With Compliments
from the Author

SPIRAZINES

A Type of Chemical Structure Bearing Upon the Constitution of Proteins and the Cause of Life

By

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THE SCIENCE PRESS PRINTING COMPANY
LANCASTER, PA.

FOREWORD

The ultimate cause and nature of life processes is a subject so intensely interesting that no further argument should be necessary to justify the presentation of this booklet to the public. When it is considered that there is not only a dearth, but a total absence in scientific literature of specific suggestions as to how such processes as growth and reproduction might be explained, it appears that any suggestion which is at all reasonable ought to be welcome. Nevertheless, when the spirazine hypothesis was first tendered to the editors of scientific magazines in the summer of 1926, it was condemned as being unscientific and contrary to known facts, and was characterized as being only one out of a thousand other equally good guesses, although the author has not yet received from the critics thereof a single suggestion as to what some of those other equally good guesses might be.

Finally after the prospects of obtaining publication through the usual channels seemed hopeless, a number of mimeographed pamphlets were prepared and distributed among those who were known to be interested. An abstract notice of them was recorded in *Chemical Abstracts,* 22, 2584 (July 20, 1928).

In order to guard against the publication of a possible fallacy, two more years were then allowed to elapse so that a critical study might be made of every phase of this hypothesis. During this time it was submitted to numerous chemists and biologists and their adverse criticisms were earnestly solicited, but until the present time not a single valid criticism has been received. Since the hypothesis seems to be consistent with known facts, and has been found to explain a host of phenomena which have not heretofore been explained, it is believed that it should not be withheld from the public merely because it is not in accordance with the personal views of certain editors.

SPIRAZINES

INTRODUCTION

The various forms of life which are encountered in nature exhibit such a variety of appearances and such a profusion of details that the casual observer is often too bewildered by the complexity of his surroundings to gain a clear conception of life processes in their entirety and to distinguish what is fundamental and indispensible from what is superficial and unessential. The presence of life is usually recognized by characteristic bodily form, spontaneous mobility, and responsiveness to external stimuli, but these properties can all be closely imitated artificially and in the lower forms of life are often entirely absent, so that they must be regarded as secondary characteristics which have developed in the course of evolution and not as primary attributes of life itself.

Every living organism is unique in that it constitutes a self-contained entity having its own laws of action, and which is capable, under favorable conditions, of producing others like itself. The phenomenon of self-perpetuation or reproduction is exhibited by every living organism regardless of its rank in the plant or animal kingdom and establishes in nature a sharp line of demarcation between living and non-living things. Reproduction in its broadest aspect amounts to nothing more than self-duplication, but is fundamentally different from any of the other processes heretofore known to science. It involves more than mere dispersion or subdivision in that the progeny retain not only the chemical composition and physical state, but also, either actually or potentially, the specific physical structure of the parent. Neither can it be regarded as merely a form of dissociation because the progeny are structurally similar to the parent, whereas the ions which result from dissociation of molecules are always dissimilar from the undissociated molecules. All living organisms, notwithstanding their diversity of form and appearance, must therefore possess something in common which gives rise to that peculiar characteristic called "life."

Self-duplication cannot be due, primarily, to specific configurations of tissues or membranes because there are innumerable species of bacteria which exhibit no internal heterogeneity whatever, even under the most powerful magnification. The real cause of life, whether it be a certain substance or a specific detail of physical structure, must exist on a scale smaller than about

1/25,000 cm = 4,000 Angstrom units, and in that region we come dangerously close to the details of molecular structure.

That the phenomenon of self-duplication must be due, either wholly or partly, to specific chemical processes is generally admitted, but there is a prevailing opinion that the molecular structures which are necessary for this purpose must be extremely complex. The failure of all previous efforts to devise some type of molecular structure which is capable of duplicating itself does not prove, however, that the solution of the problem must lie in the direction of extreme complexity. The complex molecular structures which make up the tissues of the higher plants and animals have developed gradually in the course of evolution, and the fact that they are necessary for the proper physiological functioning of the particular organisms in which they now occur does not prove that they were also the original cause of the fundamental life processes in the more primitive organisms from which these higher plants and animals have developed.

With the exception of certain plasmodia and syncytia which have no definite cell-walls, the bodies of all higher plants and animals consist of aggregates of separate living cells, all of which are formed according to the same general plan in that they consist of an outer cytoplasm containing central bodies, asters, fibrillae, plastids, chondriosomes, Golgi-bodies, etc., and an inner nucleus containing chromosomes, linin network, etc. Nucleated cells like those which form the bodies of the higher plants and animals have a definite lower limit of size, being never smaller than several (approximately five) microns in diameter. Since the diameter of the benzene ring, as measured between the centers of the atoms, is about three Angstrom units (3×10^{-8} cm), in diameter, it would take about seventeen thousand benzene rings arranged side by side to form an object as large as the smallest living cell, or about 2,500,000,000,000 to fill the volume thereof. It is probably safe to say that a structure of such complexity could never have sprung into existence spontaneously from inorganic substances. The conclusion is therefore inevitable that the typical nucleated cell does not represent the most primitive form of life, but is probably the final result of a long process of evolution.

A much more primitive form of life is exhibited by the bacteria which carry on the same processes of metabolism and pass through the same cycles of growth and cell division as their nucleated relatives, so that they must be regarded as true living organisms. These differ from nucleated cells in that they are definitely smaller in size, are usually formed according to some simple geometric figure, do not contain chromosomes, centrosomes, or other self-perpetuating bodies, and never conjugate.

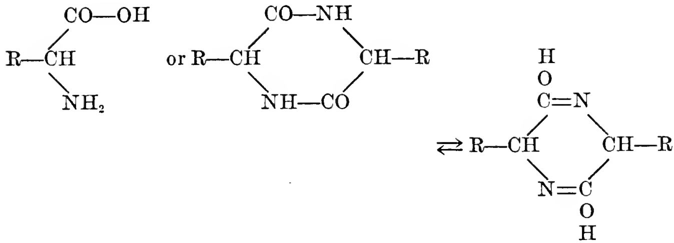
The existence of a definite gap in size between the smallest nucleated cells and the largest bacteria indicates that bacteria represent a distinctly different form of life from nucleated cells, and when we consider the extreme simplicity of their forms and the homogeneity of their internal structures we feel inclined to believe that they constitute the most primitive class of living organisms. Even the largest of them are not far above the limit of microscopic vision, and there is every reason to believe that there are innumerable species, similar in form and constitution to their larger representatives, which are too small for the microscope to reveal.

In order to avoid a confusion of issues at the outset, we shall for the present confine our attention as much as possible to the bacteria, because these exhibit life processes in their simplest form. The problem of explaining life does not require that we should explain the entire process of evolution, but only those processes and characteristics which are common to all forms of life and which must have been exhibited by the most primitive form of living matter as it first appeared on this earth.

THE CHEMICAL BASIS OF LIFE

There being no evidence to justify us in assuming that life is due, primarily, either to specific details of physical structure or to extreme complications of molecular structure, we find ourselves driven to the conclusion that life must be due to some comparatively simple principle of chemistry which has not yet been discovered. To find a clue to this we must investigate the molecular structure of proteins, because these appear to constitute the basis of all life processes. Fats and carbohydrates, although formed during protein metabolism, are evidently nothing more than by-products which may be useful at times for fuel or skeletal support but do not enter into the molecular structure of living matter in such a manner as to exert any directing influence thereupon.

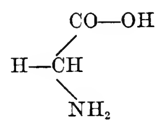
Protein substances, upon hydrolytic decomposition, always yield as their principal cleavage product a mixture of amino acids or their diketopiperazine derivatives, which may be represented generally as follows:



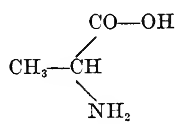
About thirty of these amino acids or their anhydrides have been isolated, the structural formulas of the more important ones being as follows:

Aliphatic monobasic monamino acids:

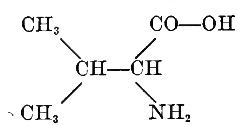
Glycine



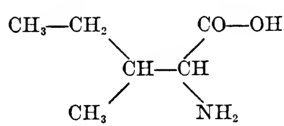
Alanine



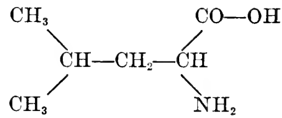
Valine



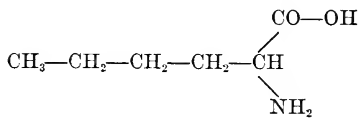
Isoleucine



Leucine

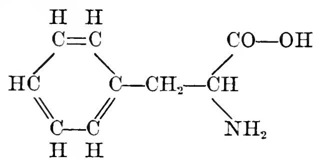


Caprine

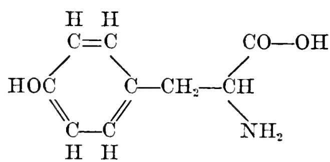


Aromatic monobasic monamino acids:

Phenylalanine

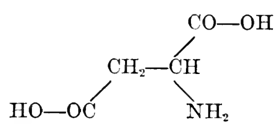


Tyrosine

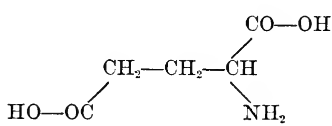


Dibasic monamino acids:

Aspartic acid

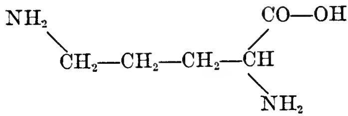


Glutamic acid

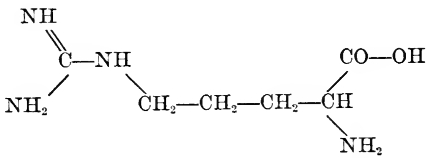


Monobasic diamino acids:

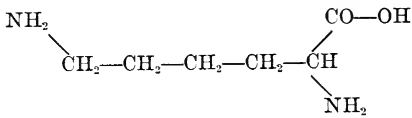
Ornithine



Arginine

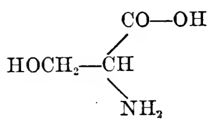


Lysine

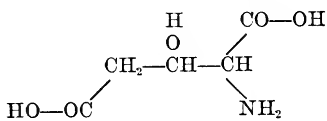


Hydroxy- and Thio-amino acids:

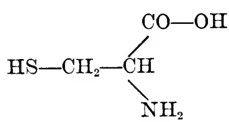
Serine



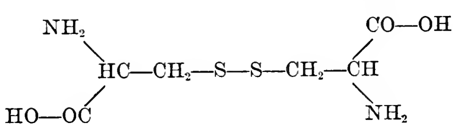
Hydroxyglutamic acid



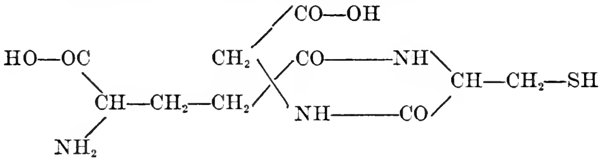
Cysteine



Cystine

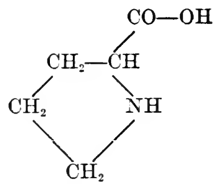


Glutathione (γ-glutamylcysteylglycine)

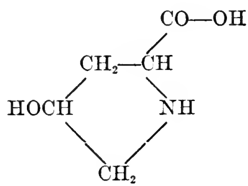


Heterocyclic amino acids:

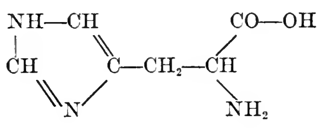
Proline



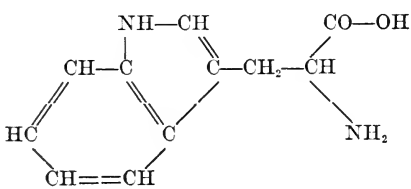
Oxyproline



Histidine

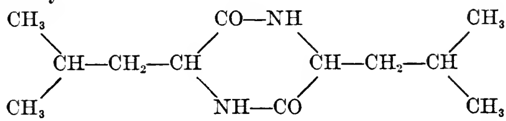


Tryptophane



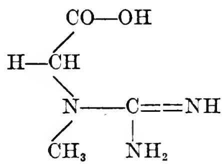
Anhydrides:

Leucine anhydride

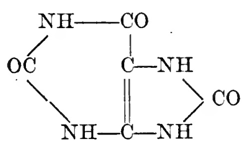


Because of their frequent occurrence in living tissues the formulas of creatine, uric acid, plant and animal nucleic acid, and lecithin should accompany the above list:

Creatine



Uric acid



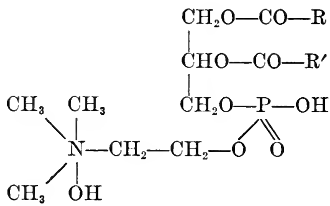
Plant nucleic acid

(Phosphoric acid)$_4$ (d-Ribose)$_4$ (Guanine Adenine Cytosine Uracyl)

Animal nucleic acid

(Phosphoric acid)$_4$ (Desoxy-Ribose)$_4$ (Guanine Adenine Cytosine Thymine)

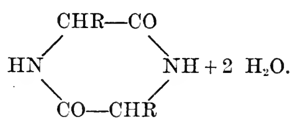
Lecithin



By suitable chemical treatment the above mentioned amino acids may be condensed, with the elimination of water, to form either chain structures known as polypeptides, or ring structures known as diketopiperazines:

$$3\ NH_2—CHR—CO—OH = NH_2—CHR—CO—NH—CHR—CO—NH—CHR—CO—OH + 2\ H_2O,$$

$$2\ NH_2—CHR—CO—OH =$$



(E. Fischer, Untersuchungen über Aminosauren, Polypeptide, und Proteïne, 1899–1906.)

Since proteins constitute the principal structure-building food for animals, and upon digestion are decomposed into amino acids, in which form they are assimilated by the tissues, it is generally thought that growth involves condensation processes of a similar character, and that amino acids exist in living tissues either as long polypeptide chains or as diketopiperazine rings. Such a theory, however, offers only an imperfect explanation for the phenomenon of growth, and fails to offer any explanation whatever for reproduction with the transmission of inheritable characteristics to the progeny or for the infallible precision with which a single germ cell will transmit its own specific pattern throughout all the cells of the organism and on to the next generation. The persistence with which living organisms will devour every bit of food material within reach and invade the entire earth's surface with their progeny shows that they must possess in the molecular structures of their tissues some contrivance which is definitely superior to ordinary chemical forces and which can function in a manner unknown to chemical science. What is needed for this purpose is not some new form of molecule but some new type of molecular structure; not some new arrangement, but some new principle.

THE SPIRAZINE STRUCTURE

Growth and reproduction being the two indispensible processes without which life is inconceivable, the molecular structure of living matter from which such life processes originate must possess the two following characteristics:

(1) It must be of such a nature that the process of growth by assimilation of amino acid molecules can take place continuously without producing any sudden variation in its molecular configuration or chemical behavior; and

(2) It must be capable of division into a plurality of portions each of which retains, either actually or potentially, all the essential characteristics of the original structure.

Of the various geometric forms which molecular structures might exhibit, the helical spiral appears to be about the only one which possesses characteristics similar to those mentioned above, and it appears that the helical spiral is also the only configuration, besides rings and chains, which the polypeptide molecule can be made to assume. The ease with which diketopiperazine rings are formed from dipeptides, and the difficulty with which such rings are broken up, seems to indicate that the valencies of the successive

The Spirazine Structure.

Fig. 1a.

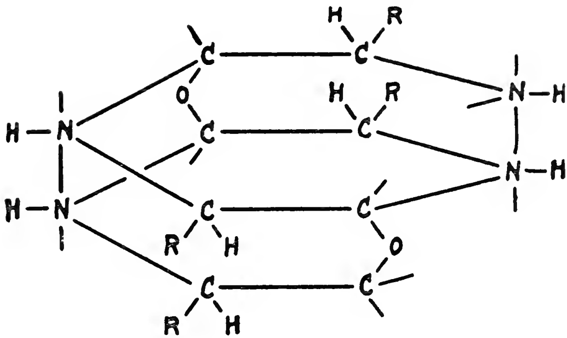


Fig. 1b.

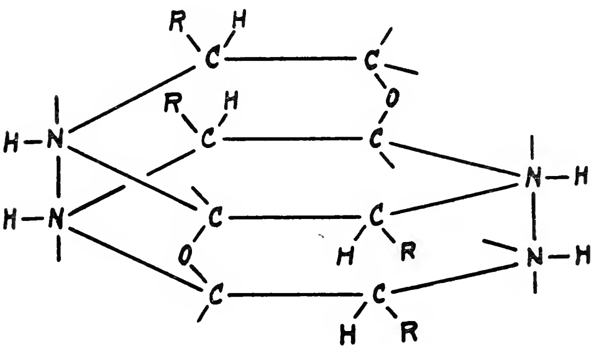


Fig. 1c.

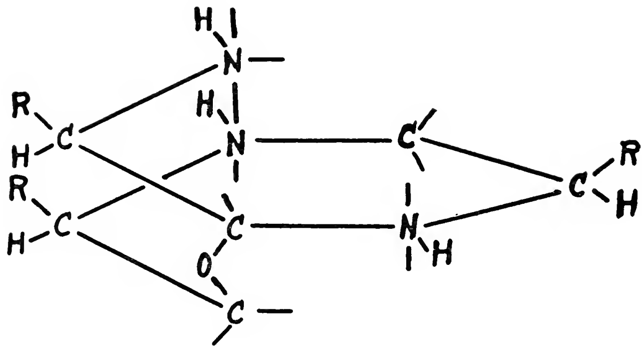
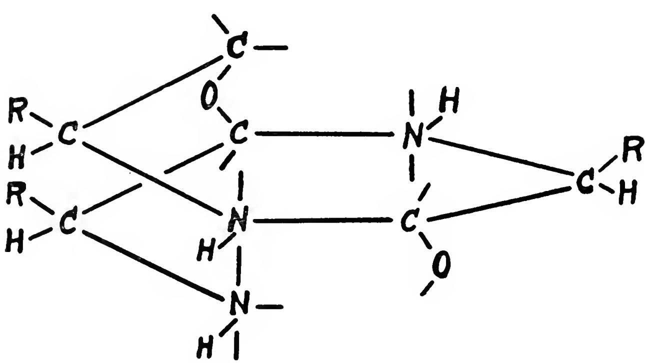


Fig. 1d.



carbon and nitrogen atoms in dipeptides are at such angles to one another as to give them a natural tendency to form six-atom rings; and if dipeptides tend to form six-atom rings, then polypeptides would tend to form spirals with six-atom convolutions, which may be referred to, briefly, as "spirazines." Since the configuration of such structures in three dimensions of space is difficult to visualize, several different views thereof are given in the accompanying diagrams.

It will be noticed that one of the valencies of the alpha carbon atom in these amino acids is always occupied by hydrogen. Chemically it would be possible to attach more complex groups in this position, but it will be found upon experimentation with atomic models that the presence of more complex groups in this position would render the spiral structure impossible, and it will be observed that complex groups never occur in this position in the decomposition products of natural proteins.

The two ends of such a spiral will be different in that one end will be formed of a negative carboxyl group whereas the other end will be formed of a positive amino group. When the dissimilarity of molecular structure at the two ends is taken into consideration, it seems highly improbable that the ability to grow by assimilation of amino acid molecules could be possessed by both ends alike. The fact that the physiological effects of different substances when injected into the blood stream are due almost entirely to the positive kations seems to indicate that assimilation takes place at the acid carboxyl ends, although the acid character of the chemically active portions of living matter may also be due to phosphoric acid radicles clinging to the positive amino groups at either end of the spiral, and acting catalytically as intermediaries to facilitate the assimilation of amino acid molecules, just like sulphuric acid acts catalytically to facilitate the combination of alcohols with organic acids to form esters. The fact that phosphorus occurs principally in the nuclear materials where such assimilation is known to take place, and even there only in comparatively small amounts, seems to indicate that it does not enter permanently into the molecular structure of proteins but is associated only with the actively growing portions thereof.

The successive nitrogen atoms along each side of the spiral will increase the basicity of the terminal nitrogen atom, just like the two nitrogen atoms in diazo compounds increase the basicity of each other. Similarly the carbonyl groups along each side of the spiral will increase the acidity of the terminal carbonyl group. We thus have a strongly basic group held firmly in close proximity to a strongly acid group but yet not permitted to neutralize the latter, which appears to account for the remarkable ability of living matter or its enzymes to digest all sorts of complex food materials and to appropriate the resulting substances spontaneously and continuously for the building up of its own molecular structures, for no matter how many additional amino acid molecules are assimilated the configuration at the end of the spirazine remains the same.

The similarity in form and appearance of a polypeptide spiral to a bacillus, a spirillum, or a connective tissue or nerve fiber will be apparent. It should be capable of growing endwise by assimilation of additional amino acid molecules, and as long as the spiral form is maintained it will possess a certain definite and characteristic morphology. It must remain permanently right-handed or left-handed which will account for the optical activity always exhibited by substances obtained from living tissues, and if transverse fission occurs, each half should retain the right-handedness or the left-handedness and the cross-sectional pattern of the original structure, so as to exhibit in a very simple manner the process of reproduction with the inheritance of parental characteristics.

THE LINKING OF SPIRAZINES

Since a single polypeptide spiral, being of about the same diameter as the benzine ring, measures only about five Angstrom units (5×10^{-8} cm.) in diameter, it is evident that even the smallest bacteria, and all other fibrous forms of living matter which are visible under the microscope, must consist of aggregates of large numbers of such spirals. The fact that about three-fourths of the weight of living tissues is water seems to indicate that the polypeptide spirals of such tissues are not arranged in closely packed formation like the molecules of a crystal, but rather in some sort of open or spaced-apart formation.

Chemical union between adjacent spirals may take place through either the amino, the carbonyl, or the alpha carbon groups. Three different things, taken two at a time, can produce six different combinations. Some of these can be eliminated immediately as representing reactions which do not take place chemically. For example, two amino groups will not unite directly with each other, nor will two carbonyl groups be very likely to unite with each other permanently. The amino hydrogen from one spiral may, however, unite with the carbonyl oxygen of an adjacent spiral so as to form water molecules and leave the carbonyl carbon connected directly to the amino nitrogen.

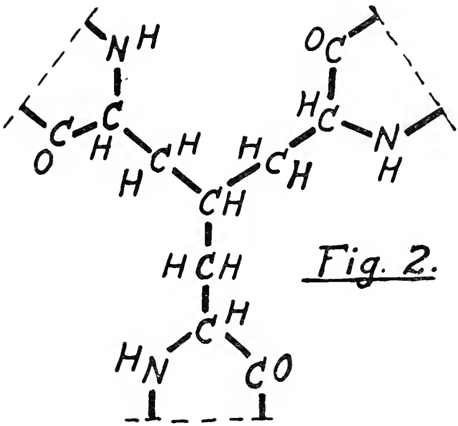


Fig. 2.

A triple junction of the gamma-gamma-gamma type.

If the connection is formed through the side chains attached to the alpha carbon atoms, then it appears that only a limited number of intermediate atoms can be involved, because at any point beyond the third or gamma carbon atom the movements of the side chains would be too much at random to form the connecting complexes spontaneously.

The branched hydrocarbon side chains connected to the alpha carbon atoms of valine, leucine, and isoleucine are evidently the fragments of the complexes which connected adjacent spirals in the original mass, because if the particular spirals which carried these branched side chains had been connected by means of their amino and carbonyl groups, then it is unlikely that they would have produced the alpha amino acid groups again upon hydrolysis. In valine and isoleucine the triple junction occurs at the beta carbon atom, whereas in leucine it occurs at the gamma carbon atom. Phenylalanine and tyrosine also exhibit a similar branching at the gamma carbon atom. No amino acid has ever been obtained from natural proteins in which such a junction occurs at any point beyond the gamma carbon atom, nor would we expect to find such structures because at more remote points the side chains would have too much freedom of movement to produce the triple junction spontaneously. Aspartic acid appears to have come from two spirals which were connected directly by means of their alpha carbon atoms without the presence of any intermediate atoms. Glutamic acid differs from aspartic acid in that it has one more CH_2 group, which evidently formed the connecting link between two adjacent spirals, although it may also have formed a triple junction between three adjacent spirals.

It appears that a triple junction between three adjacent spirals is the arrangement which occurs most frequently in nature, because a large number of spirals connected in this manner will collectively form a cluster of hexagonal compartments as shown in Fig. 3, and a hexagon is one

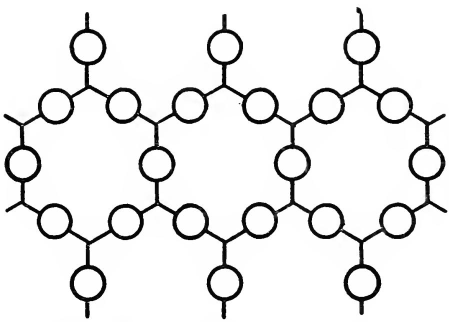
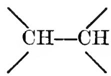


Fig. 3. Hexagonal compartments.

of the few figures which when duplicated will completely cover a certain area, like the cross-sectional area of a bacillus or a connective tissue fiber. The only other possibilities are quadrilateral or triangular compartments, but the existence of these, except at the free surfaces, appears very improbable because they would require the connection of four and six adjacent spirals respectively. It does not appear that complexes for connecting six adjacent spirals directly with one another can be formed spontaneously under any conditions, although complexes for connecting four adjacent spirals may be formed occasionally as follows:



The elementary composition of a protein will also indicate to some extent the probable nature of the connecting complexes. For example, if the triple junctions are entirely of the gamma-gamma-gamma type, then we may take as a representative portion thereof one-half of each of three adjacent spirals as illustrated in Fig. 2. This will have the following empirical formula:

$$C_{10}H_{13}N_3O_3,$$

and will have the following percentage composition:

Carbon	Hydrogen	Nitrogen	Oxygen
53.9	5.8	18.8	21.5

This differs only slightly from the percentage composition found experimentally for crystalline egg-albumin, which is as follows:

Carbon	Hydrogen	Nitrogen	Oxygen	Sulphur
51.48	6.76	18.14	22.66	0.96

(Perkin & Kipping, Organic Chemistry, p. 577, 1922.)

The percentages of carbon and nitrogen in our theoretical formula are slightly higher than those obtained experimentally, whereas the percentages of hydrogen and oxygen are slightly lower. The low percentage of hydrogen can be accounted for on the theory that the individual particles of albumin are very small so that many additional hydrogen atoms or hydroxyl groups would be required to occupy those valencies which, in our continuous three-dimensional hypothetical structure would be used for connecting different portions thereof to one another. If, for example, we assume that there is a break in one of the hydrocarbon chains at every triple junction, and that a hydrogen atom occupies each of the unused valencies, then our theoretical formula would become:

$$C_{10}H_{15}N_3O_3,$$

which will give the following percentage composition:

Carbon	Hydrogen	Nitrogen	Oxygen
53.4	6.7	18.6	21.3

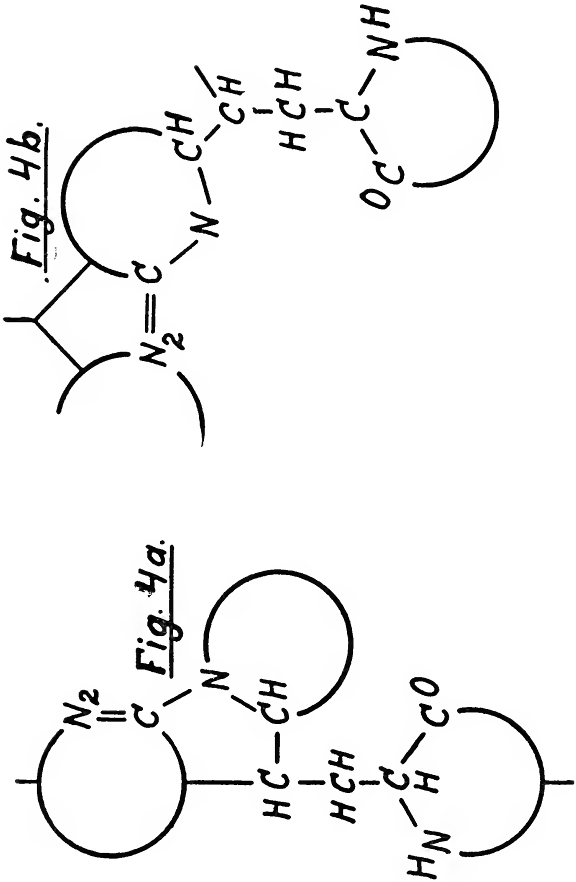
The percentage of carbon is still slightly high, but that can be accounted for by the presence in albumin of a few junctions of the beta type, the existence of which is evidenced by the glutamic acid and arginine obtained therefrom upon hydrolysis.

Sulphur occurs in the molecular structures of nearly all proteins, but is seldom present in amounts greater than two or three percent. Although several different sulphur compounds have been obtained from proteins upon hydrolysis, yet they all have their sulphur in chemical combination with the beta carbon atoms of alpha amino acids and appear to be merely different cleavage products of the same original structures. The principal sulphur-containing cleavage product is cystine, which contains a pair of sulphur atoms between two alpha amino acid groups. If we assume that all alpha amino acid groups were derived from spirazines, then we shall have to conclude that sulphur takes the place of the gamma carbon atoms at double junctions for connecting two adjacent spirazines. It probably occurs only at the surfaces and not generally throughout the interior molecular structures because the interior structures would require triple rather than double junctions, and furthermore the amount of sulphur in proteins is not sufficient for general distribution.

If we assume a sulphur content of 2.5 percent, which is more than most proteins contain, then there would be about one cystine molecule or two sulphur atoms for every eighteen spirazines, twelve triple junctions, or six polygonal compartments as seen in transverse section.

It will be observed that the molecular structures of the various triple junctions are separate and distinct from one another, except for their connections to the intermediate spirazines. Since the spirazines themselves are all exactly alike, and since they can never be separated from one another by more than three or four intermediate carbon atoms, it appears that there is a definite limit to the molecular complexity of living matter. We must not confuse manifoldness of structure with intrinsic molecular complexity. The number of variations that may be produced in the cross-sectional pattern of the simplest units of living matter by changing the connections of the spirazines with one another is enormous, and alterations of this sort in the nuclear material of the germ cells may result in all sorts of mutations during subsequent embryonic development, but the complexity is in the biological significance of the pattern as a whole, and not in the chemical behavior of its component parts. Since the maximum number of atoms in a triple junction is much less than in many of the organic molecules which have been synthesized and studied by chemists, we may confidently expect that a satisfactory

Arginine in-situ.



Purine derivatives in situ.

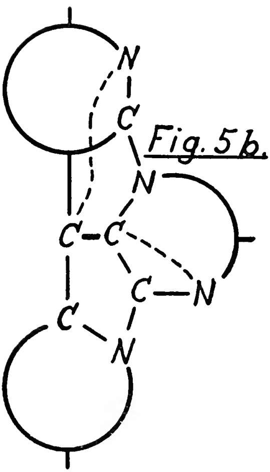


Fig. 5b.

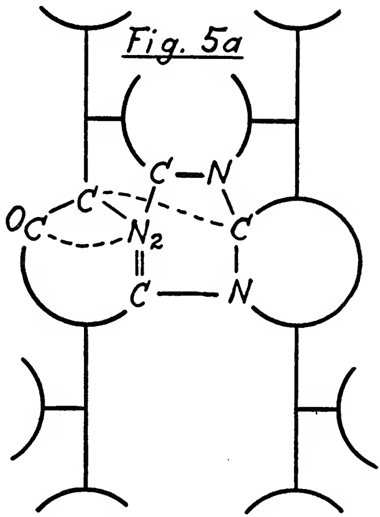


Fig. 5a

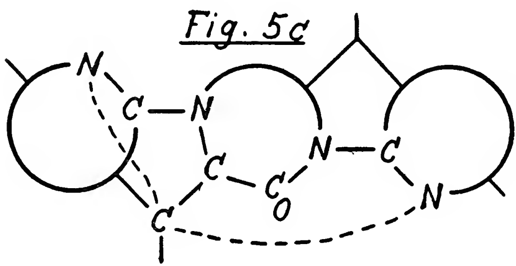


Fig. 5c

chemical explanation of all phases of vital activity will soon be forthcoming.

Evidence of direct connections between the amino groups of one spiral and the carbonyl groups of an adjacent spiral is furnished by the urea and guanidine groups which occur in the pyrimidine and purine derivatives and in arginine and creatine respectively. When protoplasmic structures are subjected to severe stresses, as must occur in the nuclear material during cell division, we would expect the hexagonal compartments to become flattened by lateral compression in one direction or another so as to bring the amino groups of one spiral directly against the carbonyl groups of another spiral, whereupon the amino hydrogen will combine with the carbonyl oxygen to form water and leave the carbonyl carbon atom of one spiral connected directly to one or two nitrogen atoms of an adjacent spiral as illustrated in Figs. 4 and 5. Since the carbonyl carbon atom is already connected to the nitrogen atom immediately adjacent to it in the same spiral, we will have produced in this manner either the urea or the guanidine complexes which occur so extensively in the products of both plant and animal metabolism. A connection between one carbon atom and two nitrogen atoms may also occur at the positive end of a single spiral as illustrated in Figs. 4a and 5a. The formation of substances like arginine and uric acid may thus be accounted for in several different ways as shown in the accompanying diagrams.

In the nucleated cells of plants and animals these urea and guanidine complexes occur principally in the chromatin material of the chromosomes. This chromatin material has a strong affinity for dyes so that it stands out very prominently in stained preparations, but the fact that it is conspicuous in appearance does not prove that it plays an important part in vital processes. If purine derivatives are formed in the manner suggested in the preceding diagrams, then it appears that the chromatin material of the nucleus, which has generally been regarded as the seat of heredity, is actually nothing more than an accumulation of waste material.

It is a significant fact that after cell division is complete, the chromatin material spreads out into irregular patches over the surface of the nucleus and is probably absorbed by the cytoplasm while a new set of chromosomes develops in the interior of the nucleus. In order to explain the supposed genetic continuity of this chromatin material it has usually been assumed, although not supported by a trace of experimental evidence, that at least a portion of it is transmitted to the new chromosomes that are being formed within the nucleus. The spirazine hypothesis, on the other hand, teaches that the seat of heredity must always consist of a coordinated system of spirazines, and that the urea and guanidine derivatives which may at times be liberated by certain configurations of spirazines in the nucleus can serve only as chemical messengers or intracellular hormones by means of which the various configurations of spirazines in the nucleus can exert their specific influences upon the other portions of the cell. It appears from the spirazine hypothesis that heredity takes place in two different ways. The inheritance of major characteristics, such as the arrangements of the various tissues and organs by which the larger groups of plants and animals are distinguished from one another, is probably determined directly by the cross-sectional pattern of the nuclear spirazine structures and would not be subject to Mendel's laws; whereas the inheritance of minor or modifying characteristics, such as the colors or textures of tissues or organs already present, is probably determined by substances in a dispersed or molecular state which have been liberated by the nuclear spirazine structures, and the inheritance of such minor characteristics would be governed by Mendel's laws.

In the accompanying diagrams it has been possible to represent the molecular structure of living matter only in its statical aspect, but it should be constantly borne in mind that the various units of living matter are not rigid crystalline structures but are plastic molecular fabrics which are almost continually in a state of metamorphosis and that it is the specific behavior of living matter and not its exact form or appearance which is carried on through successive generations. It is impossible to represent adequately on paper the various deformations of which the spirazine structure is capable, but it should be noted that besides mere flattening of the polygonal compartments in one direction or another as represented in Figs. 4 and 5, there is also the possibility of longitudinal straightening out of the spirals themselves, which can take place without the disruption of either the peptide linkings or the connecting complexes at the triple junctions, so that almost every conceivable change of shape is possible with these molecular structures without any mutilation of the pattern which is characteristic of the species.

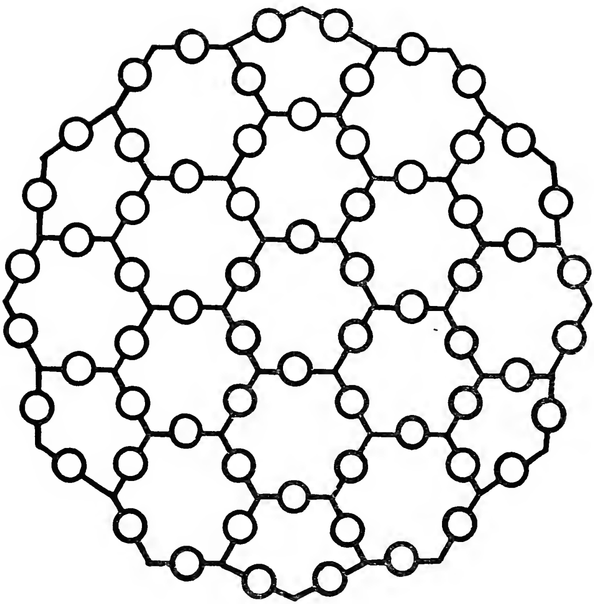


Fig. 6. Transverse section showing diagrammatically the probable molecular structure of the simplest form of life.

THE SIMPLEST FORM OF LIFE

Hypotheses concerning the origin and constitution of the simplest living organisms must necessarily be surrounded by a great deal of uncertainty, but any hypothesis, however speculative, is preferable to total darkness.

Although life must have commenced by the formation of single polypeptide spirals, yet it could not have existed in any sort of a stable and self-perpetuating form until a number of such spirals had clustered together into parallel formation and had become permanently joined to one another. It does not appear that a series of polypeptide spirals connected edge to edge to form a single polygonal compartment could constitute a permanent living organism because the exposed corners would render such a structure extremely vulnerable. Structures of this sort were probably formed temporarily when life first emerged from inorganic substances, but they must have become reinforced immediately by the addition of more spirals. If we assume that there was first formed a single hexagonal compartment, and that an additional hexagonal compartment was then formed upon each of the sides of the original one, there would have been produced a cluster of seven compartments which would be considerably more stable than a single compartment because there would not be more than two exposed corners on any one of the seven compartments. It is doubtful, however, whether even a structure of seven compartments could exist permanently because the two exposed corners on every peripheral hexagon would constitute regions of weakness, whereas if we would substitute pentagons for hexagons at the periphery then there would be too much straining of the triple junctions.

If, however, this structure would become surrounded with another layer of hexagonal compartments it would be rendered considerably more stable because only the alternate compartments at the periphery would then have two exposed corners and the remaining compartments only one, and if the compartments with two exposed corners be changed over into pentagons then none of them will have more than one exposed corner. Since each peripheral polygon now occupies only one-twelfth of the entire circumference, it appears that conditions at the periphery will not be materially changed by the addition of more layers of compartments. A cluster of nineteen polygonal compartments arranged as shown in Fig. 6 should therefore possess as much stability as any larger structure and probably represents the simplest form of life.

THE CAUSE OF CELL DIVISION

Every living organism exhibits during some period of its existence the phenomenon of cell division, which may take place either by simple fission as in the case of bacteria, by budding as in the case of yeasts, by direct amitotic division of the nucleus as in the case of pathological growths or tissues of a transcient nature, or by mitotic division of the chromosomes either with or without the formation of centrosomes and asters as in the case of nearly all higher plants and animals. The process is always entirely spontaneous, so that it must be the result of internal and not of external forces.

It has been suggested that cell division might be due to the fact that as an organism grows larger there will be a point reached where it will become physically unstable, due to the fact that its mass, which contributes to its instability, increases as the third power of its linear dimensions, whereas its surface, which by reason of its surface tension contributes to its stability, increases only as the second power of its linear dimensions. Such an explanation is inadequate because the mere presence of a large mass or volume would not cause an object to divide into fragments unless it be acted upon by external forces, and it has never been shown that physical disturbance is necessary for cell division.

Cell division cannot be attributed to surface tension because the effect of surface tension is always to hold a body together and never to separate it into fragments, but even if surface tension would act in the opposite direction from that in which it actually does act it would still be insufficient to account for cell division because the cohesive strength of protoplasmic fibers is far greater than any force that could possibly result from surface tension.

Another suggestion has been that cell division might be due to the fact that as an organism becomes larger its food requirements increase with the third power of its linear dimensions whereas the quantity of food within reach increases only as the first or second power. This explanation is also inadequate because shortage of food would only cause an organism to become under-nourished, which might retard its growth and eventually result in its death, but would not cause it to divide. Attempts to explain cell division on the basis of food economy have been due to a confusion of the principles of phylogeny with the principles of ontology.

Numerous other hypotheses have been proposed, but they have all been found untenable for

Mechanical Illustration of Cell Division

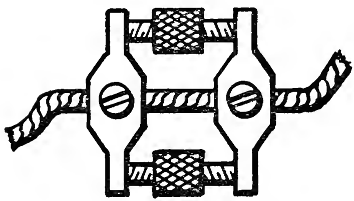


Fig. 7 a.

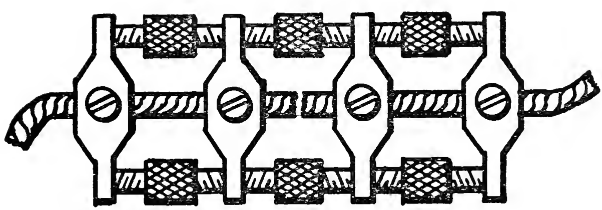


Fig. 7 b.

one reason or another. A more complete account of them will be found in E. B. Wilson's book on "The Cell in Development and Heredity."

It appears that spontaneous cell division can be explained only on the basis of a heterogeneous internal structure, such as is postulated by the spirazine hypothesis. In order to convey as clear a conception as possible of the underlying principles, a mechanical illustration will be used. In Fig. 7a two clamps are applied to a rope and their ends forced apart by means of jack screws. Let us assume that each screw is able to exert a force of one gram, but that it takes three grams to tear the rope. The structure in Fig. 7a will therefore not divide of its own accord. Let us now add to each end of this structure another rope clamp and another pair of jack screws as shown in Fig. 7b, these additional parts being identical with the homologous parts of the original structure. Each time when such additional units are added to the ends of this structure the tension of the rope is increased, so that eventually it will tear in two at the center. If, now, we substitute a polypeptide spiral for the rope, and double or triple junctions for the clamps and jack screws, then we will have conditions substantially as they exist in bacteria or other simple forms of living matter. Growth by assimilation of additional amino acid molecules will continue endwise, and if the connecting complexes are of the proper kind their mutual repulsion will eventually become sufficient to overpower the cohesive forces of the spirals themselves so that after the organism becomes of a certain length it will spontaneously divide into two halves without the intervention of any external forces.

Cell division may also be attributed to a difference in molecular structure between the outer portions and the interiors of the bacteria, chromosomes, or other elementary units of living matter. As has already been explained, the outer portions probably contain many double junctions with pairs of sulphur atoms in the places of the gamma carbon atoms, whereas the interiors must be composed mostly of triple junctions. It is highly improbable that two such radically different structures would occupy exactly equal volumes, and since the surface layers are incapable of shifting longitudinally upon the interior structures there will be a gradual increase in tension of the less voluminous structure as the organism grows in length, so that eventually it will become torn in two. This process is clearly illustrated by cell division of a bacillus. If the internal structures are more voluminous than the surface structures, cell division will begin by the formation of a circumferential groove and will result in the production of daughter cells with rounded ends. However, if the surface structures are the more voluminous, then the interior portions will separate first and leave the daughter cells with concave ends.

Although a heterogeneous internal structure is always necessary for spontaneous cell division, yet the specific manner in which it is brought about need not always be the same. A single cell may contain as many as three different kinds of self-perpetuating bodies, namely the nuclear structures (chromosomes), the central bodies (centrosomes and asters), and the plastids (leucoplasts and chloroplasts). These three are so different from one another in their structures and behaviors that it would hardly seem possible for all of them to undergo cell division by the same specific method. The nuclear structures and the plastids probably divide as the result of internal stresses which may be produced in various ways as has already been explained, but division of the central bodies is probably due to entirely different causes.

A central body consists of a radiating cluster of protoplasmic fibers called the aster, which appears to grow from a tiny central region called the centrosome. Central bodies sometimes appear to be formed de novo from cytoplasmic material and usually occur in pairs, although four or more may occur in a single cell. A constant circulation of fluid is maintained inwardly through the astral rays and outwardly through the spaces between the rays, which is probably the means employed for gathering food material for growth.

The clustering of the astral rays about common centers may be due to conditions similar to those which cause the molecules of a polar solute to arrange themselves with the same ends toward the solution. As these astral rays grow longer and become more numerous they will become more crowded in the region of the centrosome, so that the entire structure will eventually become unstable, will cave in, and two separate centrosomes will make their appearance. The rays from these two daughter centrosomes will tend to spread out in all directions and as a result of their mutual encounters will cause the two new asters to move away from each other and towards the opposite sides of the cell.

A discussion of psychical matters in a treatise on biochemistry may seem frivolous at first glance, but when we consider what a close and inseparable relationship there exists between mind and living matter, and what a powerful governing action the mind has over the body, then it would seem to be not only pertinent, but in fact necessary in a treatise of this character to give the mental factor full consideration.

The mind functions in three different ways. It gives us sense perceptions, it forms the medium for thought and memory, and it enables us to act voluntarily through the exercise of our free will.

There is no satisfactory evidence to show that mind is a separate entity capable of existing independently of living matter, or that it can reach out and act beyond those molecular structures in which it originates. It cannot be a substance because it does not possess any of the properties by which substances are recognized. Neither can it be a vibration, or, in fact, any form of energy because it will produce no effect upon even the most delicate of physical instruments.

Although many fantastic ideas prevail as to the intrinsic nature of the mind, yet if we confine ourselves strictly to the evidence presented by known and demonstrable facts, then we must regard mind not as a self-sustaining entity, but rather as a property or attribute of living matter.

Mind is synonymous with self-consciousness because whatever can be said of the mind can also be said of the self-consciousness. Without mind or self-consciousness we can have neither sensation, thought, memory, or volition.

The individual self-consciousness is coextensive with the central nervous system. Most of the cells of our bodies form parts of us physiologically but not mentally. In order for a cell to form part of us physiologically it is only necessary for the cell as a whole to be definitely coordinated in position and specifically related in function to the other cells of the body, but in order to form part of us mentally it must be coordinated with the cells of the central nervous system on a molecular scale, that is, its individual spirazines must be coordinated with or joined to those of our central nervous system in a specific manner, so that electric impulses passing along a certain spiral or polygonal compartment of one of these cells will be transmitted to a certain spiral or polygonal compartment of the other instead of being dissipated and lost in the surrounding protoplasm.

Thought and memory may be explained on the theory that a previous impulse from a sensory nerve has produced such a forceful coordination of certain of the spirazines of the cerebral cortex that the surrounding structures have become permanently modified in such a manner that they will retain the spirazines in their new positions for some time thereafter.

Free will and volition are probably due to the spontaneous activity of the spirazines in our cerebral cortex and differ from memory only in that the electric impulses which are produced by such activity have found an outlet through the motor nerves instead of being confined to the molecular structures of the cerebral cortex.

Whether the exercise of free will involves any violation of the laws of nature is a question on which there is much difference of opinion. According to the laws of nature the behavior of every physico-chemical system is fixed and predetermined, whereas the exercise of free will introduces an arbitrary and indeterminate factor. Since there cannot be two independent systems of governing forces operating in the same place and at the same time, we must either regard free will as a delusion, or we must assume that living matter does not come under the domain of those natural laws which govern physico-chemical systems.

The existence of free will is being made known to us directly through our self-consciousness, and it would be very dogmatic and unscientific for us to reject the testimony of our self-consciousness in so far as it furnishes us with a basis for our belief in free will, but yet to accept it in so far as it informs us of the operation of the laws of nature.

The classical principles of mechanics, electrodynamics, and thermodynamics, which seem to signify predetermination to the exclusion of free will, were derived from experiments upon isolated physico-chemical systems and deal only with the effects of simple elementary forces or with the combined or average effects of large numbers of atoms or molecules. There is no artificial device known which will respond to the specific behavior of a single selected atom. Even the streaks produced in supersaturated vapor by the individual alpha and beta particles of radioactive substances constitute no exception to this rule, for what is really being observed here is only the presence of a particle and not the specific behavior thereof.

It is only through the medium of living matter that the individual behaviors of the various atoms can make themselves known to us. In the molecular structure of living matter the various atoms are coordinated and connected with one another in a specific manner so that the relation of each atom to the structure as a whole is different from that of any other atom. In chemically organized structures of this sort the specific effect of each atom will be transmitted along the spirazines of the protoplasmic fibers to other parts of the cell, just like the specific effect of each atom of a molecule is transmitted to other parts of the latter. An individual atom may therefore excite a nerve or other protoplasmic fiber in such a manner as to produce a response of which we may become aware. Such responses may manifest themselves either as thoughts, sensations, or volitions and will not conform to any of the laws of nature by which the world about us is governed but will appear to us as entirely arbitrary and without natural causation, although they may actually have been predetermined by intra-atomic conditions which are beyond the reach of physico-chemical methods of exploration. Predetermination by natural law ends where atomic structure begins, because we cannot extend the laws of nature by analogy into realms where conditions are not the same as those under which such laws were derived.

The arbitrary behavior of living matter affects primarily the second law of thermodynamics because this law applies only to systems in which the variable components are capable of approaching a random state of distribution, whereas in the molecular structure of living matter the orderly arrangement of the atoms along the sides of the polygonal compartments will tend to sort out rather than mix up the molecules or ions within them. The passageways through these polygonal compartments are only about ten Angstrom units in width, which is not sufficient to permit any free flow of fluid therethrough. Since the spirazines which form the walls of these compartments are polar structures, they will render the electric fields within such compartments unsymmetrical so as to facilitate the migration of molecules or ions in one direction but retard them in the opposite direction.

The direction of migration of molecules or ions through these compartments may also be controlled by side chains extending inwardly from the walls thereof and functioning in a manner similar to check valves. These side chains may be in the form of fat or carbohydrate molecules in the process of formation which have not yet become detached. Since they consist of only single chains of atoms they will be sufficiently sensitive to respond to the approach of individual molecules or ions, and like Maxwell's demons will close or open the passageways through the polygonal compartments according to whether a certain ion or molecule approaches from one direction or from the other.

In either case the effect will be a sorting out of different kinds of molecules or ions from one another or an accumulation of molecules or ions of the same kind so as to build up osmotic or hydrostatic pressures or electric potentials. These processes will take place in contravention to the second law of thermodynamics because the energy which is thus rendered available will not have been obtained entirely from the oxidation of food material but partly from the heat of the surroundings.

Vital energy of this sort should not be confused with vital force, for the two have nothing in common. The principle of vital energy is entirely consistent with the laws of nature and supplements rather than contradicts them, whereas the doctrine of vital force assumes the existence of some mysterious power which is supposed to act in contravention to the laws of nature to control such processes as metabolism, growth, and reproduction. Vital energy is within the realm of the comprehensible and the possible existence of such a form of energy has been suggested by physicists long before the conception of the spirazine hypothesis, whereas vital force is supposed to be something which is incomprehensible to the human mind, and the existence of which would be contrary to all the principles of science.