborate description and illustration with which they present their observations leaves little to be desired for making the case trustworthy, even had it not been confirmed by other workers. Fortunately, however, C. Dawydoff, a Russian zoologist, working on the same species at the same time but wholly independently, reached results identical in every essential particular.

Dawydoff's categorical statement touching the main point is as follows: "The newly-arisen alimentary canal of *Lineus lacteus* is formed from mesoderm. It is differentiated from the parenchyma and the walls of the lateral vessels." [9] A very brief description of the experiment performed by these investigators will suffice to make the crucial part of the results clear. The nemertean has a long section of body in front of the mouth, consequently into which no part of the intestinal canal extends. From this it follows that if the animal be cut in two anterior to the mouth, the front piece will be wholly devoid of digestive organs. Notwithstanding this it was found that these gutless, mouthless pieces would not only continue to live, but would develop into complete worms, the new alimentary tract being formed, as the quotations show, from the internal tissues of the severed piece; that is, from tissues which in the normal worm have nothing to do with the digestive organs.

The demonstration of this ability of organisms to press into service certain of their parts to replace other parts that have been lost, even though the parts implicated are normally quite different, structurally, functionally and developmentally, is undoubtedly one of the most important results of the researches on animal regeneration that were so eagerly pursued a few years ago. A goodly number of instances of this in widely separated sections of the animal kingdom have been established beyond cavil.

Nusbaum has performed the useful office of summarizing these on the basis of the kinds of tissues involved, as follows:

"1. Formation of muscle elements from epithelial tissues of ectodermal origin.

"2. Formation of connective tissue elements from epithelial tissue of ectodermal origin.

"3. Formation of muscle elements from differentiated parenchyma cells of mesodermal origin (from connective tissue).

"4. Formation of nerve elements from differentiated epithelial tissues of mesodermal origin." [10]

Summary of Examination of Inadequacy of Cell-Theory

We have now passed under review several large and quite distinct groups of knowledge pertaining to those biotic objects called cells, all of this knowledge favoring the interpretation of these bodies as differentiated parts or members of the larger bodies to which they belong. They come into existence one after another as a consequence of the growth and differentiation of the organism, and in strict subordination to its needs. In a word, we are led to see that cells must be regarded as *organs* of the organism just as muscles and glands and hearts and eyes and feet are so regarded. They undoubtedly constitute a class of organs rather sharply set off from all other classes, but this should not be permitted to obscure the equally important fact of their always presenting those attributes which are most general to all organs, namely those of origination by the growth and differentiation of the organism, and of being functionally subservient to the organism.

Nor should we, while taking note of the attributes of cells which range them under the general category *organs*, neglect to note also the attributes which make them a class by themselves within that category, namely their similarity in form, constitution and size, for the whole organic world, and of still more importance, their office as the implements or tools by which the organism performs the physical changes and chemical transformations of the materials it uses.

Advance Toward the Organismal Standpoint Through Conception of the Cell Reached by Biochemistry Pursued in Accordance with the Principles of Physical Chemistry

This last statement turns us back to the concluding sentences of the chapter on The Organism and Its Chemistry.

Our explorations in that field discovered, it will be recalled, that biochemistry, prosecuted in accordance with the principles of physical chemistry, is being led to conceive the cell as a "highly differentiated system," or an "organized laboratory" consisting largely of "colloidal complexes" which constitute, "as it were, a special apparatus for performing dynamic chemical events."

Into the details of the physico-chemical conception of the cell we do not enter again here. Miserably inadequate as our presentation of the subject was in the previous chapter, it must suffice for this discussion.

By way of making the conception still more concrete and vivid, and of emphasizing its importance from the organismal standpoint I quote Hopkins a little further: "On ultimate analysis we can scarcely speak at all of living matter in the cell; at any rate, we cannot, without gross misuse of terms, speak of the cell life as being associated with any one particular type of molecule. Its life is the expression of a particular dynamic equilibrium which obtains in a polyphasic system. Certain of the phases may be separated, mechanically or otherwise, as when we squeeze out the cell juices, and find that chemical processes still go on in them; but 'life,' as we instinctively define it, is a property of the cell as a whole, because it depends upon the organisation of processes, upon the equilibrium displayed by the totality of the coexisting phases." [11]

Let us now bring closely alongside these and the previously quoted statements about the nature of the cell as seen by physical chemistry, statements about its nature as seen by natural history, these latter statements having been examined in the preceding chapter. Take this from E. B. Wilson, for example: "The real unity is that of the entire organism and as long as its cells remain in continuity they are to be regarded not as morphological individuals, but as specialized centers of action into which the living body resolves itself and by means of which the physiological division of labor is effected."

And this from Whitman: "Comparative embryology reminds us at every turn that the organism dominates cell formation, using for the same purpose one, several, or many cells, massing its material and directing its movements, and shaping its organs, as if the cells did not exist, or as if they existed only in complete subordination to its will, if one may so speak."

And this from Lillie: "The traditional view, held by many embryologists at the present day, is that the physiological unity arises in the course of embryonic development of the secondary adaptation of originally independent parts to one another. But this explanation has, in my opinion, become untenable, and must be replaced by the view that there are certain properties of the whole, constituting a principle of unity of organization, that are part of the original inheritance, and thus continuous through the cycles of the generations and do not arise anew in each."

And finally this statement by Conklin of the often expressed perception that the germ-cell and the adult organism which develops from it are one and the same individual: "Furthermore, from its earliest to its latest stage an individual is one and the same organism; the egg of a frog is a frog in an early stage of development."

Recognizing in these four statements a sort of concentrated solution of the evidence of our whole discussion of the cell-theory, that the cells of multicellular organisms are really organs of the organisms; that they are not independent, ultimate life units but on the contrary exist because of and in subordination to the organism, how escape seeing that in such general physico-chemical presentations of the nature of living substance as those quoted from Hopkins whenever the term *cell* occurs the term *organism* really ought to be used? The compulsion to such substitution is especially direct and compelling from the perception, as expressed by Conklin, that a frog, for instance, *is* one and the same organism whether in the one-celled stage, that is, existing as a *cell*, or in the many-celled stage.

But bringing the language of natural history into juxtaposition with that of biochemistry, as we are here doing, accomplishes more than merely to reveal the necessity for substituting *organism* for *cell* in the statements of biochemistry. It reveals important details of the general truth that the organism and not the cell is what physical chemistry is in reality carrying biochemistry toward. For instance, compare Hopkins' assertion that it is impossible to attribute cell life to "any one particular type of molecule" with Lillie's that the traditional view according to which cells are "originally independent parts" and only secondarily become incorporated into the "physiological unity," must be replaced by the conception that there are "certain properties of the whole" which constitute a "principle of unity" that are part of the "original inheritance" of the organism. The parity here suggested between the natural historian's objection to conceiving "life" as a phenomenon of "the Cell," as though on ultimate analysis there were only one kind of cell, and the modern biochemist's objection to conceiving "life" as a phenomenon of "one particular type of molecule" should be examined a bit closer. What Hopkins has in mind in taking a stand against "a particular type of molecule" as the explanation of life is the "ultimate physiological unit" theory which has cropped up under so many nomenclatorial garbs in later years, but has reached its most plausible form, perhaps, in the *biogen* conception, ably defended by Verworn.

To this conception, no matter what guise it assumes, physical chemistry brings the insurmountable objection, so far as the living cell is concerned, that "life" in the very simplest expression of it known to observational science, is yet a great complex of structures and activities which constitute a system. It is a space-occupying, shape-presenting, self-equilibrating complex. Its very existence is a phenomenon of multiplex dynamic unity, the parts of which though constituting the whole are yet subordinate to the whole. Hence the modern biochemist's assertion that we cannot properly speak of the living molecules *in* the cell, but must think of the life *of* the cell as a property of the cell as a whole. And hence, too, the natural historian's perception that he must, in turn, and by the very same general principles which guide the physical chemist, insist that life is a property of the organism as a whole. In Whitman's expressive language, the "organism dominates cell formation," exactly as, by implication, Hopkins' language justifies us in asserting that the cell dominates the "molecules" of the living substances of which it is constituted.

Likewise the "morphological plan of the organism" mentioned by Carrel and Burrows as something to which the tissues "must adapt themselves in their development" (see quotation in section on tissue cultures) is really the counterpart in natural history language of the cell as an "organized laboratory" in biochemical language. And the "unknown factor" which Carrel and Burrows assume must be added to the "morphological plan of the organism" to explain the compulsory adaptation of the differentiating tissues, is supplied by physical chemistry so far as the cell is concerned, in the dynamical, the self-equilibrating system of phases recognized as constituting the cell.

But when the perception is reached, as it is through our examination, that in reality the term "organism" should take the place of "cell" in biochemical language, the organism no longer appears as a morphological entity merely, but as a dynamical, a physiological entity as well, and the "unknown factor" is supplied in the organism-as-a-whole. Once such a conception of life becomes as clear as it is inevitable, a seemingly overwhelming difficulty looms up in the fact that "the organism" as natural history is compelled to deal with it is infinite in number, theoretically if not practically. For nothing is more patent than that *individual* organisms are the primary material of natural history, and no generalization of natural history is better grounded than that no two individuals are quite alike. From which it results that no individual can be fully understood, fully interpreted, without *itself* being made a subject of investigation. No generalization about organism proper can be counted on to apply *fully* to all organisms! It is probable that an ill-defined sense of this difficulty (that of the unreachableness of the *whole* of living nature by any recognized universal principle or law) accounts for the turning back of so many able biologists after they have gone far on the natural history road. For example, E. B. Wilson's failure to accept the consequences of his own conclusion, "the real unity is that of the entire organism," is very likely explicable in this way. To one who has been so indoctrinated with the metaphysics which grows naturally out of modern mathematical physics as to make him accept the pronouncement that there are "only two real things in the universe, Matter and Force," a course of discovery and reasoning which makes every individual organism, no matter how small and insignificant, a "real thing" seems preposterous even though true. But the fact that the conception as modern biology reaches it is largely due to *physics itself* through its influence upon chemistry and biochemistry, ought to contribute much to the reconciliation of science generally to the conception.

The full meaning of such an exaltation—for exaltation it undoubtedly amounts to—of the individual can be compassed only by a painstaking examination of very many biological facts and hypotheses and dogmas, this examination ranging over the whole vast realm of living nature. Indeed, the final and most convincing evidence for the essential truth of the conception will be reached only when man himself and the highest provinces of his nature have been brought into the examination. By the mode of treatment adopted in this work we shall not have sounded the deepest depth explored in it until the end of the last chapters shall have been reached, those on The Psychic Integration of the Organism.

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Chapter VIII

FURTHER EXAMINATION OF THE CELL-THEORY

So pervasive have been the efforts to interpret organic development in accordance with the cell-theory that to examine them exhaustively is impossible. All one can do is to choose some of the most prominent and assume that if the criticism succeeds with these major efforts it could succeed with the minor ones.

The Mosaic Theory

Two diametrically opposed interpretations of the early developmental states of the organism have figured largely in later biological theorizing. According to the first, the constituent cells of the earliest cleavage stages hold the relation to one another of the stones in a mosaic work; according to the second, each cell is "totipotent," that is, supposedly capable of producing the entire organism.

What the Mosaic Theory Is

What the phrase "mosaic work" means when applied to an embryo may be stated in the words of Roux himself, the discoverer of the phenomena on which the conception rests. "Mosaic work" designates those "developmental phenomena through which in many eggs, those of the frog for instance, each of the two or four first cleavage cells (or the complex of descendants of these) develop *by themselves alone* into the corresponding body part, for example into half embryos and so forth, consequently without the formative coöperation of other parts, so are fashioned *independently*, like the stones of a mosaic picture. This takes place through the 'self-differentiation' of separate cleavage cells or later separate organ-foundation or in fact artificially delimited parts, and is possible only in 'typical' development since 'atypical' development must proceed with far reaching formative regulation."[1] And along with this definition of mosaic work the definition of the mosaic theory should be noticed. "The mosaic theory is the theory which explains or at least makes intelligible the 'mosaic work.' It rests upon the assumption of different qualities in the separate cells (cell body or also cell nucleus) or organ-foundations etc. capable of 'self-differentiation'."

Obviously, were it generally true that the cells of an organism are as distinct as the individual stones in a mosaic, not only as to their form and structure, but also as to their activities, including their powers of differentiation, this fact would go far toward a demonstration that cells really are the "key to all ultimate biological problems" and the central thesis of biological elementalism, namely, that the final explanation of all organic phenomena lies in the elements constituting organic bodies, would have found an almost impregnable stronghold. On this account the mosaic theory has been far more eagerly defended and combatted than its merits as a strict scientific hypothesis warrant. For this reason too, it will be profitable for us to devote somewhat more attention to it than we could otherwise afford.

The central facts on which the mosaic theory rests are familiar to all students of embryology. Roux killed one of the two cells of frog eggs when they were in the two-cell stage of development, by pricking it with a heated needle. In some cases the other cell remaining uninjured developed into a half-embryo of somewhat such character as one would get were he to split a normally developed embryo lengthwise in the dorso-ventral plane of the body. He then killed three of the four cells of embryos in the four-celled stage, and in a few instances got something from the remaining cell quite like a quarter embryo. On these observations Roux based the somewhat bold hypothesis that "the development of the frog's gastrula and of the embryo immediately following the gastrula-stage is, after the second cleavage-period, a mosaic work of at least four vertical self-developing (or differentiating) parts." To this, however, was added the sheltering statement, "how far this mosaic work is changed by a change in position of material in the later development, cannot be determined."

So striking a series of experiments and so far-reaching an hypothesis were naturally not permitted to stand long without re-examination. O. Hertwig was the first to try the experiment again. His results were quite different from Roux's. He got no hemi-embryos at all, but on the contrary a number of whole embryos, more or less badly deformed in various ways. It should be borne in mind that Roux's method of killing the cells did not remove the injured cells. These remained in full or slightly diminished mass, but wholly inert, as originally supposed, when the operation was entirely successful. Hertwig, on the contrary, believed that usually the life of the pierced cells was not entirely destroyed, but that whether quite dead or not, they exerted an important influence on the developing part, and he hazarded the opinion that could one of the two cells be entirely removed, the other would produce a complete embryo though of reduced size.

After much discussion between Roux and Hertwig and others who came into the field, it was shown by Morgan that "when the black pole of the uninjured blastomere remained up, the blastomere developed in all cases observed into a *half-embryo*. Conversely, those eggs in which the white pole was turned upward, formed, in most cases, *whole embryos* *of half-size.*" It thus seems that the mosaic hypothesis for the frog is partly true. Under some circumstances the cells seem more or less like the stones in a mosaic, under other circumstances however they do not. Later work, particularly by Roux, Curt Ziegler, Morgan and Ellen Torelle, has in general confirmed this much modified form of the hypothesis in the case of the frog. It has at the same time shown how much more complicated the whole matter is than Roux's original simple statement would lead one to suppose.

But the frog is not the only animal in which the cells of the early embryo present something of the mosaic character. C. Chun discovered that one of the cells of the two-celled stage of a Ctenophore would develop as a half-embryo if isolated from its mate. Driesch and Morgan confirmed this discovery in general, but pointed out certain details of structure of the resulting organisms which make the latter depart quite fundamentally from half-organisms in a strict sense. For instance, a true ectoderm covered over the side that would be the cut surface were two half-animals to be produced by halving a whole one with a knife. Further, some of the internal organs, notably the endodermal pockets, were not merely what they would be in a half-animal, but were as much like those of a whole animal. The normal animal has four, so a typical half-animal would have two, but the half-animals produced from isolated blastomeres had three. Several later investigations on ctenophore eggs have been carried out, the upshot of all being that with very decided reservations the cells of the young embryos of these animals may be looked upon as the "stones in a mosaic work." A few other kinds of animals, for example the mollusc *Ilyanassa obsoleta* show something of the same sort of developmental capacity.[3]

A Modicum of Truth in the Mosaic Theory

It is, then, fully established that in some animals the cells of the early embryos are so specified or individualized that each develops to a considerable extent in its own way, that is, more or less independently of its neighbor cells, and hence may be crudely compared to the stones in a mosaic work—*crudely*, we must insist, since stones as members of a mosaic work do not develop at all.

The Theory of Totipotence

This theory is the other side of the shield, the side which looks as though the cells of the early embryo are "totipotent," that is, as though each cell were able to produce the whole organism instead of only a pre-ordained portion of it. Chieftainship, both experimental and speculative, in this theory of developing embryos is universally accorded to Hans Driesch. The discoveries by him which had such pervasive influence on biological thinking for more than two decades were first published in 1891. His recent popular account of his work in *The Science and Philosophy of the Organism*, will best serve our present need.

Experimental Facts on Which the Theory Rests

Three years after the publication of Roux's experiments on the frog's egg, above referred to, Driesch tried essentially the same experiment, but on a different animal and by a different method. He writes: "It was known from the cytological researches of the brothers Hertwig and Boveri that the eggs of the common sea-urchin *Echinus microtuberculatus* are able to stand well all sorts of rough treatment, and that, in particular, when broken into pieces by shaking, their fragments will survive and continue to segment. . . . I shook the germs rather violently during the two-cell stage, and in several instances I succeeded in killing one of the blastomeres, while the other one was not damaged, or in separating the two blastomeres from one another.

"Let us now follow the development of the isolated surviving cell. It went through cleavage just as it would have done in contact with its sister-cell, and there occurred cleavage stages which were just half of the normal ones The stage, for instance, which corresponded to the normal sixteen-cell stage . . . showed two micromeres, two macromeres and four cells of medium size, exactly as if a normal sixteen-cell stage had been cut in two; and the form of the whole was that of a hemisphere. So far there was no divergence from Roux's results. . . .

"I now noticed on the evening of the first day of the experiment, when the half-germ was composed of about two hundred elements, that the margin of the hemispherical germ bent together a little, as if it were about to form a whole sphere of smaller size, and, indeed the next morning a *whole* diminutive blastula was swimming about. I was so much convinced that I should get Roux's morphological result in all its features that, even in spite of this whole blastula, I now expected that the next morning would reveal to me the half-organisation of my subject once more. . . . But things turned out as they were bound to do and not as I had expected; there was a typically *whole* gastrula on my dish the next morning, differing only by its small size from a normal one; and this *small but whole* gastrula was followed by a whole and typical small pluteus-larva.

"That was just the opposite of Roux's result; one of the first two blastomeres had undergone a half-cleavage as in his case, but then it had become a whole organism by a simple process of rearrangement of its material, without anything that resembled regeneration, in the sense of a completion by budding from a wound." [4]

Driesch went on with his sea-urchin eggs, as Roux had with the frog-eggs, to see what cells would do if separated in the four-cell stage. He found that such cells could also give rise to whole larvæ, but of correspondingly diminished size. So far then, as the sea-urchin is concerned, taking the facts at their face value, the cells of the very young embryos were proved to be diametrically the opposite in their relation to the complex as a whole, from the individual stones of a mosaic work.

Driesch's methods of treating developing eggs were soon much resorted to by other investigators, with the general outcome that numerous animals in widely separated parts of the animal kingdom were proved to have much the same developmental ability as the sea-urchin. Wilson found that the cells of *Amphioxus* embryos separated in the two- and four-cell stage would develop from the *very beginning after isolation* like whole eggs of reduced size. It will be recalled that the sea-urchin cells separated by Driesch developed at the beginning like half-eggs, and only changed over to the whole-embryo in the blastula stage. So Wilson's discovery removed *Amphioxus* still farther from the mosaic type of development than the sea-urchin had been removed by Driesch.

The Italian zoologist, Raffaello Zoja, increased knowledge of whole-animal production from a portion of the cells of the young embryo, by showing that in the hydroid *Clytia flavidula*, not only one of the blastomeres from the two-cell stage, but one from the four- and eight- and even the sixteen-cell stage, will develop to complete organisms of diminished size, the half and the fourth at least, of the whole egg, being capable of going on with the development until the adult animal, perfect except as to size, is reached.

In view of the fact that the egg of the frog, a representative of one of the two main sections of the Amphibia (the anura), served as the starting point for the mosaic theory, it is particularly interesting to know that the egg of *Triton*, which represents the other section (the urodela), falls in with the sea-urchin, *Amphioxus*, and hydroids, as concerns the developmental ability of the separated cells of the two-cell stage. For this information we are indebted first of all to Amedeo Herlitzka.

This power of developing whole animals from portions of the egg has been proved to exist in several other groups, but enough detail has now been adduced to show conclusively that the mosaic conception of the organism contains only a modicum of truth. The observations here briefly set forth, with others of like import, led Wilson to declare: "In its original form the mosaic theory has, I believe, received its death-blow." [5]

Going still farther, Wilson said in the same discourse, "I will here point out one all-important point which is definitely established by the work of Driesch and other experimentalists, and which is accepted by all opponents of the mosaic theory, namely, that the cell cannot be regarded as an isolated and independent unit. The only real unity is that of the entire organism, and as long as its cells remain in continuity they are to be regarded, not as morphological individuals, but as specialized centres of action into which the living body resolves itself, and by means of which the physiological division of labor is effected." [6]

It was these discoveries, antithetic to those which led to the mosaic theory, that begot in Driesch's mind the conceptions of "totipotence," "prospective significance," and the "harmonic equipotential system."

The formal definition of "totipotence," and of "prospective significance" may be given here since they concern primarily the cells of the embryo. "Totipotence [is the possession by] a part of the germ as yet not at all or but slightly 'specified' of a form-producing power similar to that of the entire egg. It is therefore the power [of such a part] to develop the entire organism." [7]

The meaning of "prospective significance" is that "each blastomere is a function of its position in the whole." [8]

The extreme form of Driesch's view is set forth in his lucid and often quoted statement that the early cells of the sea-urchin embryo are "composed of an indifferent material, so that they may be thrown about at will, like balls in a pile, without the least impairment of their power of development." [9]

Balancing the Account Between the Mosaic and Totipotence Theories

Every one, it would appear, must then admit that, so far as concerns the part of the cell-theory which would see in the cell the "key" to all development, these discoveries by Roux and Driesch neutralize each other. If the cells of the frog's egg seem in their individual capacities to produce each its particular part of the organism, those of the sea-urchin's egg seem, with equal positiveness, to do nothing of the sort, but on the contrary to be entirely subject to the needs of the future organism. This, I say, is manifestly the effect which the original discoveries of Roux and Driesch have upon each other. But later researches have undoubtedly proved that more animals resemble the sea-urchin than the frog so far as the developmental attribute is concerned. And the case of Triton, the near relative of the frog should be particularly remembered. "There is no necessity," says Herlitzka, "for a predisposition of various parts of the isolated blastomere (or of the egg) to give origin to determinate organs." [10]

It is quite impossible and unnecessary to follow all the details of the Rouxian and Drieschian views of the relation of cells to the organism in development; but we must notice in a general way the course pursued by Roux relative to the observations by other biologists and by himself which are clearly hostile to the mosaic theory. To meet the fact that under some conditions, even in the frog, not a half-embryo but a smaller whole embryo develops from the isolated blastomeres, he advanced the notion of "postgeneration." By this he means the "*supplementary* restoration, completely or incompletely, of a half- or quarter-embryo, or other '*Partial-product*' formed in consequence of the destruction of a part of the egg." [11]

By coupling this idea with an earlier speculation of his about the nature of the cell nucleus, he tried to make the nucleus, instead of the cell, the really responsible element in the mosaic, at least in those cases in which the whole cell clearly does not conform to the mosaic conception.

Provision for retreat to the nucleus upon occasion, is made in his definition of mosaic theory already quoted.[1] It will be recalled that the theory rests on the "assumption of different qualities in the individual cells (cell body or cell nucleus, etc.) capable of self differentiation."

Alongside this modification of the original mosaic theory made by transferring the rôle of building stones from the cells to the nuclei, it is instructive to place what is in effect another modification of an opposite nature invented by G. Born, in connection with his extensive experiments on grafting together the larvæ of various amphibians. Born found that larvæ, not only of different species, but even of different genera and families, could be made to unite to some extent, the union between the more closely related species being in general the easiest to accomplish and the most permanent, but that in any case each component of the grafted specimen maintained its specific attributes uninfluenced by the individual with which it was united. In other words, animal grafts, so far as these experiments went, follow the well known rules of plant grafts. The maintenance of identity of the parts, Born interprets as supporting the mosaic theory. He says: "From our beginning stage on, the development rests essentially upon self-differentiation of the particular (einzelnen) parts a correlative influence of the neighborhood (Nachbarshaft) as of the whole cannot be recognized—neither negative nor positive; the development therefore corresponds throughout from our beginning stage on to the mosaic theory of Roux. The organ-forming germ regions are parceled out (His)." [12]

That an individual plant or animal made up of parts of the bodies of two or more other plants or animals grown together, each constituent maintaining its identity wholly unmodified by the other parts, has as much resemblance to a mosaic picture as can well be imagined for any living being, must be granted. No one should, however, fail to see the difference between a mosaic of this sort and one of the sort conceived on the basis of the developmental facts which were the starting point of Roux's theory. In the first place "mosaic pictures" of the kind produced by grafting are genuinely man-made affairs. They never occur in nature. A "mosaic theory" contributes nothing substantial to their interpretation. Indeed it is difficult to see that there is room here for any such theory. Such a composite creature undoubtedly resembles somewhat a mosaic picture and that would seem to be all there is to it. But undoubtedly such a creature also differs very much from a mosaic picture. For one thing, the creatures are alive and mosaic pictures are not. However, I have no wish to make all that might be made against the mosaic theory because of its high degree of artificiality. The main purpose in bringing forward Born's work and ideas at this point is to direct attention to his proposal touching what might be called the scientific aspect of the mosaic theory. The organ-forming germ areas (organbildende Keimbezirke) of His to which Born refers, and which unquestionably played a large part in Roux's original theory, are surely features of the earliest stages of ontogeny, even of the unsegmented egg. A passage from His's *Unsere Körperform* quoted by Wilson makes this clear. "The material of the germ is already present in the flat germ-disc, but is not yet morphologically marked off and hence not directly recognizable. But by following the development backwards we may determine the location of every such germ, even at a period when the morphological differentiation is incomplete or before it occurs; logically, indeed, we must extend this process back to the fertilized or even the unfertilized egg. According to this principle, the germ-disc contains the organ-germs spread out in a flat plate, and conversely, every point on the germ-disc reappears in a later organ. I call this the *principle of organ-forming germ-regions.*" [13]

But notice now that the organ-forming germ-regions which were Born's "beginning stages" in his grafted larvæ, were by no means "germ-regions" of the unfertilized or even fertilized egg. They were parts of larvæ, *i.e.*, of individual animals well advanced in development. The pieces in his mosaic works were not single cells or parts of cells but great groups of cells, many of them already considerably differentiated from one another, but yet so correlated in their activities as to enable the grafted parts of the animal to maintain their specific identity.

A fundamental question, then, raised by the mosaic theory as formulated to-day is, What is an organ-forming germ area? or, more briefly, What is germinal material? Is it the material of each of the first two, or in some instances four blastomeres as indicated by the frog's egg? Is it nuclear material as conceived by Roux's modification of his original theory? Or is it in accordance with Born's idea, the material of any group of cells no matter how large the group and how many kinds of cells in it, so long as the group is able to develop true to the kind of organism to which it pertains? A critical examination of both the original theory and the modifications of it, in the light of the questions just raised will, I believe, discover that the modifications have in reality destroyed whatever of scientific value the original theory may have had. There can be no objection to comparing a living being with a mosaic picture on the basis of the fact that the former is composed of a great number and variety of living particles called cells, just as the mosaic picture is composed of a great number of particles of stone, but the comparison has at best but little scientific value, and at worst may be very harmful. The little scientific value in the comparison is purely subjective and logical; it concerns the problem of the unity in spite of the composite quality of both organism and picture as objects of perception.

The harmfulness of which the comparison is capable lies in the wholly fallacious inferences that may be drawn as to the mode of origin of the objects compared. The fundamental difference between them is that while all the myriad cells of the organism arise by the repeated auto-division of one cell, the fertilized ovum, the picture is composed of pieces of stone cut one by one from rocks which had nothing to do with it, until the pieces were assembled and put in order to produce it, by men, beings again originally quite independent of the picture. The undivided egg-cell would then have to be compared to one such stone block, and a mountain of trouble looms up. In the first place, we know for an absolute certainty that there is no one block of the picture from which all the others are produced either by division or in any other way; and in the second place, while any particular stone block of the picture is nearly or quite homogeneous so far as the general design of the picture is concerned, and represents only a small piece in the design, the undivided egg-cell is itself the whole organism in one stage of its growth, and contains within itself a considerable design, or composition; so much, that is, as is distinctive of the organism in this period of its life.

Nor can we let Born's modification of the theory off without looking at it from another and quite different angle. The larvæ and portions of larvæ entering into the graft complexes have, he shows, no correlative influence on one another, nor is there any influence of the whole on the parts, and therefore the *whole* is a mosaic work. But how about the cellular and tissue elements composing the larvæ and parts of larvæ within the complex? May we look upon these elements also as comparable to stones in a mosaic picture? Is not the fact that the portions of an organism entering into a graft-complex maintain their specific if not individual identity, peculiarly strong evidence of correlative influence of the *elements of these portions* upon one another? The *organized* and *organizing* power of living beings hardly manifests itself in any way more strikingly than in the fidelity of grafts to their own kind whether in plants or animals. But the very essence of organization and organizing power is, as everybody recognizes, correlative influence or activity. A mosaic picture is about as near an antithesis to an organization as can be found. So while we may willingly grant that an organism made up of parts of other organisms grafted together resembles to some extent a mosaic work, we must at the same time recognize that when looked at in its real nature it not only does not support, but really refutes the mosaic theory if that theory is held to any definite and significant meaning.

The "Promorphology" of Germ-Cells

Although a critical examination of the mosaic theory found it to be of exceedingly little value at its best, and downright noxious at its worst, yet we were led to recognize a measure of forcordination in each of the first two cells of the dividing egg, as in that of the ctenophore, and under some circumstances, the frog. Even before division begins, this intimation of specific structure of the egg arrests our attention. Our standpoint makes organization important wherever found and of whatever grade.

(*a*) *Facts of Immediate Observation on Which the Conception Rests*

The truth is we now know that the undivided egg-cell stage, in the individual life histories of animals so far as they have been carefully studied, is already rather highly organized and to a considerable extent *specifically organized* with reference to the kind of organism which the egg-cell represents. Otherwise stated, we know that a thoroughgoing account of the life history of any organism must include its structure and function *in* and *before* the undivided egg-cell stage, as well as its structure and function *after* cell-division begins. The science of germ-cell structure and function previous to the egg-cell division is known to embryologists as promorphology and prophysiology.

The inductive evidence in support of the conceptions of promorphology and prophysiology is altogether too voluminous and complicated to be fully presented in a work like this; but the matter is so important that the reader must not be left in doubt about its conclusiveness.

I call attention first to an aspect of the evidence which though well known in a general way, is rarely if ever given the consideration which in my opinion it merits. Reference is made to the fact that many species of animals, even belonging to the same genus in numerous cases, have been distinguished from one another in all their stages of development down to the undivided egg-stage. Investigation has gone so far in this direction as to make it probable that all species whatever might be thus distinguished were the examinations sufficiently searching.

The most extensive studies in this field have pertained to groups of animals whose economic or ecological relations to man are such as to render it important to recognize the different stages of their lives. Thus in the interest of the great marine fishing industries of northern Europe, elaborate investigations have been undertaken for identifying the eggs and embryos of numerous species of fishes. Worthy of special consideration is the partnership work by Fr. Heincke and E. Ehrenbaum.

After asserting the indispensability of exact specific determination of floating eggs and young fishes as a basis for any reliable deductions concerning the distribution of the eggs, the authors say that the possibility of such determination can be affirmed only conditionally; and their research had for its object to show in general how far the identifications can be made, and in particular to ascertain the extent to which size is distinctive of the different species. Agreeing with seemingly all zoologists who have attended to the matter, they say that the oil drops and pigmentation occurring in so many floating eggs furnish important distinguishing marks. The time of escape of the embryo from the egg membrane seems also to be distinctive for many species. Concerning pigment, they affirm that in the advanced embryonal stages, nearly all fish species can be recognized with great certainty. Included in the elaborate study is a "table for determining the floating fish eggs in the German North Sea." [11] This is a "key" in the ordinary sense of the taxonomist and deals with some thirty species belonging to about twenty genera. The attributes used chiefly in constructing this key are found in the oil drops, pigment spots, and size of the eggs.

Mosquitoes are another group of animals which have drawn considerable attention to their early developmental stages because of their importance to man; and here again "keys" for the identification of the species are frequently given for the larvae as well as for the adults. I have seen no work on the subject in which the eggs are treated in this diagnostic way, but in the "*Report of the New Jersey State Agricultural Experiment Station upon the Mosquitoes occurring within the State, their Habits, Life History, etc.*" by Dr. John B. Smith, we read, "Dr. Dupree tells me that he has found good characters in both eggs and larvæ; but that they are observable only with the compound microscope." [15]

The truth arrived at in other connections from more theoretical considerations, that the fertilized egg from which an individual animal develops is that individual in the one-cell stage of its life, comes most vividly to view in just these purely practical studies. Thus in one of the many reports by Fr. Heincke on the food fishes of the North Sea, the author says: "The first condition for a right understanding of the habits and habitats of the food-fishes of the sea, and in general, of the production of the sea as regards useful fishes, is an exact knowledge of the occurrence and distribution of these food-fishes *at all the various stages of their life, from the egg on to the adult mature form.*" [16]

Facts of the sort here set forth have seemed to most biologists too trivial to deserve consideration in theoretical discussions, and so far as they have been studied, this has been done for the most part either incidentally, or, as in the cases here adverted to, for practical ends.

(*b*) *Grounds for Believing Minute Observable Specific Differences Between Germ-Cells Important*

No matter how minute and superficial may be the attributes which distinguish the egg-cell stages of species, if these attributes are indubitable and constant they differentiate the species *in that stage of the individuals' lives,* and so from the strictly logical standpoint have the same order of importance as have smaller discriminative attributes of any other stage in the individual life; furthermore, from all that modern research is bringing to light on the correlation of attributes, to assume that these minute differences are really as detached and insignificant as they seem is biologically quite unwarranted.

To illustrate, what careful biologist would dare affirm, having due regard for what we now know about the chemical interaction of the parts of an organism, that the difference in the size and distribution of the oil globules, let us say, of the eggs of two species of fish, stops with just that difference? We are certain, are we not, that the formation of these globules is connected in some way with the metabolism of the egg? And this means that the truly living substance and vital processes of the egg are involved. So it becomes not only possible but highly probable that oil-drop differences between the eggs are indices of far more deep-seated differences.

And we must not fail to note that in addition to the probability of important correlations among these seemingly trivial morphological details through the metabolism (i.e., through the *chemical* processes) of the cell, correlations through the *physical* processes are also to be presumed in accordance with the conceptions of the cell justified by physical chemistry. The reader should recall the quotations from Hopkins on the conception of the cell as a system in equilibrium. But an additional statement from the same author will be especially germane at this point. Speaking of certain metaplasmic constituents of the cell, Hopkins writes: "These last comprise not only the fat droplets, glycogen, starch grains, aleurone grains, and the like, but other deposits not to be demonstrated histologically. They must be held, too,—a point which has not been sufficiently insisted upon, to comprise the diverse substances of smaller molecular weight and greater solubility which are present in the more fluid phases of the system—namely, the cell juices. It is important to remember that change in any one of these constituent phases, including the metaplasmic phases, must affect the equilibrium of the whole cell system, and because of this necessary equilibrium-relation it is difficult to say that any one of the constituent phases, such as we found *permanently* present in a living cell, even a metaplasmic phase, is less essential than any other to the 'life' of the cell, at least when we view it from the point of view of metabolism." [17]

Biology will sooner or later surely have to take seriously in hand this matter of the differences between organic species in all the stages of the lives of the individuals representing those species, the germ-cell stages with the rest. There is urgent need for the extension of ordinary taxonomic investigations to the entire ontogenetic series of organisms, the germ-cell stages included. Such work as that by Dr. Th. Mortensen on the comparative larval stages of echinoderms is in this direction and should be far more widely prosecuted than heretofore.

The classical systematic studies of Gustav Retzius on the spermatozoa of the animal kingdom are on the whole the most complete we have in this field; but it must be remembered that the differential attributes of species at this level are likely to have somewhat less correlational significance than similar attributes of the eggs, for the reason that the sperm-cells are more highly differentiated for their special environment and habits and offices. We may confidently predict extensive researches in the future on the taxonomy of germ-cells according to the frankly descriptive standpoint, and on the promorphology of germ-cells according to the morphological standpoint.

The term promorphology has usually been restricted to a very different use from that to which I have here put it, namely, to structural features of the ovum which influence the early stages of cell-division, and the shape, size, structure and so forth, of the "blastomeres," i.e., the product of the early egg-cell divisions. These phenomena have been considered more significant than the differences between eggs of different species above referred to, and have been investigated by embryologists rather than by systematists; and it is to a large extent on evidence from this source that the fact that the "egg is not one being and the embryo another and the adult a third, but the egg of a human being is a human being in the one-celled stage of development" [18] has gained theoretical interest.

Several of the most thoughtful embryologists who have investigated the earliest stages of numerous animals by the best modern methods have expressed views more or less like this, and so are in accord with zoologists who have been led to the comparative investigation of eggs by practical considerations.

A quotation from E. B. Wilson will serve well as a starting place for our inquiry as to what promorphology is in this restricted sense. "It is a remarkable fact," writes Wilson, "that in a very large number of cases a precise relation exists between the cleavage products and the adult parts to which they give rise; and this relation may often be traced back to the beginning of development, so that from the first division onward we are able to predict the exact future of every individual cell. In this regard the cleavage of the ovum often goes forward with a wonderful clocklike precision, giving the impression of a strictly ordered series in which every division plays a definite *rôle* and has a fixed relation to all that precedes and follows it. But more than this, the apparent predetermination of the embryo may often be traced still further back to the regions of the undivided and even unfertilized ovum." [19]

This preordination of the future animal in the egg before the beginning of development, strictly understood, about reaches its zenith among the insects. According to W. M. Wheeler, a French investigator, P. Hallez, states the matter thus with reference to the cockroach, water-beetle, and locust: "The egg-cell possesses the same orientation as the maternal organism that produces it: it has a cephalic pole and a caudal pole, a right side and a left side, a dorsal aspect and a ventral aspect; and these different aspects of the egg-cell coincide with the corresponding aspects of the embryo." [20] "My observations," Wheeler says, "based on some thirty different insects, accord perfectly with those of Hallez;" and he adds as details that the head end of the future embryo is usually marked by the micropyle and that the dorsal and ventral sides are foreshadowed by a slight flexure of the elongated egg in its longitundinal axis, the concave surface of the egg corresponding finally to the dorsal side of the embryo. To understand more specifically the meaning of this for the point under consideration, it is necessary to have in mind that such insect eggs as Wheeler is talking about are largely yolk, so far as bulk is concerned, and that the very young embryo arising from division of the protoplasmic part of the egg occupies but a relatively small portion of its whole surface. This small embryonal patch or blastoderm, after it begins to elongate and to show traces of the jointed body of the adult insect, is called the germ-band. "The practical value of Hallez' law," Wheeler says, "was shown in studying the *Xiphidium* [a locust] egg; all the movements of the germ-band could be at once referred to the axis of the mature embryo. When the eggs of other insects are oriented in the same manner, it is seen that the germ-band invariably arises on the ventral surface of the yolk with its procephaleum directed towards the cephalic, and its tail toward the caudal pole. No matter what positions it may subsequently assume, it always returns to its original position before hatching." [20]

This statement about the movements of the germ-band has reference to the fact that the actively developing part of the egg makes a series of remarkable journeys, as one might say, within and upon the rest of the egg, which consists mostly of yolk. In other words the topography and orientation of the very young insect are so far and so firmly established *before cell multiplication begins* that the details of cell splitting and cell movement and arrangement have seemingly little or no influence in determining these relations, but on the contrary, though going on for a time quite independently of such relations, are finally brought into conformity with them.

In another group of animals, those to which "pill bugs" and "sow bugs" belong, the eggs, like those of insects, contain a great quantity of yolk but the protoplasm is sharply separated into two portions, the one superficial and non-nucleated for a time, the other deeply imbedded in the yolk and nucleated. Only the centrally situated nucleated portion undergoes division at first. This division is so thoroughgoing that the resulting cells, the blastomeres, become widely separated from one another and scattered through the yolky part of the egg. Later these scattered blastomeres migrate into the surface patch of protoplasm and uniting with it form the blastoderm, the forerunner of the embryo proper. Investigating this mode of development, J. P. McMurrich emphasizes the fact that all details of cell-formation and migration and final arrangement have reference to structural peculiarities some of which are present before cell multiplication begins, while others pertain only to the later embryo. Both the direction taken by the spindle of the dividing nuclei, and the aggregation of the blastomeres in the surface layer of protoplasm are, says McMurrich, "simply precocious preparations for a differentiation which will later become pronounced; they refer to the final form of the embryo, and are instances of Sachs' law that growth determines division and not division growth." [21] And the author continues: "Each stage of the development appears to stand in relation not only to what has preceded it, but to what will succeed it, and is a link in a chain one end of which is lost in the obscurity of the past while the other stretches into the future." And still further: "We must, I believe, recognize the fact so forcibly discussed by Dr. Whitman in his lecture on the *Inadequacy of the Cell-Theory of Development* and so clearly shown by centrolecithal ova, that in embryological development the differentiation which occurs is a differentiation of the entire organism and not of the constituent parts or cells of which it is composed; physiologically, if not morphologically, every organism is a syncytium, and future theories of heredity must take this into consideration."

I will do no more in the way of comment than to call attention to the fact that the phrase "in embryological development the differentiation which occurs is a differentiation of the entire organism and not of the constituent parts or cells," is one way of expressing specifically my general proposition that the organism is an explanation of its parts or cells.

While the elementalist may admit himself compelled to grant that in animals having eggs of the type dealt with by Hallez, Wheeler and McMurrich, i.e., eggs of the insect type, the organism seems as much a causal explanation of the cells as the cells are a causal explanation of the organism, he will be likely to say that eggs of this type are rather the exception than the rule, taking the whole animal kingdom into account, and hence that the cases cited do not justify a sweeping generalization of the sort I am trying to establish as to the causal power of the whole over the parts in organic development.

We must consequently consider how this matter stands with animals generally. Attention may first be called to

Wilson's statement already quoted, that "it is a remarkable fact that in a very large number of cases a precise relation exists between the cleavage-products and the adult parts to which they give rise." [19] The frog's egg, one of the earliest and most persistently studied of all eggs, was long ago discovered to have certain features about it, even before cell-multiplication set in, that are adumbrative of the structural relations of the future embryo and adult. This was partly recognized, as Wilson points out, by Karl Ernst Von Baer, the "father of Embryology"; and the fact that the first division plane of this egg corresponds with the plane of symmetry of the adult frog was discovered more than a half century ago by George Newport.

Another group of animals in which promorphology in this restricted sense is quite as conspicuous as in the groups already mentioned is the mollusca. Especially noteworthy are molluscs of the octopus kind. A research in this field well known and much admired among embryologists is by S. Watase on the common squid. Wilson epitomizes Watase's results touching this matter as follows: "Here the form of the new-laid egg, before cleavage begins, distinctly foreshadows that of the embryonic body, and forms as it were a mould in which the whole development is cast." [22]

Watase's own statements are peculiarly instructive since, as is well known to biologists, he has been an extremist on what we might call the aggregative theory of the multicellular organism. The *fact* of a definite organization of the squid in the one-celled stage of its life he fully recognizes. This organization is, he says, such "that the plane of the first cleavage furrow may coincide with the plane of the median axis of the embryo, and the sundering of the protoplasmic material may take place into right and left, according to the pre-existing organization of the egg at the time of cleavage; and in another case the first cleavage may roughly correspond to the differentiation of the ectoderm and endoderm, also according to the pre-organized constitution of the protoplasmic materials of the ovum." [23] How is this organization of the squid before cell multiplication begins to be explained in accordance with the conception that the creature's cells are more fundamental than the creature itself and are the cause of the creature? Watase's radical elementalism made it almost obligatory upon him to try to answer the above question. Something of the difficulty which the protozoan colony theory of the higher organism has to face in such cases as this, he seems to have felt, and his way of meeting it certainly has the merit of being ingenious. "Even if we admit," he says, "that the unicellular ovum irrespective of its stages of growth, represents actually the condition of the ancestral protozoan, a highly differentiated axial symmetry of a certain metazoan ovum cannot be said to be an aberrant feature unrepresented in the ancestral protozoa, so long as the existing forms of the protozoa often show such a high degree of differentiation in that particular respect." [23] As though the high degree of axial differentiation in some protozoan imagined to be the far-away ancestor of a squid were an explanation of the axial differentiation of a squid in its unicellular stage! It is hardly possible for speculation to soar on less restrained wings than this and maintain its claim to being scientific.

So much by way of illustration of animal groups in which the promorphology consists in a considerable measure of observable differentiation while the individual animal is yet in the one-celled state, or, in other words, of animals in which the individual development has gone some distance in the egg before cell multiplication begins.

(c) *Reflections on a Promorphology of Germ-Cells Beyond the Limits of Visibility*

To make the generalization that the egg is an individual animal in the one-celled stage of its life, we have now to consider those animals in which the egg does not observably foreshadow the adult by any such axial or other differentiations as do those we have just been considering. Eggs of this sort, of which those of the sea-urchin and amphioxus are examples, are preëminently the ones called totipotent by Driesch. Reference to what was set forth in our discussion of totipotence will bring before the reader the fact that eggs of this kind look to be quite devoid of organization forecastive of the adult stage, but yet are so profoundly stamped in some way with the nature of the species that not only the undivided egg-cell may develop into an adult animal, but each of the first two or four or in some cases even eight blastomeres, may develop into complete animals if the blastomeres be entirely separated from one another.

All analogy of observable structure and development warrants us in believing two things as to the promorphology of these eggs; first, that there is some sort of organization characteristic of the species to which the particular animal belongs beyond the limits of our present knowledge, and second, that we have little or no means of predicting what that organization is. This second point is of much importance from its involvement of embryological speculations on the nature of the germ. The fundamental fact lost sight of in almost all these speculations is that the transformations and metamorphoses characteristic of all organic development are in their very essence unforeseeable. The history of biology, and especially of comparative embryology, is absolutely conclusive on this point. Over and over again has it happened that certain developmental stages in the life cycle of animals have been discovered before the complete series of stages were known, and that these stages were so different from the adult stages that the predictions made as to the species to which the stages belonged were entirely wrong. The larva of *Balanoglossus* is a famous instance of this in the history of zoology. This larva resembles the larva of enchinoderms so much that its discoverer believed it to belong to this group and for a long time zoologists accepted this view, the truth about it coming out only when the transformation of the larva into the adult was actually observed. For non-zoological readers it may be stated that Balanoglossus is a worm-like creature about as unlike a sea-urchin or a starfish as can be imagined. The truth is, it is only by *observational comparative* studies that embryologists are able to predict at all either the earlier or the later unobserved stages, pertaining to the developmental career of an animal.

If speculation on the nature of germ-cells had followed consistently these familiar and universal principles, the literature of biology would be unburdened to-day of a vast load of useless writings. Let any biologist ordinarily practiced in the methods of embryology ask himself candidly what he would expect to find in the living fertilized egg of a starfish, for instance, were some manufacturer of microscopes to furnish him with an instrument that would magnify with good definition to a million diameters. Can he consistently suppose he would see something "carrying" all the innumerable characters of the adult starfish? Why has he any more right to suppose he would recognize the characters of the adult in the germ-cell than that he can recognize them in the larva just before metamorphosis, or in any other stage? Yet what embryologist has ever talked about the characters of the adult starfish being "carried" by elements of the larva? What we are justified in believing on the basis of the inductive evidence in our possession is that such a microscope would enable us to recognize many structural features peculiar to the particular species of starfish at that particular stage of the individual's life, and that as development proceeded these egg-stage features or characters would disappear and other characters distinctive of the embryonal stage, the larval stage, and so on, would appear in regular succession till the adult stage with its distinctive characters were reached. The great point to be emphasized is that if we are guided strictly by the observational and rational methods by which all our knowledge of organic development has been built up, we see that the effort to conceive germ-cell promorphology or prophysiology in terms of representative units succeeds only in so far as we deceive ourselves into believing that we know what we do not know, and probably never can know, about the structure and functions of the germ, and by thus deceiving ourselves, believe ourselves relieved of the necessity of endeavoring to learn what the actual structure and function of the germ is.

The metaphysical promorphology and prophysiology of the germ which, culminating in the "determinants" of Weismann, have befuddled the thinking of many biologists, hold exactly the same place in the logic of biology that phlogiston held for well nigh a century in the logic of chemistry. There is surely something in the wood that is a cause of the flame, so why not say the characters of the flame are "carried" in the wood by units capable of doing that sort of thing? And how easy and complete the explanation of flame would be on that basis! For minds of such cast as that of Joseph Priestley (about the last ardent defender of phlogiston) and as those of Weismann and his disciples, explanations of this sort appear to have great fascination.

It is probably implied, if not definitely contended, by some present-day geneticists, that the methods of analysis employed by them, those, namely, of experimental breeding, the application of Mendelian principles of inheritance, and the correlation of these with chromosomal studies, are a refutation of the conceptions above set forth. As a matter of fact, though, the results of genetical analysis, so far as they are *objective and not purely speculative*, are entirely confirmatory of the conceptions.

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Chapter IX

ORGANISMS CONSISTING OF ONE CELL

A. ADULT FORM AND STRUCTURE

Remarks on the Conception of the Cell as an Elementary Organism

WE saw early in the chapter on The Organism and its Cells that the cell may be advantageously looked upon as an "elementary organism." The warrantableness of thus regarding it as set forth by Carl Brücke, who first clearly reached the perception, should be recalled. This conception is warranted, Brücke said, by the fact that the cell possesses an organization of another sort than that pertaining to its molecular structure. While we may not subscribe to the implication of his doctrine that the cell has an organization wholly independent of its molecular structure, yet we must endorse his conception that it has a structure genuinely unique as contrasted with that of any non-living body; and must reckon the perception of this fact as a forward step of first rate importance in biology.

While we are now to devote a chapter to an inquiry into that peculiar structure of the cell which justifies us in viewing it as an *elementary organism*, we should recognize that this discussion falls properly under the general head of cell-theory taken in the comprehensive sense indicated in chapter six. As there defined the cell-theory concerns itself with the structure of the cell as well as with the participation of cells in the make-up of multicellular organisms. It is only for the didactic purpose of making this part of the theory stand out in the discussion with a prominence proportionate to its importance that we give it independent titular recognition. So our present discussion will intersect at various points the discussion of the Cell-Theory specifically. The first intersection is at the place where we brought out the fact that the conception "organism" is historically prior to "cell," and hence, that in reaching the conception of the cell as an elementary organism, Brücke and those who followed him have literally used the organism to explain the cell. We must now push this idea further in both its logical and its factual aspects.

First as to the logic of it. When we state that the cell is an elementary organism, we are speaking in the technical language of logic, recognizing the cell as a species of the genus organism. An *elementary organism* is obviously *one kind* of organism, the implication being unescapable that there are other kinds; one other kind implied being a not-elementary, that is, a more complex kind. Organism is a broader and higher category than elementary organism, another designation for cell. From the natural history standpoint, then, Haldane's efforts to raise organism to the dignity of a category in the Kantian sense are superfluous, this having already been done in the real sense through the establishment by Brücke and the acceptance by biologists generally of *elementary organism* as a defining designation for cell. This aspect of the logic of the cell-theory is of so much practical importance that it is desirable to state it more definitely if possible.

The term cell now universally accepted in biological terminology is a *general name* applicable to a vast class of natural objects, the name having become fully established and defined after years of patient examination and description by many investigators, extending to the whole range of objects brought under the designation. If one reflects on all this he will see a vast difference of meaning in the word *cell* when used in the two assertions: "this object under the microscope is a cell," and such generalizations as "the key to all ultimate biological problems must be sought in the cell." In the first case the term performs the comparatively simple office of a name for a particular object, endowed, as one might say, with great ability to make intelligible certain phenomena of living beings.

Undoubtedly the name stands for an idea in both cases, and undoubtedly too, the ideas in the two cases must have something in common, but equally certain is it that there are important elements of difference in the two ideas. Of the elements in common, one, we know very well, relates to certain structural features, cytoplasm, nucleus, and so on, experimentally settled upon as essential to any object entitled to be called a cell. Another is the conception that all bodies so entitled are a kind of organism, i.e., elementary organism, this conception being based on the observation that great numbers of cells are, in the language of O. Hertwig, "endowed with the attributes of life." Now notice: by virtue of what is the cell conceived to be the key to all biological problems? Surely not in the mere presence in it of bodies that may be called nucleus, cytoplasm, and so forth, but rather because it is endowed with the attributes of life, is an organism, even though of an elementary character. In other words, since typical cells are universally admitted to be very simple in structure as contrasted with those bodies to which the term *organism* was first applied, and since it is now only one among such bodies, and that an elementary and simple one, to assert that it is the "key to all biological phenomena" is a logical contradiction, if by being the "key" it is implied that the cell is an ultimate explanation of such phenomena, for with such an implication the assertion is virtually that part of a thing is greater than the whole of it.

Comparison of the Structure of Organisms Consisting of a Single Cell with That of Organisms Consisting of Many Cells

This chapter will be concerned primarily with the factual side of the structure of the cell viewed as a species of organism, and will confine itself to the structure of the cell in organisms indubitably such in the strict sense, even though they ordinarily consist of but a single cell.

The narrowing influence of elementalism in biology finds striking illustration in the application of the cell-doctrine to unicellular organisms, that is, to the protozoa and the protophyta, or collectively, the protista. In fact, if one wishes to bring before him in the clearest possible fashion the contrast between what a great province of living nature is when seen as it actually is and when seen through the medium of elementalist theory let him compare some of the great modern objective treatises on the protozoa, like Brady's report on the Foraminifera and Haeckel's on the Radiolaria, in the Zoology of the Challenger Expedition, or Haecker's *Tiefsee Radiolarien*, in *Wissenschaftliche Ergebnisse der deutschen Tiefsee-Expedition,* with the statements one finds in ordinary text books of zoology concerning the same organisms. Hardly anything could be more misleading than the almost universal practice in elementary teaching of introducing beginners to the protozoa by showing, very superficially, an amoeba and emphasizing its simplicity, and then keeping it in the foreground of the learner's thought as an exemplification of the doctrine that the protozoa are "extremely simple" animals, that they are undifferentiated into organs and tissues—that in fact they are hardly "true animals" at all. In even so advanced and usually excellent a work as Lang's *Lehrbuch der vergleichenden Anatomie* we are told that the metazoa or "true animals" (*echte Tiere*) are "set over against the protozoa or pro-

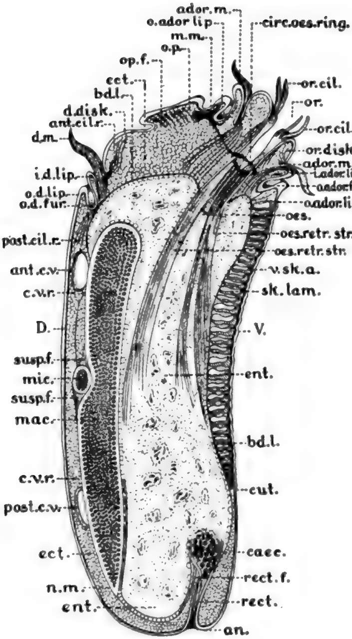

FIGURE 1. DIPLODINIUM (AFTER SHARP).

ador.m., adoral membranelles. an., anus. ant.cil.r., anterior ciliary roots. ant.c.v., anterior contractile vacuole. bd.l., boundary layer (ectoplasmic). cir.oes.r., circumesophageal ring. caec., caecum. cut., cuticle. c.v.r., region about contractile vacuole. D., dorsal side of body. d.disk, dorsal disk. d.furrow, dorsal furrow. d.m.str., dorsal motor strand. d.m., dorsal membranelles. ect., ectoplasm. ent., entoplasm. fd.v., food vacuoles. i.ador.lip, inner adoral lip. i.d.lip, inner dorsal lip. L., left side of body. l.sk.a., left skeletal area. mac., macronucleus. mic., micronucleus. m.m., motor mass (motorium). o.ador.fur., outer adoral furrow. o.ador.lip, outer adoral lip. o.d.fur., outer dorsal furrow. o.d.lip, outer dorsal lip. oes., oesophagus or cytopharynx. oes.f., oesophageal fibers. oes.-retr.str., oesophageal retractor strands. op., operculum. op.f., opercular fibers. or., oral opening, mouth, or cytostome. or.cil., oral cilia. or.disk., oral disk. post.cil.r., posterior ciliary roots. post.c.v., posterior contractile vacuole. R., right side of the body. rect., rectum. rect.f., rectal fibers. r.sk.a., right skeletal area. sk.lam., skeletal laminæ. susp.f., suspensory fibers. V, ventral side of body. v.sk.a., ventral skeletal area. n.m., nuclear membrane.

tista,"[1] the implication being that the protozoa are not "true animals." "Organless organisms" is an appellation one not infrequently finds applied to protozoa.

(*a*) *Comparison of Certain Ciliates and Metazoans*

By way of introduction to the commentary I wish to make on this mode of thinking, I ask the reader to compare the pictures, figures 1 and 2, keeping the idea of cell as much

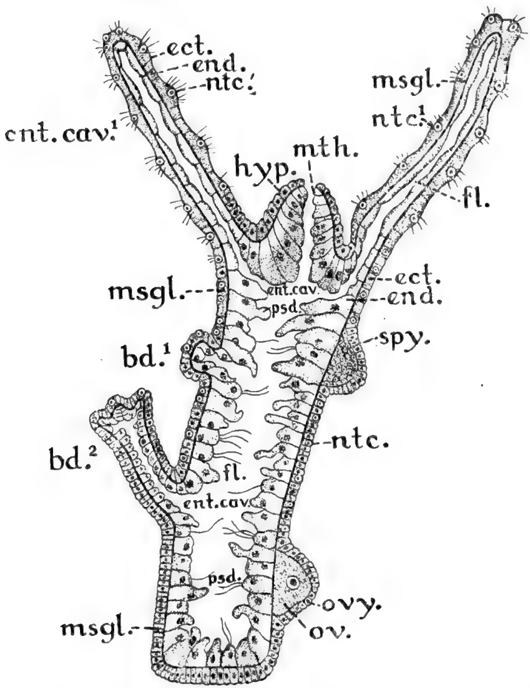

FIGURE 2. HYDRA (AFTER PARKER AND PARKER).
ect., ectoderm. end., endoderm. ent.cav., enteric cavity. mth., mouth. hyp., hypostome. msgl., mesogloea. ntc., nematocysts. psd., pseudopods. fl., flagella. bd., buds. spy., spermary. ovy., ovary. ov., ovum.

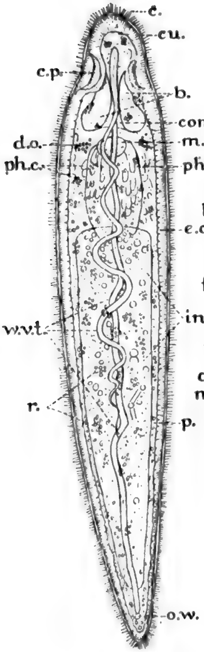

FIGURE 4

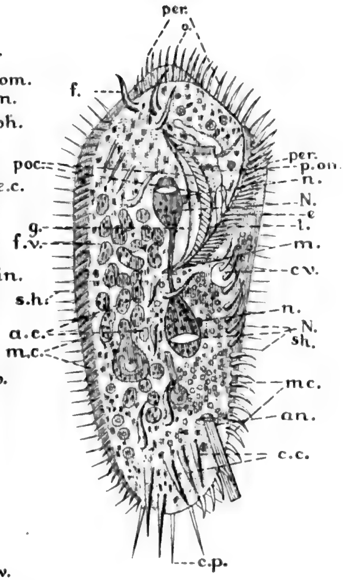

FIGURE 3

FIGURE 4. STENOSTOMA LEUCOPS (AFTER OTT).

c., cilia. c.p., ciliated pits. cu., cuticula. b., brain. com., brain commissure. d.o., dish-shaped organs. m., mouth. ph., pharynx ph.c., pharyngeal cells. e.c., epithelial cells. in., intestine. w.v.t., water vascular tube. r., rods. p., parenchyme. o.w., external opening of water vascular tube.

FIGURE 3. STYLONYCHIA MYTILUS (FROM HARTOG, AFTER LANG).

a.c., abdominal cirrhi. an., anus discharging the shell of a Diatom. c.c., caudal cirrhi. c.p., dorsal cirrhi. cv., contractile vacuole. e., part of its replenishing canal. f.c., frontal cirrhi. f.v., food vacuoles. g., internal undulating membrane. l., lip. m., mouth or pharynx. mc., marginal cirrhi. N., N., lobes of meganucleus. n, n, micronuclei. o., anterior end. per., adoral membranellæ. poc., preoral cilia. p.om., preoral undulating membrane. s.h., sense hairs.

in the background of consciousness as though he had before him for comparison a cat and a hen, for instance. Do the figures give the impression that one presents a very simple animal while the other represents a very complex one? Which, may well be asked, is the very simple one? Does one give the impression that it represents an organless animal, while the other represents an animal with organs? Does one seem organized while the other is unorganized? Does one look like a true animal while the other is an untrue or pseudo-animal? Yet there is now unanimity among zoologists that the creature represented by figure 1 is a protozoan, while that represented by figure 2 is a metazoan. The protozoan shown is a species of Ciliate which inhabits the stomach of the ox. Its techincal name is *Diplodinium ecaudatum.* The figure is from R. G. Sharp. Figure 2 is of the common fresh water hydra.

Or compare in detail a *Stylonychia*, a protozoan, with a *Stenostoma*, a worm. For the former, the description and figure of *Stylonychia mytilus*, figure 3, given by Hartog in the Cambridge Natural History will serve our purpose well. A good description of a *Stenostoma*, figure 4, is furnished by Ott. A rough and ready way of estimating the degree of complexity of the two animals is to notice the number of named parts or organs in the two descriptions, presumably intended to be about equally thorough.

The activities of these two species have also been well studied, so they can be compared from this as well as from the anatomical standpoint. To any one who has watched both creatures somewhat attentively in their normal lives, the great animation and diversity of movement of the protozoan as contrasted with that of the metazoan are striking enough. Concerning the general character of the movements of *Stylonychia*, Hartog writes, "It moves through the water either by continuous swimming or by jerks, and can either crawl steadily over the surface of a solid or an air surface such as an air bubble, or advance by springs, which recall those of a hunting spider." [2] The rapid movement ahead, running against obstacles, backing off, changing directions, and turning around, remind one of the performances of an ant under similar surroundings. Jennings' statement that they are "usually found running about on the bottom, or on the surface of objects in the water," [3] is no more a figure of speech than would be a similar remark about a rabbit.*

FIGURE 5. STYLONYCHIA MYTILUS (AFTER PÜTTER).

With reference to their food habits, Maupas's characterization of them as "hunter ciliates," is truly descriptive.

By contrast the movements of *Stenostoma* are slow and simple indeed. In it locomotion is accomplished almost entirely by surface cilia, and the well-nigh complete absence of differentiation among these, as contrasted with the high degree of differentiation and specialization of the cilia of *Stylonychia*, may be taken as a reliable index to the difference in locomotor activities of the two creatures.

(*b*) *Comparison of a Radiolarian and a Jelly-fish*

Carrying the comparison of unicellular, "simple" or "untrue" animals, with multicellular, "complex," "true," animals still farther, we will take up a Radiolarian for brief consideration. Non-technical readers are particularly urged to look through the volume of 140 quarto plates which illustrate Haeckel's great Challenger Report on this group.

* Jennings copies this diagram from Pütter showing a *Stylonychia* "creeping along the surface," which shows well the "belly" and the "back" sides of the creature and the way in which it uses its cilia as legs.

Nearly all large libraries have sets of the reports of this famous exploring expedition.

So astounding was the wealth of life both as to number of species and elaborateness of structure of the individuals described and depicted in this report, that many zoologists who had been properly impressed in their formal training with the doctrine of the simplicity and minuteness of the protozoa, were disposed for a long time to accept the report with some "grains of salt"—to suspect that many of the specially remarkable species were, partly at least, creatures of the lively imaginations of Haeckel and his artist. But later researches, particularly those of V. Haecker, already mentioned, on the same animals collected on the cruise of the *Valdivia*, of the German Deep-Sea Expedition, have driven away all shadows of doubt about the essential truthfulness of Haeckel's narrations. Indeed, we now know, if anything, he fell short of full justice to the Radiolarians.

I take this opportunity to remark that one of the serious, even though perhaps unavoidable, defects of formal instruction in elementary zoology and botany is the tendency to fix in the learner's mind the notion that nature is far more simple than it really is. Of course, the only right antidote for this falsification is contact with nature itself in its plenitude. But since school books and school lessons are mainly responsible for the wrong inculcuations, on the principle that like cures like, books again, though this time of the elaborate monographic sort, even though no more than hastily run through, ought to be of considerable use to young students. Quite as much with the hope of sending the reader to Haeckel's or one of the other great monographs on the Radiolaria, as for the purpose of impressing him with the elaborateness of organization of these animals, I will refer specifically to a section of Haeckel's Report.

One entire new family discovered in the Challenger's collections, Haeckel named *Medusetta*. The author gives us the reason for the choice of this name: "Some species are among the most admirable forms of Radiolaria, and are similar to small elegant *Medusae*. The form of the shell exhibits the same varieties as the similar umbrella of the Medusa. . . . The similarity with the umbrella of a Medusa is so great, that in many species the large lower opening on the mouth of the shell is surrounded by a prominent ring or diaphragm, comparable to the velum of the Craspedotae or Hydromedusae." [4] This general resemblance to certain medusae is made still more striking in such a species as *Gazelletta crytonema* by the phaeodium, a mass of cell-like pigment-bearing structures "in the lower half of the shell cavity," [5] sometimes, as in the figure referred to, protruding from the mouth of the shell. No one can compare this figure with those of various medusae which bear gonads or buds on the manubrium or the subumbrellar region without being struck by the general resemblance between them.

The reader must not infer from this comparison that the points of resemblance signify anything like close correspondence in structure. As a matter of fact the two animals are no more alike than a bat and a butterfly. The sole point of significance, so far at least as this discussion is concerned, is that judged by the facts of actual structure and function of the radiolarian and the coelenterate, the first is hardly if at all more simple than the second—is not a whit less a true animal.

(*c*) *Comparison of the Shell of a Rhizopod and of a Nautilus*

One more comparison between a "simple" unicellular animal and a complex multicellular "true" animal is as far as we can go in the strictly comparative-anatomy part of this presentation. Take, for example, the shell of *Operculina*, the detailed structure of which was worked out by W. B. Carpenter. Some of the schematic figures in his work are reproduced in many of the larger textbooks and handbooks, Bütschli in particular giving specially good figures. The remarkable resemblance of the shell of this and of allied genera to the shell of the chambered nautilus has long been a common subject of remark. According to the prevalent view, although the variety and complexity of the shells of great numbers of foraminiferae are universally recognized, they do not militate against the conception of the animals as "simple," because they are only secretory structures, or in many groups only structures built up from foreign substances. But what right have we, I ask, to assume but slight protoplasmic differentiation in a creature that can produce in any way whatever such a system of chambers and septa and canals and pores, as is presented by the shell of *Operculina?* This query becomes particularly searching when one considers that each of the various genera and species has its own type of shell.

In his *Monograph of the Foraminifera of the North Pacific Ocean* Dr. J. A. Cushman remarks that being single-celled animals, the structures of the Foraminifera "do not need explanation on the basis of organs and tissues." [6] This naive manner of dodging difficulties is characteristic of elementalist notions about explanation—the method of making an implied theoretical definition take the place of searching examination. The particular difficulty evaded by definition in this case pertains to the nature of the outer portion of the protoplasm or sarcode, which constitutes so large a fraction of the living body of both the Foraminifera and the Rhizopoda. As is well known, the sarcode produces the shell either by secretion or by the selection and placement of foreign particles. In many Foraminifera, as *Operculina*, the sarcode extends over the whole exterior of the shell, thus making the shell an internal structure. The highly elaborate canal and pore systems above referred to are passage-ways for the semi-fluid sarcode.

Intimately connected with the network of sarcode situated within the substance of the shell and on its surface is the wonderful pseudopodial system, i.e., the system of innumerable filamentous, anastomosing, expanding, withdrawing, and shifting strands of living material. As is well known, at least for many Rhizopoda, the pseudopodial system is nutritional in function. First of all, the pseudopodia are prehensile organs and operate in much the same way and apparently with as great effectiveness as the corresponding organs of higher animals. By means of them the animals seize their prey consisting of living micro-organisms. In some species the seizure is accompanied by a stunning and paralyzing action. After capture the food is, in many species, transported by the grasping organs through the mouth of the shell and into the deeper portions of the sarcode there to undergo digestion. But in some groups the nutritional office of the pseudopodial system goes much farther than the mere procurement of food. Digestion, and so of necessity circulation in part, are performed by the same system. Calkins [7] mentions the Reticularia particularly as Rhizopods whose digestion is thus performed. What could be more far-fetched and distracting of attention from the true nature of the animals, than to call organs that perform all these functions "feet," false feet, or feet of any other kind?

The locomotor appendages of many animals are brought into the service of the nutritive function; and in such animals, as many of the Crustacea, where this change of function has gone so far as to divert the organs entirely from their original office and transform them both structurally and functionally into mouthparts, comparative anatomists never think of still lumping them all together as locomotor organs. In no higher animal whatever, so far as I know, has conversion of the locomotor into nutritional organs gone so far as to make them not only food-seizing but fooddigesting, as is the case in the Reticularia. Consistency in descriptive treatment and clear thinking demand that the sarcode processes of those protozoans in which the structures are wholly or even chiefly nutritive in function should no longer be called pseudopodia. Some such term as *trophorhiza* ought to be applied to them, especially where, as in the Reticularia, they are digestive. Whether or not the structures "need explanation on the basis of organs and tissues," they certainly need description and definition that shall set forth their true nature. Fortunately considerable study has been devoted to them and the rest of the peripheral sarcode in the Rhizopods, and to the extra-capsular sarcode of the Radiolaria, so we already know much about the facts.

Calkins [8] has well summarized the information we possess concerning the "pseudopodia" of Sarcodina. From this knowledge we are able to say with the greatest assurance that these creatures lead their lives—maintain their locus in space, whether of fixity or movement, respond to external stimuli, procure, ingest, digest, and assimilate their food, solid and gaseous, and propagate their kind—no less definitely and hardly less variedly than the larger multicellular animals. All these things they do through the instrumentality of definite and definable anatomical elements; and I would insist that we can justify the refusal to call these elements organs and tissues because they occur within the limits of single cells only by having first so defined *organ* and *tissue* as to exclude from them all organic elements not composed of cells.

The Unjustifiable Conception that Unicellular Organisms Can Have No Tissues

As a matter of fact this illogical course is exactly the one that is widely followed. "A tissue is, therefore, a complex of similarly differentiated cells." [9] This definition of tissues, occurring in one of the most generally used text-books of miscroscopical anatomy, turns up in substance again and again in the common instructional writings of the day. "The foundation-stone of the tissue is the cell." [10] According to this doctrine the cell is the building-stone of the tissue, so no matter what may be found within the cell, it cannot be a tissue. Undoubtedly this way of treating the term tissue has been useful, especially didactically, and undoubtedly too it is on the whole justified so far as multi-cellular organisms are concerned, though even here the scientifically scrupulous teacher finds himself under the necessity of doing much uncomfortable wriggling to make many of the connective tissues fit into it. But when the view is extended to the whole animal kingdom, to the protozoa as well as to the metazoa, one sees how inadequate and cramping such a conception of tissue is.

The fact is, when we consider the real meaning of the word *tissue*, and still further, when we consider what the anatomical parts are to which the early anatomists thought the term could be appropriately applied, we see that with the possible exception of some of the connective tissues of the higher animals, we can hardly point to a more typical tissue than that of the network of strands into which the peripheral sarcode of many of the Rhizopods forms itself, or than the extra-capsular "plasm" of a Radiolarian like *Thalassicolla*. I mention this genus especially because a species of it which has been well figured and described by Haeckel, is frequently used in text-books as a type of the group. The "meshes constituting the *sarcodictyum*," the "alveoli of the *calymma*," and the pseudopodia arising in the deep zone, or *sarcomatrix* and "forming a network through the other capsular parts," are the terms in which the "plasm" of these animals is described. And notice how contrary to good biological usage it is to employ an anatomical nomenclature which starts out by calling the major parts of the body of this organism "plasm," and then names all the details of organization in keeping with this. It would be quite as consistent and quite as useful to call all that part of a fish, for example, situated outside the viscera "extra-visceral *plasm*," and then name the skin, bones and muscles "dermoplasm," "osteoplasm," "myoplasm."

True Organs in Some Protozoans

But objectionable as is the usual treatment of the term *tissue* when viewed from the standpoint of a theoretical biology that is adequate and generous, even more objectionable is the treatment of the term organ. What could be more absurd than to contend that an animal like *Diplodinium* (see figure 1) has no true organs, while one like *Stenostomum*, figure 4, has such organs! No zoologist who becomes so interested in any of the higher protozoa as to rise above the theoretical notions into which he may have been schooled as to what an organ is, hesitates to call many of the parts of these creatures organs. Thus speaking of his discovery of what he regards as functionally a supporting apparatus for the gullet in an infusorian related to *Diplodinium*, A. Günther says: "I have found an organ lying in the ectoplasm. . . ."[11] Sharp's excellent description and illustrations of this organ (or these organs, for there are three of them) in *Diplodinium*, establish its indubitable right to be called *an organ*.

Both historically and biologically there are two criteria for an organ. One, the more important, is that a part shall perform a definite office or function in the economy of the organism; the other, that it shall be composed of definite elements to which usually the term *tissues* may be applied. As to how the organ in question of *Diplodinium* measures up to these criteria, we will let Sharp tell us. Concerning the first he writes "That the above described structure functions as a true skelatal (supporting) structure, not only for the retractile oesophagus, but also for the entire body, seems altogether certain."[12] The illustration shows something as to its composition (figure 1 *sk. lam.*, indicating skeletal laminæ). It is composed of plates or laminæ, running lengthwise of the organ, and placed edgewise relative to the surface of the creature. This organ is said to be the most rigid and brittle of any in the animal, and is conjectured to contain silicic acid. One does well to note the section headings of Sharp's description: "Organs of Locomotion,"[13] "Organs of Food-taking,"[14] "Organs of Defecation,"[15] "Organs of Erection."[16] An examination of figure 1 by the aid of letterings accompanying it, will give the reader some idea about each of these sets of organs.

One of these organ systems must be attended to more specifically. It is called by Sharp the *neuromotor apparatus* (labelled in the figure *m.m.* and *circ. oes. ring*). The discovery of this remarkable system may well be regarded as epochal in the history of knowledge of the protozoa, for it seems to indicate the presence of a nervous system in the higher members of this great subdivision of the animal kingdom no whit less well differentiated and elaborate than in some of the metazoa and that by no means the lowest of them. "This apparatus," says Sharp, "consists of a central motor mass or motorium, from which definite strands radiate: one to the roots of the dorsal membranelles (dorsal motor strand); one to the roots of the adoral membranelles (ventral motor strand); one to the circumoespohageal ring (circumoesophageal ring strand); and several pass out into the ectoplasm of the operculum (opercular fibers). Each of these strands may send off one or more branches. In the walls of the oesophagus, both nervous and contractile fibers may be distinguished."[17]

A True Nervous System Probably Present in Some Protozoa

Should further investigations confirm these discoveries, as one may predict they will, nothing but purely speculative considerations can restrain comparative anatomists from putting the nervous system of the Diplodinium type alongside that of some worms, so far as structural elaborateness and functional effectiveness are concerned. Of course there can be no possibility of homology between the two types, if the term homology be used with the meaning generally attached to it in comparative morphology.

If the possession by a protozoan of a nervous system thus elaborate should be fully established, the fact would have far-reaching consequences on our theories about these animals. A few remarks are therefore in order as to the probable general correctness of Sharp's observations. In the first place, Mr. Sharp's statement, "Whatever there may be of merit in the methods used and the results so far obtained, is due to the kindly and helpful suggestions and interest of Professor Kofoid, under whose direction the work has been done," [18] should be noticed. It may be taken for granted, I presume, that Professor Kofoid's wide knowledge of the protista, and his long experience in the technique of such research as that here involved constitute a weighty guarantee for the trustworthiness of the results. The general "internal evidence" of carefulness, for which well-practiced biologists come to have so keen an eye, will, I think, be recognized by all who read Mr. Sharp's memoir. From the morphological side, the point most open to question is that of the trustworthiness of the differential action of the stains used. A modification of Mallory's connective tissue stain seems to have been Sharp's main reliance, and it is unfortunate that he does not inform us how this affects fibers positively known to be nervous. Furthermore, it must be remarked that the seeming identity of staining of this system and the micronucleus does not fall in very well with accepted views touching the general character of these two kinds of substance in the metazoa. But the general anatomy of the system, and its relation to other organs undoubtedly favor the belief that it is nervous. "All parts," says Sharp, "connected with the neuromotor system act in perfect co-ordination." [19] And it should be said that this assertion was based on attentive study of the living animals. "In watching these phenomena of retraction and expansion in the living, active animals one cannot help but be impressed with the wonderful co-ordination of parts." [20]

The idea that neural elements occur in the protozoa is, as is well known, not new. The most definite report to this effect previously made, is that by Neresheimer. This author describes fibers in *Stentor* running parallel with and in general accompanying the myonemes. He believes these to be nervous and calls them neurophanes. The observation has not been confirmed so far as I am aware; and one observer, O. Schröder, believes that Neresheimer is in error as to the existence of any such fibers in these animals. Neresheimer's, and particularly Sharp's, reports will undoubtedly call forth renewed studies in this important field.

A More Critical Examination of the Term "Organ"

The parts of the protozoa occupied with determining the creature's place in space are perhaps those to which the application of the term organ is avoided with greatest difficulty. "In the majority of Protozoa," says Calkins, "movement is accomplished by the activity of special motor organs, which may be either changeable processes (pseudopodia) or permanent vibratile appendages (flagella and cilia)." [21] This is a favorable place to remark on the justifiability of calling pseudopodia (and other transitory cell parts for that matter) organs. Science demands consistency. There are many transitory structures among multicellular organisms notably connected with reproduction, for example the hectocotylized arms of some cephalopods, which we never hesitate to call organs. And taking the animal kingdom as a whole, think of the innumerable organs occurring in the embryonal and larval lives of animals; for instance the placenta in mammals and the gills of frogs in the tadpole stage. No one hesitates to call these "organs" because they are transient. As long as this is so, we cannot consistently let the transitoriness of cell parts stand in the way of calling them organs.

"The cilia and the stalk (of *Vorticella*) are definite, permanent organs, the first of the kind we have met with." [22] One can justify the use of the term organ as applied to the Protozoan by quoting indefinitely from practical writings by the best authorities. Yet when we come upon definitions of "organ" framed to meet the needs of cellular elementalism, we find that the practice above referred to would be illegitimate. Some of these definitions are wonderfully naive. Take this from the *Handwörterbuch der Naturwissenschaften*, under the heading "Organs of the Animal Body." "By *organ* we understand, in accordance with the original sense of the word *organon* (*Werkzeug*, instrument) any body-part, either internal or external of a multicellular living being, (*Lebewesen*) such part being of regular form, regular position, and definite, intimate, histological structure, and having to perform instrumentally a special function or operation in behalf of the living individual as a whole, this whole being designated an organism because composed of such organs," etc.

The naiveness here displayed lies in the recognition of the term *organ* as going back in use and meaning to the ancient Greeks, and in the same breath restricting its application to multicellular organisms. When Aristotle recognized that "each sense is confined to a single order of sensibles, and its organ must be such as to admit the action of that kind or order," and went on to point out that the organs must be "heterogeneous," (that is, as later anatomy came to say, composed of tissues); and when William Harvey spoke of the heart as an organ and described its shape, structure, blood capacity, density and movements, and the passage of the blood through it, beyond a shadow of doubt these men had a perfectly clear conception of the most essential attributes of an organ, though of course they knew nothing about cells. And does any one believe that had they seen the locomotor parts, let us say, or the mouth of *Diplodinium*, they would have hesitated, though still wholly ignorant of cells, to call these parts organs, doing so on the same basis on which they had called the sensory parts and the heart of larger animals organs? Can any one either fail to see the point or refuse to admit the validity of the argument?

The term organ stands for certain kinds of natural objects. First and foremost these objects are definite parts of an organism; definite that is, in that they have a certain form and character of their own, perform definite offices in the economy of the organism as a totality, and are in turn composed of definite elements. Thus understood the term has had a place in the science of living beings for centuries, as we have just seen. How now, has the advance of knowledge affected the earlier understanding of the nature of organs? Undoubtedly it has expanded that understanding in a number of directions; it has made it *fuller*. One of the directions of enlargement pertains to the composition of the organs. It is found that for a large part of the organic world, namely the *multi*cellular animals and plants, the elements of the organs are *tissues*, all of which are derived from still another kind of elements, namely *cells*.

The discovery of cells has greatly enriched and clarified the *definition* of the term organ; but there is no shadow of right in the view that the discovery has at the same time narrowed the *application* of the term. As the preceding discussion shows, historically, logically, and biologically, the mouth or the locomotor appendages of a protozoan have exactly the same right to be called organs as have the same parts of a metazoan. The dodging in this matter, as seen for example in the proposal to keep the organs of the protozoa quite apart from those of the metazoa, by calling them "organelles," "organoids," "cyto-" one-thing-and-another, is indefensible so far as animals themselves are concerned. And no one should wish to minimize the importance of the point at issue by imagining the question to be merely one of terminology—of what the objects dealt with shall be named. That this is by no means all there is to it may be discovered by noticing the warmth with which a genuine cellular elementalist will come to the defence of his terminology when its legitimacy is seriously questioned. The truth is, and let us not miss it, behind this "mere matter of terms" there is in hiding the scientifically reprehensible practice of trying to disguise or obscure *facts* in the interest of a *theory*. And the practice entails, as the defence of false theories always entails, contradictions and obscurations of all sorts. To illustrate, it is said by cellologists that a protozoan's mouth must not be called a mouth but a cytostome because being *in* a cell and not *composed of* cells it is only analogous, but not homologous with the metazoan or "true" mouth. From which it follows by clear inference that all metazoan mouths are homologous, those of a lobster and of a dog, for example! But the anatomical absurdity of the situation is easily met by those who are committed to the defence of the theory regardless of facts, by simply pointing out that the mouths of a lobster and a dog are homologous just because they are both multicellular. If one wishes to prove that no wooden building is a true house, he can do this to his satisfaction, if his mind works that way, by defining house as a building which must be composed of brick or of stone.

More Detailed Examination of the Anatomy of Higher Protozoa

In behalf of the treatment of reproduction and heredity which will engage us later on, we must now extend our acquaintance with the finer structure of some of the more highly developed protozoa. *Stylonychia*, about which something has already been said, may be the first object of closer scrutiny. Pütter, who has given special attention to the activities of many protista, remarks, "One may take a hypotrichous infusorian (*Stylonychia* being typical) as an example of the highest complication of body-form which a single cell is able to reach, for in addition to differentiation into dorsal and ventral sides and the very complicated form of the periphery, we find no less than six different groups of cilia." [23]

Pütter's representation of a side view of *Stylonychia mytilus*, copied in various books and shown in figure 5, illustrates his statement. He describes in detail the movements of the cilia in crawling; and from all this and from what others have written on the subject, it is entirely permissible to call these main cilia limbs or legs. The elaborate system of fibers connecting and coordinating these limbs will be spoken of in a later section. The statement by Pütter about the extent of complication of body possible in a single cell prompts one to wonder, in view of the elaborateness of these animals, whether the limits of possibility of structural differentiation is much narrower for single-celled than for many-celled animals. In none of the metazoa, excepting the arthropoda and higher vertebrata, do we find a more highly differentiated, and, seemingly, integrated system of locomotor organs than in *Stylonychia* and its congeners.

Figure 6 shows numerous details of the system of external organs of *Stylonychia histrio.* The figure was made from a section of the peristomal field. Special attention is called to the finely striated appearance of the membranellae, *m l,* and the

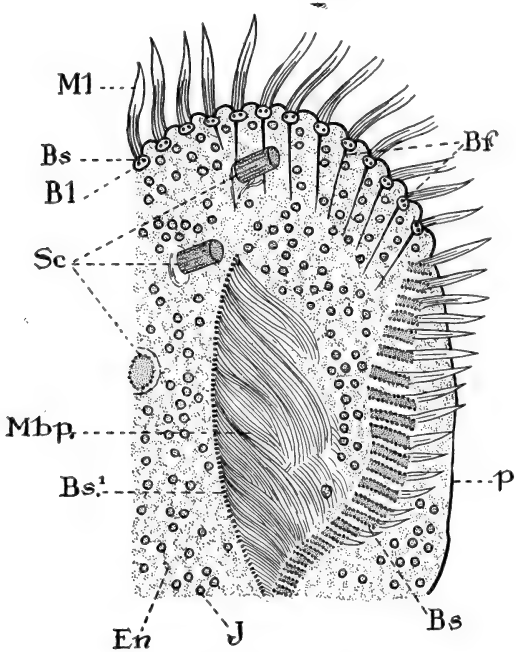

FIGURE 6. STYLONYCHIA HISTRIO (AFTER MAIER).
Mbp., preoral membrane. Sc., frontal cirrhi. Bs., basal strand. Bs.[1], basal strand of membranellæ. J., endoplasmic inclusions. Bf., basal fibers. p., pellicula. En., endoplasm.

pre-oral membrane, *m bp,* these striae being evidence that the organs are produced by a fusion of cilia. The distinction between the basal lamella, *bl,* and the basal granules should also be noticed. The investigation from which this figure is taken is particularly instructive because it is based on a large number of representative genera and because the discussion brings out various inferences concerning certain important aspects of development, even though the observations were mostly limited to the completed organs. To these latter we shall return in the chapter on development and heredity.

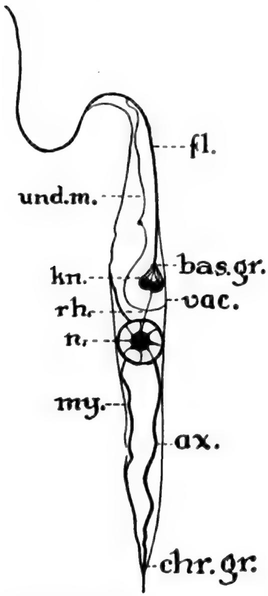

FIGURE 7. CRITHIDIA LEPTOCORIDIS (AFTER McCULLOCH).
ax., axostyle. bas.gr., basal granule. chr.gr., chromatin granule. fl., flagellum. n., nucleus. rh., rhizoplast. und.m., undulating membrane. vac., vacuole-like area about the "kinetonucleus." kn., kinetonucleus.

So far our glance at the complication of structure occurring among the protozoa has been directed chiefly to the organs of contact with the outside world. These organs are particularly characteristic of the large species, and in general of those leading the freest, most active lives. From the relative conspicuousness of these organs and the ease with which they can be observed it has naturally come about that they have been studied most and are the most accurately known of all the organs of these small animals. But extensive researches in recent years have brought to light a whole system of organs in one group of protozoans, the flagellata, that was entirely unknown a generation ago. The subdivision of the flagellata referred to contains the trypanosomes, animals which have come into prominence lately because many of them are parasitic in man and beast, pro-

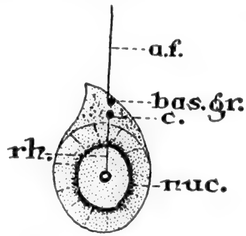

FIGURE 8. CRITHIDIA LEPTOCORIDIS (AFTER McCULLOCH).
a.f., axial filament. bas.gr., basal granule. c., centrosome. rh., rhizoplast. nuc., nucleus.

ducing a long list of diseases of which sleeping sickness is probably the most generally known. As we are now more interested in the organisms than in the effects they have upon their hosts, other species akin to the trypanosomes, but unknown except among specialists, will best serve our purpose. The examples I select are shown in figures 7 and 8. The species illustrated by figure 7 is *Crithidia leptocoridis* McCulloch.* This species has been chosen for the purpose of showing the newly discovered system of organs mentioned above, so structural details other than those of the system are not shown in the drawing.

* This occurs in various parts of the United States. The description of the creature is by Miss Irene McCulloch (An Outline of the Morphology and Life History of *Crithidia leptocoridis,* n. sp. Univ. of Calif. Publ. Zool., Vol. 16, pp. 1-22, 1915), one of the group of students in protozoology working under the guidance of Professor Kofoid.

The flagellum marks the anterior end of the creature; and along with it there is an undulating membrane, the two forming an efficient locomotor apparatus.

The explanations accompanying figures 7 and 8 name the parts of the system. Special attention may be called to the following points:

The *nucleus, n,* with its distinct membrane, central *karyosome,* and clear space between the latter and the membrane; the *kinetonucleus* (always written with quotation marks by Miss McCulloch, for reasons which we shall mention later); the *rhizoplast,* a fine thread connecting the karyosome of the nucleus with the kinetonucleus; the *basal granule* with its numerous very fine connections running to the kinetonucleus; and the *axostyle,* a thread extending from the basal granule to the posterior end of the body.

Concerning the function of all these parts our knowledge is very fragmentary. The reader should never forget the difficulty of observing these organisms. The largest individuals of this species are 40 or about 1/625 of an inch long, and as the figure shows, narrow in proportion to the length. Because of this minuteness several of the parts, for example the rhizoplast and the various granules, are at the very limit of visibility by the best microscopes. This fact, combined with the peculiar conditions under which the animals live, make it impossible to study a single individual during its whole life or even a considerable portion of it. Probably the impossibility of studying the parts as they do their work is chiefly responsible for the meagerness of what we know about the functions of the organs. The nucleus of a large number of protozoans, including this one, is often called a trophonucleus from the theory that it is chiefly concerned with nutrition.

The term *kinetonucleus* has been applied to the organ thus labelled from the conjecture that it has specially to do with the movements of the animal. As the figure shows, the flagellum is connected, though indirectly, with this organ, and this means that the undulating membrane is also related to it. But the fact that there are plenty of flagella and undulating membranes in other species which have no kinetonucleus, makes it certain that its rôle in the production of motion can not be exclusive or very fundamental. Concerning the office of the several granules, the rhizoplast and the axostyle, nothing positive seems to be known. When, consequently, the whole complex is spoken of as a "system of organs," we must keep in mind the fact that we are certain of its being a single system only in a morphological sense. The mere fact that several organs are structurally connected with one another does not by any means signify that they are all concerned in a single operation. For example, such complexes as muscle-nerve and gland-nerve-duct are morphological systems which perform several quite distinct functions.

A matter of much theoretical interest is involved in the application of the terms *chromatic* and *chromatin* to several of the parts of the system. The karyosome of the nucleus is called chromatin, as are the kinetonucleus, the basal granule, and the granule in the axostyle near the posterior end of the body. And the axostyle itself is said by Miss McCulloch to be "present apparently in the form of a chromatic thread." The flagellum and nuclear membrane are not held to be chromatic, even though they seem to take stains quite as well as the other parts which are called chromatin primarily because they are thus acted on. Mention may be made too, of the fact that some of the parts, notably the karyosome, which are considered to be chromatin, are shown by Miss McCulloch to stain with unequal intensity at different times. The subject of chromatin and chromatic bodies, has played a prodigious part in recent theoretical biology, especially in speculations about heredity. We shall consequently be obliged to give more attention to it in the discussion of how organisms reproduce themselves. What has been described is only the adult stage, or as it is often called, the vegetative stage in the creature's life cycle, this being sufficient for our present aims. Considerable is known about several other stages of this and related species; but our purpose now is only to get in mind as clear a picture as possible of the make-up of the animal in the culminating stage of its life.

The other species selected to illustrate this new system of internal protozoan organs shown in figure 9 is *Giardia muris,* the specific name referring to the fact that the creature is an inhabitant of mice. The figure and description are by Kofoid and Christiansen. The facts to which special attention is invited in this animal are the way in which all the various granules and bodies are connected with one another by fibers, the almost perfect bilateral symmetry of the animals, and particularly the presence of two nuclei, *nuc.* The binuclear condition of this protist is not merely a stage in the life history of the organism. No uni-nucleate stage occurs and the creature is typically organized on the binucleate plan. It should be noted that the two nuclei are alike morphologically and presumably physiologically, so they do not correspond to the macro- and micro-nuclei of some ciliates. The animal may consequently be

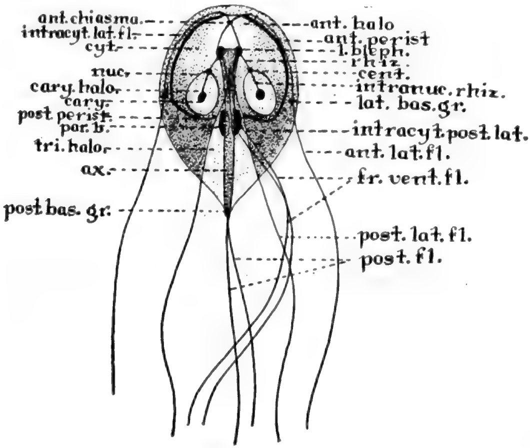

FIGURE 9. GIARDIA MURIS (AFTER KOFOID AND CHRISTIANSEN).
ant. chiasma, anterior chiasma. ant.halo., anterior halo. ant.lat.fl., anterior lateral flagellum. ant.perist., anterior peristome. ax., axostyle. cary., karyosome. cary.halo, karyosomal halo. cent., centrosome. cyt., cytostome. fr.vent.fl., free ventral flagellum. intracyt.-lat.fl., intracytoplasmic part of the postero-lateral flagellum. intranuc.rhiz., intranuclear rhizoplast. lat.bas.gr., lateral basal granule. post.fl., posterior flagellum. post.lat.fl., posterior lateral flagellum. post.perist., posterior peristome. l.bleph., left blepharoplast. rhiz., rhizoplast. tri.halo., triangular halo.

justly regarded, as Kofoid and Christiansen remark, as the "simplest (from the standpoint of numbers only) possible multinuclear organisms." [24] Special notice should also be taken of the *blepharoplasts* (l. bleph.), the *axostyle* (ax.) and the *parabasal bodies* (par. b.)

Worthy of mention is the fact that this system of organs, called by the authors the *neuromotor system,* is so well differentiated from the rest of the body substance, and so permanent that it may remain intact after the softer, more plastic parts of the body have undergone dissolution. It reminds one of a skeleton quite as much as of any other system belonging to the higher animals, though this remark is not intended as a suggestion that it may be of this nature. But the fact of capital importance to the present discussion is the remarkable degree of structural unification, or in accordance with the terminology favored by us, the structural integratedness of the animal through this organ system. All analogy warrants the supposition that functional integration of some sort corresponds to this structural integration, and if ever research discovers what that function is (or those functions are, for the possibility that there may be several should never be lost sight of), the insight thus obtained into the nature of these creatures would be another long step toward banishing the doctrine of the simplicity of the protozoa.

The Fiction of Structureless Organisms

Having informed ourselves concerning the highest grades of organization known among unicellular beings we must inquire about the lowest grades. The immediate question is, are genuinely structureless or homogeneous or amorphous living beings known? The next and far more searching question is, if such beings are not known (and they surely are not) does the nature of the inductive evidence demand or even warrant the supposition that they must exist somewhere or must have existed at some time although we can get no evidence to this effect?

The supposed existence of beings of this sort has cut a large figure in speculative biology. One need only refer to the moneron theory of Haeckel and its wonderful vitality shown by its cropping out everywhere, even in elementary and popular writings, and by its receiving a show of assent simultaneously with the admission that actual observation tends to disprove the theory. A good example of the persistence of the teaching is shown by Haeckel's *The Evolution of Man.* In the fifth edition, English, 1903, we read, "The earliest unicellular organisms can only have been evolved from the simplest organisms we know, the *monera*. These are the simplest living things that we can conceive. Their whole body is nothing but a particle of plasm, a granule of living albuminous matter." [25] So far as the protozoa are concerned, no zoologist who is both well informed and intellectually free and candid pretends any longer that such beings are known. "In all protozoa that have been examined in recent times, at least one nucleus has been found to occur without exception." [26] It hardly needs to be remarked that even the possession of a nucleus is sufficient to take an organism out of the category "organisms without organs." But as a matter of fact the nucleus is not the only differentiated part that has been demonstrated in the simplest protozoa.

The Structure of Bacteria

The visible living beings to which the term structurelessness can be ascribed with the greatest plausibility are the heterogeneous myriads known as the *bacteria*. Whether or not these organisms are true cells, that is, are "nucleated masses of protoplasm," has been extensively debated in recent years. This much may be regarded as settled: If by nucleus one is to understand a cell organ of such structure as that which is characteristic of ordinary plants and animals, then the bacteria are not nucleated. But this is far from meaning that the organisms are structureless.

(*a*) *Membrane and Surface Structures*

In the first place, there seems to be almost complete agreement among authorities that in bacteria the body is differentiated into at least one outer coat or membrane and an inner mass. It should be specially noted that the membrane is by no means a mere passive, wholly extrinsic thing, like the cover to a base-ball. It is an essential, active, living part of the organism. It seems to correspond more to the skin of a higher animal than to a man's coat, or to the shell of a mollusc or of a walnut. "Unlike the cell-wall of the higher plants, it [the outer layer of the bacterium] gives usually no reactions of cellulose, nor is chitin present as in the fungi, but it consists of a proteid substance and is apparently a modification of the general protoplasm." [27] This appears to express the most common view, especially among bacteriologists proper. Some authorities, as Kolle and Wassermann, speak of the ectoplasm and endoplasm, and declare that a "cell-membrane, such as is present in plant cells, is not to be thought of" [28] in the bacteria. If the membrane is comparable with that of the cells of any multicellular organisms at all, it would seem to be more akin to that of the animal cell than the plant cell, for nearly all authorities consulted agree that only in exceptional cases does cellulose occur in it, and W. Beneke says that the repeated assertion of the presence of cellulose in many bacteria is unproved. Even the presence of chitin, still more frequently affirmed by writers, is doubted by this author, and he tells us "we know nothing concerning the chemical structure of the wall." [29] Arthur Meyer takes vigorous ground against the views above indicated as to the nature of the bacterial membrane. He believes these organisms are more closely related to the fungi than to any other group and that through these their kinship to higher plants is established. But even he admits that "It is very easy to recognize that the bacteria possess a cell-membrane morphologically similar to the membrane of fungi, even to that of higher plants." [28] And he thinks that perhaps there is more similarity between the epidermis of aquatic higher plants and the bacterial wall than between the latter and the cell wall of higher plants.

Aside from the question of the chemical composition of the bacterial membrane, two facts seem to indicate its active character: the presence in many species of a mucous envelope, presumably secreted by the membrane, and the presence in many others of cilia which in some cases are almost certainly outgrowths of the membrane. It seems to have been proved that in *Spirillum giganteum*, the ciliary tuft with which each end of the body is armed arises from the inner body mass and passes through a chink in the membrane. Meyer and a few other authorities consulted are of the opinion that this is the typical mode of origin. But too many capable observers are positive about their having demonstrated the origin of the cilia from the membrane in widely separated species to permit us to believe that this is not in fact the mode of origin in many species. Thus V. A. Moore: "The flagella appear as hair-like appendages or filaments, which radiate from the bacteria. They are given off from the cell wall of the germs of which they appear to be continuations or projections." [30]

So meager is our knowledge of the individual activities of these minute beings that the simplest trustworthy observations in this field are welcome, and the following from Moore's paper is worth quoting even though its bearing on the membrane question is only indirect. Speaking of the behavior of the organisms when the cilia of several individuals become entangled with one another the author says they exhibit "a trembling motion, then a jerking, reeling and pitching movement, until finally they are free and move across the field," and "it seems highly probable that detachment or breaking of the appendages is produced during these voluntary movements, by their contact and possible entanglement with each other." [31]

The probable active participation of the membrane in the division of the bacterium is evidence from another direction that the structure is a real part of the organization of the being.

(b) *Structure of the Inner Portion*

We now pass from the consideration of the peripheral parts of the bacteria to an examination of the internal body mass. Recent discussion of this subject having been mostly carried on from the elementalist standpoint, with either nucleus or chromatin as the guiding star, gives the distinct impression of having for its end not full and accurate description of anything and everything that exists in the organism, but proof that a nucleus or chromatin either do or do not occur there. Writings under this head are so numerous and voluminous as to make a comprehensive review out of the question, and the diversity of opinion is so great and so strenuously set forth in some instances as to make satisfactory judgment of just what has been found difficult. The one thing that stands out with great clearness in the illustrations and descriptions of such recent works as those of Bütschli, Schaudinn, Arthur Meyer, Guillermond, Menol, Ruzicka, Swellengrebel, and Dobell, is that the main body substance of the organisms is far from homogeneous. A considerable variety of objects are undoubtedly differentiated within the protoplasm. Difference of opinion among the latest investigators concerns only the *nature* of these objects. Perhaps the most generally observed differentiations are granules of various sizes, shapes and behavior toward stains. The next most common structures seem to be networks and strands of varied character. The materials of these appear to differ generally from those of the granules in "taking" stains with less avidity. Vacuoles are another type of structure which present-day methods are discovering to play an important part in these minute organisms, as they have long been known to do in many protozoa, and in the cells of higher plants.

The narrower needs of our undertaking do not require us to examine farther these internal parts. The bare fact of their existence is conclusive proof that the main body of the organisms is not structureless; and almost conclusive proof too, when the extreme minuteness, and hence difficulty of observation is taken into account, that not only are they not structureless, but that their structure would amount, could it be seen as readily as that of larger organisms, to a very considerable degree of complexity of organization. And this, be it noticed, follows even though considerable portions of the body substance, especially in some stages of the individual life cycle, still look structureless or homogeneous under the highest magnifications and best conditions of lighting and staining. Although this phase of our discussion does not require us to go farther into the interpretation of the structure thus generally looked at, it is nevertheless desirable to attend to the subject a little more specifically.

(*c*) *The Question of a Nucleus in Bacteria*

We may first speak of the present status of the nuclear problem as touching the bacteria. The most prevalent view still is that the bacterium is a non-nucleated cell, if by nucleus one is to understand the organ that goes by that name in higher plants and animals. But there is plenty of dissent from this view, and seemingly this is growing in volume. Those who believe in the presence of a nucleus are still far from agreement as to what shall be regarded as this organ. One group of observers speak of a "diffuse nucleus," the idea being that certain of the granules mentioned above are chromatin or something close of kin thereto; and since according to a widely prevalent theory, this is the most essential constituent of the nucleus in the cells of higher organisms, they believe it justifiable to consider bacteria nucleated. Schaudinn and Richard Hertwig are prominent advocates of this view, the former basing it primarily on his studies of *Bacillus bütschlii*, and the latter making use of the bacteria as one illustration of his now well-known chromidial network theory.

Another view, proposed by Bütschli in 1890 and since favored by several students, is that the whole body of the bacterium is equivalent to the nucleus of a typical cell. A recent strong advocate of this view is Vladislav Ruzicka. This author defends the theory mainly on the evidence he believes he has obtained that bacteria as well as mammalian red blood corpuscles, familiar examples of non-nucleated cells, resist digestion in gastric juice in the same way as do the nuclei of typical cells.

Still another group of authors believe nuclei not fundamentally different from typical nuclei are present in bacteria. But again as soon as this view is examined in detail, the widest possible differences are found as to the criterion of what a nucleus is, and as to what objects in the organism are nuclei. Arthur Meyer, one of the most conservative supporters of this general view, believes he is able to demonstrate a nucleus in several genera and species, in the form of a minute granule more highly light-refracting than the surrounding cytoplasm as seen in the unstained condition, and reacting differently from all other substances toward various stains. It is most readily seen in the spore stage of the organism's life, and has so far been demonstrated in only a comparatively few species, taking the bacterial group as a whole. Dobell on the other hand, believes himself justified, after an examination of many species belonging to nearly the whole bacterial series, in declaring, "I think I may fairly claim from what has been pointed out in the preceding pages that not only do my own observations furnish conclusive evidence with regard to the nucleus in bacteria, but that in almost every case in which careful investigation has been made by others, the results are not inconsistent with mine," his results being that "the Bacteria are, like the Protista generally, nucleated organisms."[32] But the most cursory examination of Dobell's figures makes it obvious that what he regards as the nucleus is not what Meyer believes to be this organ, excepting possibly in the coccus forms. Dobell's nucleus is, in most of the elongated species, an axially elongated, usually extremely irregular, more or less fragmentary affair, varying greatly for different stages and conditions of the organisms. These two investigators are severe in their criticism of each other's work and conclusions.

Various other structures are described and figured, and various interpretations given, of the supposed nucleus of the bacteria, but we need go no further at present with the examination. Our main contention may be regarded as established: structurally viewed there is no longer any room for doubt that the bacteria are organisms in the usual sense of that term, that is, in the sense of possessing parts devoted to particular activities; but that there is unlimited room for doubt how, if at all, the conception "cell" as a nucleated mass of protoplasm is to be applied to these organisms. Structurally viewed, I say, the case stands this way. But if we approach the bacteria from the chemico-physiological side, the case against the cellular and for the organismal conception is still stronger.

Bacteria Undoubted Organisms Whether "True Cells" or Not.

It has been often remarked that Bacteriology is pre-eminently the department of biology that relies on functional rather than on structural attributes for its determinations. This character of the science results from the extreme minuteness of the creatures which renders morphological study of them so difficult. One of the most striking, indeed one of the most remarkable facts about "microbes" is that they are so like ordinary living things in their general modes of life despite their excessive minuteness, and, as judged by ordinary anatomical standards, despite their structural simplicity. Like other organisms they feed and respire and propagate their kind; and they survive in an active condition only within a range of temperatures not greatly different from that which conditions the lives of other beings. But striking as is their similarity to organisms generally in these attributes-in-common, still more striking is their *specific diversity among themselves.* That organisms so small as to be barely visible, or even invisible to the highest powers of the microscope, should still be subject to the general principles of specific differentiation in habits of life and hereditary transmission as are the largest, most complex organisms, seems to me one of the marvels of the living world.

In this field as in so many others, the facts which touch human welfare the most vitally are best known. Take the case of smallpox and chickenpox. These are both diseases of the human skin and are so much alike as to be often confused even by physicians not especially experienced in this field; yet to the expert the difference between them is declared to be positive and unmistakable. "Smallpox has rather severe prodromes, backache, head-ache, fever, and sorethroat, the rash appearing on the third and fourth day. Chickenpox usually has light or no prodromes, the rash appearing on the same day or within twenty-four hours as a rule. In both diseases the face, chest, back, arms, hands, legs, and feet are likely to show eruptions, but chickenpox tends to show the greatest number of spots 'under cover,' i.e., on the parts usually covered by clothing, while smallpox tends to show the majority on the face, neck, arms, wrists, and hands, rather than on the body. The skin lesions themselves differ very markedly, the typical lesions of chickenpox being superficial, thin-walled, high, rounded, and filled with clear liquid; those of small pox being deep-seated, tense, opaque, covered with a tough skin. There are many other points of distinction, and any one familiar with the two diseases can hardly fall into error when dealing with typical cases at whatever stage they are encountered." [33]

This is the type of discriminative description that occurs everywhere in the writings of biological taxonomists. It is as characteristic of zoological and botanical, as it is of medical "diagnoses." Yet the organic species themselves implicated in the diseases are invisible under the highest magnifications so far produced, the specific discriminations being based exclusively on the effects arising from the different activities of the two kinds of organisms! Now what are the probabilities as to the structural attributes of these invisible beings? Answering in the light of what is well known about all familiar organisms, can we say anything else than that the microbes of smallpox and chickenpox, not only possess differentiated and coordinated parts, that is, are organized, but that the two species are to some extent *differently* organized? Nor is the evidence of specificity in this case at all exceptional for ultra-minute organisms, as every one knows who has given attention to the popular subject of "germ-life." Some of the disease producers, as those of rabies, it is true, are able to flourish in a considerable range of hosts; but this is also the case with many protozoan and even metazoan parasites. The microbe of hog cholera is, according to present knowledge, as closely restricted as to possible hosts as that of any disease producer whatever; and judging from its ability to pass through filters, it is one of the smallest of the ultra-microscopic species. So on the whole it appears that the principles of host adaptability are essentially the same throughout the whole range of parasitic life regardless of size.

But while this statement about the conformity of bacteria to the general rules of species differentiation and constancy is undoubtedly true as a general proposition, at the same time the group presents a degree of structural and functional plasticity which surpasses, probably, anything occurring in any other group. Under the term "pleomorphism" this multiform character of bacteria has been the subject of much investigation and no little heated discussion. One party, headed by the German botanist Nägeli, has maintained that the organisms are not classifiable in the usual sense of biological taxonomy at all—that any form is susceptible of becoming almost any other form, depending on the external conditions under which it is placed. The other party, of whom Cohn seems to have been the originator, has stoutly insisted that species and genera are as definite in bacteria as in any other group, and that every infectious disease has its specific germ agent. The evidence and the controversy need not be followed into details. The truth undoubtedly lies somewhere between these extreme views. "Bacterial species exist, but they are all of the kind called in the language of the science of classification '*ill-defined.*' "[34]

The great body of facts instanced in the foregoing pages furnish the answer to the question raised early in this section, namely, does the inductive evidence warrant the supposition that homogeneous or structureless or organless organisms actually exist? No, appears to be the only reply permissible, and this in spite of the fact that the observable organic world taken as a whole does undoubtedly show a general simplification with diminution in size.

If we feel compelled to speculate, but yet resolve, as we must when fully committed to the inductive method, to hold speculation to strict accountability to observational evidence, then are we driven to the conclusion that simplification of structure and diminution in size of organisms go hand in hand, but that neither ever reaches the vanishing point, even though we know nothing about the limit of possibility as to size or as to simplicity of structure. This examination of the protista brings into clear light a difficulty not otherwise recognizable in the way of applying the cell-theory to this section of the living world. The concept cell being primarily one of structure and only secondarily one of function, necessarily becomes inapplicable to invisible beings so far as special objectivity is concerned, while the concept organism being primarily one of function and only secondarily one of structure, is quite as applicable to invisible as to visible beings if, as in the case of disease-producing microbes, we have observational evidence on the functional side of their nature. No discoveries in the whole biological realm have more clearly revealed the fatuousness of the claim made by the cell-theory to being the "key to all biological problems," than have those establishing the existence of barely visible and invisible living things. On the other hand, these discoveries taken along with those concerning the structure of the protozoa and visible bacteria, have contributed greatly to the expansion and clarification of the organismal conception.

B. DEVELOPMENT

False Conceptions About Development in Protozoa

We have now seen something of the disastrous effects of trying to squeeze the whole adult structure of the protozoan into the theoretically "simple cell." It remains to look at the still worse effects of trying to keep the facts of development of the individual protozoan down to the same theoretical limitations. We will first examine the notion constantly inculcated by text-books and in formal instruction, that there is "no true development" in these creatures. Embryology is almost always defined and treated so as to exclude from its scope development in the protozoa. Thus the preface to the monumental *Treatise on Comparative Embryology* by F. M. Balfour contains this: ". . . the work is, I believe, with the exception of a small but useful volume by Packard, the first attempt to deal in a complete manner with the whole science of Embryology in its recent aspects. . . ." [35] But the introduction tells us specifically that the actual scope of the work is not to be thus ambitious after all. "The present treatise deals only with the Embryology of Animals, and is further confined to those animals known as Metazoa." [36] It will be noted that nothing in this statement compels the inference that Balfour conceived Embryology as being actually limited to the metazoa. In fact, if anything, the opposite might be inferred. Considerable reference is made to protozoan reproduction in the Introduction, which however has to do only with conjugation and spore formation and the problem of the origin of the metazoa from the protozoa and especially the origin of sexual reproduction. But the theory of the "formation of the individual from the *structureless germ*" (italics mine),[37] and of the individual metazoan as "equivalent to a number of Protozoa coalesced to form a single organism in a higher state of aggregation," [38] adumbrates the fallacious doctrines about the relation of the organism's cells to the organism which have come to dominate biological theory, and against which we are taking strong ground.

"Inasmuch as the individual Protozoan has the morphological value of a single cell, the embryology of the Protozoa belongs to the province of cell morphology. For this reason it is usually excluded from the domain of comparative embryology of animals in the stricter sense; in this book too, it will receive no consideration. Comparative embryology has to do accordingly with the development of the Metazoa." [39] It is satisfactory to note that in the later general part of the great text-book from which this paragraph is quoted, the authors have given a much more adequate definition of development (*Entwicklung*) and embryology (*Entwicklungsgeschichte*). "By development," they say, "we understand the course of those form-changes through which organic figure is produced."[40] And "embryology is a descriptive presentation of the developmental processes of the organism."[41] But development of the protozoa is as rigidly excluded from all the discussions in this newer general part as it was from the older special part.

"The science of embryology," we read, "has for its subject-matter the growth of animals from the time when they first appear as germs in the bodies of their parents until they reach the adult condition and are able to produce similar germs themselves."[42] Though this statement seems broad enough to cover the development of many, at least, of the protozoa, yet when one turns to the body of the work to see how these animals have fared, he is quite taken aback to find that they simply are not mentioned at all. So the inference seems unescapable that according to the views of the embryologists responsible for the above statement, in this great section of the animal world there are no such things as germs contained in the bodies of parents, which grow to reach the adult condition. According to their *views*, I say, because not for a moment is it to be supposed they are unaware of the fact that one of the primary subdivisions of the protozoa, the sporozoa, receive their name from the almost universality among them of reproduction through sporulation, the spores or germs being in most cases formed within the encysted parent animal. And the authors are, of course, familiar with the conjugation of male and female gametes in many species to produce the zygote, the parent of the spores, from which in turn the adult animals are developed.

Although it is unfortunately true that there is dearth of observational knowledge on the growth of the adult from the spores, yet the dozen and more developmental stages of the sixteen-millimeter-long *Porospora gigantea* described by E. van Beneden and discussed and figured by Bütschli shows us an ontogeny or individual development in one case no less positive, and probably little less complex were all

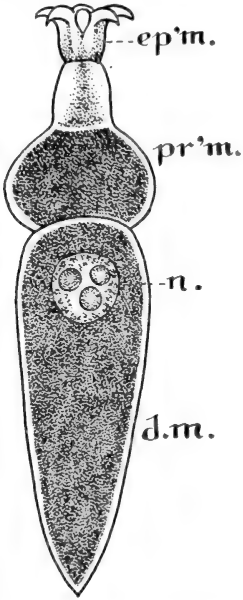

FIGURE 10. CORYCELLA ARMATA (FROM WASIELEWSKI, AFTER LÉGER).
ep'm., epimerite. pr'm., protomerite. d.m., deutomerite. n., nucleus.

the details known, than that of many endoparasitic worms.*

But how could a zoologist hesitate to recognize that so elaborate an organism, as for example a *Corycella*, figure

* With reference to the development of this species, it should be remarked that although later researches have proved that the amoeboid stages considered by van Beneden to belong to this series in reality have nothing to do with this animal, yet the later stages leading up to the final one, or "trophozoite" seem not to have been questioned; and these constitute the evidence of *an ontogeny* with which we are now specially concerned.

10, the body of which is sharply differentiated into the three distinct parts called the *deutomerite, protomerite* and *epimerite*,[13] (the latter being a fixation organ of greatly varied form in different species, and often highly specialized), must imply an ontogeny of no mean extent? Nor are we any longer without knowledge, at least in outline, of the developmental series in this part of the sporozoan cycle for several other series. The investigations of Léger and Dubosq are especially noteworthy in this connection. From their account of the development of *Pyxinia möbuszi* we learn that in this species the full grown animal, the slender epimerite not included, is five times the length of the sporozoite; and the epimerite attaining a length greater than that of the rest of the animal, penetrates through the entire length of the epithelial cell of the intestine of the host. The whole of the adult animal except the epimerite projects free into the intestinal cavity.

Misuse of the Term "Ontogeny"

I give only one other quotation showing the extent to which this obscuration of the facts of protozoan development has gone in the interests of cellular elementalism. This quotation is specially telling because it is genuinely up to date and displays the extremity of the tendency by not being restricted to the meaning of the term embryogeny, concerning the scope of which there is good historical and biological ground for difference of opinion, but goes to the term ontogeny, concerning which there is no such ground. "*Ontogeny* includes, as the developmental history (*Entwicklungsgeschichte*) of the separate individual, all those changes of form which the individual undergoes from its point of origin, the fertilized egg cell, to the state of sexual maturity." [44]

The terms *ontogeny* and *ontogenesis*, introduced into biology by Haeckel, have been exceedingly useful, and their usefulness depends largely on the fact that the root *ontos* refers to a living being, an organism as a totality, so that coupled with the term *genesis*, the reference is to the entire cycle of the being, and not merely to some particular stage of that cycle, as is the case with the term embryogeny. The word *embryon*, the back-bone of *embryogeny*, *embryology*, and the like, means, as the Greek dictionaries tell us, "the fruit of the womb before birth." It is synonymous with the Latin *foetus*. In other words, the center of reference of all terms containing the root being primarily to one stage, and that a very immature one, of a higher organism, it may be held with considerable justice to be inapplicable to the development of such lowly creatures as the protozoa. But to define *ontogeny* so as to exclude reference to the development of the protozoan or any other organism is not only utterly unjustifiable, but deserves unqualified scientific condemnation, because, as we have seen, it gives persons not well informed and so not in position to be on their guard against being misled, a narrow and false conception about organic development. The full mischievousness of this sort of limitation is seen only by looking a little more into details.

Development of Stentor as an Example of Protozoan Ontogeny

The familiar "trumpet animalcule," *Stentor*, found in fresh water ponds almost everywhere and figured in many books, will serve our purpose well. Numerous zoologists have made this animal the object of their studies, one of which only, by H. P. Johnson, will be drawn upon. The case of *Stentor* is the more instructive in that its mode of propagation is chiefly if not entirely that of "simple cell division"—to use a phraseology that is pleasing to simple elementalism.

Before entering upon an account of the development of

Stentor, it is to the point to hear what Johnson has to say touching the reality of the process as compared with the development of a metazoan. "The conception," he says, "that the development of a new infusorian by the process of fission is an ontogenetic development, comparable in some respects to the development of a metazoön, has impressed itself strongly upon me in the study of fission in *Stentor*." [45]

The course of events in the multiplication and development of the animal is so illuminating that I reproduce four of Johnson's figures, figures 11, 12, 13 and 14, and would urge the reader unacquainted with the subject but wishing to get at the kernel of the position here defended to consult the original memoir, especially for the anatomy and ontogeny of the organism.

The main exterior body-parts to which attention should be directed and which are indicated on the figures are: *a. z.*, aboral zone, *b. p.*, buccal pouch, *cl.*, cilia, *c. v.*, contractile vacuole, *ex. p.*, excretory pore of contractile vacuole, *l*, line of division, *l.b.s.*, left boundary stripe of ramifying zone, *o*, mouth, *p.*, peristomal band, *r. z.*, ramifying zone, *vel.*, velum.

The processes of division and development are so intimately associated as to be inseparable. "The first sign of fission," says Johnson, "is the formation of a rift (the anlage of the new aboral zone) in the pellicula and ectoplasm near to and almost parallel with, the left boundary stripe of the ramifying zone." [46] (figure 11 a. z.) By examining the figures the reader may follow quite satisfactorily the main events. The first step in the development of some of the new parts should be specially noticed. The aboral zone, for example, as indicated in the quotation, is initiated as a rift through the ectoplasm running down the side of the animal's body, hence having no connection whatever with the original aboral zone. A point of special interest in this fact is that the organ in question for the new individual does not arise from the same organ of the old, or parent individual, either by division or budding. And this *de novo* mode of origin is that followed by a whole series of organs and tissues; the cilia and membranellae of the aboral zone; the mouth, velum, and pharynx; the frontal field; the ramifying zone; and the con-

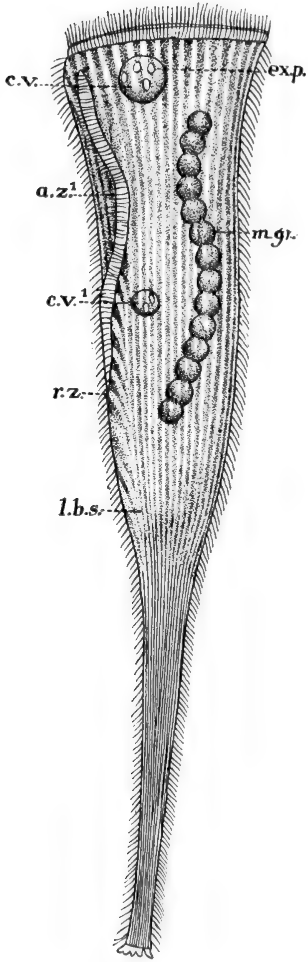

FIGURE 11

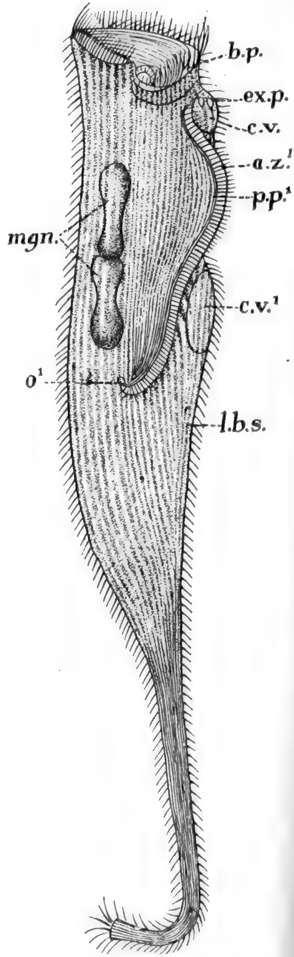

FIGURE 12

FIGURES 11, 12—STENTOR CAERULEUS (AFTER JOHNSON).

a.z.,[1] adoral zone. b.p., buccal pouch. c.v., c.v.,[1] contractile vacuole. d.a.z.,[1] distal extremity of adoral zone. ex.p., excretory pore of contractile vacuole. f, f[1], frontal field. l, l,[1] line of fission. mgn., meganucleus. o, o[1], mouth. p, p[1], peristome band. r.z., r.z.,[1] ramifying zone. vel[1]., velum.

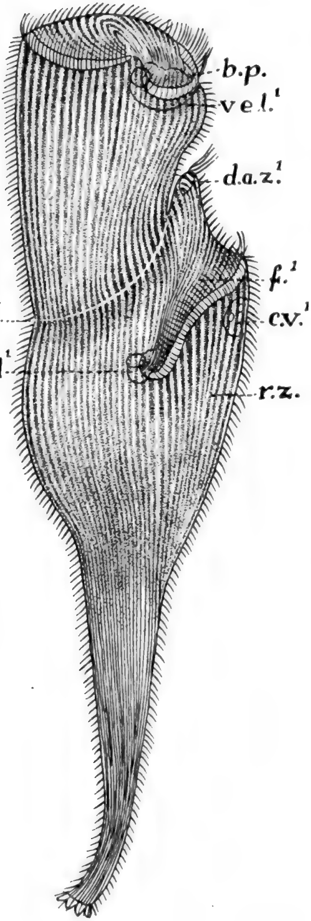

FIGURE 13.

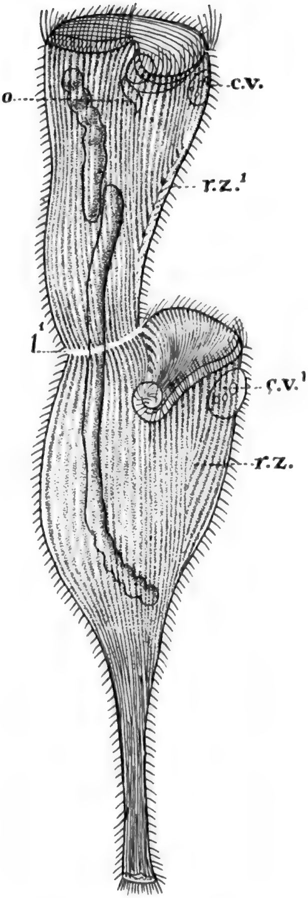

FIGURE 14.

FIGURES 13, 14

tractile vacuole and excretory pore. The origin of the membranellae in this way particularly appealed to Johnson. "The gradual evolution," he says, "of structures so complicated as membranellae, from a mass of indifferent protoplasm, is very striking." [47] What he has especially in view is that these "organula," as he calls them, arise not from the ectoplasm, to which in the adult they seem to pertain, but from the endoplasm.

Although Johnson was not much of a speculator, he was still on the lookout for questions of general interest. "Our ignorance," he remarks, "of the *primum movens* to a neoformation is complete. We can only say it lies in some peculiar molecular condition that incites the duplication of existing organs. And the working out of the impulse thus given is only partly dependent upon temperature, food, the size of the individual, or even as Balbiani's and my own experiments in merotomy show, upon the intact condition of the organism." [48] The reader should not fail to see that this is an obvious, though somewhat indirect, recognition of the organism *as a cause* of developmental phenomena—of appealing to the organism as a causal explanation of observed occurrences. In saying that the *primum movens* to organ production lies in "some peculiar molecular condition," the *just* claims of the potency of elements (of some sort) is recognized. But no one should fail to notice the qualifying term *peculiar* appended to molecular. The molecular condition capable of producing the observed results is no general condition; it is a particular condition. And particular how? To the organism possessing the organs to be duplicated. When the discussion of a purely objective case like this proceeds normally, the reference is entirely to the organism and its organs and tissues, and the conception *cell* does not enter into it in any way. For example, there is no occasion whatever even to refer to the nucleus. If the idea of the cell is brought in at all, it is lugged in purely arbitrarily.

One of the things that has given embryology its great interest, since the doctrine of evolution became established in biology, is the fact of rudimentary, often transitory, organs which appear in the course of the individual development. Johnson gave special attention to two such organs in Stentor, the *ring-canal* and the *peristomal-band*. The former is a canal in the endoplasm, just beneath the aboral zone and running parallel with it. It is present only in the newly produced posterior zooid, its complete atrophy occurring soon after fission. Johnson proved it to originate in connection with the contractile vesicle.

The peristomal band (figure 12 p. p.) is a narrow, clear band inside of and running parallel with the aboral zone. It also entirely disappears some time after fission. It is believed to represent the peristome of the lower Heterotricha; that is, like so many rudimentary organs of the metazoa, it is supposed to be an ancestral structure; to have, in other words, a racial significance. It will be noticed even from this imperfect description of division and development that one of the two new animals, the posterior, resulting from division, undergoes most of the development. It alone, or very nearly alone, takes on new organs. It may therefore very well be called the offspring, the anterior animal being distinguishable as the parent.

The Terms "Embryology" and "Ontogeny" Inevitably Used by Investigators of Protozoan Reproduction

The futility of supposing practical science will conform to a definition drawn up in the interest of a grand theory but in defiance of a great body of facts, could hardly find better illustration than in the persistence with which students of the Protozoa speak of the ontogeny and embryogeny of the creatures despite efforts like those quoted above to restrict the term to the metazoa. Looking at these illustrations a little further, let us take Valentin Häcker's work on the Radiolaria. In the general part, entitled *Form and Form-development in the Radiolaria*, of his splendid report on the collections of this group made by the German Deep-Sea Expedition, not only do we find a section *Ontogenesis of Variations*, but facts and questions of "*ontogeny*" are scattered throughout the whole part, thus: "The other sort of variability may be in large part referred back to changes in some of the elementary processes which normally coöperate in the ontogeny of the skeleton, especially to be considered being the secretory and sprouting operations." [49] And Häcker laments that in spite of the great quantity of excellently preserved material at his disposal he was unable to work out the "complete embryology" (*Entwicklungsgeschichte*) of a single group of Tripylea, though he was able to add largely at many points to previous knowledge.

From the standpoint of descriptive embryogeny probably the most serious gap in our knowledge of the development of the Radiolaria is the scarcity of information about the growth of the adult animal from the swarm spores. Thanks to several zoologists, among the latest of whom is Borgert particularly, we know quite fully the mode of spore or gamete production in several species. The great number, small size, and simple structure of these germinal elements in species like *Aulacantha* leave no doubt that their growth to full sized animals is an elaborate operation involving many stages and kinds of differentiation.

We have now gone far enough into the structure and development of the higher protista to make it indubitable that there is a morphology, individual and comparative; an embryology, also individual and comparative; and a physiology, likewise individual and comparative, of this great subdivision of the animal kingdom, not a whit less definite and hardly less rich and varied, though less elaborate as to individual animals than in the subdivision known as metazoa. In the light of the great body of knowledge now available, only a tithe of which has been used in this review, it is hard to see how any one can avoid recognizing that the fact that the animals usually consist of a single cell, is really of secondary importance. Neither descriptively nor interpretatively (if one insists on making a sharp distinction between the two) do the generalized elements cytoplasm and nucleus, held to be the irreducible minima of the cell, throw any but the vaguest, most general light on innumerable of the structures and processes brought under notice.

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Chapter X

HISTORY OF THE ATTEMPT TO SUBORDINATE THE PROTISTA TO THE CELL-THEORY

IT is important to learn how the attempt to subordinate protozoans and other protista to cells has fared in the history of knowledge of these minute organisms. It was a genuine surprise to me, as I imagine it may be to many zoologists orthodoxly drilled in the cell-theory, to find how much dissent there has been and still is among the able investigators of the protozoa, from this mode of treating the little creatures.

Clash Between Ehrenberg and Dujardin a Special Case of the Conflict Between Organismal and Elementalist Conceptions

The erroneous appraisement by many recent authors of the work of Ehrenberg will serve as a starting point for what needs attention under this head. Few names are better known in protozoology than C. G. Ehrenberg, whose monumental work, *Die Infusionsthierchen als volkommene Organismen,* holds some such place in protozoology as Linnaeus' *Systema Naturae* holds in zoology and botany generally. Yet it is the custom of most writers to regard it as a great depository of facts, but antiquated and erroneous in its interpretations. The view expressed by Locy is typical: "His publication was almost simultaneous with the announcement of the cell-theory (1838-1839), the acceptance of which was destined to overthrow his conception of the protozoa, and to make clear that tissues and organs can belong only to multicellular organisms." [1]

If one looks into Ehrenberg's conception that "was destined to be overthrown," and the controversies it provoked, a very significant thing comes to light. He finds repeated reference to the fact that prominent among those who helped to overthrow Ehrenberg's false teaching was Felix Dujardin. The current form of statement of the difference between these two naturalists may be illustrated by the following from Calkins: "A formidable opponent soon appeared in France—Felix Dujardin—who, influenced by long study of the *Rhizopoda*, came to the conclusion in 1835, that the marine forms (*Foraminifera*) which up to that time had been classed with cephalopod molluscs, are in reality the simplest organisms, composed of a simple homogeneous substance which he called 'sarcode.'" [2]

The reader will recognize in the clash here indicated only another special instance of the ages-old conflict between the organismal and elementalist conceptions of living beings. But this instance is sufficiently important in both its theoretical implications and its practical consequences to merit a somewhat close examination. To begin with, particular notice should be taken of the type of elementalism upheld by Dujardin, namely, that of a *simple homogeneous substance* as the basis of all life. This finds expression in his sarcode theory, which has cut a large figure in later speculative biology. The conflict between Dujardin and Ehrenberg was first and foremost theoretical. The kernel of the former's theory was that there must be a *substance* of organisms more fundamental than organisms themselves, while Ehrenberg stood for the view that organisms, no matter how simple, must still be organized. He contended that all the organisms we actually know, including "Infusionsthierchen" (and for him practically all microscopic organisms came under this term) are demonstrably organized, that is, possess organs.

That there may be no question as to the essential correctness of the statement that this conflict was primarily one of theory, let us listen to Dujardin himself. "Among the authors," he says, "who have written on the Infusoria, some, as Leeuwenhoek, have attributed to these animals a very complicated organization, while others, as Müller, would see only a glutinous homogeneous substance * (mera gelatina). This last opinion, adopted by Cuvier, Treviranus and Oken, appeared henceforth the most probable, when M. Ehrenberg came boldly forward in 1830 to show to the learned world evidences which he believed he had found, but which unfortunately no one else has been able to confirm, of a richness of organization of the Infusoria." [3]

From this passage alone the inference could be drawn that the difference between the two men was strictly one of ability in observation—of what each was able to see when examining very minute creatures. But another passage lets the cat out of the bag. "M. Ehrenberg, who, guided by false analogies, has gone even beyond Leeuwenhoek in ascribing to the Infusorians a prodigious wealth of organization, supports himself on the principle that 'the ideas of size are relative and are of little physiological importance.' This principle is only a consequence of a preconceived idea of the unlimited divisibility of matter. Now in supporting the absence of all limitations to the divisibility of matter to be a law of nature—and a mass of chemical and physical phenomena seem to prove the contrary—that law would not suffice to prove the possibility of a very complex organization beyond a certain minimal limit of size; for it is known that many physical and dynamical phenomena are considerably influenced or even inhibited by molecular action when the

* The original wording should be noted: *"n'y ont voulée le plus souvent qu'une substance . . ."*—the old familiar story of seeing what one wants to see rather than what is actually before his eyes.

bodies or intervals which separate them are very small. . . . It is more in keeping with the laws of physics to admit that in these small animals, liquids are taken in by simple imbibition; as it is more in keeping with rules established by analogy not to assume that the plan of higher organisms can be reproduced in these very small beings, since we see the elements of these organisms, blood globules, muscle fibers, and capillary vessels, instead of undergoing a progressive diminution in size in the smaller vertebrates, showing almost the same size in the mouse and in the elephant." [4]

In other words, the physical theory supported by certain facts of structure and function in larger animals (rather than any theory of organic evolution) led Dujardin to believe that such minute living beings as Infusorians must be structureless and beyond question these theoretical views largely influenced, and influenced harmfully, the results of his observational studies. This fact deserves emphasis because current presentation of the subject makes it appear that Ehrenberg was theoretically all wrong while Dujardin was theoretically all right.

Ehrenberg went astray not in defending the theory that *Infusionsthierchen* possess organs, but in claiming for them *particular kinds* of organs which they do not possess. Convinced as he was, largely on *a priori* grounds, that they must be organized, and knowing no other kind of organization than that of the larger animals with which he was familiar, he brought to his microscopic researches a mind prepared to make the most possible of the general resemblance many of the little creatures he studied bear to ordinary animals. From pole to pole and in all depths of the ocean, he said, live minute animal forms which resemble higher animals "*wie Abdrücke einer Schablone*"—like the impress of a mould. And that the little creatures are genuine organisms seemed to Ehrenberg to be supported by the fact that the myriads of them fall into species, genera, families, and so on, as do higher animals. His position cannot be fully understood without taking into account his view that the protozoa, being part and parcel of the animal kingdom, are subject to its general laws, that is, modes of life, distribution and classification of that kingdom.

In this fact hardly less than in the structure of individuals, he saw proof that the Infusoria are complete organisms. Guided by these theoretical views, the warrantableness of which later researches have made many times greater than they were when Ehrenberg propounded them, it is not surprising that he was led to interpret into various parts he could see only imperfectly, resemblances to the organs of higher animals, which resemblances did not as a matter of fact exist. The stomachs, hearts, genital organs, and so on, which he believed he saw in many of the species, disappeared before the criticism of Dujardin, Köllicker, von Siebold and others. But here is the point of chief theoretic importance. Although these *particular organs* went down before criticism, criticism by no means deprived the animals of *all* organs. It is in neglect of this last fact that current teachings do Ehrenberg injustice. His "conception of the protozoa" was destined to be overthrown only as to the *sort* of organization he believed them to have. It is gratifying to find that in this conclusion I am in essential agreement with so eminent an observational student of the protozoa as C. C. Dobell. In a recent quite remarkable essay this author writes, "To my mind, Ehrenberg (1838) in spite of his incorrect interpretations in matters of detail, was far nearer to the truth when he saw Protista as '*volkommene Organismen*' than any more modern biologist who regards them as analogues to parts of multicellular beings."[5]

As between the conception of organization in all living beings, no matter how small and simple, and the conception of living beings so small and simple that they are without organization, there can be no question that all inductive knowledge favors the former and tends to refute the latter; and in so far as Ehrenberg stood for the former and Dujardin for the latter the evidence surely supports the views of the German and opposes those of the Frenchman.

This brings us to a highly important practical point. I mentioned a little while ago that Dujardin's theoretical views influenced harmfully his observational work. In support of this statement the reader is asked to compare the monographs by Ehrenberg and Dujardin already mentioned, giving special attention to figures of the same animal presented in each. No one will fail, I believe, to recognize the greater truthfulness (disregarding the relative merit of draftmanship and publication) of many of Ehrenberg's illustrations, especially as regards the internal structure of the organisms. That the difference cannot be attributed altogether to Ehrenberg's superior powers of observation seems certain from the fact that Dujardin made out numerous points about the cilia of various species which were unknown to Ehrenberg. Both Dujardin's observations and his scheme of classification appear to have been largely influenced by his sarcode theory: i.e., his theory of structurelessness. "The numerous genera which one establishes," he says, "in the family of the monadinians, are distinguished therefore only by the number and position of the locomotor filaments and by the most habitual form of the body and of the appendages." [6]

Prepossessed by the idea of structural diversity and complication in the creatures of the microscopic world, Ehrenberg directed his attention primarily to their internal makeup, described things that do not exist there, and overlooked various external parts. Dujardin, on the other hand, prepossessed by the idea of internal structurelessness, of homogeneity, fixed his attention more on the external parts and so was able to surpass Ehrenberg in describing these, but also to correct various of his opponent's erroneous interpretations of internal structure. But while Dujardin's greater merit in these respects was undoubted, his lesser merit in describing the internal structure is quite as undoubted, and more vital in that it involved serious practical consequences. *The difference in preconception of the two naturalists made Ehrenberg the better practical anatomist of the protozoa.* It will have been noted that Dujardin's opposition to Ehrenberg did not primarily involve the question of the application of the cell-theory to the protozoa, both men having published their main works before that theory was propounded.

Modern Opposition to the Effort to Make the Protista Conform to Cellular Elementalism

We now pass on in our examination of historical opposition to the conception that unicellular plants and animals are "organisms without organs," into the strictly modern period during which the effort has been to bring the protista "into conformity with the narrow bounds of cellular elementalism."

(*a*) *The Position of Friedrich Stein*

I suppose all protistologists would agree that there has been no greater worker in microscopic natural history during this period than Friedrich Stein. His *Der Organismus der Infusionsthiere* (*nach eigenen Forschungen*) is no less a fundamental and indispensable part of the library of every student in this field than is Ehrenberg's great work. That Stein "was never an ardent advocate of the simplicity of the Protozoa," as Calkins expresses it, is well known to all zoologists acquainted with his writings. Both Calkins and Dobell quote the following sentence from him, which not only shows his skepticism about the unrestrained applicability of the cell-theory to the protozoa, but indicates the sort of limitation to that application which he believes necessary. "One must ever hesitate to consider the fully developed Infusoria as unicellular organisms, for they are not merely cells that have undergone further simple growth, but the original cell structure has given place to an essentially different organization which is entirely foreign to cells." [7] That is, the cell conception applies to these animals, according to Stein, only when they are in the earliest or germinal stages of their lives. This view is brought out still more clearly by the following comparison which he makes between the individual development of a unicellular and a multicellular organism. "The germinal spheres or embryonal cells of the Infusoria do not behave at all like the egg cells of the higher animals. By a process of fission [these latter] break up (*zerfallen*) into an aggregate of smaller embryonal bodies, the constituting cells (the germinal spheres of the Infusoria), which transform themselves just as they are into the embryonic body sarcode, the kernel [*kern*] becoming the nucleus, of the young Infusorian. The embryo of the Infusorian is therefore in the strictest sense of the word a unicellular organism." In this sense, and in this sense only, Stein goes on to say, he subscribes to the doctrine that the Infusoria are unicellular. Stein's conception of the adult Infusorian as contrasted with the embryonic Infusorian was probably influenced by his having mistaken an Ascinetan, parasitic in certain ciliates, for embryos of the hosts, and on this error he based his theory that these ciliates pass through an ascinetan stage in their ontogeny. But this error does not invalidate his statement of the fundamental difference between unicellular and multicellular organisms as to the sort of transformation undergone in their individual development. Wherever sporulation occurs, growth of the spores into the adults would exemplify Stein's main point, and this point is of capital importance as we shall contend more at length later.

(*b*) *Position of Huxley, R. Hertwig and Others*

The views of Huxley on the nature of organisms and cells give him an interesting place among those who protest against the current cellular interpretation of the protista. After mentioning *Vorticella*, *Caulerpa* and "Roesel's Proteus," as organisms in which there is little or no histological differentiation, he says: "It is true indeed that the difficulty with regard to these organisms has been evaded by calling them 'unicellular'—by supposing them to be merely enlarged and modified simple cells; but does not the phrase 'unicellular organism' involve a contradiction for the cell-theory? In the terms of the cell-theory, is not the cell supposed to be an anatomical and physiological unity, capable of performing one function only—the life of the organism being the life of the separate cells of which it is composed? and is not a cell with different organs and functions something totally different from what we mean by a cell among higher animals? We must say that the admission of the existence of unicellular organisms appears to us to be virtually giving up the cell-theory for these organisms." [8] While the argument Huxley is making differs in important respects from that which we are developing, these statements make it obvious that, as Dobell remarks, Huxley realized "there was something wrong in the application of the cell theory to the protista." We shall speak further of Huxley's views in another connection.

Even Richard Hertwig, staunch believer as he is in the conformity of the Protozoa to the "laws of cell-life," recognizes that harm has been done by pushing the cell-theory too hard in the interpretation of the protozoa. "A whole series of instances," he writes, "show how the effort to subordinate the protozoa to experiences with metazoan cells and to adapt them to the straight-jacket scheme devised for metazoan cells has led to errors." [9]

Many other expressions of dissatisfaction with prevalent notions about the simplicity of the protozoa could be cited from the very latest writings touching the subject from quite other directions than those of morphology and development. Thus Jennings says concerning the activities of the protozoan, "The writer is thoroughly convinced, after long study of the behavior of this organism, that if *Amoeba* were a large animal, so as to come within the every-day experience of human beings, its behavior would at once call forth the attribution to it of states of pleasure and pain, of hunger, desire, and the like, on precisely the same basis as we attribute these things to the dog." [10]

And M. M. Metcalf in a recent address reviewing the nuclear phenomena lately discovered in various species of Amoeba, said: "With such phenomena as these demonstrated in an amoeba, no zoologist can dare again to apply to any organism the adjective simple. In the behavior of its nuclear elements *Amoeba* is as complex as is man himself."

But the most radical and violent pronouncement against the cellular conception of the protista that has ever been made, comes from one of the ablest and most active students of these organisms, C. Clifford Dobell, whose writings have already been incidentally cited. A closer acquaintance with his view will appropriately terminate the historical part of our discussion.

Dobell's notable essay leaves no reader in doubt about the nature of this author's disaffection, or as to the doctrinal reformations he holds to be necessary. The application of the cell-theory to the Protista is wholly unjustifiable and has been and is now more than ever before a serious hindrance to the advancement of positive knowledge and sound interpretation of this great subdivision of the organic world. Coming to closer quarters, his contention is that the protist body does not correspond to a minute fragment of the metazoan body, one of its myriads of cells, but to the whole body.

"The body of a protozoan is not the homologue of a single cell in the body of a metazoan, and hence the succession of individuals formed from one conjugation to the next, is not comparable with a metazoan body any more than a swarm of bees is comparable with an elephant." [11]

The reformation proposed is to cease calling the protista *unicellular* and to recognize that they are *non-cellular.* "The essential difference between the structure of protista and that of other organisms is properly and objectively expressed when we describe these as cellular, those as non-cellular. The concept 'cell,' derived from a study of cellular organisms, is a fairly simple one. It is quite clear that the correct antithesis in the present case is between cells and not-cells, and not between many cells and one cell—as has hitherto been universally assumed." [12]

The cell concept which Dobell believes to be "fairly simple" is presented thus: "The investigation of an immense number of organisms has brought to light a most important fact, namely, that the protoplasm of a living organism always consists of two elements, a nucleus (or nuclei) and cytoplasm.

"Now in a very large number of multinucleate organisms the cytoplasm is subdivided into a number of definite compartments, each of which encloses a nucleus. These cytoplasmic subdivisions with their enclosed nuclei we may call—following the ordinary usage—cells." [13] The denial of cellularity to the Protista, Dobell bases on the fact that the individual organisms are not divided up into nucleate masses of protoplasm.

Other and quite distinct aspects of Dobell's standpoint are his contention that the terms "higher" and "lower" have no valid applicability to organisms, and that the protista are not "primitive" and "ancestral" relative to man and other large animals and plants, in an evolutional sense. "There is no more reason," he says, "to suppose that these organisms, with their complex and peculiar structures and life-histories, are the beginnings of man than that man is the beginning of them."[14] The far-reaching consequences of Dobell's views, should they prevail, are indicated by his remarks about evolution. "Why should it always be taken for granted that by 'Evolution' is meant 'an upward progress from Protozoa to Man'? This is only one hypothesis of organic evolution. That evolution of some sort has taken place in living beings I regard as certain. But, that evolution of the Haeckelian 'Amoeba to Man' type has not occurred I regard as equally certain. We can certainly believe in evolution without believing in this dogma."[15]

General Conclusions From Examination of Knowledge and Views as to the Nature of Uni- and Multi-cellular Organisms

We may now ask ourselves, what comes of this somewhat extensive examination of the structure and function of the Protista, and of the history of discovery and opinion concerning them? Whatever else comes, I do not see how any open-minded person can escape seeing that the practice of thinking about these small beings as conforming in essence to the "simple cell" is unnatural, impedimental of progress in sound knowledge, and ought to be abandoned forthwith. But how abandon a practice based on a general theory which has served to unify so vast a multitude of diverse and, at first sight, apparently quite isolated facts? That the cell-doctrine applied to the Protozoa has served such a purpose is beyond question.

The point deserves concrete illustration. There has recently occurred in the dinoflagellate collections of the San Diego region an organism so different from any hitherto described as to elicit the exclamation "a remarkable thing!" That Doctor Swezy, to whom has fallen the task of describing it, was able to make the hypothesis that the creature is unicellular, was undoubtedly a very great help toward making out the details of the structure and instituting the comparisons preliminary to assigning the organism to a place in the system of classification. The generalized observational knowledge which is the backbone of natural science is impossible without a central concept or mental construction of some sort to which new observations can be brought for testing and standardization, and finally for assignment to their proper place in the general scheme. Sound science as well as common knowledge refuses, consequently, to abandon its general views, especially if these have been truly helpful, even though their inadequacy, or actual erroneousness may have become manifest. The oft-repeated statement that a wrong theory is better than no theory has the sanction of psychology and logic, as well as of the universal concatenation of nature. Outgrown or erroneous theories must be supplanted rather than abandoned. Their places must not be left vacant, but filled by other and better theories.

These general considerations taken by themselves make it extremely improbable that Dobell's proposal to reform interpretation of the protista as non-cellular instead of unicellular will meet with wide approval. Non-cellularity is pure negation, and so lacks the essentials of a "working theory." Furthermore, from the side of clear objectivity, a proposal which involves the denial of cellularity to such an organism as an amoeba or a gregarine because only one cell is present in it, violates the principles of sobriety and consistency, so vital to true science, and ought not to be sanctioned.

The reformation of theory touching the cellular nature of the protista which it seems to me is demanded by the facts will, I hope, be apparent to any one who has followed the discussion to this point. The concept cell must be held in strict subordination to the concept organism in this as in all other portions of the living world, and to make this effective the concept organism must be given greater *definiteness* than it has generally had. The classes of fact which have been sampled in the preceding pages furnish the basis for both these readjustments.

First as to the subordination of cells to organism. Let attention be directed to the myriad of natural objects called living beings and cells rather than to concepts about them. Wherever in the living world structures occur which competent judges agree to call cells, these are structurally part of and functionally dependent upon, and therefore strictly subordinate to, living beings. This subordination is seen in the fact that cells arise as a consequence of the activities of living beings. This mode of origin is most obvious in the individual development of the larger plants and animals where growth is accompanied by a resolution of the growing body into a great number of such structures.

It seems that racially as well as individually, cells were produced by living beings. This I say *seems* to have been the case, for be it always remembered that certainty as to how either living beings or any of their parts arose in the first instance—if indeed there was a first instance—is wholly impossible for positive science. However much we may speculate on the subject we have no right to permit the speculations to exercise more than a secondary influence on observational and interpretative results touching actual living beings.

So far as the bacteria and other living beings near or below the limits of microscopic vision can be supposed to represent earlier stages in the evolution of the living world, they indicate that beings much smaller and considerably simpler than cells existed long before cells.

And functionally as well as developmentally, cells are subordinate to the living beings to which they belong. This is most manifest in animals which, like man and other higher vertebrates, perform a great number of voluntary acts. In such cases as those of the voluntary muscles, the muscle cells are *used by* the living being for its needs as strictly as are the whole muscles or the limbs and other primary voluntary members of the body.

But while the functional subordination of cells to the living being is seen most conspicuously in the active use of them by the higher animals as they perform their voluntary acts, this sort of subordination is exceptional, taking the whole world and all its operations together. The most fundamental, and as it seems, the strictly universal aspect of the functional subordination of cells is in the assimilation of food and concomitant breaking down of synthesized organic substances to produce the basal processes distinctive of each individual and kind of living being. In its *metabolic* processes the living being's supremacy over its cells is most universally manifest. The identity, structural and functional, which the individual organism maintains by converting nutrient matter into its own self, and for its own use, is accomplished largely if not wholly by means of its cells.

The supposition that the cells themselves, taken independently of the organisms to which they pertain, have power to develop and perform the metabolic operations characteristic of each species and each individual organism, seems a necessary consequence of the cell-theory in its full modern development, in the conception, that is, which sees in the cell the "key to all biological problems." But it is hardly necessary to remark that there is not an iota of direct evidence that cells possess such power. The only observations we have upon which such an interpretation could be forced, even by the most intellectually unscrupulous methods of forcing evidence, are those on the viability of isolated cells and tissues (see Chapter 6).

As a matter of fact the evidence from this source not only does not support the doctrine of the supremacy of cells but strongly favors the supremacy of the organism. Let us suppose, for example, a specially skillful technician has isolated all the voluntary muscle cells of a cat and kept them alive indefinitely. Would any cellular elementalist be so courageous as to contend that the cells would undergo the contractions coördinated in quantity, force and speed, which are involved in the animal's crouch-and-spring to catch a rat? But suppose such coördinated contraction of the isolated cells should take place. How could the fact be explained? Surely in no way that did not recognize that they were merely doing under the new conditions what they were accustomed to do under the old; that, in other words, in endowing them with the ability to perform these contractions, the organism had also endowed them with such a measure of independence of metabolic activity as to enable them to keep up these operations after separation from the organism.

One of the most essential things toward putting ourselves straight in theory as to the relation of the cell to the organism in unicellular beings, is to get straight on the relation of the cells to the organism in multicellular beings. An indispensable step toward this latter consummation is to remove from our thought and terminology the conception which holds the metazoa and metaphyta to be "cell-states," "cell-colonies" or "cell aggregations," when these terms are used as though the cells were originally independent entities. The embryology of the metazoa furnishes overwhelming evidence that the egg is the organism in its one-celled stage, and that cell-division during ontogeny is a resolution of the organism into minute parts very much like one another.

Once we have gone this far in revising the cell-theory we come to realize the weightiness of the truth that the theory was originally concerned with parts or elements of larger plants and animals, and not with these organisms themselves. It was the appreciation of the significance of this fact that made the theory seem to Huxley wholly inapplicable to the protozoa. "How," he said, "imagine structures which are professedly only elements in the make-up of one kind of organisms, to be the same as structures which are the whole organism in other kinds of beings?" This same difficulty seems to have been the chief influence in leading Dobell to deny that the Protista can be legitimately brought under the cell-theory.

I wish to point out that while there can be no doubt about the great importance of the fact that in metazoa and metaphyta cells are *parts* of the organisms, I am unable to see that the fact necessitates, as held by Huxley and Dobell, the exclusion of protozoa from the cell-theory. It simply establishes in the most uncompromising way the subordination of the cells to the organism in the metazoa and metaphyta. If the idea be grasped that cells are among the instrumentalities produced by organisms in the course of their development, individual and racial, with which to carry on their various activities, it will become apparent that there can be no objection to modifying the conception of the cell to make it apply to any structure whether a part of, or the whole of an organism, which satisfies certain well-established criteria. When, for example, it is recognized that certain species of amoebae resemble so closely the white corpuscles of the blood of many animals as never to fail of recognition by good observers, the established principles of biological definition and classification dictate that the two sorts of bodies be given a common, that is, logically speaking, a generic name.

But now comes another principle of description and classification which, though no less fundamental than that just mentioned, has not been as adequately heeded by defenders of the cell-theory; the principle, namely, that a genus always implies species and that these must each be as carefully described as the genus itself. In other words, sound scientific procedure requires that if amoebae and white blood corpuscles are classed together as cells, their differences must at the same time be given full recognition. If this be done, among the many differences that will come to record are sure to be this: amoebae are organisms, each individual being complete and independent in itself, while blood corpuscles occur only as elements of the blood and lymph of other organisms. This is a simple statement of fact in the interest of pure description. But notice what it reveals. *Amoeba* appears in a two-fold rôle, that of cell and that of organism. But cells of the metazoa are, as we have seen, subordinate to the organisms to which they belong. What, consequently, are we to conclude as to the relation of the cell of the amoeba to the organism amoeba? Manifestly that the one cell of the amoeba is no less subordinate to the organism amoeba than the many cells of a worm are subordinate to the organism worm.

While this is merely a presentation of the logic of the situation, it corresponds to the objective facts of the protista, and I think must be admitted by any one who will weigh fully and candidly what has been presented in the section on that subject.

So much for that part of the reformation of the cell-theory, in its application to the protista, which concerns the subordination of cells to organisms in these as well as in metazoa and metaphyta.

It remains now to see what can be done with the other aspect of the reformation, namely, that of securing for the concept organism greater definiteness than it has hitherto had. For reasons partly valid and partly not valid the terms "organism," "organism as a whole" and "organization" are believed by some biologists to be too vague to be scientifically useful. Indeed, a few good authors charge that these terms have a mystical implication. In reply to this last charge it may be pointed out that any objective term, no matter how exact and rigidly scientific, is capable of being given a mystical twist. Think for example, of how the words *substance* and *force* had been and still are being abused in this way! Were positive science to eliminate from its vocabulary all words that have had mystical meanings imposed upon them, there would be left only words that have never come into wide and general use. The truth as touching the mystical implication of *organism* and *organization* is that while no careful thinker would venture to deny that they may have been thus misused, they have suffered distinctly less than many other common biological terms the utility of which when properly used no one ever questions.

These palliative remarks about the charge of mysticism are not intended to lessen in any degree the need of giving greater definiteness to the concept.

We may take as a starting point for this effort the fundamental truth that living beings exist whose organization is so radically different from any with which ordinary observation acquaints us, as to have been wholly unpredictable before they had been actually studied. Research on the protista and especially those prosecuted during the present era, have established their uniqueness beyond cavil, and no other general result of these researches is of greater importance than this.

The appraisement of the fruits of protistology thus indicated came to me gradually in the course of my studies preparatory to writing the chapter on this subject, and I was greatly interested to find later that Dobell had reached the same conclusion. "The great importance," he writes, "of the protista—to my mind—lies in the fact that they are a group of living beings which are organized upon quite a different principle from that of other organisms. . . . The protista offer us, in other words, a new point of view for looking at the phenomena of life." [16]

Something of what has been gained or may be gained in the way of limbering up and broadening our minds as to the nature of living beings is illustrated by the work of Ehrenberg examined in a previous section. So rigidly limited, as we saw, was this zoologist's idea of an animal that it seems to have been impossible for him to believe an animal could be organized on a plan essentially different from familiar animals.

Having regard to the whole range of knowledge of protistan anatomy in our possession, two things stand forth prominently. First, the organisms present a type (if indeed we ought not to say types) of organization fundamentally different from any known among the larger plants and animals; and second, the observational evidence is to the effect that organization of some sort is present in all Protista. Nor is the phrase "organization of some sort" void of definite meaning. For a living being to have organization is to have parts of different kinds whose existence and operations are dependent upon one another, all corresponding to the activities of the special being taken as a whole. "Of some sort," used in the most general way possible, that is, as applicable to all organisms whatever, means just so many sorts as there are sorts of plants and animals in all the world. Man's sort of organization is man's total structure, his externo-topographic body members, his gross anatomic parts, his histologic parts, and his chemico-biologic elements. Likewise *Stylonychia's* sort of organization is that protozoan's total structure, macro- and micro-morphologic and chemico-biologic and so on for all living beings.

And this brings before us one of the great merits of the organismal as contrasted with the cellular mode of viewing living beings. The concept organism being committed to not *one* sort of organization but only to *some* sort, is open to whatever particular organization may be discovered in any being. On the other hand, the concept "cell" being committed to *a single* type to which it strives to reduce whatever being it approaches, is locked, as one might say, against the vast diversity that actually exists in the living world. Not only has the cell-theory, strictly understood, no explanation of the structural variety of living nature, but by its very essence it tends to minimize the significance of that variety, and to divert attention from it. That the theory always has been and is now narrowing in its influences no candid student will try to deny.

The injury that the science of microörganisms has suffered and to which attention has been called in preceding pages is a notable instance of the tendency of the cell-theory here criticized.

But does almost limitless diversity in the conception of "organism" deprive it of value as a generalization? Has it any of the unifying quality upon which the usefulness of a scientific theory depends? The answer to this is two-fold. In the first place, there is just so much unity in the concept organism as there is in the larger and smaller groups of the plant and animal kingdoms. On this side the conception is rooted in comparative anatomy and physiology and taxonomy.

But the conception's unifying quality *par excellence* is seen in another direction, namely, that of the elements-in-common of organization in all organisms whatever, so far as their structure is known to us. In all living beings from the largest and most complex to the smallest and simplest, if still visible, the body is differentiated into a surface layer or coat somewhat firmer and denser than the underlying more voluminous parts. We know of no living thing without a skin of some sort. Frequently this is spoken of as a mere lifeless protective structure. But as a matter of fact it is the organism's organ of contact with its environment, and so of the utmost importance for the nutritional, respiratory and responsive functions. Possibly skin and inner mass may be organization in its lowest terms, though this is not probable. The inner mass is probably never entirely structureless. Even the bacteria, formerly described as homogeneous in their body substance, are now being shown to have considerable structure.

So our guiding star in the study of living beings whose structure is not known, as for example the ultra-microscopic beings to which hog cholera is supposed to be due, is that they are organisms whose organization may be assumed to consist of at least an outer layer and an inner mass. We may presume, too, that portions of the protoplasm of the inner mass are more or less definitely and permanently differentiated chemically from the rest, but of this there is less certainty than of the differentiation of the outer layer.

Our contention that cells are subordinate to organisms everywhere and always, whether in unicellular or multicellular beings, we may now regard as established.

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PART 1

CRITIQUE OF THE ELEMENTALIST CONCEPTION OF THE ORGANISM

B. The Production of Individuals by Other Individuals

Chapter XI

THE NATURE OF HEREDITY AND THE PROBLEM OF ITS MECHANISM

Heredity the Chief Present-day Stronghold of Biological Elementalism

BIOLOGICAL elementalism of to-day undoubtedly has its chief stronghold in the realm of heredity. The germ-plasm theory, accepted by probably a majority of biologists as an absolute monarch in the empire of biological thought, was elaborated for the sole purpose of explaining heredity. In the third chapter of the present work we looked at certain subsidiary aspects of this theory. The time has now come for scrutinizing the theory itself.

Heredity has come so conspicuously to the front lately in connection with plant and animal breeding, in social questions, and in eugenics, that almost every educated person has learned something about the splendid progress of knowledge concerning it. All who have glanced through some of the numerous books on the subject have seen the pictures of chromosomes represented as the bearers or the mechanism of heredity. They have also learned more or less about unit characters, so prominent, biologically speaking, in connection with the mode of inheritance discovered by Gregor Mendel. If the learner's efforts have gone beyond the rudiments of the subject he has become acquainted with "determiners" and "unit factors" of the germinal substance which are held to explain the characters of full-grown organisms.

There is something bewilderingly fascinating in the quality and scope of these discoveries, and it is not surprising that many of the leading investigators in the field have been swept off their feet with enthusiasm for the rehabilitated germ-plasm theory. Thus we hear one prominent student declare that individual traits are a "veneer," and another that "analysis of the constitution of the germ-plasm is admittedly the fundamental problem in the study of heredity." In other words, the interpretations placed upon the indubitable results of the new researches have effected a rejuvenation of the germ-plasm theory of Weismann. Rejuvenation, I say, because that theory was approaching death and decay when the rediscovery of the Mendelian mode of inheritance occurred. It seems as though some students have lived so exclusively and intensely in the invisible world of "determiners," "factors," "bearers," etc., that for them the ordinary world of plants and animals has lost most of its interest if not its reality.

This Due Particularly to the Discovery of the Interdependence Between Adult Characters and Chromosomes of Germ-Cells

In what immediately follows I want to fix attention on the remarkable way in which a long series of discoveries highly interesting in themselves, and pertaining to fields quite remote from each other have conspired to increase the plausibility of the old theory that organic beings are caused by the activities of pre-existent, simple representative units or elements of some sort.

On the face of the matter two fields of biology could hardly be more sharply separated than that in which falls the study of the nuclei of cells, and that which occupies itself with the way color, size, and similar attributes appear in successive generations of plants and animals. Yet the first, or cytology, on the one hand, and breeding experiments conducted under the guidance of Mendel's discoveries, on the other, have almost if not quite demonstrated some sort of interdependence between the chromosomes of the germinal cells of several species of sexually propagating plants and animals, and such attributes of adults. These demonstrations are perhaps the most important achievements of biology in the last decades, and they must ever hold high rank in the history of the science.

How do the new discoveries appear when viewed from the organismal standpoint? A study of recent writings on heredity gives one the impression that elementalist conceptions have left cells behind and passed on to chromosomes, elements which lie at a deeper level as one might express it, of organic constitution than do cells. Much recent discussion of the mechanism of heredity has not been cytological so much as chromosomological. Somewhere in the first few pages of nearly all semi-popular books on genetics one finds diagrams of the egg-cell with the nucleus and its chromosomes represented in due particularity, but with the body of the egg left blank, the implication being that this part contains nothing significant for heredity. So much has recent thinking on the "hereditary substance" kept chromosomes in the foreground as "carriers of heredity" that the most radical elementalists might, quite conceivably, grant that the main mass of each cell, whether germ-cell or soma-cell, may be an organ and so subject to the organism, yet contend that the chromosomes are not so subject. In fact, speculations like those recently published by the late E. A. Minchin on the evolution of the cell appear to claim just this sort of primacy for chromosomes, or at any rate for chromatin.

Revised Conception of Heredity Essential to Interpreting This Interdependence

On the basis of the objective evidence what is the probable meaning of the interdependence between attributes of full-grown organisms and chromosomes of the germ-cells? There is the utmost diversity of view as to what heredity is and as to what facts come under it. It seems almost as though the more the subject is investigated the more diverse the views become. This I think is literally true for the theoretical side of the subject, though it is certainly not true with reference to the factual side. The discovery by Mendel of the principle of segregation of characters while they are still latent in the germ-cells, and the elaboration of this principle by later investigators, is a positive achievement of high rank, destined to stand for all time. And such negative results as those of the disproof of telegeny, of the influence of "maternal impressions," and of the inheritance of acquired characters in the old pre-Weismannian sense, must be counted as factual achievements of much practical importance.

Unwarrantable Tendency to Restrict Heredity to Sexual Propagation

Heredity as used in biology has to do with the reproduction of plants and animals. That the growth of an oak tree from an acorn and of a rooster from a hen's egg illustrate heredity there can be no doubt. These typify a great number of cases, all those in which the plant or animal develops from a germ-cell, an exceedingly minute, simple body as compared with the full grown organism. But what about reproduction through other means than such cells? Is there heredity in propagation by other means? Much of the recent discussion of the subject is practically restricted to heredity among germ-producing organisms; and some of the foremost writers on the subject are explicit on this limitation. Thus in the glossary of *Heredity and Environment in the Development of Man* by E. G. Conklin, we read that heredity may be defined as "the appearance in the offspring of characters whose differential causes are found in the germ cells"; [1] and since nowhere in the volume does Professor Conklin even mention any but germ-cell reproduction, we are obliged to assume that for him heredity is a phenomenon of germ-cell reproduction alone. This seems to be a case of trying to escape through definition the difficulties encountered by a theory; in other words, to circumscribe the theory for the purpose of excluding from its scope phenomena which can not be made to fit in with it. It is surprising that so careful a reasoner and observer as Conklin should have fallen into this pit. A definition of heredity that would exclude from its operation the growth of a tiger lily from a bulb, of a sponge from a gemmule, and of an ascidiozooid from an ascidian bud, is so obviously forced that it ought to raise a suspicion that consciously or otherwise it is framed with some other motive in view than that of telling what heredity is; and it is unbelievable that such a definition can gain general and permanent approval.

While not many authorities are so definitely extreme as this, a large majority of the recent books in which heredity occupies a prominent place tend to lead the reader thus to restrict his conception of heredity. Another class of writers, while tacitly allowing that heredity manifests itself in cases where germ-cells do not occur, yet take the ground that sexless propagation is very exceptional and does not need to be taken particularly into account in elaborating theories about heredity. Thus in so excellent a book as J. Arthur Thomson's *Heredity* we are told that "the exceptions are trivial compared with the vast majority of living creatures in regard to which it is certain that each life begins in a fertilized egg-cell." [2] And on a later page this author italicizes the sentence: "In asexual reproduction the resemblance of the offspring to the parent tends to be very complete, and the reason for like producing like is no puzzle, while the separated-off portion is a representative sample of the whole organism." [3]

One would like to know how Professor Thomson would reconcile the first statement with the sum total of facts of reproduction. We know from his numerous books that few biologists are more broadly learned on the subject of organic reproduction than he. It is therefore hardly possible that he would hesitate to admit that if a complete census were made at this hour of the individual organisms composing the living world, the enumeration taking note of all individuals produced sexually and all those produced asexually, the asexually produced would probably exceed in numbers those produced by the other process. And be it remembered that in some of the most prolific sub-divisions of the bacteria, the dinoflagellates, the diatomes, the trypanosomes, the sarcodinians, various groups of algae, and even some of the higher plants and insects, sexual reproduction, with rare exceptions, has never been seen.

Nor should one fail to recall that in the many groups of both plants and animals where sexual and asexual reproduction alternate in the same species, the individuals produced asexually are almost, if not always, far more numerous than those produced sexually. So far as numbers of individuals are concerned all zoologists know how small a part sexual propagation plays in some of the coelenterates, as the coral-producing polyps; in most bryozoa; in several groups of tunicates; and in some flat-worms. If one objects that coral polyps, bryozoan polypides, and ascidian zooids ought not to be counted as "individuals," the reply sufficient for the present discussion is that whatever they should or should not be called they are what give rise to the sex-cells, the things which are central in the theories of heredity. "Germinal continuity," so fundamental in these theories, is certainly non-existent so far as germ-cells are concerned in many of these species.

The aim so far has been merely to fix attention on the tendency of present day theorizing on heredity to restrict the conception to phenomena presented in reproduction through the instrumentality of germ-cells of two sorts, male and female. It is hoped that this brief statement of the tendency has revealed its unwarrantableness to the uncommitted reader. But since our general enterprise requires us to perceive its fallaciousness we shall have to examine it in considerable detail.

Unwarrantable Tendency to Restrict Heredity to Adult Characters

Another serious shortcoming in the way problems of heredity are treated must be noticed. Reference is made to the practice particularly by recent geneticists of treating heredity as though it primarily concerns only the attributes of adult organisms. To be sure both popular and scientific observation depart to some extent from this rule. Notice is often taken of the resemblance to their parents of young, even newly born humans and lower animals, but even here the basis of comparison is the adult, the parent. Rarely are resemblances of the embryo in its many stages of development to the *embryos of its parents at the corresponding stages of their development* thought of as phenomena of heredity. Raymond Pearl, in his *Modes of Research in Genetics*, has pointed out this defect more comprehensively than any other writer so far as I know. Under the topic, "The Embryological Methods of Research in Genetics," after remarking that embryology has been cultivated mainly for its own ends, he writes, "Only in a relatively small portion of instances, has it been directly and purposefully used as a mode of research in genetics. Yet embryology is the science of somatogenesis, which was shown at the beginning to be one of the fundamental elements of the problem of heredity," and he remarks further: "It is a little difficult to understand why, with such splendid opportunities as the embryological method offers, so little light regarding the hereditary process seems to have come from the embryologist." [4]

Importance of Recognizing Heredity as Working by Transformation Rather Than by Transmission

Another weak spot in much thinking about heredity even by some biologists is due to the fiction of "transmitting" characters from parent to offspring. This appears to have come from the original meaning of the terms *inheritance* and *heredity*, which have to do with heirship to property. Several recent authors have dwelt on the confusion of ideas that has arisen from this equivocal mode of expression. No one fails to recognize the difference between the transmission of stature and the transmission of a farm by a father to his son. That the difference is partially recognized even in ordinary discourse is seen by the stated beliefs that biological heredity is always associated with resemblance. Indeed, the universality of this association is one of the basal truths in theories of heredity. The real inappropriateness about speaking of organic propagation in terms of economic inheritance is that attention is not called to the fact that the former is accomplished through a long, regular systematic series of transformations to which there is nothing comparable in the latter.

The objection here made against the transmission idea is different from that made by most geneticists. Their point is that the germ-plasm conception excludes the possibility of any sort of transmission from parent to offspring. *Continuity* of germ-plasm is the kernel of their objection. My main point, on the contrary, does not concern the hypothetical germ-plasm so much as the observable fact that organic development, whether hereditary or not, is first and foremost transformative rather than transmissive.

Tendency to Confuse Heredity with Causes of Heredity

Again there is appearing in the strictly modern studies of heredity a conception that seems both scientifically unwarrantable and fraught with possibilities of much harm. This is the failure to distinguish between heredity itself and the causes of heredity. Pearl has given this the most positive expression I have come upon. "By heredity is meant the complex of causes, not now further specified or defined, which, taken together, determines this likeness or resemblance between individuals genetically related to each other." [5] It is to be hoped Doctor Pearl would not wish to be taken quite literally in this. Indeed, other passages give some ground for supposing he would not. The point here raised is probably more an aspect of the general theory of natural causation than of the specific question of cause and effect in heredity.

The concept "cause" is meaningless except in relation with the concept "effect," and since causes and their effects can not be identical, effects must be as much realities of nature as causes are; so if science is to maintain its claim to objectivity it must devote itself as sedulously to the ascertainment of what the effects are in any given case as to what the causes are. The eye-color of a child which resembles the eye-color of an ancestor is an effect and not a cause, and must be accepted whole-heartedly as such before the student is in a proper frame of mind to consider the question of what the cause or causes may be of the observed effects. To define heredity in a way that implies a disregard of this general principle can but lead to unbalanced thinking and effort and to results strongly tinctured with error. If the position be taken—and unfortunately it is taken by many men of science—that the investigation of causes is the main if not the exclusive function of science, this can mean nothing else than that in the eyes of natural science at least one-half of all nature is of less importance and interest than the other half, and that science is privileged to decide which is the important part. This is another way of criticizing the practice now so dominant in biology of exalting the concept of causality and degrading that of description. An important fruit of the present discussion will be, it is hoped, an exposure of the injury that has befallen theories of heredity from this practice. Nor does our position imply the notion, held by a few men of science, that the category of causality is useless in science and ought to be dropped. Far from it. The causal explanation of heredity is not only a legitimate but an exceedingly important object of investigation. But it is by no means the whole problem or even the most important problem, the subject of heredity being regarded in the large and for all time. Perhaps in the present stage of progress of biology it is the most important; but if so I would maintain that at some later time, when the knowledge of causes shall have been advanced out of proportion to other aspects of the subject, some of these retarded aspects will become for a period the center of genetic interest.

The Definition of Heredity Adopted in This Discussion, with Remarks on Its Application, Especially with Reference to the Chromatin Theory

We are now in position to fix upon a definition of heredity which shall recognize that its mechanism is as much a part of and subordinate to the organism as are all its other parts and organs. Or, employing the form of expression current in recent genetics, a definition which shall tactily recognize that chromosomes, even though bearers of heredity, are causally explained by the organism in the same sense that the hereditary attributes of the organism are causally explained by the chromosomes.

Of the many definitions the one that most nearly expresses the conception that will pervade this discussion is that given by W. E. Castle: "By heredity, then, we mean organic resemblance based on descent."[6] The commendable things about this definition are its non-commitment to any theory, and the fact that it puts resemblance in the front line along with the recognition that resemblance is due to descent. Any adequate definition of heredity must hold the phenomenon of resemblance always in clear sight, and this in spite of the fact that in the Mendelian mode of inheritance the resemblance may skip one or more generations.

Our further discussion will fall under two heads. First, we shall make a wide survey of resemblance due to descent for the purpose of learning how far its connection with chromosomes actually extends; whether in a word, the connection is a universal principle. Second, we shall then have to see what we are justified in supposing to be the nature of the connection.

It will be noticed that the first statement admits in advance that *to some extent* resemblance between ancestors and progeny is *in some way* connected with the chromosomes. This admission relieves us of the necessity of an exhaustive review of the evidence which necessitates the admission. Though the evidence has practically all been brought out during the last twenty-five years, it is large in quantity and widely scattered. Nearly all the semi-popular books, not to speak of the many serials in technical biology, present some of it. We may therefore restrict ourselves to such aspects as will serve our purpose from time to time.

Throughout the vast range of living beings the rule *like produces like* holds sooner or later. I say sooner or later because there are many exceptions were we to limit the statement to parents and their immediate offspring. No individual salpa, for example, ever produces its like. In some species parent and offspring are very unlike, so much so that were they not actually observed to be parent and offspring, they would be regarded as unrelated and belonging to different genera. But instead of being wholly unique, though so unlike its parent, the young returns to its grandparent for a pattern; so if we jump a generation the rule holds after all. This scheme of reproduction, technically known as alternation of generations, occurs in a considerable number of groups of both plants and animals. Another exception is presented by the Mendelian mode of heredity. One of the most characteristic things about this kind of inheritance is the skipping of generations as regards heritable attributes. When gray and white mice are mated the issue are all like the gray parent; but some of the grandchildren, if inbreeding be followed, are like their white grandparent. This departure from the rule of like is so important and peculiar that some biologists have felt it necessary to frame the definition of heredity so as to make it cover the appearance in offspring of difference as well as of resemblance. In truth though, if the term descent be understood to pass over one or more generations, as in the case of Salpa, the rule holds. Indeed, Mendelian inheritance in hybrid races might be described as a sort of alternation of generations.

Another aspect of the law of like must be noticed here. Not only do organisms come from ancestors but we have not a scrap of trustworthy evidence that they are or ever have been produced by any other means. In other words, the law of biogenesis, the law, that is, that negatives the theory of spontaneous generation, is the same in large part as the law that like produces like. So starting from any given individual, problems of genesis and resemblance look in two opposite directions, backward into the past, and forward into the future. Viewing heredity from this standpoint compels us to consider closely the *degree* of resemblance between descendants and ancestors. Full consideration of the question may be deferred for the moment, though attention must be called to the fact that resemblance even of this sort, never, so far as we know, amounts to identity, even though in many instances it is wonderfully close. Difference is a no less universal rule than is similarity and from this it results that science is absolutely prohibited from attempting to minimize the importance of either truth. The problems of organic likeness and difference are inseparable, and those biologists are so far right who contend that heredity has to do with both. In the interest of clear thinking however, it is necessary to recognize that resemblance is one fact and difference another; and that the idea of heredity has rightly grown up in connection with the former. Heredity and variation are not simply one fact and one problem. They are two distinct, though essentially interrelated and wholly inseparable facts and problems. This way of putting the matter seems unescapable when we consider a cirsumscribed group of organisms, as for example the horses, in which much is known about the ancestry in geological time and the species and varieties now existing. The student of such groups is alert for both points of resemblance and points of difference between the members of the group. He knows that his scientific integrity depends on his preserving an exact balance of effort towards the two kinds of characters, and the degree of resemblance is his sole criterion of degree of kindred. Particular note should be taken of the difference of starting point relative to problems of heredity held by students of genetics and by students of natural organic groups. For the former the descent aspect of the definition we have adopted is observationally known and is the part in which their main interest lies, while for the latter the genetic connection is, in a vast majority of cases, forever beyond the reach of observation. With him it has to be inferred or ignored. But what is his basis for inference? Degree of resemblance and that alone. So the comprehensive and balanced study of resemblances-and-differences is far more important with the student of organic groups than with the geneticist. The former must perforce devote himself to resemblances more broadly and more deeply than does the geneticist, and so is sure to have an ampler mass of facts at his command.

Looking at the phenomenon of heredity from the vantage point now reached, a fact that cannot escape attention is that the infinite number and kind of resemblances presented by the living world co-exist with a likewise infinite number of differences. This fact brings us to where we can state sharply the problem now before us: If the resemblances among completed individual organisms are explained, as prevalent theory holds them to be, by referring them to the chromosomes which constitute only a small fraction of the total mass of organisms, and which have little observable variety as compared with that among organisms, how have all the differences among the organisms come about? Of the vast total mass of material that enters into the make-up of living nature and which is composed of chromosomes plus whatever else the living body contains, how has the relatively small mass of relatively undifferentiated chromatin produced the great mass of relatively highly differentiated cytoplasm entering into the tissues and organs?

It should be stated at the outset that so utterly insignificant is the positive evidence of the production of cytoplasm by the chromosomes as compared with the evidence of the fundamental coexistence and cointeraction of these substances, that very few biologists are so bold as to contend that either ontogenetically or phylogenetically are chromosomes literally first, and producers of other parts. The extreme form of the germ-plasm theory probably implied this, although Weismann never followed the logical consequences of his speculations into phylogenetic history.

E. A. Minchin, as previously noted, has taken the bull by the horns in his address on *The Evolution of the Cell* and contended that the chromosomes or their immediate ancestors, chromatic granules, were the primal organisms. Minchin's ideas deserve examining as an example of where elementalist speculation may lead even at this late day of supposed fidelity to objective evidence. Minchin accepts the classification of biologists made by a poet writing for *Punch* into "cytoplasmists" and "chromatinists" and declares himself a "whole-hearted chromatinist." "All the results," he says, "of modern investigations into the structure, physiology, and behavior of cells on the one hand, and of the various types of organisms grouped under the Protista, on the other, . . . appear to me to indicate that the chromatin-elements represent the primary and original living units or individuals, and that the cytoplasm represents a secondary product." [7] These "hypothetical primitive organisms" Minchin thought might well be called *biococci*, the name used by Mereschkowsky for certain primal beings imagined by him. The author's desire to keep in sight, at least, of objective reality is obvious, and leads him to say frankly, "We have as yet no evidence of the existence of biococci at the present time as free-living organisms." [8] How this admission fits in with the statement previously quoted about all the results of modern investigations, he appears not to have felt it necessary to consider. Nor did he neglect to dwell upon the similarity between these chromatin-elements, with their continuity through simple division, and the germ-plasm. This aspect of the subject appealed to him especially, and some of his terminology is highly characteristic of the elementalist standpoint and especially instructive for the present discussion. The conception which has become familiar to us in late years that the germ-cells of the metazoa "throw off, as it were," a soma, has a prominent place in Minchin's comparison of the germ-plasm of multicellular organisms with the chromatin-elements of the Protista.

One of the most significant things about this particular development of chromosomal elementalism is its relation to the plasmic elementalism as first set forth by Dujardin, and later by Haeckel in his Moneron theory. An essential aim of the last mentioned theory was to reduce "life" to an ultimate simplicity in the sense of conceiving it as once manifesting itself without organized substance—in "organless organisms," as Haeckel liked to express it. Minchin criticizes with due severity the "phantom" Moneron which has been "permitted to masquerade for many years under the false appearance of an objective phenomenon of Nature." [9] But curiously, he appears not to have noticed that so far as objectivity and logic are concerned his proposal is merely to displace the phantom Moneron by the phantom Biococcus. The question of structurelessness versus organization is no less pressing in the one case than in the other, as indeed Minchin's own statement shows. "The earliest forms of life were 'Biococci,' minute ultramicroscopic particles of mycoplasm, without organization," he says in presenting Mereschkowsky's theory.[10]

A theory of chromatin hegemony less startling than this by Minchin, but hardly more satisfactory when viewed in the full light of fact and logic, has recently been elaborated by H. F. Osborn. Osborn's theory does not, he thinks, require him to conceive chromatin to be actually the primal organic substance. It is more probable, he holds, that "chromatin and protoplasm are coexistent in cells from the earliest known stages." [11] But the author's central purpose, that of working toward "an energy conception of Evolution and an energy conception of Heredity and away from the matter and form conceptions which have prevailed for over a century," [12] permits him to pass over rather lightly the morphology of the hypothetical first Life. It is clear, though, that "*heredity-chromatin*," a term which he uses as a synonym for germ-plasm, holds a commanding place in his mind. This is clear from many direct statements, as for example that of the conception that chromatin is the "*seat* of heredity," while protoplasm is the "*expression*" of it.[13] But a "seat" as thus used is always something far more fundamental and interesting than an "expression." For instance, in Osborn's enterprise the "matter and form" which, as indicated above, he proposes to move away from, would come under the head of "expression" rather than "seat." There are several highly significant things about these speculations, only one of which is it justifiable to mention here. That is the curious dualism into which Osborn is led. As between Body- and Heredity-chromatin, he conceives a sort of independence which reminds one of the independence of Body and Mind assumed by the hypothesis of psycho-physical parallelism. His theory of heteroplasy conceives that "we are studying not one but four simultaneous evolutions."[14] Of these four one is the Inorganic Environment and another the Life Environment. That is, two pertain to the Environment, so that the other two pertain to what in ordinary biology is considered the organism. But in Osborn's theory the "developing organism (protoplasm and body-chromatin)" is only one of the two evolutions, the other being "heredity-chromatin." In other words, so far as evolution is concerned, the organism is one thing, having its laws of evolution which are pretty well known, while the heredity-chromatin is quite another thing, the evolutionary laws of which are still to be discovered.

This will suffice to indicate how uniquely dominant a rôle chromatin, or the heredity variety of it, plays in this significant speculation. A direct examination of it is not necessary, since our whole argument will be recognized as incompatible with it. We may, however, call attention to the unmistakable indications scattered through the theoretical part of *The Origin and Evolution of Life* that so far as chromatin enters into his theory the author is faced toward metaphysics, and metaphysics of a distinctly mystical cast. One of the moderate expressions showing this trend occurs on the first page of the preface: "Some of these miracles [of adaptation] are recited in the second part of this volume to show that the germ evolution is the most incomprehensible phenomenon which has yet been discovered in the universe." The author's *emotional attitude* toward his theory is to me one of the most significant things about the book. And my criticisms of the theory, implied rather than expressed, are not at all against the *fact* that an emotional attitude is displayed by the author but only that the focal point of this attitude should be chromatin, whether heredity-chromatin or any other—especially when the author is a palaeontologist!

Meaning and Criterion of "Mechanism of Heredity"

If we decide to apply the term "mechanism" to the means by which organisms produce other organisms like themselves, we obviously ought to consider carefully what a mechanism would be that could serve such a purpose. Obviously, I say, such a consideration is due because nowhere else in the world, either the natural or the artificial world, do we find need for any such mechanism. Heredity is surely one of the most distinctive phenomena presented by living beings, so its mechanism must be unique. We have already called attention to the familiar but often ignored fact that "heredity" is the term applied to the universal truth that as the organism unfolds itself from the relatively minute and simple stage known as the germ into the relatively large and complex stage known as the adult, it does this in accordance with a scheme or pattern characteristic of the species to which the organism belongs, so that any particular individual in the series resembles those which have gone before it. And this unfolding, we have pointed out, consists essentially of a great intricacy and succession of transformations. From this it follows that the "mechanism of heredity" would be the materials and structures by which these transformations are accomplished. To think of the hereditary substance, or the "mechanism of heredity" as belonging to the germ-cells alone is utterly unwarranted by the obvious facts, as everybody must see who will reflect broadly and candidly on the subject.

A truly objective study, consequently, of the mechanism of heredity must be a study not only of the materials and structures in the germ-cell stages, but in all stages whatever, by which the production of hereditary parts and attributes is accomplished.

In other words, a real study of biotic genesis, whether the generating parts be hereditary or variational, that is, like or unlike those of ancestors, must be first and essentially by the methods of descriptive ontogenesis. The only direct evidence we have or can have of the origin of a part or an organ is the observed transformations by which that part or organ is produced from preceding parts, and the materials participating in the transformations are the hereditary substances, if that term is to have any legitimate meaning.

To illustrate: the lens of the vertebrate eye originates from a patch of ectoderm exterior to the optic globe. The optic globe itself arises by an outpocketing of the primitive brain. Since both lens and globe resemble the corresponding parts of the eye of ancestors near and remote, their development comes under the principle of heredity; and the ectodermal patch giving rise to the lens, and the part of the primitive brain giving rise to the optic globe are mechanisms of heredity; and the whole observable series of embryonic parts which culminate in the completed eye are the *only direct* evidence for the mechanism of heredity for the eye. So is it with all biotic ontogenesis whatever. This brief statement is in essence nothing more than the gist of the facts discovered and principles laid down by Wolff and von Baer, and the truth expressed has been the foundation of all solid achievement in embryology throughout the history of the science. It is strange that conditions should arise at this time of advanced progress in biology which involve what seems decidedly like an abandonment of this foundation.

It could hardly have been believed in the hey-day of descriptive embryology, in the decade, for instance, following the publication of Francis Balfour's "Comparative Embryology" that the time would again come when the dominant theories of organic genesis would have regard to the completed organism at one end of the series, and the germinal elements at the other, with well-nigh complete neglect of all the intervening stages. Yet this is essentially what has happened. One cannot avoid seeing this if he examines with open mind almost any of the literature produced by the modern school of geneticists, especially if the work has been under the spell of Mendelism accepted as a creed to which conformity must be reached by hook or crook, and not as an instrument to be used when applicable and useful. Unless observation is to be denied a primary place in biological method, and unless that place can be unreservedly given over to inference and deduction, I see no escape from the necessity of testing by the familiar methods of embryology the hypothesis that chromosomes or any other particular bodies are the mechanism of heredity; that is, of showing in what particular way the bodies participate in the origin of a given part or organ from its forerunners in the developmental series: If, for example, it be contended that a particular portion of a chromosome causally explains eye color, then some activity or transformation, morphological or chemical, of that chromosome, not away back in the germ-cell, but in the cells of the part from which the color-bearing cells immediately arise, should be proved. This alone would be direct evidence for the chromosomal hypothesis of heredity.

And thus it comes to pass that evidence on the problem of the mechanism of heredity will be of two sorts, direct and indirect. Direct evidence will be that obtained by immediate observation of the actual transformation of substances and parts into other substances and parts known to be hereditary. The methods here will be those of ordinary histogenesis and organogenesis, only carried on with reference to the hereditariness of the parts produced. Indirect evidence, on the other hand, will be any sort of evidence which does not come from immediate observation as above indicated, but depends upon some measure of inference interposed between the observation and the conclusion. By far the greater part of the evidence of this kind being used at present in researches on heredity comes from observations on the germ-cell stages at one end and on adult stages at the other end, of the ontogenetic series. From these observations the inference is drawn by various courses of reasoning that the observed adult structures and attributes are dependent upon and explained by the observed germ-cell structures and attributes.

Our next task will be that of examining both these sorts of evidence with special reference to the problem of hereditary substance as it presents itself in present-day genetic research, namely that of whether nuclear substances, especially chromatin, or cytoplasmic substances, are the "mechanism of heredity."

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Chapter XII

EVIDENCE FAVORABLE TO CHROMATIN AS "HEREDITARY SUBSTANCE"

A. DIRECT EVIDENCE

Evidence from the Ontogeny of Some Protozoans

WE conform to the time-honored custom in zoology of beginning the examination at the lower end of the taxonomic scale.

As a first example we take the trichocysts (*tr.* figure15) that occur in some protozoa of the class Ciliata. *Paramecium*, for instance, is well armed with these organs. Briefly characterized, they are elongated, spindle-shaped bodies situated in the ectoplasm perpendicular to the surface of the body. Each has a short bristle-like process at its outer end which probably pierces the pellicula, or outermost layer of the body, and is in contact with the surrounding world. They are organs of offense and defense, and under proper stimulation are explosively converted into long, somewhat rigid threads which project from the surface of the animal.

As the animal on which the investigation we shall make use of is not *Paramecium*, but a less generally known relative, *Frontonia leucas*, our figures will be taken from this latter species (figure 15). The work referred to is by C. Tönniges and is so recent as to have had hardly time to receive the confirmation by other students which unexpected results should generally get before being used in a work like this. But Tönniges is an experienced and trustworthy worker; and since there is nothing inherently improbable in the results, it seems justifiable to take them as conclusive, at least in main outline. The observations on the develop-

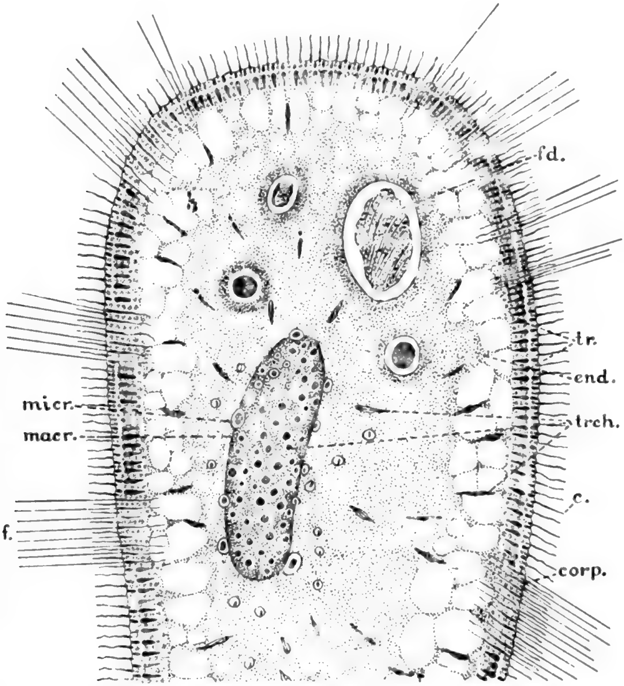


FIGURE 15. FRONTONIA LEUCAS (AFTER TÖNNIGES).
c., cilia. corp., cortical plasma. end., endoplasm. fd., food. macr., macronucleus. micr., micronucleus. tr., trichocysts. trch., trichochromidia.

ment of the trichocysts that specially concern us now may be stated in a short paragraph.

The organs (*trch.* figure 15) originate in the macronucleus (*macr.*) and migrate through the nuclear membrane and cytoplasm of the animal's body to their final position in the ectoplasm. An essential constituent of the germ, as it may be properly called, of each trichocyst, is a body which from its familiar characteristics as to density, light refraction and stainableness, Tönniges does not hesitate to regard as chromatin. It seems undoubted, consequently, that chromatin of the macronucleus contributes directly to the origin of the trichocysts in *Frontonia* and probably in all related protozoans. Figure 15 shows the germinal bodies, *trch*, in the macronucleus, *macr.* and various stages and positions of the trichocysts as they develop and make their way through the cytoplasm. The details of development are highly interesting and will be examined more closely in a later section. The very brief account given here suffices to show chromatin acting *directly* as "hereditary substance" in the production of trichocysts. But, as we shall see later, while chromatin is here an undoubted physical basis of heredity, it is not the only substance that plays such a part in this particular case. Nor should the reader neglect to notice that the chromatin functioning thus belongs to the macronucleus which, according to current interpretation, is not concerned with reproduction but with nutrition, its chromatin being called "vegetative."

Perhaps the clearest cases among the protozoa of direct contribution of the nucleus to the production of organs are furnished by the origin of the flagella in some groups. A good example is furnished by the soil amoeba *Naegleria gruberi* upon which Professor Kofoid has recently published a short paper (figure 16a, 16b, 16c, 16d). Individuals of this species change "on slight provocation under conditions of laboratory culture," from an amoeboid, non-flagellate phase (figure 16a) to a non-amoeboid flagellate phase (figure 16d). The nucleus of the animal is in the form of a single karyosome situated within a heavy nuclear membrane. (Figure 16a). Professor Kofoid's description of the development of the flagella is clear. He says: "When it enflagellates the karyosome sends out a chromatic process (Figure 16a) which traverses the nuclear membrane, forms a marginal

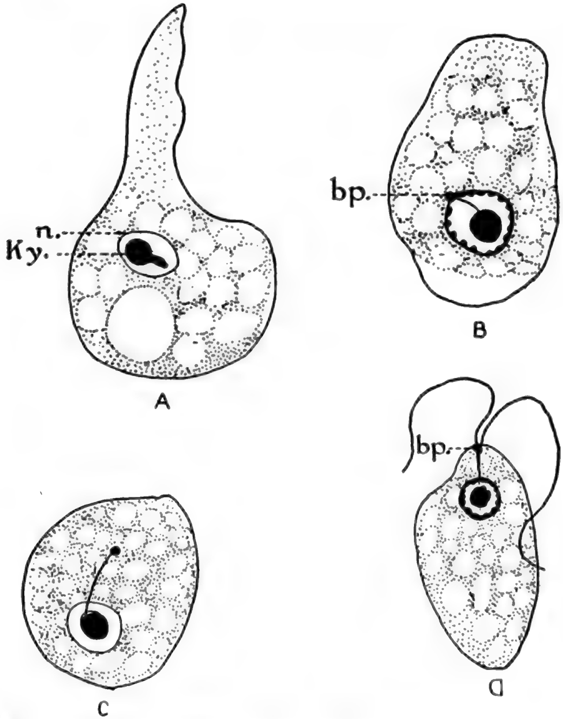


FIGURE 16. NAEGLERIA GRUBERI (AFTER KOFOID).
bp., blepharoplast. ky., karyosome. n., nucleus.

blepharoplast (Figure 16b *bp.*) and emerges as two long flagella. (Figure 16d). The body assumes a rigid, asymmetrically curved shape and the organism swims away in the typical spiral course." [1] Since the regularly recurring flagella of this animal, two in number, constitute a resemblance between the corresponding stages in the life of each individual, and undoubtedly between an individual and its progeny, they are an instance of heredity; and since their development is directly contributed to by the chromatic body of the nucleus, we have here a clear instance of chromatin acting as a mechanism of heredity.

The reader will recall that in *Crithidia leptocoridis* and in *Giardia muris*, two protozoans quite different from each other and both very different from the amoeba-like creature just described, the flagella of the adults are also connected, by way of a blepharoplast, with the central chromatic body of the nucleus. The same connection is known to occur in numerous other protozoans. Indeed, its occurrence is so frequent that some authorities now regard flagella in general as belonging to the nuclear system. Minchin particularly is a supporter of this view. Starting from species like *Mastigina setosa* in which Goldschmidt has shown that the flagellum seems to arise directly from the nucleus, Minchin presents a scheme of "possible phylogenetic origin of the different types of flagellar attachment in flagellates."

An important element in the general problem of the relation of flagella and cilia to nuclei is the question of the origin and nature of the blepharoplast. The statement was made when we were examining the adult anatomy of *Giardia muris* that the blepharoplast question would receive further consideration in the discussion now occupying us. This question is fundamentally connected with a cell organ which, though of undoubtedly high importance, has not hitherto figured in our treatment. Reference is made to the centrosome.

The term "blepharoplast" (from the Greek *blepharon,* eyelash) came into biology from the botanical side. It was applied by Webber to a body occurring in the spermatogenous cells of *Ginkgo* and *Zamia,* "because of their special function as cilia-formers," the spermatozoids being derived from the body in these plants. That the production of cilia is the main if not the exclusive office of the body in these and other plants, Webber and other observers have made certain. The question of the relation of this body to the centrosome, which latter is generally held to be part of the nuclear-divisional apparatus of the cell, has been much discussed. In the plants mentioned Webber believed, seemingly with full justification, that the blepharoplast arises *de novo* in the cytoplasm and at no time has connection with any part of the division apparatus. It seems to have no office other than that of producing the cilia. Almost certain it is, consequently, that in several distinct groups of plants, Ginkgo, cycads and mosses for example, the main portion of the motile organ of the sperm cell is derived from the cytoplasm of the cell and not from chromatin or any other nuclear material.

But such an origin does not hold for the corresponding organ of all sperm cells. In several animals, insects and salamanders for example, there is practical agreement among authorities that the axial filament of the sperm "tail" grows out from the centrosome.[2] Furthermore, it seems to be accepted that in some animals, e.g., some echinoderms and worms, the centrosome arises from the nucleus.[3] Viewing these facts in connection with the recent tendency to exalt the nucleus as the "seat" of all sorts of cell capacity, and putting them alongside those above sketched concerning the nuclear connection of flagella in some cilia-bearing protozoans, one readily sees the strong temptation to homologize the motor apparatus of the spermatozoan with that of the protozoan and conceive a common basis for both in the nucleus. If the centrosome could be held to have arisen, phylogenetically, from nuclear chromatin; and if the blepharoplast, which is unquestionably a cilia-producer, could be counted as fundamentally a centrosomal structure; and could such a generalization be established, it would certainly be a considerable achievement in support of the theory of universal nuclear and chromatinic hegemony in development. We must, consequently, scrutinize somewhat closely the evidence which points in this direction.

Evidence from Certain Cells of Multicellular Organisms

A decade ago the centrosome problem held a commanding place in cytological investigation and an extensive literature gathered around it. Nothing like an exhaustive review of the observations and hypotheses can be thought of here. But our present interest in it, namely the question of whether or not flagella are originally and fundamentally part of the nuclear system, requires us to acquaint ourselves with some of the main results reached by investigations into the structure, function and origin of the centrosome.

As regards structure, what most concerns us is whether the minute central granule, deeply stainable in certain special dyes, is the essential thing, and so should be regarded as the centrosome, or whether this granule, together with the more voluminous, less dense, less easily stainable substance around it, are fundamental so that the whole should be regarded as the centrosome. Such an examination of the writings on this question as a general student is able to make almost forces him to conclude that the application of the names centriole, micro-centrum, cytocentrum, astrosphere, attraction sphere, etc., to the various objects treated under the general designation "cellular centers," is at present largely a matter of personal choice. This results from the great structural variety, taking the whole animal kingdom together, of the parts dealt with, and the meagerness of positive knowledge as to the functions of these parts. Thus, on the question which chiefly concerns us now, that of what shall be called centrosome, great difference of view and hence of nomenclatural usage prevails.

The term centrosome was first used according to Wilson, by Boveri and was applied to a small protoplasmic spherule differentiated from the surrounding cytoplasm "in the center of which one or two exceedingly minute spheres, the centrioles, are enclosed." [5] In a word, as originally conceived, the centrosome conformed to the second alternative indicated in what was said above about what a centrosome really is. But later investigations produced facts, chiefly concerning the penetration of the astral rays during indirect cell division into the less stainable substance around the central granule that led many investigators to regard the granule alone as the centrosome. This is the position held by E. B. Wilson in the 1899 edition of *The Cell* and also by O. Hertwig in his *Allgemeine Biologie*. But Hertwig tells us in the fourth edition (1912) of his book [6] that the arguments produced by Heidenhain in *Plasma und Zelle* have convinced him that the term centrosome ought to be used in the original sense, the name centriole, used by Heidenhain and others for the central granule, being favored by Hertwig.

Heidenhain's statement that the centrosome problem has recently entered a new stage, largely, according to him, through the researches of Vejdovsky and Mrazek, seems justified by the observations. "Evidently," says Heidenhain, "in the centrosomes of large cells (eggs, blastomeres,) we have to do not with any sort of sharply differentiated bodies of definite organization, not with organs whose capability rests upon a definite, intrinsic constitution reached through systematic development, but with *structural material* transported from place to place through the activity of the radially differentiated cell substance and heaped up for further use." [7]

One can hardly avoid reflecting that this statement by Heidenhain seems to accord much better with the physical-chemistry conception of the cell, that is, with that of the cell as a system of phases in dynamic equilibrium, than with the older idea of the centrosome as in some peculiar way a "dynamic center" of the cell. Nevertheless for the purpose of a general discussion like that in which we are engaged, we may leave the question of what the term centrosome ought to be applied to undecided, and fix attention upon the central granule as belonging structurally to the "cellular center," this phrase being understood to cover a very wide range of objects none of which are simple and some of which are quite complex.

As to the function of these "centers" there appears to be unanimity among the authorities that they are in some way "dynamic centers of the cell" as originally expressed by Boveri. There is some satisfaction in this unanimity even though the range of possibility in "dynamic" is so wide as to make the unanimity rather indefinite. For one thing, it is certain that the centers take an active and important part in indirect cell division. This is a basal tenet of modern teachings concerning cell division. The rôle of the centers as force- and activity-producers which concerns us here is in connection with flagella and movements characteristic of these organs.

Evidence from the Spermatozoan.

There appears to be nearly complete agreement among authorities that the axial filament of the tail of the spermatozoa of many animals arises from a basal granule or centriole of the spermatid. Illustrations of this may be seen in many of the recent studies of spermatogenesis. If one compares early stages of the transformation of the spermatid into the spermatozoan, like those of the rat (figure 17) with some of Miss McCulloch's figure (8) of *Crithidia*, already described, the resemblance between the two is unmistakable, when one considers the difference in the animal species to which each belongs. In both there is the relatively voluminous cytoplasm, the large nucleus (*nuc.*),

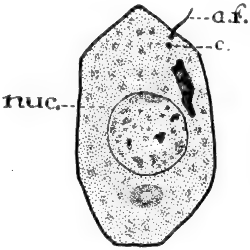


FIGURE 17. SPERMATID OF THE RAT (AFTER DUESBERG).
a.f., axial filament. c., centrosome. nuc., nucleus.

the filament (*a.f.*) connected with the granule (*bas. gr.*), and between this granule and the nucleus another chromatic body (*c.*). To be sure the resemblance falls far short of identity; but it is nevertheless so striking that hardly any one can avoid recognizing it, nor can he well avoid asking what it means. Can it be a resemblance due to descent and hence an instance of heredity? That it is due to descent in the meaning of the term as used in our definition of heredity is certainly not the case. Descent in that definition means *observed* descent as when the ancestry of a child is a matter of family record. Such resemblance is declared due to descent because the ancestry is known on *other grounds* than that of such resemblance as appears between the adult unicellular *Crithidia* and the developing sperm cell of the rat. The only ground for supposing descent in the latter case is the resemblance itself. We have, consequently, no right to reason about the corresponding parts of these two organisms as though we had other proof of their kinship than that of the resemblance indicated.

Similar needs and activities and surrounding conditions tend to make organisms resemble one another. No biological principle is better established than this. And surely as between *Crithidia* and a rat sperm there is much similarity of need, of activity, and of environment. Both are single cells of approximately equal size, and in both a high degree of locomotor ability adapted to a fluid or semi-fluid environment is essential; so we are bound to recognize on purely anatomical and physiological grounds and quite apart from descent in any strict sense, that considerable resemblance between the two might be anticipated. In other words, the well-known and widely operative fact of parallel adaptive modification in development is at least as likely to be the explanation of the resemblance here as is descent.

Appeals to recent cytological discoveries for evidence to support the theory of germ-plasm continuity as the basis of heredity have been altogether too unmindful of this biologic principle of adaptive parallelism. With such a fact before us, as for example that of the "practical identity" in minute structure of the heart muscle of the horse-shoe crab and of vertebrates [8] where there is hardly a glimmer of probability that the resemblance is due to anything else than adaptive parallelism, how escape recognizing that the resemblance between a protozoan and a vertebrate sperm-cell is probably due to the same cause? And innumerable instances hardly less striking than this presented by the hearts of *Limulus* and vertebrates could be pointed out.

Origin of the flagellum from the chromatin of the nucleus in any or many protozoans has little weight as proof that the axial filament of the spermatozoan is phylogenetically of the same origin. While, as stated above, it may be accepted as proved that in some animals the centrosome arises from the nucleus, in a far larger number of animals the

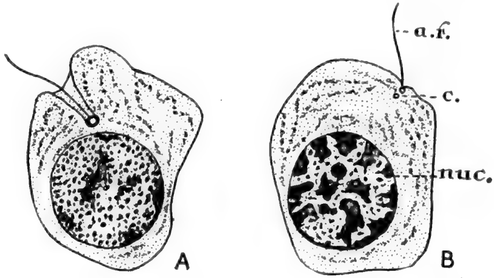


FIGURE 18. SPERMATID OF SALAMANDER (AFTER HEIDENHAIN).
a.f., axial filament. c., centrosome. nuc., nucleus.

evidence is all against such an origin. Furthermore, in many animals a pair of "cromioles" occur, seemingly homologous to the chromosomes, situated in the cytoplasm of various

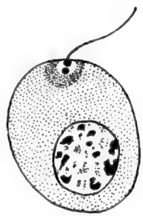


FIGURE 19. SPERMATID OF SNAIL (AFTER HEIDENHAIN).

cells at a point as remote as possible from the nucleus; and from one of these in the sperm mother cell the axial filament of the spermatozoan grows out.

The development of the spermatozoan from the spermatid in two widely separated animals, a salamander (figure 18, a and b) and a land snail (figure 19), illustrates several interesting aspects of the point before us. In both the spermatid possesses a lash or flagellum which arises from the outermost of a pair of granules or centrioles situated in the cytoplasm just beneath the surface of the cell. In an early stage of the transformation of the salamander spermatid the pair of centrioles moves inward toward the nucleus, the inner member of the pair finally entering the nucleus and becoming the middle piece of the sperm head, while the outer membrane is converted into a ring which finally contributes the undulating membrane of the tail of the completed sperm.

Connection between the centrioles and nucleus in the snail's sperm is accomplished in a different manner. Instead of an inward migration of the pair as in the salamander, the inner member of the pair sends an ingrowth toward the nucleus, the centrioles themselves remaining at the surface of the cell and remote from the nucleus. This ingrowth becomes much elongated and produces finally the axial thread of the sperm, the anterior end of which is embedded in the nuclear part of the head. Much this same sort of thing occurs in many other animals, both vertebrate and invertebrate.

There can be no question then that in a large number of animals the centriole of the sperm is primarily quite independent of the nucleus, and only becomes connected with it as the sperm develops. Consequently, to speculate that originally or ancestrally the nucleus gave rise to the centriole and axial thread of the sperm is to go exactly contrary to the most direct and positive evidence we have bearing on the question. To this direct evidence drawn from the study of spermatogenesis, that the centriole is in its origin quite independent of the nucleus, should be added the extensive evidence that the centriole is self-propagating by division and passes on from cell generation to cell generation somewhat as the nucleus does. But this fact is so familiar a part of elementary cytology as to need no special treatment.

The upshot of this discussion is that while as regards flagella in some protozoa there is solid observational ground on which to rest the theory that chromatic bodies of the nucleus are "bearers of heredity", the effort to make the facts presented by the protozoans support the general theory of chromatin as the "hereditary substance" by comparing the nucleus-blepharoplast-axial filament of the spermatozoan, is quite unwarranted. Indeed, due regard to all the facts involved in this comparison finds in them very strong evidence against the conception that chromatin is the exclusive "hereditary substance."

Evidence from Pigment Cells

Another set of facts brought out by recent studies which connect the nucleus directly with the production of definite hereditary attributes, concerns the ontogenetic origin of certain colors. A paper on an investigation in this field published in 1915 is introduced by this sentence: "The more recent work on the formation of melanin seeks to derive this pigment from chromatin elements".[9] One may remark the form of expression here. Recent work "seeks to derive" melanin from chromatin, rather than "seeks to learn whether, if at all, and in how far melanin is produced from chromatin". No biologist speaking as a proponent of the "scientific spirit" will, I think, hesitate to admit that the latter mode of stating the problem is more in accord with that spirit. Yet when a specific situation arises, the tendency to depart from the seeking-to-learn spirit and to assume that of seeking confirmation for an adopted hypothesis is still well-nigh irresistible even in science. The temper of the day in a considerable section of biology is one of thorough going partisanship in behalf of chromatin.

The "seeking to derive" things from the chromosomes is not by any means limited to melanin. Neurofibrils, muscle fibrils, and glandular secretions are among the things which so far have appeared as conspicuous claimants for such an origin. And one familiar with the discussions of ontogenesis in the period of the *Gastrea* theory, can hardly fail to recognize the same tendency that prevailed then to force the evidence. Forecasting in the light of history alone, we may anticipate that out of the chromosome theory of heredity will emerge proof that these bodies are of great importance in actual development, but that their importance consists in their being indispensable tools or agents of the organism rather than entities, ultimate and supreme in their power over the organism. Thus already the demonstration is almost if not quite complete that the nucleus plays an important part in the production of melanin and other organic pigments, and so is a mechanism of heredity to some extent, so far as colors are characteristic in genetically related organisms.

A notable forward step toward solving the problem of pigment formation was taken by E. Meirowsky. Besides producing important evidence bearing on the old and much discussed question of whether pigment arises in the epidermis or cutis or in both, Meirowsky turns his attention to how the melanin arises within the cells. He concludes that it is the result of the transformation of a colorless substance originating in the nucleus. From the intense red it assumes when treated with the basic stain pyronin, this substance is called by the author pyrenoid nuclear substance. It is said to pass through the nuclear membrane into the cytoplasm. The particles gradually turn brown, this color appearing first on their surfaces. The transformation of color is said to begin in some of the substance before it leaves the nucleus. It is not contended that the pyrenoid substance is derived from the chromatin of the nucleus, but merely that it arises in and is extruded from the nucleus.

The latest contribution to this subject which has come to my notice is by Davenport Hooker. Studying the development of pigment in various tissues of the embryo of a frog, *Rana pipiens*, this observer has shown conclusively that the melanin granules all arise in the cytoplasm at its line of contact with the nucleus. The first pigmentation appears in a very thin layer over the whole outer surface of the nuclear membrane. From here it increases uniformly all around the nucleus and gradually fills the entire cytoplasmic part of the cell, the nucleus itself, however, remaining free from pigment. The absence of pigment from the nucleus of pigmented cells is, as is well known, of wide occurrence. In this case at least the evidence seems conclusive, as the author says, "that the nucleus plays an essential part in pigment formation".[9] What that part may be is the important question, and one as yet by no means fully answered.

Several investigators hold that the chromatin of the nucleus is the direct source of the pigment. Thus, for example, Aurel von Szily reports that in the vertebrate eye the melanin granules are produced from the colorless rod-like bodies derived directly from the chromatin of the nucleus. These bodies he calls pigment bearers (*Pigmentträger*).[10] They pass out of the nucleus through the nuclear membrane and become disseminated through the cytoplasm, where they are gradually transformed into melanin granules.

Much more evidence might be brought forward on the morphological side that the nucleus at least and probably its chromatin takes a direct part in the production of brown pigment. And the supposition is strengthened and extended by evidence produced in recent years of how, chemically speaking, the nucleus does its work. The idea that the nucleus is specifically concerned in the oxidative processes of the cell had been gradually gaining definiteness for several years before 1902, at which time R. S. Lillie produced apparently conclusive evidence to this effect so far as concerns frog tissues. He subjected living active cells to reagents which indicate oxidation in the animal body by change of color.*

* Several such reagents are known but the one chiefly relied on by Lillie and which has since been frequently used for the same purpose is

Although some investigators report having failed to get the differential reaction described by Lillie, on the whole his evidence with much more of like purport that might be cited, makes the conclusion seem unescapable that for a considerable range of animals the "nucleus plays an essential part in pigment formation by some activity which greatly resembles an oxidizing action."

How far the chromosomes are responsible for this activity, is by no means settled. Hooker could find nothing similar to von Szily's "pigment bearers", or evidence of any kind that the melanin granules come from chromatin. Indeed, he brings forward a number of weighty considerations against the theory that in the frog at least the chromatin is directly concerned in pigment production. He holds that his observations demonstrate that in this animal "melanin is formed in the cytoplasm of the cell at the point of known greatest efficiency of the nucleus as an oxidizing agent."

Summarizing our examination of the direct evidence favorable to the theory of chromosomes, or at least chromatin, as the mechanism of heredity, we find that in the origin and growth of flagella and pigment in some organisms the theory receives a certain amount of support.

B. INDIRECT EVIDENCE

The indirect evidence favorable to the theory will now be considered. Significantly enough the theory is supported chiefly by this sort of evidence. To such an extent is this true, and so sterling in quality and great in quantity is the

a mixture of one of the naphthols with a derivative of one of the benzenes. This mixture produces a deep violet-colored fluid on oxidation. By treating kidney tissue, for example, under proper conditions with this indicator, Lillie found that the "nucleus of the tubule cells remains comparatively clear and uncolored, and that the coloration of the cytoplasm is diffuse, but *typically deeper in the immediate neighborhood of the nucleus than elsewhere*—a clear indication that oxidations are especially active at the nuclear surface."

evidence of this class, that many students devoting themselves exclusively to genetics seem not to realize that they are dealing with such evidence. Reference is here made to the truly brilliant researches of the last years proving beyond a doubt that in the sexual mode of propagation of many plants and animals some sort of interdependence exists between the attributes of the developed organism and the chromosomes of the germ-cells.

Since it is taken as proved that such an interdependence exists we are not required to examine critically the evidence itself. Rather are we to inquire concerning the nature and meaning of that interdependence.

The Chromosomes of Germ-Cells in Fertilization

The field is one of magnitude and complexity, and we can touch only its prominent landmarks. The earliest known class of facts, as well as one of the weightiest, favorable to the theory concerns the part played by the chromosomes of the male and female germ-cells in fertilization, the structure and behavior of the male cells being especially important. It is now an established fact that the head of the male reproductive cell, the spermatozoan, consists mainly of the transformed nucleus of the spermatid, that is, the cell from which the sperm is immediately derived, and that by far the larger mass of the head comes from the chromosomes. In fact, so demonstrably large a portion is thus derived that the statement is made over and over again in recent discussions that the sperm head is "practically entirely" of chromatin. And since this part of the spermatozoan is proved to be the predominant element in fertilization, and since the offspring inherit from the father no less than from the mother, the inference has been widely drawn and firmly held that the chromosomes must be mainly, if not exclusively, the "hereditary substance". It is, however, generally admitted that in no case among animals, so far as known, is the sperm head derived quite exclusively from the chromosomes. A small amount of the cytoplasmic part of the spermatid appears always to be carried on into the spermatozoan as a surface layer of the head. And the "middle-piece" or part immediately behind the head, seems always to contain material not derived from the chromosomes. We shall have to examine these extra-chromatinic portions of the sperm more fully when we undertake to find what substances, whether in germ or somatic cells, participate directly in actual development.

In the meantime we must recognize the important part taken by the chromosomes, or more exactly by chromatin, in fertilization and in the first steps of development of the individual. The evidence is especially weighty in some of the higher plants where according to one eminent botanist, Eduard Strasburger, the nucleus only of the pollen-grain enters the ovum. Summing up the results on the point, Strasburger writes, "In these plants (the flowering plants) the male sexual cells lose their cell-body in the pollen-tube and the nucleus only—the sperm nucleus—reaches the egg. The cytoplasm of the male sexual cell, is therefore not necessary to ensure a transference of hereditary characters from parent to offspring. I lay stress on the case of the Angiosperms because researches recently repeated with the help of the latest methods failed to obtain different results." [11] Should this statement receive confirmation by future investigation it would mark the flowering plants as the group of organisms in which specialization has gone farther than in any other so far known toward making chromatin the sole genetic intermediary between male parent and offspring.

But the sperm head, composed almost exclusively of chromatin, unites with chromatin only of the female germ-cell, the quantity of the male chromatin being apparently equal to that of the female chromatin. These facts are clearly very weighty as evidence that chromatin plays a very important part of some sort in heredity.

Fertilization of the Ova of One Species by the Sperm of Another Species

The class of facts next to be noticed as supporting the chromosome theory of heredity has come to light through experimental researches, and concerns the cytological results of fertilizing the eggs of one species with the sperm of another. During the last fifteen years considerable work of this sort has been done. Most of it has produced equivocal results, but some of the positive results favor the chromosome theory, while others oppose it. At present we will consider only those which favor it. Boveri, one of the most intellectually resourceful and manually deft investigators in this as in so many other aspects of cytology, writes: "The egg protoplasm is with reference to these qualities [i.e., of individual and species] only the material for the formative activity of the equally potent but opposite male and female nuclear parts." [12] Although this formulation was made with special reference to Boveri's own observations, as a matter of fact the evidence which seems to support it most strongly has been produced not by Boveri but by Curt Herbst. Herbst's most telling case is presented in his *Studies in Heredity.* The evidence obtained "is almost convincing, I think," says Morgan, "in favor of the view that chromosomes are the essential bearers of the hereditary qualities." [13]

Herbst conceived the interesting experiment of giving spermatozoa a chance at eggs which had already received the impulse to develop without the intervention of sperm, that is, parthenogenetically.[14] By using the eggs of one species and the sperm of another, he thought he might be able to recognize the difference in effect of the female and the male chromosomes, should development ensue under the impetus of both artificial parthenogenesis and artificial fertilization. The animals used were species of two genera of sea-urchin *Sphaerechinus* and *Strongylocentrotus*, the eggs being from the first and the sperm from the second. A few minutes after the impetus to parthenogenetic development had been given by treating them with a weak solution of valerianic acid, the eggs were removed to normal sea water and mingled with the sperm of *Strongylocentrotus.* The sperm fertilized some of the eggs, but since the nuclear changes of the male nucleus within the egg always lagged a little behind the changes of the female nucleus, it happened in some instances that the male nuclei passed into one only of the two first blastomeres, the result being that in the embryos in the two-cell stage, one cell contained only a female nucleus, while the other contained both a female and a male nucleus, which in some cases fused in the usual fashion making a larger nucleus than that of the other cell. This could be made out by direct observation. It was further observed that in batches of eggs where a two-cell stage of this sort occurred, the resulting larva possessed a typical hybrid skeleton on one side, and a skeleton typical in several respects of *Sphaerechinus* on the other.

"The female skeletal side," says Herbst, "corresponds to the small nucleus designated as left, and the hybrid to the large one designated as right." Although no details are given as to the exact relation of the two kinds of nuclei to the skeletal elements presenting characters from two diverse species, the inference is hardly to be escaped that the relation is one of actual causal dependence. But Herbst's attitude of caution and restraint must not be ignored, as it seems to have been by some of the supporters of the chromosome theory whose enthusiasm seems to be too strong for their judgment. He is careful to point out that he found no larva in which the part of the skeleton presenting maternal characters, were these characters exclusively maternal, in spite of the fact that in some of the embryos in the two-cell stage the nucleus of one of the cells seemed to be purely female. That the variations from pure femaleness toward the hybrid condition of this part of the skeleton were due to fragments of chromatin from the male nucleus having passed into the female nucleus, he regards as probable, for he could observe that in the reconstruction of the nuclei, both male and female, from the chromosomes during fertilization, the male chromatic granules did not always remain together, but were scattered about more or less, sometimes mingling quite intimately with those from the female nucleus. This would seem to give opportunity for contamination, as one might say, of the female nucleus with male chromatin even in those cases where, after the nuclei were reconstructed, nothing of such contamination could be observed. But Herbst is quite conscious of the danger in this sort of explanation, that namely, which having found some observational ground on which to base an explanatory assumption, proceeds to push that assumption to whatever lengths may be necessary in order to explain the facts as it is desired they should be explained.

The weight of this piece of evidence in favor of chromatin as *one* "hereditary substance" is undoubtedly great, and is enhanced not a little by the conservatism of the investigator who presents it. How far it goes toward proving that chromatin is *the* hereditary substance is quite another matter, and one to be dealt with later.

The Connection of Sex with a Particular Chromosome

The proof recently brought out that in some organisms sex is connected with a particular chromosome in the germ-cells is another point scored for the chromatin theory of heredity. The first phase in this discovery consisted in making out that there are two sorts of spermatozoa from one and the same male in certain insects, the difference between the two being that the head of one kind contains an element or body not present in the other. At first there was difference of view as to the anatomical nature of this extra element. Some regarded it as akin to the nucleolus rather than to the chromosomes. The idea of dimorphic spermatozoa was first clearly expressed by H. Henking as follows, "I believe every unbiased observer will view with me this spherical element [of the sperm head] sharply distinguishable from the other chromatin, as the nuclear body [present in part of the spermatids]. Thus is revealed the important fact *that we have two kinds of spermatozoa: one kind possesses a nucleolus, the other does not*." [15]

C. E. McClung, another student of spermatogenesis, first suspected that these two kinds of spermatozoa have something to do with the two sexes. The important paper in which this hypothesis is set forth was published in 1902, and within the brief period since that date, the hypothesis has been supported and extended by such a mass of observation that its universality for at least the animal kingdom seems not improbable.

The exact terms in which McClung stated the hypotheses merit attention. He says, "Briefly stated, then, my conception of the function exercised by the accessory chromosome is that it is the bearer of those qualities which pertain to the male organism, primary among which is the faculty of producing sex-cells that have the form of spermatozoa." [16] Noteworthy for our discussion is the difference of view concerning the chemico-morphological nature of the extra element in the spermatozoan as shown by these two quotations. It was regarded as sharply distinguished from the chromosomes by Henking, but as a true chromosome by McClung. The great preponderance of later opinion has sided with McClung, but very recently the question has been raised again, though in a quite different form.

This demonstration of the existence of two kinds of spermatozoa and McClung's guess as to its meaning came at an opportune time for their influence upon investigation. On several accounts interest in cell structure was already largely centered in the chromosomes. Furthermore, the Mendelian mode of inheritance was rediscovered almost simultaneously with the publication of McClung's hypothesis. Now the most fundamental thing so far recognized in connection with this sort of heredity seems to be separateness and stability of the attributes of organisms; the unit character concept, it has been usually called. As soon as the natural suggestion was made that sex itself might be a unit character, the alluring surmise was close at hand that attributes of adult organisms which segregate in inheritance, that is, which come out in pristine purity in the children, no matter how much they may have been obscured in the parents, might be connected with particular chromosomes. Add to these circumstances the more general one that the established facts and proposed hypotheses were congenial to the elementalist spirit already powerful in biology, and the tremendous impetus to work on the fascinating problems of the mechanics and cause of heredity in so far as sexually propagating organisms are concerned, can be easily understood.

It is doubtful whether in the whole history of biology any other fifteen-year period has seen greater intensity of investigation or a larger number of notable observations and discussions on any topic than has the period since 1900 on the problem of heredity and sex. And "determinants", (hypothetical somethings in the germ which "carry" and so explain characters of the adult), modified into "determiners" apparently for the purpose of disguising the unpalatableness of Weismannian metaphysics, have played a very great part in the efforts that have been made. Indeed, there seems to have been something talismanic in the word, it having inspired workers with the belief that since determiners belong to the realm of causality, quest after them absolves the seeker from the humble task of telling in ordinary descriptive fashion what they themselves are. Although no serious effort has been made in this period to give an account, either morphological or physiological, of determiners, excepting that they determine, the fact that evidence has been forthcoming in abundance that chromosomes act as though they were depositories, or carriers of determiners if such exist, has increasingly vivified and strengthened faith in them, and so has made the determiner hypothesis a stimulant to research in even greater measure than did its immediate predecessor, the determinant hypothesis of Weismann.

If the value of a "working hypothesis" is to be judged solely by the amount of work incited by it (though for reasons which it is beyond the scope of this volume to present I deny the adequacy of such valuation), this hypothesis has surely justified itself. If one mentions only the foremost workers in this field the list is by no means short and contains biologists of the first rank. The names of Boveri, Correns, Doncaster, Goldschmidt, Guyer, R. Hertwig, King, McClung, Meves, Montgomery, Morgan, Stevens, and E. B. Wilson, would be sure to appear in any list of students distinguished for what they have contributed to the advancement of biology during the last two decades, and the problem of the cytological basis of heredity has received a generous share of the attention of all these.

The fruitage of effort since McClung published his hypothesis must now be summed up, though naturally only the baldest essentials can be included. McClung conceived the accessory chromosome to be the bearer of those qualities which pertain to the male. In other words, he conceived that maleness in the insects to which his studies related was caused by the extra chromosome of the sperm cell. Two distinct questions suggest themselves to the critically minded: assuming it proved that spermatozoa having extra chromosomes do induce eggs to develop into males in some animals, how generally is this true for sexually propagating organisms? And assuming it true either universally or only in a few animals, what is the real meaning of the statement that the accessory element of the sperm is the "bearer of those qualities which pertain to the male organism"?

The answer to the first question alone concerns us now, though the answer to the second is far more fundamental and upon it depends in large measure the significance of whatever answer may be forthcoming to the first.

The arguments by which McClung supported his hypothesis were rather general and indirect, and it is possible to state in a single sentence the main outcome of later research relative to it. A connection between sex and particular chromosomes has been definitely proved for a large number of animals; but the particular connection supposed by McClung, namely, that the accessory chromosome of the sperm produces a male, has not been proved. In 1911 Wilson, epitomizing the results of his own researches and those of others using terms necessitated by discoveries since 1902, said, "The observed relations of the X- and Y-chromosomes to sex are not theories, but facts." [17] The evidence seems undoubtedly to justify this statement; so information as to what the X- and Y-chromosomes are will furnish information of the dependence of sex upon chromosomes.

Discoveries were made soon after the enunciation of McClung's hypothesis that seemed almost certainly to connect the extra chromosome of the sperm not with the production of a male, but of a female. "The decisive evidence," writes Wilson, "in regard to this question was first produced by independent investigations upon Hemiptera and Coleoptera by Miss Stevens and myself in 1905-1906." [18] This evidence was obtained by a comparative study of the chromosomal number and character in the body cells as well as in the germ-cells of both males and females. Miss Stevens's statement of results may be given. Referring to the previous investigations by herself and Wilson on a considerable list of species of insects belonging to the orders above mentioned, she said that in all cases where an odd chromosome occurs in the male germ-cells, a pair of such chromosomes occurs in the body cells of the female; from which the conclusion follows that an egg fertilized by a spermatozoan containing an odd chromosome must produce a female insect.

But a variation from this scheme was found which, though not contradictory to the principle involved, made it necessary to give this chromosome some other designation. The designation chosen by Wilson was X-chromosome, or as later observations seemed to justify, sex chromosome. "X-chromosome" is then, essentially synonymous with "accessory chromosome," and "Y-chromosome" refers to a chromosome in some species as a mate to the X-chromosome. But since the Y-chromosome constitutes a further complication, though not a fundamental modification of the principle of the relation of chromosomes to sex, the purpose of this discussion would not be furthered by going into the subject in more detail, interesting as it is from various other standpoints.

The other kind of evidence which we will mention connecting sex with chromosomes has come from animals which, like some bees and wasps, propagate by fertilized eggs part of the time and by unfertilized or virgin or parthenogenetic eggs the rest of the time. As soon as the fact had been discovered that a chromosomal difference between the two sexes occurs in some animals which always reproduce bisexually, the likelihood of a difference between the chromosomes of parthenogenetically produced females, ordinary females, and males of the same species, readily occurred to biologists, and a study of the subject has been made by several investigators. The state of things found in the honey bee, perhaps the most familiar example of virgin propagation, illustrates the principle involved. It has long been known that female bees (queens and workers) are produced from fertilized eggs, while males (drones) are produced from non-fertilized eggs. If the dependence of sex on chromosomal peculiarities known to occur in some insects be true generally, then the eggs of bees which develop parthenogenetically might be expected to differ as to their chromosomes from those which develop after fertilization. This expectation has been definitely realized. Before maturation the male germ-cells have sixteen chromosomes and the female cell thirty-two. Reduction by one-half in the number of chromosomes which occurs in typical spermatogenesis does not take place here, so the spermatozoan receives the full sixteen chromosomes. From this it results that the fertilized egg, containing thirty-two chromosomes (sixteen having been added by the spermatozoan), has undergone the usual reduction of chromosome-number during maturation, leaving it sixteen. "The fission spindle of the unfertilized egg contains only the haploid number of chromosomes (16), the fertilized egg contains naturally the diploid number (32)." [19]

"Here, then," says Doncaster, "is a clear case of sex determined by, or at least in connection with, the presence of a definite number of chromosomes; when the full, or double, number is present, the individual is a female; when only the half number is present, it becomes a male." [20] With important variations for the different animal groups, the first part of this statement has been found to be true for quite a list of animals which reproduce parthenogenetically a portion of the time, among these being certain wasps, gall flies and phylloxerans.* And observations have lately been published which strongly indicate the dependence of sex upon chromosomes in other animals in which parthenogenesis and hermaphroditism occur. This is notably true of aphids, certain nematode worms, and a pteropod mollusc. Summing up, we may say, then, that in a considerable number of animals sex is proved to be hereditary and to be connected with the chromosomal condition of the germ-cells.

The Connection of Mutation with Particular Chromosomes

Finally, the most surprising evidence in favor of the theory that chromosomes are bearers of heredity, is the discovery that certain attributes in some animals and plants, not necessarily peculiar to either one sex or the other, but which arise as mutations and are transmitted in Mendelian fashion, are connected with particular chromosomes. The best investigated examples are furnished by the evening primroses, plants which have become famous in connection with the mutation theory.

Mr. R. Ruggles Gates, one of the foremost workers in this specialty, has lately epitomized the facts and views held relative to the chromosomal characters of plants. He writes

* The investigators who have contributed most to the descriptions of the chromosomal conditions of the honey bee are J. F. Meves (*Die Spermatocytenteilungen bei der Honigbiene*, Arch. f. Mikr. Anat. Bd. 70, p. 414, 1907) and H. Nachtsheim, referred to above. Meves and J. Deusberg (*Die Spermatocytenteilungen bei der Hornisse.* Arch. für Mikr. Anat. Bd. 71, 1908) have investigated the wasp. The gall flies have been studied by L. Doncaster. (*Gametogenesis of the Gall fly* NEUROPTERUS LENTICULARIS Proc. Roy. Soc. B. 82, 1910, p. 88 and B. 83, 1911, p. 476.) The germ-cells of certain Phylloxerans have been the subject during the last ten years of some of T. H. Morgan's most important studies. His first paper, (*The Male and Female Eggs of Phylloxerans of the Hickories*, Biol. Bull. Vol. 10, p. 210) was published in 1906. In all he has written something like a dozen papers on the subject, the last so far as I know having appeared in 1915 (*The Predetermination of Sex in Phylloxerans and Aphids.* Jour. Exper. Zool. Vol. 19, Oct. 1915, p. 285).

". . . in the genus *Oenothera* the original number of chromosomes is 14. This is true of *Oe. Lamarckiana* and many other species. Duplication of one of these chromosomes through an irregular mitotic division has led to 15 in *Oe. lata,* a characteristic mutation which has occurred both in *Oe. Lamarckiana* and in certain races of *Oe. biennis.* The same chromosome number occurs in *semilata* and in a very different form from Sweden which I have called *incurvata.* De Vries has recently described still another form having 15 chromosomes. It was derived from *Oe. biennis semi-gigas* pollinated in part from *Oe. biennis* . . . Hence we may say that whenever a germ-cell having 8 chromosomes fertilizes a normal germ-cell a new form is produced. . . . *Oe.* mut. *gigas* is a prototype of another series of still more closely parallel mutations in which the chromosome series is doubled —28—the plant being a cell giant and not merely gigantic in its external dimensions. . . . A third series of morphological mutants is the *semigigas* series, having 21 chromosomes. . . . Another important feature of mutations which has not hitherto been emphasized is the fact that each is the result of a cell change which is represented in every part of the organism. The cells of *Oe. lata* constantly have 15 chromosomes, in whatever part of the plant they have been examined. Similarly in *Oe. gigas* even the most specialized tissues retain the double number of chromosomes transmitted to them." [21]

The examples of connection between mutations and chromosomes which are now attracting most attention are furnished by the fruit flies (*Drosophila*). Biology is especially indebted to Professor Morgan's genius for experimentation for the investigations in this field. The explanation of the behavior in heredity of mutant attributes in *Drosophila* elaborated by Morgan and his co-workers is admittedly hypothetical and is consequently not really entitled to a place in this section, the aim of which is to present cases of actually proved connection between hereditary attributes and chromosomes. Morgan's hypothesis is, however, so interesting and seems so likely to be proved partly true (that is, true to the extent of there being *some sort* of connection between the attributes in question and chromosomes), that it seems desirable to present the most salient parts of the theory.

That the case is, as above indicated, still in the hypothetical stage, seems not to be appreciated by some enthusiasts, though fortunately Morgan is *not* one of these. In the preface to the volume *The Mechanism of Mendelian Heredity* Morgan writes: "But it should not pass unnoticed that even if the chromosome theory is denied, there is no result dealt with in the following pages that may not be treated independently of the chromosomes; for we have made no assumption concerning heredity that cannot also be made abstractly without the chromosomes as bearers of the postulated hereditary factors." [22]

The observations on which Morgan's hypothesis rests belong to two very different categories, and these categories pertain to parts of the organism anatomically far away from each other, namely, to the union and separation or "segregation" of the hereditary attributes of adult organisms that propagate bisexually, and to the union and separation of chromosomes of the germ-cells during maturation and fertilization in these same organisms. As an illustration of the first part of this statement take one of Mendel's own cases, that of the table pea having roundish seeds crossed with a variety having angular and deeply wrinkled seeds. All the seeds of plants arising immediately from this cross (the F_1 generation) are round. But if now the plants of this F_1 lot are pollinated among themselves, their immediate progeny (the F_2 generation) will have both round and angular seeds in the proportion of three round to one angular. In a word, since the F_2 plants produce seeds corresponding in form to the seeds of both their grandparents, it is certain that the germs of their parents must have contained some sort of a combination between round-producing and angular-producing capacities of the germs, even though those parents revealed nothing of that capacity so far as their own seeds were concerned. And it is certain, too, that whatever the nature of the combination in the germs of the F_1 generation, it is such as to permit a separation of the capacities for the seeds of the F_2 generation.

In 1865, when Mendel announced these observations, nothing was known about pea germs, or for that matter about any other germs, that could remotely suggest what their constitution is in virtue of which they possess peculiar capacities. Nor was it until cytological research had accumulated a good deal of knowledge of the chromosomes that positive light from the side of germ morphology and physiology was thrown on the subject.

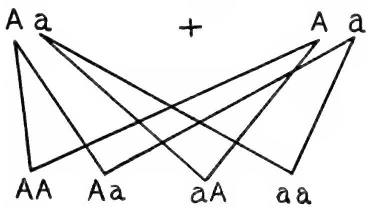
Chromosomes and the Mendelian Mode of Inheritance

The pregnant hypothesis that the combination and the separation of hereditary attributes in the fashion discovered by Mendel is not only paralleled but explained by combinations and separations of chromosomes in the germ-cells, was, according to Morgan, Sturtevant, Bridges, and Müller, first stated "in the form in which we recognize it to-day," by W. S. Sutton. E. B. Wilson has informed us how the idea came to expression almost simultaneously by Mr. Sutton, then a student of zoology in Columbia University, and W. A. Cannon, a botanical student in the same University.

The basis and formulation of the hypothesis are presented by Mr. Sutton in two papers published in the same volume of the *Biological Bulletin*. In order to appreciate the full cogency of the argument in favor of the hypothesis, it is necessary to go a little farther than we have hitherto into the structure and maneuvering of the chromosomes of the germ-cells during the "ripening" of the germ-cells. The facts usually taken as the starting point for the hypothesis are that all the cells, both body and germ, of an ordinary sexual plant or animal have a constant number of chromosomes, the number being characteristic for the species; that before fertilization, an essential feature of which is the union of male and female chromosomes, the chromosome number of both male and female cells is reduced by one half, excepting in those cases where there is an odd or accessory chromosome, so that the union of the chromosomes in fertilization restores the number typical of the species; that the final adjustment gives the fertilized egg and all the cells arising from it supposedly equal portion of chromatin from each parent; and finally, that the chromosomes of the germ-cells in many animals, if not in all, are not all alike either in form or size.

Proceeding from these facts Sutton studied the germ-cells of the lubber grasshopper with reference to the question of whether the differences in size and form of the chromosomes are haphazard and meaningless or have some constancy, especially in relation to their maternal and paternal sources, and in the way they couple with one another in fertilization. Summarizing the results for the germ-cells as they grow and multiply before the ripening process sets in, he concluded that during this period the chromosome group of each germ-cell is composed of two equivalent chromosome series, each series consisting of eleven chromosomes differing among themselves in size, and that in all probability one of these series comes from the father and the other from the mother. Furthermore, he believed that the reduction in number which takes place in this ripening stage and is known as synapsis, is accomplished by the union of two series in such fashion that each member of the maternal series unites with one of corresponding size, its mate of the paternal series, and that in the very last division before the transformation of the unripe cells into eggs and spermatozoa, a separation of the chromosomes which united at synapsis occurs, so that each egg and each spermatozoan gets the full series of eleven, characteristic of the species, some, however, being of maternal and some of paternal origin.

In his first paper, Sutton merely mentioned Mendelian inheritance in connection with the chromosome scheme he had considered. "I may finally call attention," he said, "to the probability that the association of paternal and maternal chromosomes in pairs and their subsequent separation during the reducing division . . . may constitute the physical basis of the Mendelian law of heredity." [23] His second paper is devoted to an elaboration of this suggestion. Mendel pointed out that where attributes of hybrids behave in heredity in the peculiar way discovered by him, if one of the constant characters, for example, the dominating one, be designated by *A* and the other, the recessive, by *a*, and the hybrid form in which the two are combined by *Aa,* then these two differentiating characteristics of the development series in the progeny of the hybrids will give the formula: $A + 2Aa + a$. This comes about on the supposition that the uniting of these characteristics follows the law of chance; that is, that a male hybrid with attributes *Aa* pairing with a female hybrid having the same attributes, gives:



or A + 2Aa + a, since *AA* and *aa* can be nothing more than *A* and *a* as here used.

What in essence Sutton did was to show that such a chromosome scheme as he had partly proved and partly conceived to exist in the germ-cells of the lubber grasshopper, could be brought under the identical expression that we have just seen Mendel deduced for the attributes of peas. If, Sutton reasoned, each chromosome of any series, has a corresponding one in any other series, and if these have such an identity and freedom to combine and separate as the discussion had assumed, then if a given chromosome of the father be designated by A and its mate in the mother by a, in synapsis there would arise Aa, which on reduction division preparatory to ripening of the eggs and sperm would produce two kinds of eggs and two kinds of sperm relative to this set of chromosomes, namely male A and female A; and male a and female a. These if equal in number and equally free in their movements would give in fertilization:

$$
\begin{array}{llll}
\text{Male } A + & \text{Female } A & = & AA \\
\text{"} \quad A + & \text{"} \quad a & = & Aa \\
\text{"} \quad a + & \text{"} \quad A & = & aA \\
\text{"} \quad a + & \text{"} \quad a & = & aa
\end{array}
$$

Or since Aa and aA are alike the expression becomes $AA + 2Aa + aa$ as the distribution, or again $A + Aa + a$ as the sum of possibilities of each chromosome pair. "Thus," Sutton says, "the phenomena of germ-cell division and of heredity are seen to have the same essential features, viz., purity of units (chromosomes, characters) and the independent transmission of the same." [24]

We must now return to the truly remarkable discoveries made by Morgan and his students and collaborators on mutations in *Drosophila* and on the behavior of the mutant attributes in heredity. These have consisted in showing that such a relation between attributes and chromosomes as that assumed in this relatively simple scheme worked out by Sutton may be carried out in much detail both as to attributes and chromosomes. An especially ingenious and fascinating aspect of the theory as it has been elaborated largely under Morgan's leadership, is that which shows the possibility that different parts of one and the same chromosome may correspond to several distinct attributes of the adult; that these attributes may or may not be inseparable from one another, and that when they are separable they may be transferred from one sex to the other, presumably by the transferrence of factors in one part of a chromosome of a given pair to the other chromosome of that pair.

So rapidly have come the striking observations in this field, and so striking have been the theoretical interpretations set forth that many biologists who have been admiring onlookers, have seemingly failed to discriminate just how much of what has been presented is fact, how much legitimate inference, and how much hypothesis in the strict sense. It is, consequently, eminently fortunate that Morgan himself has, as noted above, given us an explicit even though an inadequate statement of how the case stands in this regard. The sentence quoted some pages back, "We have made no assumptions concerning heredity that cannot also be made without the chromosomes as bearers of the postulated hereditary factors,"[22] should be recalled. The case standing thus, the present discussion would not be furthered by going into more of its details.

And so we come to the end of our examination of the observational evidence favorable to the theory that hereditary attributes in bisexually propagating organisms are in some way and to some extent dependent upon the chromosomes of the germ-cells. The conclusion must be, it seems, that not many of the major theories in biology are more securely established than this. Thus stated, the chromosome doctrine not only takes its place along-side the cell-doctrine, but it supplements, and in fact, partly supplants the cell doctrine. Never again, for example, can the cell be conceived, as many earlier cellular elementalists were wont to conceive it, as The Ultimate Unit of organic beings.

In several instances presented by the foregoing review of the chromosome theory of heredity, notably in that of the pollen grains of flowering plants where the final act in fertilization appears to be accomplished by the chromatin alone (see p. 343), the chromatin manifestly constitutes a unit beyond the cell and hence nearer to ultimateness than is the cell.

REFERENCE INDEX

Chapter XIII

EVIDENCE FROM PROTOZOANS THAT SUBSTANCES OTHER THAN CHROMATIN ARE PHYSICAL BASES OF HEREDITY

TAKING it as proved that in most sexually propagating organisms heredity is dependent on chromosomes, thus making the view that chromosomes are bearers of heredity legitimate in a certain sense, a fundamental question must be examined before the discussion can be regarded as having even an approach to comprehensiveness. This question may be stated thus: is heredity dependent on the chromosomes *alone*, that is, to the exclusion of other parts of the cell; in other words, are chromosomes the sole "bearers of heredity"?

At the outset of this inquiry we must recall what heredity is as understood in this treatise. It is resemblance between living beings due to descent. This is the definition which in an earlier section we decided is more satisfactory than any other when due consideration is given not only to the phenomena of organic propagation themselves, but also to the historic usage of the word. Another thing about heredity insisted upon on earlier pages should be recalled: all stages in the development of an individual are as truly manifestations of heredity as is the final or adult stage. And finally, the reader is asked not to forget the deprecation expressed early in the discussion of the unwarrantable practice with many recent writers on heredity of either ignoring asexual propagation altogether or tossing it aside as presenting no problem or anything of significance to the geneticist.

If we hold firmly to this broad but, in the light of facts, only adequate conception of heredity, the general answer to the questions stated above as to the relation of chromosomes to heredity will come without equivocation. We may give the answers now categorically, then look at the facts which compel them. Neither chromosomes nor chromatin are the sole bearers of heredity. Factors for hereditary attributes, if the term has any real meaning as thus used, are "carried" by the cytoplasm no less than by the chromatin. Many, probably all living parts of the cell, and not the chromatin and chromosomes alone, are the physical bases of heredity.

Evidence From the Ontogeny of Various Protozoans

Beginning the discussion again with the lower organisms and advancing to the higher, we first examine the development of a few protozoans; and the reader is urged to take what follows in connection with the chapters on the structure, and especially on the development of protozoans.

(*a*) *Stentor*

The development of the "trumpet animalcule," *Stentor*, having been instanced as a genuine, often complex ontogeny in protozoans, our study of heredity in the protozoa may well begin with this animal. The figures 11, 12, 13, and 14 accompanying the earlier presentation will serve us now. Reference to the account given in the former discussion finds that one of the main points brought out was that in reproduction a whole series of the *Stentor's* external organs arise *de novo*, that is, independently of the corresponding organs of the parent; and that these take their origin in the surface layer or ectoplasm, and outer part of the endoplasm. "And this *de novo* mode of origin," we read, "is followed by a whole series of organs and tissues; the cilia and membranellae of the aboral zone; the mouth, velum and pharynx; the frontal field; the ramifying zone; and the contractile vacuole and excretory pore." The question which chiefly concerns us now, but which received no consideration in the earlier treatment is, what part, if any, does the chromatin of the nucleus play in the initiation and development of these organs? One of two courses must be followed if the chromatin theory is to be proved in a specific instance like this: either the developmental facts presented must be shown not to be subject to heredity or it must be proved that they are caused by the chromatin.

That many modern students of heredity have strongly tended by implication if not expressly to pursue the first mentioned course, cannot be successfully disputed. This was dwelt upon in the early part of our discussion of heredity and we may hope its utter unwarrantableness was revealed. As a consequence our only task now is to inquire what the evidence is that the developments before us are causally explained by the nuclear chromatin—or for that matter by chromatin of any other kind.

The method of handling the evidence, not only in this particular case, but in all others with which we shall deal, must be stated at the outset. Briefly, our task is not to prove what chromatin does not do, but to point out what cytoplasm and other substances *do* in connection with the development of the organs under consideration. Otherwise stated, just as in the effort to decide whether or not chromosomes and chromatin are the physical basis of heredity, we sought for evidence of the direct participation of these in the production of organs and parts, so now we have to inquire as to whether or not extra-nuclear and non-chromatic parts of the cell participate in the production of organs and parts.

"The first sign of fission," Johnson has already been quoted as saying, "is the formation of a rift (the anlage of the new aboral zone) in the pellicula and ectoplasm, near to and almost parallel with the left boundary stripe of the ramifying zone." The list of structures enumerated as arising *de novo* should be recalled and the further fact recognized that like this first sign of fission, they all pertain to the superficial part of the animal's body. "The gradual evolution," we previously quoted Johnson as saying, "of structures so complicated as membranellae, from a mass of indifferent protoplasm, is very striking."

What of the nucleus while these parts are being started in the indifferent protoplasm? Considering the time at which Johnson did this piece of work, his account of the behavior of the macronucleus during fission is very full. "At the beginning of fission," he says, "the meganucleus has its usual spiral disposition in the body. The first alteration, just previous to the appearance of the new pharynx, is a straightening of the nucleus and disappearance of the commissures, the nodes becoming appressed." [1] The various positions and conditions of the nucleus here referred to are shown, *mgn*, of the figures.

The complete obliteration of the nodulation typical of the resting nucleus, the great elongation of the nucleus and its gradual reformation at each end, and the final division after the preparation for body-fission is far advanced, are indicated in the figures. Johnson speaks of the great activity of the nucleus in some of its stages showing something approaching an amoeboid character; but there is no intimation either by position or by activities that the nuclear changes are correlated in any detail with the formation and growth of new organs of the body.

But, it will be said, prevalent views about the macronucleus would not lead one to expect it to participate in the development of organs. The micronuclei of the group of organisms to which *Stentor* belongs, being chiefly concerned in reproduction, would be presumed to contain the hereditary substance, and so to them and not to the macronucleus ought inquiry to be directed for evidence, if such there be, of nuclear participation in the development of organs. Johnson's observations on these nuclei were very incomplete, but such as he made are significant. He found undoubted evidence that some of them divide when the animal divides; but in no case was he able to follow all the details. The points made out which seem to bear on the main question before us are: "I made out," he says, "65 micronuclei adherent to the two [pieces of the macronucleus], but none were found in the spindle stage except the two above-mentioned." [2] The point of interest for us is that so far as the evidence goes, the dividing micronuclei were closely related spacially to the macronucleus, which is another way of saying that they were *not* closely related spacially to the developing organs, so that if they played any direct part in this development they did so through some "action at a distance"—a sort of action which, though as we now know may be a real factor in organic development, can be invoked as an explanation of morphogenesis only with the greatest caution.

Another point of interest touched by Johnson's observations concerns the time of the division of the micronuclei relative to the division of the macronucleus. When the dividing micronuclei were observed the macronucleus was "at complete condensation and in two distinct pieces." [2] Turning to the account of the behavior of the macronucleus during division of the animal, we read, "the meganucleus has assumed the spherical shape [state of condensation] when the pharyngeal funnel has begun to form"; [1] in other words, at a time somewhat earlier than that shown in figure 12. That is to say, so far as the observations go, the indications are that fission of the animal begins in the cytoplasmic part of the body not only before the macronucleus undergoes any change, but also before the division of the micronuclei.

Apparently the behavior of the micronuclei during asexual fission and development in *Stentor* has not been reëxamined since the publication of Johnson's paper, so all the light we have on the part played by the micronuclei in the ontogeny of these animals is still fragmentary and indirect so far as the particular point now before us is concerned. Muslow [3] presents certain observations on these bodies during conjugation that bear on the point indirectly. For one thing, he confirms Johnson's observation that the micronuclei are situated typically close around, indeed are adherent to the macronucleus. But perhaps the most significant point for us brought out by Muslow's studies is the indication which he finds that the wandering micronuclei, that is, those that pass from one animal into the other during conjugation, are carried passively, in part at least, by the cytoplasm of the animal.

In a later section we shall consider the question of how the recent studies on the migration of chromatin granules from the nucleus into the cytoplasm, and also on the chromidia and on the mitochondria, affect the problem of nuclear participation in organ development. But our general position relative to this whole matter may be stated here as touching specifically the organogenesis of *Stentor*. In this section we are trying primarily to find what rôle the extranuclear parts of the cell play in development, so what the nucleus does or does not do concerns us only secondarily. This being the case, when Johnson says (and it should be remarked that descriptions of like purport by other students concerning other protozoans, are almost numberless), the "gradual evolution of structures so complicated as membranellae from a mass of indifferent protoplasm," we take the description at its face value and hold that no matter what outside influences may operate on this protoplasm, *it itself* plays an active and essential part in bringing about the results. And from this we further hold it to follow that since these results are a number of organic *parts which* *because of their resemblance to the corresponding parts in the parent organism are manifestations of heredity, the "indifferent protoplasm" which gave rise to the parts is more certainly a "physical basis of heredity" than would be any extraneous part or substance that might be shown to "influence" the substance which itself transforms into the parts.*

The essence of my contention may be briefly stated thus: recognizing as every biologist must, that transformation is an absolutely indispensable element of organic development, when the transformation of an "indifferent mass of protoplasm" into definite organs or parts takes place before our eyes, we are bound by principles of objective science to believe that the transforming substance *itself* is actively and not entirely passively concerned in the operation. We are thus bound since, by supposing that if we cannot "causally explain" the observed process we must assume that the real cause, the ultimate explanation, lies deeper and in some other substance, we are committing ourselves to a course which, if consistently followed, denies the validity of all observational knowledge. Such repudiation would result from the fact that as soon as we succeed in bringing the "other substance" under observation we are always confronted with the same difficulties as to causal explanation which we met in the first instance. In observing a cause, or the "seat" of a cause, in actual operation, we are never able to satisfy ourselves as to exactly how or why it operates as it does. Supposing, for example, we were able to see the atoms or even the electrons of nitrogen, carbon, oxygen and so on, at their work in producing membranellae in *Stentor*, does any one suppose we should be able to see fully why and how they do it? Who in modern times refuses to believe that the force of gravitation is partly inherent in the earth itself and in every other body, though no amount of examination of the bodies can make out fully how and why the bodies have such a force?

He who persistently denies that a sensible object is explanatory in a causal sense of the forces and activities it manifests because he cannot see the whole rationale of the manifestations, but insists that the final explanation must lie deeper, is at heart an apostate to observational science, and it matters not at all so far as principle is concerned, whether the invisible "deeper" cause, supposed to be final, be conceived as pure Matter, pure Energy, pure Spirit, or a Divinity.

To recapitulate: the only conclusive proof of what bodies, whether chromosomes, mitochondria or any other substances, are "bearers of heredity," is either direct or indirect observation that these bodies or substances transform into organic parts which after transformation are seen to resemble the corresponding parts of the organism's parents. And only such hypotheses concerning the nature of germcells as are made in strict accordance with the rule of evidence thus formulated, are legitimate hypotheses.

So far as fundamental principles are concerned, we might consequently go no further with the examination of details. However, since the principles are in reality only the generalized details, and the details are the mother liquor, so to say, of the science of heredity, we can hardly avoid pushing our examination somewhat farther. We will look at a few more examples among the protozoa where cytoplasm and various substances other than chromatin are a physical basis of heredity, these examples being chosen to connect with our studies of the anatomy and development of protozoans in a former chapter. It will be recalled that from the great and highly developed class of Ciliata to which *Stentor* belongs we examined *Diplodinium* and *Stylonychia*, shown in figures 1 and 3.

(*b*) *What Study of the Ontogeny of Diplodinium Will Probably Discover*

Unfortunately, next to nothing is as yet known about the ontogeny of *Diplodinium.* Mr. Sharp, who has taught us so much about its adult anatomy, has its development under investigation, but until his studies are brought to a conclusion we can do no more than ask questions pertinent to the discussion in hand. Let us fix attention upon the skeleton and the neuromotor apparatus, for example, figure 1 (*sk. lam., m. m.* and *circ. oes. ring*). When the origin and growth of these organs come to be studied, judging from our general knowledge of development, what will be observed will be a transformation in one way or another of a portion of the cytoplasm into these parts. Nor is it at all unlikely that, assuming that the work is done with the best technical methods available, chromatic material from the micronuclei will prove to play a part in the differentiation. Does any one suppose that the investigator will be able to prove that the seeming participation of the cytoplasm is a delusion and that the only form-determining agent is the chromatin? Yet nothing less, we must insist, will be required to prove the hypothesis that chromatin is the hereditary substance in these animals.

(*c*) *The Origin of Flagella*

When presenting evidence of the direct participation of the nuclear chromatin in the production of organs, we pointed to the growth of the axial filament of the flagellum in certain protozoans as an especially clear case. Now we must inquire about the origin of the other part of the flagellum—for the fact of its having an axial part or core necessarily implies that there is another part. Seemingly it is fully established that the axial core is enclosed in a contractile sheath or envelope as described and figured by Bütschli and others, figure 20. Nor is it questioned apparently, that the envelope is ectoplasmic. Even Minchin, partial as he always is toward chromatin, does not refuse to admit this. But his way of describing the flagellum is highly interesting. "A flagellum consists in an elastic axial core enclosed in a contractile sheath or envelope. . . . The flagellum takes origin from a more or less deeply-seated granule, the blepharoplast, or basal granule, which will be described in dealing with the nuclear apparatus. The elastic axis, arising from the blepharoplast, can be regarded as a form-determining element of endoplasmic origin, the sheath as an ectoplasmic motor substance." [4]

As this statement illustrates both the factual point with which we are concerned and the perverting influence of elementalist theory on supposedly straightforward description, let us examine it. If a flagellum is composed of a core enclosed in

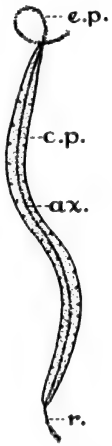


FIGURE 20. FLAGELLUM OF EUGLENA (AFTER BÜTSCHLI).

ax., axial filament. c.p., contractile protoplasm enveloping the axial filament. e.p., end piece of the flagellum. r., root of the flagellum passing into the body.

a sheath, what justification is there for saying that the organ arises from a basal granule? According to the clear implication contained in the latter part of the statement, only the axial core arises from this source. And if the statement be correct, as it undoubtedly is, that the sheath is ectoplasmic, what occasion is there for throwing into the definition the purely hypothetical notion that the elastic axis is a "form-determining element"? In view of the fact that there is as much observational ground for supposing the sheath to be "form-determining" as there is for supposing the axial core to be so, either both parts should be mentioned if a guess about form-determination is to be made, or neither should be. The consensus of view among authorities that flagella are either ectoplasmic or endoplasmic structures ought to be a sufficient refutation of the speculation that the basal granule, whatever its source, is the "form-determiner" of the organs; but when an erroneous speculation has become an imperative idea, as the chromatin hypothesis seems to have become for some biologists, nothing seems to suffice short of going through the operation of killing it time after time even though it has been dead for many months.

The truth is that if we speculate about "form-determination" of flagella, and do so on the basis of the objective evidence, we have to recognize that in some cases neither axial core nor blepharoplast can be the determiner for the sufficient reason that no such structures exist. For example, Patton has shown conclusively that in the species he studied the flagellum arises from the cytoplasm of the cell quite independently of both the nucleus and the blepharoplast. "The flagellum, about 40 in length, consists of a single stout filament which arises from the achromatic space just anterior to the blepharoplast and passes out of the anterior end. The intracellular portion does not differ in structure from the remainder and it has no basal granule in connection with it."[5] The absence of the axial core in this animal is emphasized as follows: "It is important to note that the flagellum under a high magnification consists of a single thick filament and not of a number bound together."[6] This case is especially convincing in that although technical methods were used that are held to be specially trustworthy for differentiating chromatic material, so that the nucleus with its chromosomes and the blepharoplast were brought out sharply against the surrounding faintly stained cytoplasm, the beginning of the flagellum in the less deeply stained part of the cell was clearly recognizable.

The importance of the main issue here is so great as to justify my repeating what I have said many times. The central question is not whether there may be a granule (or some other substance not made visible by the methods used) which may be form-determining for the flagellum, but whether we shall refuse to accept the observational evidence that the achromatic substance contributes, at least, to the origin of the organ. In other words, the question is, are we going to reject the positive evidence we actually have, in the interest of a pure speculation? Even should further study find that, contrary to Patton's observations, there is a granule at the base of the flagellum of *Herpetomonas lygaei* which gives rise to an axial core, the observation that the achromatic substance of the cell participates in the formation of the flagellum would not be set aside thereby.

(*d*) *Various Organs of Stylonychia and Paramecium*

In the chapter on the anatomy of the protozoa we took *Stylonychia* as an example of the high degree of specialization and integration which the sensory-locomotor system may reach in a one-celled animal. While the ontogeny of this genus has not been studied as fully as is desirable, yet the combined knowledge we have of its structure and regeneration is sufficient to leave no room for doubt that the ectoplasm and the outer strata of endoplasm take an active part in producing the elaborate sensory and motor organs. For example, the basal fibers (*b. f.*, figure 6) are shown by Maier to be attached to the basal edge of the membranellæ and to run inward in the endoplasm, where they gradually taper to very fine endings not connected with either the macronucleus or micronuclei or granules of any kind. The inference seems unescapable that ontegenetically at least they arise in the ectoplasm and grow inward. Again, as to the ectoplasm itself, Maier points out that in some parts of the animal this is laid off into definite areas, each one of which is deeply cupped outwardly and bears a cilium with its basal granule at its center. This disposition is specially clear in *Paramecium caudatum*. To suppose that such a differentiation of the ectoplasm is due to the "influence" of the basal granule, the ectoplasm itself being passively moulded, would be so gratuitous that probably no biologist would be bold enough to make it definitely; yet exactly that assumption would be necessary were "form-determination" to be denied to everything but chromatin.

Only one other developmental point can be noticed in connection with *Stylonychia,* that concerning the production of the undulating membrane (*m b p.*, figure 6). That this organ belongs to the ectoplasm is generally recognized, and the considerations advanced in favor of the view that it is partly determined by the ectoplasm, are essentially the same as those for the view that the flagella are thus produced. The particular point to which attention is now called is the view held by Maier, and apparently well supported by observations, that the membrane is the result of a fusion of a row of cilia. The evidence for this is the cross-striation of the membrane and the presence of a row of thickly set, darkly staining granules at its base. If this supposition is correct the question arises, where is the "seat" of the developmental tendency which brings about the fusion of the

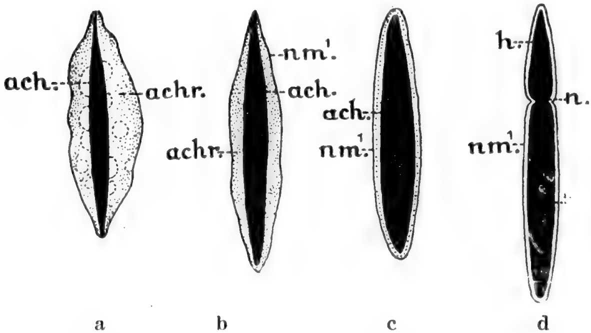


FIGURE 21. FRONTONIA LEUCAS, TRICHOCYST (AFTER TÖNNIGES).
ach., axial rod. achr., achromatinic substance. h., head. n., neck. nm.,[1] nuclear membrane.

cilia? Is it the basal granules or some other elements aside from the material of the cilia themselves? Or is it produced, as Maier says, by an "adherence of the neighboring cilia through a plasmatic substance"? Obviously there can be but one answer if it is to be based on the observational evidence.

Let us now return to the development of the trichocysts of *Frontonia* which we partly examined in the last section (figure 15, p. 327). That the chromatin of the macronucleus contributes directly to the organs was shown in the section dealing with the direct evidence that chromatin may be "hereditary substance." But it was there stated that the chromatin was not alone concerned in their production. Now we must instruct ourselves as to what besides chromatin enters into their production. The following paragraph from Tönniges tells the story in outline. "Trichocysts in the act of origination which I have designated as trichochromidia, present two substances. One is intensely colored with the nuclear staining medium employed (*ach,* figure 21), so must be regarded as chromatin. The other remains uncolored and consequently is held to be achromatic substance (*achr,* figure 21). The first produces the axial rod of the future trichocyst, while the latter, the achromatic substance, produces the external envelope and the myoneme-like structure." [7] Four stages in the development of a trichocyst are shown in figure 21 a, b, c, d. Naturally many detailed structural changes not here noticed in both the axial part and the enveloping part occur before the organ is completed and ready for use. But these need not concern us since they in no way affect the main point, namely that evidence that the achromatic substance of the macronucleus is the physical basis of heredity of organs under consideration, comes from exactly the same source and is exactly as valid as is the evidence that chromatin plays such a rôle.

The question of whether the cytoplasm of the animal plays a direct part in the development of these organs, while very important were we seeking for an adequate general theory of development or for complete knowledge of the factors involved in this particular development, must not detain us since all we are concerned with in this section is to find whether any substances other than chromatin are determiners of hereditary attributes.

(*e*) *The Skeleton of Radiolaria*

With these illustrations from the infusoria of substances other than chromatin which serve as the physical basis of heredity, we must turn from the endless examples that might be drawn from the same group, and pass to another great sub-division of the protozoa, the Radiolaria, for a few illustrations. In the chapter on the general ontogeny of the protozoa we spoke particularly of Häcker's studies on the development of the skeleton in the Aulospheridae. We will now look a little further into the development of portions of these animals.

Häcker's hypothesis of "directing centers" in some of these animals is particularly interesting for us. What the general purport of the hypothesis is can be readily under-

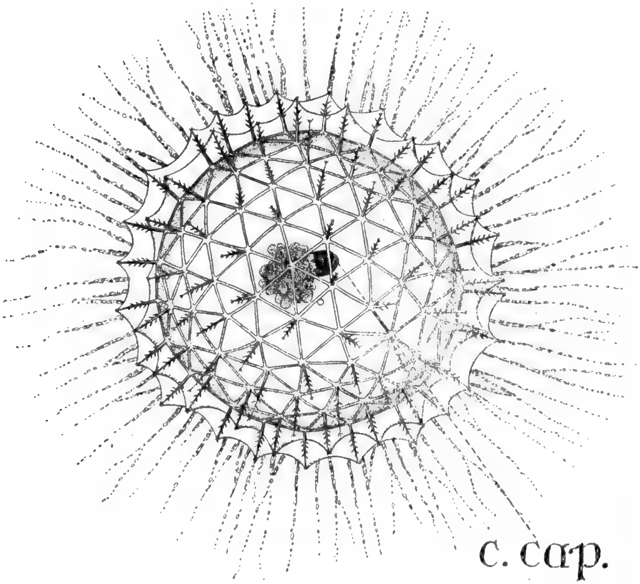


FIGURE 22. AULOSPHAERA (AFTER HAECKER).
c.cap., central capsule.

stood by the help of figures 22 and 23. The skeleton of the genus here represented is a "lattice-sphere," in Häcker's terminology, consisting of a network of tubes joining one another in such a way that six pieces unite at each nodal point. This scheme makes each mesh of the net a triangle. A radial piece or spine bearing short branches arises from each nodal point. The lumen of the tubes contains a gela-

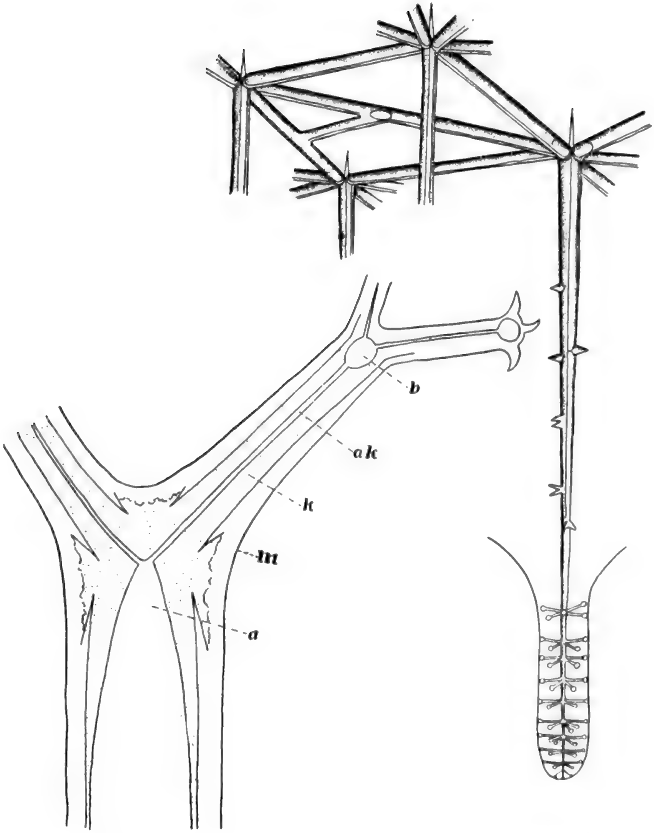


FIGURE 24.

FIGURE 23.

FIGURE 23. AULOSPHAERA ELEGANTISSIMA (AFTER HAECKER). DETAIL OF STRUCTURE.

FIGURE 24. AULOCEROS (AFTER HAECKER). DETAIL SECTION OF SPINE. a., lumen of shaft. ak., axial canal. b., vesicular enlargement of axial canal at forking of spine. k., secondary silicification. m., membrane.

tinous material and in the center a fine axial filament. As shown in figure 24, the tubes and the radial pieces are not in uninterrupted continuity at the nodal points but meet one another in a common joint.

The entire skeleton is embedded in the extra-capsular substance, and the central capsule, figure 22, *c. cap.*, containing the nucleus is, as in most Radiolaria, relatively quite small. The pattern of the skeletal net Häcker conceives to be determined by "directing centers," one for each of the nodal points.

This conception is, as Häcker fully recognizes, purely hypothetical, and consequently ought not, in the strict letter of the formulation, to be made much of. Nevertheless certain of the facts call for something of the sort, if an explanation of the peculiar skeletal features in accordance with the principles of heredity is insisted upon. The following quotation brings out the most salient of these facts: "In the stereometric 'dissimilarity' which may exist between the external body- and skeletal-form and the shape of the central capsule . . . it is difficult to imagine that the locations of the nodal points, especially in the regular triangular and quadrangular conditions, are determined (projected outward) by the nucleus. Rather one ought to think here of distributing and arranging processes which have their seat in the external layers of the sarcode body itself and are conditioned either by the competition (*Konkurrenzkampf*) of the pseudopodia or by the interplay of 'spheres of attraction.'" (Häcker's Monograph, Lief. 3, p. 627.)

Whether "directing centers" are the right things to conceive as "explaining" such a skeleton as that before us may be questioned; but I do not see how it is rationally possible to avoid believing that the main seat of the forces at work is in the extra-capsular part of the animal, as Häcker says, and not in the nucleus, and that these forces are hereditary forces. And such belief is the more unescapable by the facts that, as Häcker points out, skeletal production is no mere matter of simple secretion, or still less of crystallization, but of genuine organic growth, as a detailed study of the completed structure and histogenesis of the parts shows; and by the further fact that the parts concerned present characteristic differences for the different species. Thus in the genus *Aulosphaera* to which belongs the species we have taken as an example, Haeckel recognized twenty-one spe-

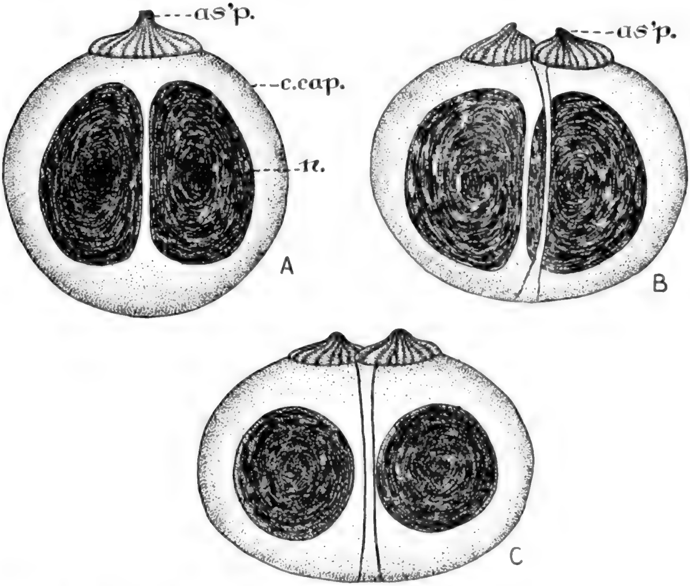


FIGURE 25. AULACANTHA (AFTER BORGERT).
as'p., astropyle. c.cap., central capsule. n., nucleus.

cies. Häcker re-examined about a third of these and added four new ones. And the specific distinctions are furnished largely in skeletal details.

(*f*) *Openings in the Central Capsule of the Radiolaria*

Along with these facts of skeletal development may be considered the development of the openings of the central capsule. A. Borgert, in particular, has recently investigated this subject. These openings, known as astropyles, *as'p*, figure 25, a, b, c, and parapyles, are characteristic organs of many Radiolaria. They are the communications between the body substances situated inside and outside of the central capsule. Borgert had shown in an earlier paper that when fission of the animal takes place new parapyles arise *de novo*, and not by division of the original organs.

In the memoir now before us he confirms his former observation on the origin of the parapyles and shows that new astropyles arise by division of the old. The chief interest for us in this later study lies in observations on the relation of the development of the organs to the behavior of the nucleus. Besides the indirect or mitotic mode of division of the nucleus proviously studied, Borgert now describes two other modes, one of which is a peculiarly modified indirect division, and the other a quite unique performance which he characterizes as "ruffle-like" (*Manschettenform*).[8] Into the details of these modes of division we need not go. Sufficient for us is it to point out that the great nuclear mass *n.* figure 25, consisting of a veritable throng (a thousand or more) of chromosomes, retains its massed character through all the division stages. The author lays special emphasis on the facts that at no time does the nuclear membrane disappear; and that the endoplasm within which the nucleus is embedded takes no "active part in the process of division," nor does it undergo "any sort of special structural change." The division of the astropyle and the origin of new parapyles are correlated *in time* with the nuclear division; but even this correlation is incomplete. Interestingly enough, the formation of new parapyles is far advanced, the author says, "when the condition of the nucleus indicates the first beginning of the process of division." And Borgert remarks: "It appears therefore that the foundation of the new structure results before the beginning of nuclear division, i.e., at a time when no sort of visible sign of division is recognizable anywhere on the central capsule." That the account of the mode of division in this species is essen-

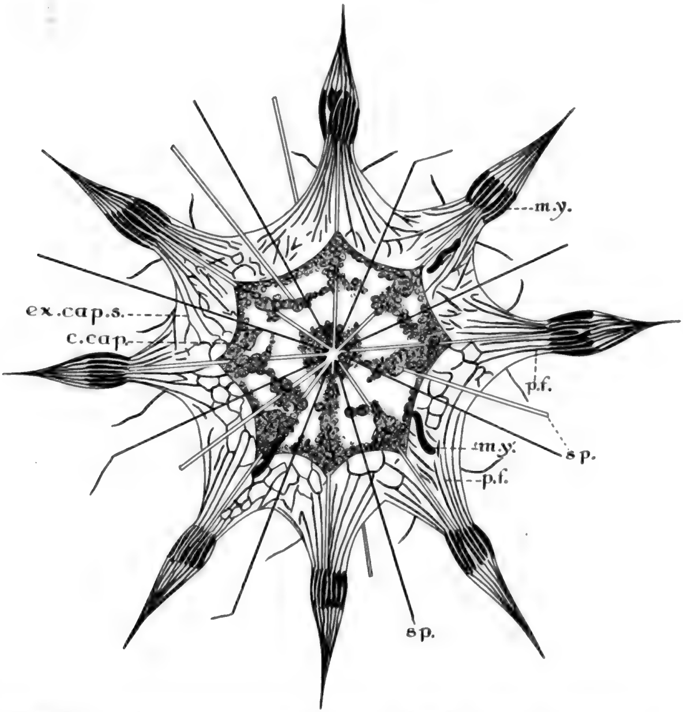


FIGURE 26. ACANTHOMETRON PELLUCIDUM (AFTER MOROFF AND STIASNY). c.cap., central capsule. ex.cap.s., extra-capsular sarcode. m.y., myophrisks. m.y'., migrating myophrisks. p.f., pulling fibers. sp., spines.

tially correct can be accepted with more assurance from the fact that Borgert has studied the mitotic mode of division in the same animal, so that the description is rigorously comparative, It seems, therefore, entirely justifiable to extend the application of Häcker's hypothesis of active developmental centers for skeletal production in the extra-capsular sarcode to organ production in the capsular membrane.

In the absence of a systematic investigation of the development of the adult Radiolarian from its swarm spores, we have to be satisfied with such fragments of ontogenetic knowledge of the group as students have had opportunity to get. A few years ago Moroff and Stiasny studied at Triest several developmental aspects of the well-known genus *Acanthometron,* figure 26. Besides their observations on the complicated multiplication processes which take place in the central capsule, involving both the chromatic and achromatic substances, and according to the authors, implicating both macro- and micronuclei as well as merozoites, schizozoites and swarm spores, the attention was also given to the structure and to certain developmental phenomena of the extra-capsular parts.

The investigators were able to extend previous knowledge of the adult extra-capsular parts. The extensions which especially concern us pertain to the myophrisks *m.y.*, and to the system of plasmic fibers (*p.f.*, figure 26) surrounding the radiating spines (*sp*) of the skeleton. These fibers were found to be much more numerous than previously described. Some of them extend to the distal ends of the spines. "Around each spine there is grouped a whole system of such fibers, constituting the sheath of the spine, which in its form resembles a tent." [9] The individual fibers pass down into the general extra-capsular mass where they anastomose with others of the same tent and with those of the tents of other spines. There are about twenty of these tents. The authors believe these fibers to be not merely supporting, as hitherto supposed, but pulling fibers.

The myophrisks are distinct rod-like bodies arranged in regular fashion around the spines some distance from the tips, together making a sort of barrel-shaped collar. They become deeply colored when treated with nuclear stains, while the fibers above described remain nearly or quite unstained. "The myophrisks do not insert, as previously described, by their proximal ends into the superficial ectoplasmic layer, and by their distal ends into the spines, but lie in the pulling fibers."[10]

The developmental point made out is that the myophrisks arise from chromatic material lying in the central capsule and migrate out to their definite positions (*m.y'.*, figure 26). The origin takes place, according to the authors, in two ways. By one method the entire nucleus of a merozoite transforms into the myophrisk; by the other, the chromatic bodies of the macronuclei unite to produce these structures. Numerous details are given of the development and structure of the myophrisks which we can not enter into. Enough is it to recognize the direct part played by chromatic substance in the production of these bodies.

Now comes the point which specially concerns the present discussion: The authors believe, from observations of their own, that Richard Hertwig's supposition that the bodies are contractile, is correct. Assuming this to be their office, and assuming the authors to be right in their account of the relation of the bodies to the pulling fibers and of the fibers to the spines, we have here a composite apparatus consisting of the spine, the pulling fibers, and the contractile elements, one portion of which, the contractile, is derived from chromatic substance, and two portions, the spine and the pulling fibers, are derived from non-chromatic substance. A slight reservation must be made in the part of this statement which concerns the spine and the fibers in that we are without direct observational knowledge as to the origin of the spines and the fibers. However, it is almost certain that the fibers are entirely differentiations of extracapsular plasm; and that the spines are at least partly of

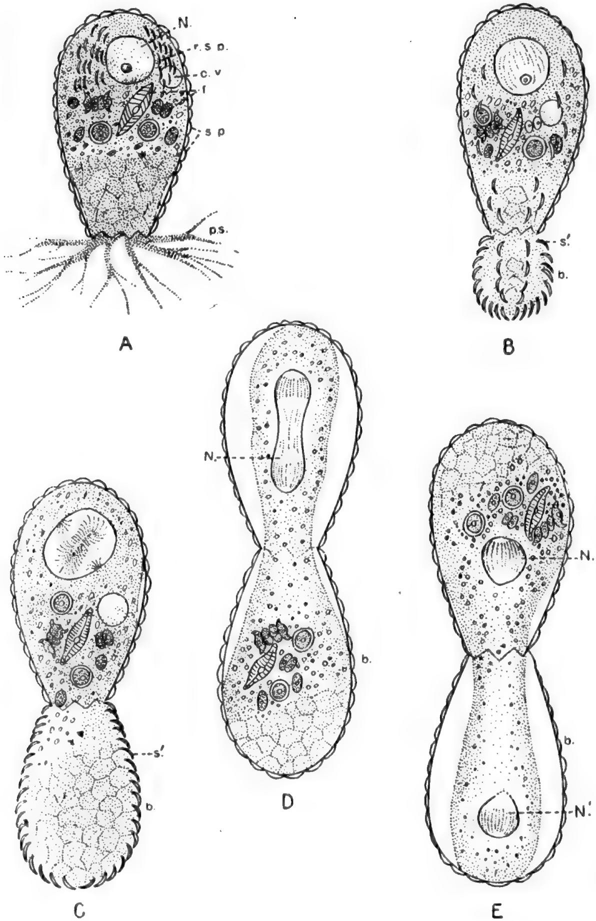


FIGURE 27. EUGLYPHA ALVEOLATA, DIVISION STAGES (AFTER MINCHIN).
N., nucleus. b., daughter-cell. p.s., pseudopodia. c.v., contractile vacuole. f., food materials. s.p., shell plates. r.s.p., reserve shell plates. s'., reserve shell plates moving into position on daughter-cell.

like origin.

So here again, as in the flagella of various flagellates, and the trichocysts of *Frontonia*, we find both chromatic and non-chromatic substances of the cell acting as the physical basis of heredity.

(*g*) *The Shells of Foraminifera*

Some of the most striking examples of what may be called general cytoplasmic activity in the production of heredity structures are furnished by many of the shell-forming Foraminifera. The case of *Euglypha alveolata* may be taken as illustrative. I take this animal not only because its reproduction is a telling case in favor of my general contention, but also because it is often used in text-books and other general zoological works, and so is readily available for study so far as literature is concerned. As shown by figure 27 a, b, c, d, e, the animal is egg-shaped, of regular outline, and enclosed, except for an opening at the small end, in a thin shell made up of little plates. The plates are silicious and are glued by a substance supposed to be silicious. The mode of reproduction exhibited is usually considered to be a form of budding. By examining the figures in connection with the following description taken from Calkins, the points of chief interest will be readily seen. "This bud (b) grows until it has reached its definitive size (usually about that of the original cell) when the shell-coating for the new individual *s* is deposited. The building material for the shell of the daughter-individual is formed within the protoplasm of the maternal cell (*r.s.p.*). If regular plates of silica or chitin, these plates are secreted long before division and stored up in the protoplasm which surrounds the nucleus (*Euglypha, Quadrula*). If quartz crystals, or any other foreign bodies, these particles are picked up and stored in similar manner, to be used later for the test of the daughter-cell. When the bud has reached a certain size, the plates or particles which are to form the shell move out through the mouth-opening of the parent shell and form around the protoplasm of the bud. In the meantime the nucleus (N) undergoes division, and, in the case of *Euglypha* at least, the daughter-nucleus is the last element to leave the parent organism."[11]

Assuming this account to be essentially correct—and there seems no reason to doubt that it is—can any candid person refuse to believe that the protoplasm is at least in part the actual cause of its own extrusion from the mouth-opening of the shell, of the production of the plates (in species in which these are secreted), of transporting them to their final position, and of arranging them into the shell of the new individual? And can any one refuse to admit that the whole formative process is a manifestation of heredity? But if one admits these contentions he perforce admits that the cytoplasm is a physical basis of heredity if any substance at all can be properly so considered.

(*h*) *The Clinging Organs of Sporozoa*

The Sporozoa being poor in organs of locomotion and of contact with the external world, in comparison with the higher Ciliata, Flagellata and Radiolaria, afford less opportunity than these latter for studying the participation of different substances of the body in organ production. However, the differentiation of the body into segments in many species, and the appearance of anchoring spines and hooks by which the creatures cling to their hosts, make them favorable for such studies. The developmental stages of *Pyxinia möbuszi* shown in figures 28 a, b, c, should be recalled, as should also the question whether the probability that the root-like epimerite *ep'm* which penetrates deep into the host cell, is "determined" largely if not wholly by the cytoplasm of the cell, as observation indicates. While the development is in progress the nucleus with its membrane, chromatin mass and nuclear sap appears to remain intact and holds its place in the deutomerite far removed from the developmental changes under consideration. It is not

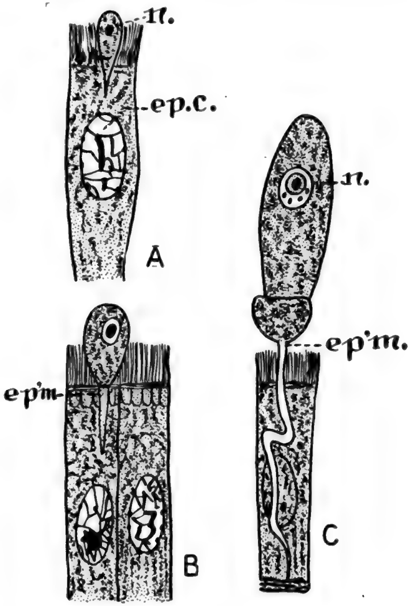


FIGURE 28. DEVELOPMENT OF PYXINIA MÖBUSZI (AFTER LÉGER AND DUBOSQ). ep.c., epithelial cell. ep'm., epimerite. n., nucleus.

impossible, indeed not improbable, that future investigation will find that the nucleus is not so passive during this development as the account here given indicates. Chromatin granules may be proved to escape into the cytoplasm and possibly to migrate to the region of developmental activity. But supposing all this should be proved, there still would remain the fundamental query: would such observation prove

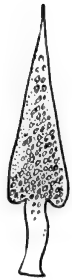


FIGURE 29. EPIMERITE OF PILEOCEPHALUS HEERII (AFTER LANKESTER).

FIGURE 30. EPIMERITE OF GENEIORHYNCHUS MONNIERI (AFTER LANKESTER).

FIGURE 31. EPIMERITE OF ECHINOMERA HISPIDA (AFTER LANKESTER).

that the transforming cytoplasmic substance is not actively participating in the transformation? After what has been said in the preceding pages, the reader will not doubt what

FIGURE 32. EPIMERITE OF BELOIDES FIRMUS (AFTER LANKESTER).

the author's reply is to this query. The activity of the nucleus would furnish no evidence whatever for a denial.

As bearing on the question of whether the development

FIGURE 33. EPIMERITE OF COMELOIDES CRINITUS (AFTER LANKESTER).

of the epimerite of gregarines can rightly be regarded as an exhibition of heredity, I present in figures 28 to 32, illustrations of the great variety of form of this organ in different genera and species of the group. The very essence of the conception of heredity, i.e., resemblance due to genetic kindred, is obvious in the reappearance of a particular type of epimerite in every generation of a given species, while in the group as a whole there is so great a variety of types.

(*i*) *The "Division Center" of Noctiluca*

Thus far in this section we have been considering the contribution of non-chromatic substances to the production of permanent organs in the protozoan body, mostly to organs by which the animals maintain their relation to the external world. We will now examine a few cases wherein

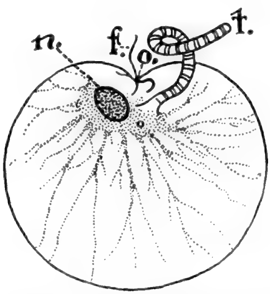


FIGURE 34. NOCTILUCA MILIARIS (AFTER HERTWIG).
n., nucleus. o., mouth. f., filament. t., tentacle.

such substances play a leading rôle in propagation. Perhaps the most striking example is furnished by the well-known marine protozoan *Noctiluca* (figure 34). To state the point as compactly as possible, division in this animal is started off and led throughout by a large, dimly staining body situated in the cytoplasm adjacent to the nucleus. The division of the nucleus seems to be a process attendant upon, and probably dependent upon the division of this body, known as the "division center." (Fig. 35a *a.sp.*)

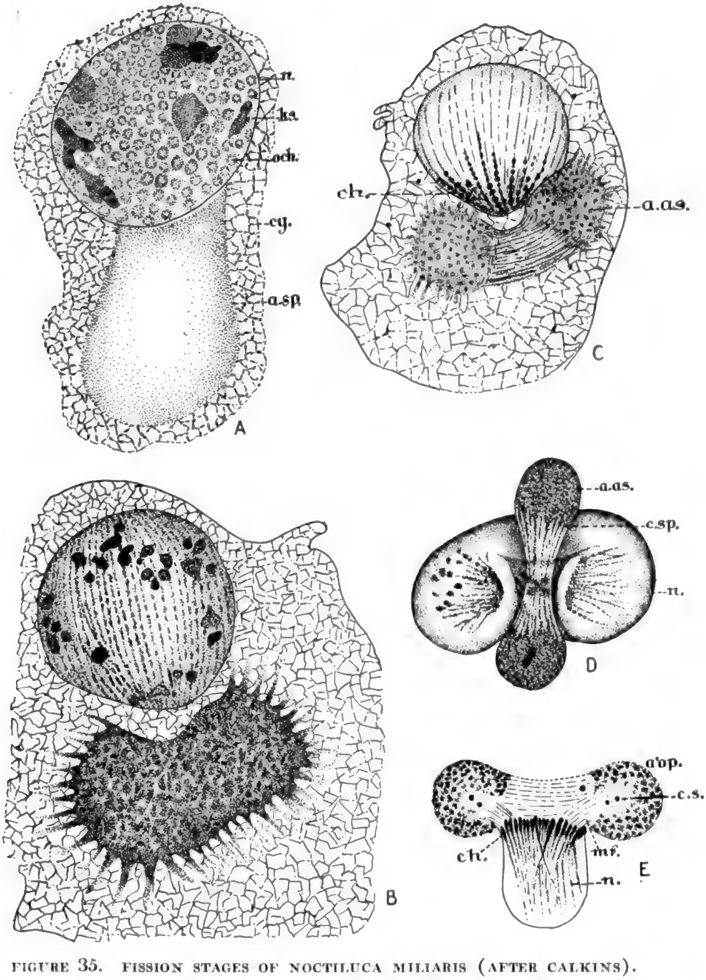


FIGURE 35. FISSION STAGES OF NOCTILUCA MILIARIS (AFTER CALKINS).
c.s., centrosome. m.f., mantle-fibers. n., nucleus. ch., chromosomes. ks., karyosomes. cy., cytoplasm. a.sp. "division center." c.sp., central spindle. a.as., amphiaster. och., oxychromatin.

Owing to the wide distribution, great abundance, and conspicuousness of *Noctiluca*, it has been a favorite animal for study at the sea-side during many years, and its mode of division has proved to be one of the most interesting features about the creature. The most important observations on division in *Noctiluca* were made by Calkins (figures 35 a, b, c, d, e, taken from the original paper), and a few quotations from Calkins' writings will set forth the cardinal facts. "On the outside of the nucleus in *Noctiluca*, in the cytoplasm and close against the nuclear membrane, is a large, faintly staining spherical mass, which acts as a division-center. During the early stages of nuclear activity, the sphere divides into two similar halves, connected by a strand composed of fibers which are formed from the substance of the sphere. These fibers compose the central spindle, and are homologous in every way with the central-spindle fibers of the usual type of mitosis in Metazoa. The nucleus then elongates in a direction at right angles to the central spindle, and at the same time bends in the centre in such a way that the central spindle sinks into a depression in the nucleus, which surrounds it upon three sides. In this way the nuclear plate is finally wrapped about the central spindle in the form of an incomplete ring. . . . The nuclear membrane then disappears in that part of the nucleus which is turned toward the central spindle, while it is retained unbroken in all other parts of the nucleus. Thus the chromosomes, as in the higher types, are brought into contact with the central spindle fibres. They then split longitudinally, and through the agency of the mantle-fibres are separated into two equal groups, each group drawn toward its own daughter-sphere. Within the sphere the fibres are focussed in a centrosome which, at this period, can be demonstrated with the greatest ease. The division is finally completed by the separation of the remainder of the nucleus and the re-formation of the daughter-nuclei, while the chromosomes disintegrate into granules, which again form the large chromatin reservoirs, characteristic of *Noctiluca.*" [12]

The matters of chief interest for us in this account are the extra-nuclear position of the division center; its large size, making the observation of it almost as practicable as observation of the nucleus itself; the sharp distinction, indicated by the difference in staining, between the material of the division center and the nuclear contents, particularly the chromatic part of the contents; the unmistakably independent and leading part played by the center in division, the split chromosomes, for example, being separated "through the agency of the mantle-fibres," these latter a part of the sphere; and finally the strong direct evidence that the activities of the center pertain to the substance of the center itself and are not caused entirely by a "force" or "influence" of the centriole. With reference to the last point it should be said that Calkins found considerable evidence that the centrioles (centrosomes according to the nomenclature employed by him) which are easily recognizable in the division center during advanced stages of nuclear division, are in the nucleus during the resting period and only migrate into the center during the divisional activity of the center and the nucleus. But granting to this minute granule all that actual observation entitles it to, the most that can be said is, that it is an active participant in the complex series of changes and transformations which constitute the propagation-division of the animal. Calkins' statement that "A cytoplasmic substance, corresponding to the centrosphere of many metazoan cells, is invariably present. It is a permanent organ of the cell, often as large, or larger, than the nucleus; it divides to form an amphiaster, consisting of two asters with connecting mantle-fibres, the central-spindle," [13] should be taken at its face value. What I mean by this is that we have no right to pin our faith to a speculative view based on something other than evidence contained in this particular statement, that would eviscerate this statement of its essential meaning. And such would be the effect were one to speculate that the centriole is "generative chromatin" and so the causal explanation of the phenomena presented by the center. The "cytoplasmic substance" which, Calkins says, constitutes the central sphere, is a "physical basis of heredity." It is such because it does that by which, and by which alone, any substance can be proved to be a physical basis of heredity. It takes a direct, active part in a series of structural transformations "to form an amphiaster, consisting of two asters with connecting mantle-fibres," that closely resemble one another in many individual animals genetically related and constituting the species *Noctiluca miliaris* (figure 34.)

(*j*) *The Centrosphere of Protozoa Generally*

We must carry a little further the examination of the centrosphere, or division center, as itself a physical basis of heredity. The wide occurrence among the protozoa of a body, or at any rate of substance, which does not stain readily and hence is not chromatin, but which plays a fundamental part in cell division, seems to be recognized by all students of these animals. As we are now concerned with the question of how general in the group as a whole is the active participation of this achromatic substance in propagation, a summarized account of what is known on the subject will meet our purposes.

Since, as has been previously pointed out, Minchin is a strong chromatinist, we shall be safe from bias in the other direction if we rely chiefly on his late book for the account. Speaking broadly, protozoologists recognize two types or classes of achromatic substance, dependent upon its location in the cell. In one class, of which *Noctiluca* is an example, it is outside the nucleus; in the other class it is inside the nucleus. As an example of the first, several heliozoans may be mentioned, notably *Acanthocystis* and *Sphaerastrum;* and as examples of the latter, several species of *Coccidium,* belonging to the Sporozoa, *Euglesia,* a flagellate, and *Arcella,* a sarcodinian. Then there are combinations and intermediate states between the two types. The following quotations from Minchin's book not only indicate this, but bear directly on our main point. "A most instructive series, showing how extranuclear elements come to collaborate in the mechanism of division, is furnished by some examples of the Heliozoa, and especially by the nuclear divisions of *Actinosphaerium,* which have been the subject of extraordinarily thorough investigation by Hertwig. . . . In the ordinary karyokinesis of *Actinosphaerium* an equatorial plate is formed, composed of a large number of small, rodlike chromosomes, imperfectly separated from one another, which divide transversely. The spindle arises from the achromatinic framework of the nucleus, and terminates in two conspicuous polar plates lying within the persistent membrane. External to the membrane are two large conical masses of archoplasm, termed the 'polar cones.'"[14] In a word, three distinct substances are here observed in collaboration: two, the chromatic bodies and the achromatinic framework, being intra-nuclear; and one, the archoplasmic cone, being extra-nuclear. The observations indicate that the archoplasmic substance is a less active collaborator in the division than are the other two substances. But, passing to another species, "In *Actinophrys* the karyokinesis appears to be of a type similar to that of *Actinosphaerium,* with persistent membrane, but with more activity in the extra-nuclear archoplasmic elements."

And finally, relative to the degree and character of the collaboration of the various elements: "In *Acanthocystis,* however, the nuclear membrane disappears completely from the karyokinetic figure, and it is no longer possible, in consequence, to distinguish the parts of the achromatic spindle which are of intra nuclear and extra nuclear origin respectively. Nuclear and cytoplasmic elements are in complete coöperation."[15]

Minchin's reference to the researches of Hertwig on the Heliozoa, indicated in the above quotation, makes this an appropriate place to call attention to the great interest, from our standpoint, which attaches to Hertwig's denial of Absolute Power of the nucleus in the life of the cell, as indicated by his well-known theory of nuclear-protoplasmic relation. Recognizing the great weight of the views of this investigator as touching the main issue here does not necessarily commit us one way or the other as to all the details of the "nucleo-plasmic relation" hypothesis.

The reader's attention is called again to the argument that the morphological elements and the activities displayed in this reproduction are in themselves manifestations of heredity, based on the fact that they pertain to different though rather closely related species of animals, each one of which presents its own particular type of the phenomena. *Actinosphaerium* and *Actinophrys* are closely related genera, among the differential attributes of which is this very matter of difference in the structure and relations and activities of the various elements collaborating in their propagation. Each genus is true to its type in these attributes as well as in others. How then is it possible, consistency and fair dealing being assumed to be cardinal virtues of science, to refuse to recognize that not only the behavior of the chromosomes in the two cases, but likewise that of the achromatinic framework and the archoplasmic bodies, are *themselves* manifestations of heredity, and that the substance of each in the initial stage of the series is a "physical basis of heredity?"

Concluding Remark on Evidence Presented

Our objective study of the production of hereditary structures and activities in the protozoa may well end with a comment on a paragraph occurring in one of Calkins' able and useful papers. In the general conclusions of this paper we read: "The chromatin, in addition to being the recognized agent in heredity, is also generally recognized as the center of formative changes in the ordinary vegetative activities of cell life. Recent observations have been interpreted to show that it is the seat of oxidative processes and the direct agent in metabolism. These various supposed functions of the chromatin are, in large part, inferential, and there are no observations to show whether it alone is the center of these various activities, or whether it plays the part of middleman in the cell. I do not know whether it is possible to determine such a point."[16]

I ask the reader to note attentively this group of statements. According to the opening words chromatin is "the recognized agent in heredity," while according to the last sentence not only is such a rôle of the chromatin "largely inferential" and there are "no observations to show" that "it alone is the center" of such activity, but the author frankly admits himself in doubt as to the possibility of determining such a point.

What I chiefly wish to do in connection with this is to insist that such facts as we have just been examining, some of which were discovered by Calkins himself, relative to the participation of non-chromatic parts of the cell in the ontogeny of many protozoans, are, according to my interpretation, conclusive evidence that chromatin is *not* alone the "center" of activity of hereditary development. For the rest I do no more in this chapter than call attention to the fact that further discussion of the matter at issue is not biological in a strict sense, but is part of the problem of the validity of observational knowledge and the nature of suppositions and of inferences.

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