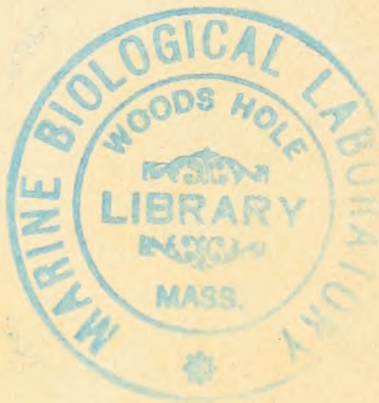
UNIVERSITY OF KANSAS

SCIENCE BULLETIN



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INTRODUCTION

At a meeting in 1957 of an informal faculty discussion group at the University of Kansas known as the Evolutionists, it was proposed that a series of lectures and seminars on aspects of evolution might be an appropriate means of focusing the University's attention on the biological and geological sciences during the approaching Darwin-Linnaeus Year. The academic year 1958-1959 was designated Darwin-Linnaeus Year by reason of its being the bicentennial of publication of the Tenth Edition of the "Systema Naturae" by Carolus Linnaeus (1758) and centennial of Charles Darwin's "On the Origin of Species . . ." (1849). A general plan for the series was laid before the University's chapter of the Society of the Sigma Xi, through its president, Dr. Robert E. Beer, and the two groups jointly appointed a committee to arrange details. Headed by Dr. Robert R. Sokal (Entomology), the committee included Dr. Albert A. Benedict (Bacteriology), Dr. Ronald L. McGregor (Botany), Dr. Philip Newmark (Biochemistry), Dr. Charles W. Pitrat (Geology), Dr. Frederick E. Samson (Physiology), Dr. John A. Weir (Zoology), Dr. Byron S. Wenger (Anatomy) and Dr. Robert W. Wilson (Zoology). It was decided that the program should consist of a series of lectures by distinguished biologists and geologists from other institutions and a number of interdepartmental seminars in which members of the various departments of biological sciences of the University would discuss the relationships of their particular fields of research to the development of evolutionary theory.

The program received generous financial support from the University, largely through the interest and assistance of Chancellor Franklin D. Murphy, Dean John H. Nelson of the Graduate School, and Mr. Raymond Nichols, Executive Secretary of the University. Continuing administrative and financial support in connection with publication of the Darwin-Linnaeus Year papers has been obtained with the help of the present Chancellor of the University, Dr. W. Clarke Wescoe, and Mr. Nichols.

In conjunction with these lectures and seminars, the Watson Library of the University of Kansas prepared an exhibition of the

works of Darwin and Linnaeus and of related materials. This exhibition was arranged by Mr. Joseph Rubinstein and Mr. Thomas R. Buckman. In addition, the already established Humanities Lecture Series included, on 21 April 1959, a presentation by Dr. William Irvine, author of "Apes, Angels and Victorians."

The contributions to the Darwin-Linnaeus Year series are arranged below in the order of first the invitational lectures followed by the interdepartmental seminars, the papers appearing in the order of presentation within each of these groups. The rather long elapsed time since the close of the series has resulted, in one instance, in the publication elsewhere of the general contents of an invitational lecture, and in sufficient duplication of material covered in two of the seminars that these are here presented in summary form only.

GEORGE W. BYERS,
Editor.

THE UNIVERSITY OF KANSAS
SCIENCE BULLETIN

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Natural Selection in Human Populations

A. C. ALLISON [1]

I welcome this opportunity for adding my tribute to the many already paid to Darwin and Linnaeus. It is appropriate that the two names should be linked in centenary celebrations because their work was complementary. Everyone now accepts that problems of speciation and systematics cannot be considered apart from those of genetics and evolution. Since my own background is medical and my researches have been concerned mainly with man and disease-producing microörganisms, I have had little to do with the traditional problems of systematics, apart from recognizing the still unresolved difficulties presented by the classification of bacteria and viruses. But like all students of population genetics and evolution, I have derived inspiration from reading Darwin's works. His approach to the problems with which he was faced is a model of the scientific method.

As so often happens, the unifying concept came early. While a young man of twenty eight on the voyage of the *Beagle,* Darwin was struck by the relationship between animals on islands (notably the Galapagos) and their closest continental neighbours. The species were often near akin and yet quite distinct, as were species living or recently extinct and those found fossil in the same country. He concluded that the findings were due to transmutation of species. This was an induction from observation and led him to search for a mechanism by which transmutation of species might occur. On his return to England the following year (1837), Darwin began his notebooks on the subject. Information was collected which he early recognized to be critical: chiefly on the tendency to geometrical increase in the number of each species (partly derived from Malthus, whose *Essay on Population* appeared

1. National Institute for Medical Research, London, N. W. 7, England. Lecture presented on 18 September 1958.

in 1838), on variation, and on artificial selection by man. For twenty years the information increased and with it Darwin's conviction that natural selection was the main cause of evolution. He had completed half a treatise on the subject when he received for comment a manuscript from A. R. Wallace, who was then in the Moluccas. The manuscript included a complete summary of the theory of natural selection. This was a bitter disappointment to Darwin, and might have led to a serious quarrel, with recriminations about priority. As it was, Wallace's manuscript and an abstract of Darwin's were read before the Linnaean Society on the same day (1 July 1858), with a preface making it clear that the two authors had reached the same conclusion independently. Such gentlemanly behaviour has not always characterized the history of science; nor is it universal today. Incidentally, I commend to you Darwin's *Autobiography,* the full text of which has recently been released. The impartiality and candour that shines through all his work appears in this self-analysis, and makes it unique among autobiographies.

Just a century ago, on 24 November 1859, Darwin's complete treatise appeared with the title, *On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life;* the whole edition of 1250 copies was exhausted on the day of issue. Darwin based his theory of natural selection on three observable facts of nature and two deductions from them. The first fact is the tendency of all organisms to increase in a geometrical ratio. Such a tendency exists because offspring, in the early stages of their existence, are always more numerous than their parents. This holds good whether reproduction is sexual or asexual, by fission or budding, by means of seeds, spores or eggs. The second fact is that, in spite of the tendency to progressive increase, the number of a given species actually remains more or less constant.

From these two facts Darwin deduced the struggle for existence. For since more young are produced than can survive, there must be competition for survival. In amplifying his theory, he extended the concept of the struggle for existence to cover reproduction. The struggle is in point of fact for the survival of the species; if its survival is aided by greater fertility, an earlier breeding season, or other reproductive function, these should be included under the same heading.

Darwin's third fact of nature was variation: All kinds of organisms vary appreciably. And the final deduction from the first deduc-

tion and this fact was natural selection. Since there is a struggle for existence among individuals, and since these individuals are not all alike, some of the variations among them will be advantageous in the struggle for survival, others unfavourable. Consequently, a higher proportion of individuals with favourable variations will on the average survive, while a higher proportion of those with unfavourable variations will die or fail to reproduce themselves. And since a great deal of variation is transmitted by heredity, these effects of differential survival will in large measure accumulate from generation to generation. Thus natural selection will act constantly to improve and maintain the adjustment of animals and plants to their surroundings and their way of life.

Darwin's later work, *The Descent of Man* (1871), aroused even greater public controversy. The main conclusion reached was "that man is descended from some less highly organized form. The grounds upon which this conclusion rests will never be shaken, for the close similarity between man and the lower animals in embryonic development, as well as in innumerable points of structure and constitution . . . are facts which cannot be disputed." Indeed, in his bodily structure man shows such obvious resemblances to the lower animals that it now seems astonishing that his kinship with them should ever have been controverted. His skull and skeleton are composed of the same bony elements, his muscular system is made up of identical muscles disposed in the same pattern, his heart and blood vessels are constructed on the same plan, and even his brain, though large and elaborate, is clearly organized in the same way as that of lower animals. Then there is the remarkable series of stages that the human embryo undergoes in common with the embryos of other vertebrates, including the transitory appearance of gill slits, pharyngeal pouches, non-functional kidney precursors and other vestiges.

But some of the most convincing evidence of all comes from the study of fossils, for they provide the opportunity for examining the actual remains of those intermediate stages which presumably must have occurred in the evolutionary transformation of one type into another. When Darwin wrote *The Descent of Man*, there was almost no fossil evidence for his thesis of human evolution. Today the situation is very different. I shall trespass on Professor Romer's ground only so far as to recall that a number of fossils intermediate in many respects between apes and man have been discovered in the last half-century, from the Australopithecinae of the late Pliocene in South Africa to the Javanese and Chinese species of *Pithe-*

canthropus and the Neanderthal and Cromagnon types found in Europe. Doubtless future research will provide a more complete series of "missing links." But the evidence that man has evolved from some ape-like creature is so compelling that only the most bigoted can now close their minds to it.

The question then arises, has human evolution occurred through the agency of natural selection and does it still continue? There is a widespread belief that the struggle for existence depends largely upon predation. It is generally conceded that some sort of natural selection may have occurred in primitive societies, when man the hunter pitted his skill and energy against wild beasts. The lions, tigers, buffaloes and mammoths, as well as the giant animals whose fossil remains have recently been recovered in East Africa, were certainly formidable enemies of stone-age man, without resorting to the anachronism of bringing dinosaurs into the picture, as is commonly done by cartoonists in the popular press. Indeed, it is obvious that this situation, and also warfare between tribal groups (for it is likely that war is as old as man himself), would produce selection in which the physically fitter and more intelligent human beings would tend to survive at the expense of others. Nevertheless, it has been argued that once man was established in communities, especially urban communities, he was protected from the struggle for existence, so that natural selection ceased to exert any significant effects. The purpose of this lecture is to summarize evidence showing how mistaken this view is, for natural selection has in fact continued in human populations with only slightly reduced intensity to the present day, when its effects can still very easily be demonstrated.

Before summarizing the evidence, it is worth pausing to consider how Darwinism stands in the light of a century of research. Darwin's first fact has remained unchallenged: All organisms possess the potentiality for increase of geometric type. Equally unquestioned is the second fact, the approximate constancy in numbers of most species. Man provides one of the partial exceptions to this rule, since his numbers are increasing at an alarming rate in many countries. But even here the actual increase is less than the potential: some young fail to survive. Again, we now know that many species undergo cyclical fluctuations in their numbers, but this finding, although it has certain interesting evolutionary consequences, does not invalidate the general principle. These two facts being accepted, the deduction from them also holds: A struggle for survival must occur. It is the third fact that has been most modified

by subsequent research. Darwin assumed that the bulk of variations are inheritable. As the Danish geneticist Johannsen put it, "heredity was seen in the light of evolutionary theory, that is to say, in a very deep shadow." Early in the study of experimental genetics it became clear that the original interpretation is only a half truth. If in a pure line one selects the heaviest beans, the beans of the next generation are no heavier than if one selects the lightest, as Johannssen (1909) first showed. The consideration of natural selection is in fact still handicapped by vocabulary. The same word is used for phenotypic and genotypic selection, although only the latter has any bearing on the future of the population. The problem is particularly difficult in human genetics; except in the case of rather few characters whose genetic determination is simple and well understood, we can only measure phenotypic selection in man. This is nicely illustrated by the selection for birth weight which will be described below.

In spite of the difficulties, data on natural selection in man are more adequate than those for any animal species in the wild state. In particular, it is quite impossible in most animal species to estimate the number of offspring begotten by a given male, though it is possible to do so in monogamous species such as most birds, about the genetics of which next to nothing is known. Hence data on natural selection in man are not only of interest to anthropologists, physicians, sociologists, and so on, but to every student of evolution.

Variation in Man

We recognize today that variation in all species is due to inheritable and environmental components. The inheritable variation results from *mutation*—sudden, nearly random changes in the structure of individual genes or sections of chromosomes—and *recombination* of existing genetic units, which may both produce and modify inheritable variations. Recombination cannot occur without sexual reproduction, the importance of which in providing the possibility of speedily recombining several favourable mutations doubtless accounts for the universal presence of some sexual process in the life cycle of organisms—from the transductions mediated by bacteriophages to the elaborate mechanisms preventing self-fertilization in angiosperms.

The first type of variation to be analysed in man was discontinuous, the occurrence of distinct changes from the common form with no intermediate types. This kind of variation includes the numerous hereditary abnormalities affecting every bodily organ

listed in textbooks of medical genetics. Soon after the rediscovery of Mendel's laws in 1900, the mode of inheritance of these defects became clear. Some, such as achondroplasia, were classified by Bateson (1909) and others as "dominants," by which it is meant that they have a distinct manifestation in the heterozygous phase. In fact, none of these characters seems to be truly dominant, in the original and correct sense in which that word was used, which implies that single-and double-dose effects of the gene are the same (as in Mendel's tall peas). Allison and Blumberg (1958) have summarized evidence that double doses of such abnormal genes produce more severe effects than single doses.

Other characters, such as alcaptonuria and albinism, were shown by Bateson to behave as recessives. Finally, the discovery of sex-linkage in heterogametic *Drosophila* males by Morgan (1910) at once explained the inheritance of sex-linked recessives, such as haemophilia and the common form of colour blindness, in man. Again, these characters are recessive only in the sense that persons carrying a single dose of the gene in the presence of the normal allele do not develop overt disease. Detailed investigations often show some abnormality. Thus, Hsia, Driscoll, Troll and Knox (1956) have demonstrated that the apparently normal parents of mentally defective children with phenylketonuria have significantly higher blood levels of phenylalanine, and are less well able to metabolize ingested phenylalanine, than normal subjects. Carter and Simpkiss (1956) reported that the capacity to concentrate urine is significantly reduced in female carriers of the gene for sex-linked nephrogenic diabetes insipidus. Considerable variability in the single-dose expression in the female of the gene for sex-linked ocular albinism is also known; occasionally this is as severe as in affected males (Waardenburg and van den Bosch, 1956). The recognition of carriers of recessive traits is useful from the eugenic point of view. The identification of female carriers of the haemophilia gene, for instance, would be a valuable contribution to knowledge. As it is, the sisters of haemophilics have the lamentable choice between remaining childless or possibly watching their sons bleed to death.

With regard to the general problem of dominance, it is clear that in man, as in other species, dominant genes are readily modifiable by other genes. Early in the study of experimental genetics it became apparent that the effects of many genes are not constant, but are modified, often to a great extent, by the presence or absence of other genes. In 1928 Fisher pointed out that if modifiers

enhanced or suppressed the effects of a gene in single dose, the heterozygote would resemble one of the homozygotes, so that, by definition, the character would become dominant or recessive. This hypothesis was soon confirmed experimentally in animals, and there is evidence that in man also the expression of individual genes is not fixed but is often profoundly altered by the gene complexes in which they are placed, even to the extent of modifying the dominance relationships of a character from one generation to the next. The evidence is summarized by Allison and Blumberg (1958), who discuss the general problem of the evolution of dominance and give reasons why it is less likely to be complete in human populations than in populations of lower animals, either in the wild or under domestication.

Included under the same heading of discontinuous variation are such common or polymorphic characters as the blood groups, haemoglobin types and serum-protein types. Their inheritance is simple and in most cases reasonably well understood. Many human proteins complex carbohydrates have been found to vary in different subjects, so that the total amount of variance produced in this way must be enormous, much of it still unrevealed. The individuality of tissues from different subjects expressed in the reaction against homografts bears out this conclusion.

Characters controlled by major genes, such as those described in the preceding sections, show an important property: the variation they produce is discontinuous and segregates in families. On the other hand, traits concerned with physique, skin colour, mental and physical ability and resistance or susceptibility to most diseases do not lend themselves easily to exact genetical analysis. But they can often be measured, and when measurement is undertaken it nearly shows that these characters have continuous variation. This was demonstrated for stature by Galton (1889), who also developed the first statistical analyses of family likeness. His method was to take a group of men of the same stature and to find the mean stature of, for example, their brothers. Thus, the mean stature of brothers of men 72.2 inches tall was found to be 70.3 inches, whereas the mean stature of all men in the population was 68.2 inches. On the average, the brothers stood about halfway between the group specified and the normal level in the population. In general, if the deviation from the population mean of a given man is D_1 and the mean value of the deviation, from the same origin, of his brothers, is D_2, $\frac{D_2}{D_1} = r^1$, or the regression coefficient. In a case

such as this, where the distribution is symmetrical because it is immaterial which brother is taken first, the variances of the two compared groups are equal, and r is equal to the correlation coefficient, for which a value of 0.5 is obtained. In the more general case where, say, parents and children are studied there are two regression coefficients, differing from one another because of the different variances of the two classes compared; the correlation coefficient is then the geometric mean between the two regression coefficients.

The genetical background of the regression or correlation value of 0.5, which was so frequently found by Pearson (1909a) in comparisons of measurements of pairs of sibs or parents and children, is a direct consequence of the fact that a parent transmits to each offspring half his genetic material (apart from a small segment of the sex chromosomes and possible cytoplasmic factors.) The argument can be extended to any degree of relationship; where the number of hereditary steps in a relationship is N, the degree of hereditary likeness is 0.5^n.

Fisher (1918) showed how these effects could come about when genes are multiple and additive, and he analyzed the deviations due to allelism, dominance and assortative mating. The theoretical analysis has been considerably extended in recent years and applied to experimental populations of flies and other organisms, as well as to characters of economic importance in domestic animals. Elegant expositions will be found in the Cold Spring Harbour Symposium (1955) entitled *Population Genetics.*

There is considerable difficulty, however, in proceeding much further in this field when dealing with human material because very few critical tests are available for distinguishing between different genetical hypotheses. The number of genes controlling a character such as stature, weight, blood pressure, intelligence or skin color, the frequencies of the genes and the amount of dominance are all indeterminate. A correlation of 0.5 for sibs or parents does not necessarily imply a simple multifactorial genetical explanation; it may indicate similarities of other kinds. Some factors, such as dominance and recessivity, tend to diminish likeness between relatives, while other factors, such as assortative mating and similarities in environment, tend to increase likeness. For these reasons, the observed values of correlation coefficients intended to measure the influence of heredity on polygenic characters must be interpreted with caution. Various alternative methods have been suggested for estimating the influence of heredity and en-

vironment on such characters. All of these, including twin studies, have serious limitations that need not be discussed here.

In general, it can be stated that discontinuous variation in man can be analyzed genetically with reasonable precision. The effects of environment on this type of variation are usually slight. Occasional difficulties arise from gene interaction, producing suppression or dominance modification, and these introduce uncertainties into the estimation of mutation rates. The analysis of continuous variation is much less satisfactory. Positive correlations for sibs or parents suggest genetical influence on the character in question, but the relative importance of heredity and environment is difficult to assess accurately. As will appear below, the effects of natural selection on such characters are also far from obvious.

Selection

Selection depends upon inequalities in the survival of different genotypes up to and throughout reproductive age, or inequalities in the reproductive efficiences of different genotypes. Evidence will be summarized that in each stage of development, from the first stages of fertilization, implantation and growth of a foetus, through birth to reproductive age, inequalities in the survival of different human genotypes occur. These findings will then be applied to particular examples of natural selection in man. Evidence is also available that different genotypes vary in fertility, but the effects of this phenomenon on population trends are still uncertain.

A concept which is indispensable in the theoretical study of evolution is that of gene frequency. Many of the results of natural selection can be expressed in terms of progressive increase or decrease of gene frequencies. The elementary mathematical results were discovered independently by Hardy, Pearson and Weinberg in 1909. Let the frequency of a given gene, *A*, in the population be represented by p. Then the frequency of the allelic partner-gene, *a*, is 1-p. Every chromosome is represented twice in the same person, so that three classes of individuals are found in the population: (1) *AA*, those homozygous for *A*; (2) *Aa* those heterozygous for *A* and *a*; and (3) *aa*, those homozygous for *a*. The frequencies of these three classes will be p^2, 2p (1-p) and $(1\text{-}p)^2$, respectively. Provided that there is no change in gene frequency, the ratios of the various genotypes in the population will remain constant. The matematical results of agencies changing the frequency of a gene, as a consequence of its being advantageous or disadvantageous, were exploited by Fisher (1930), Wright (1931) and Haldane (1932).

From that time forward, a gene could no longer be regarded as a static element in the population. Its qualities had to be understood in relation to evolutionary trends. If a gene increases fitness—that is, the viability or fertility—of its possessors, its frequency will increase; a gene which diminishes fitness will tend to be eliminated. It was shown, further, that under certain conditions selective agencies can bring about a stable gene frequency or equilibrium. These principles are now being applied to human genetics.

Selection before birth

In all species that have been investigated, there is a considerable loss of fertilized ova before birth (Brambell, 1948; Boyd and Hamilton, 1952). Thus Brambell concludes that in wild rabbits at least 43.3% of ova ovulated are lost before parturition, of which 10.2% are lost before implantation and the remainder before mid-term. In man the most conservative estimate is that one-fifth of ova implanted fail to develop to term. There is general agreement that this loss is partly attributable to embryonic defects. These may appear very early: Hertig and Rock (1944) examined a series of twelve early human ova and found that seven were normal and five showed distinct pathological changes. The ova were implanted in apparently normal endometrium, so it is presumed that the abnormal development was due to intrinsic defects in the ova.

If this loss affects different genotypes unequally, it would bring about powerful selection. In some mammals unequal prenatal mortality of different genotypes, leading to departure from Mendelian ratios at birth, is well known (Hammond, 1952). Several instances in mice, including the lethality of the homozygous yellow condition shown by Kirkham (1919), are quoted by Grüneberg (1947). A gene in Dexter cattle has been described by Crew (1923) which in the heterozygous phase gives rise to the short-legged type and in the homozygous produces the "bull-dog" calf, an abnormal embryo in which lengthening of bones fails to take place and which is usually aborted at the fifth to seventh month.

Many of these lethals are recessive, and it seems likely that a proportion of the mortality in human embryos and foetuses is due to homozygosity for deleterious recessives. Some of these would be autosomal and others sex-linked, the latter being at least partially responsible for the higher mortality in males which will be mentioned below. For example, a pedigree recorded by Bickers and Adams (1949) showed that one type of congenital hydrocephaly could be attributed to a single sex-linked gene. Böök and Rayner

(1950) consider that anencephaly may be due to a single recessive gene, but this is not the only possible explanation for their observations. In France perinatal mortality (that is, stillbirths and deaths in the first week) is high in the offspring of cousin marriages (Sutter and Tabah, 1950; 1952). This strongly suggests that recessive genes at single loci, the manifestations of which are increased by the homozygosity resulting from inbreeding, play a part in the causation of perinatal mortality. Incidentally, since a gradual reduction of the amount of inbreeding in European communities has been in progress for several generations (Haldane and Moshinsky, 1939), it may be supposed that a small part of the reduction in stillbirth and neonatal death rates has been due to this cause. Further evidence pointing to a genetical component in foetal abnormality comes from the finding of monozygotic twins with the same abnormality; in contrast, pairs of dizygotic twins showing the same abnormality are very unusual (Penrose, 1954). Although the data which have been summarized are far from complete, it seems reasonable to conclude that differential mortality between conception and birth falls most heavily on malformed embryos and foetuses, at least some of the abnormalities being genetically determined. In other words, selection operates in such a way as to eliminate unfavourable genes from the population.

Further evidence of unequal mortality comes from a study of the sex ratio. In any species, such as man, in which one sex is heterogametic (XY or XO) and the other homogametic (XX), the two kinds of gametes (X and Y, or X and no X) are theoretically formed by heterogametic individuals in equal numbers. It follows that if fertilization takes place at random there should be equal numbers of homo- and heterogametic zygotes; in other words the primary sex ratio should be unity. Any departure from unity is referable either to an unequal production of the two kinds of gametes by the heterogametic sex or else to their unequal participation in fertilization. If the secondary sex ratio—that which obtains among the newly-born—differs from the primary sex ratio, then a sexually selective prenatal mortality must have been operating between conception and birth.

As everyone knows, vital statistics in many countries show a preponderance of male births in human beings, usually between 105 and 106 male to 100 female births being registered. However, there is a remarkable swing in the sex ratio as the successive five-year age groups after birth are reviewed. Numerical equality of sexes is reached in the 15 to 19 year old group, and thereafter

follows a female ascendancy which increases progressively until amongst the 80-year-olds there are twice as many females as males. Thus the mortality among males after birth is higher than that among females. Among stillbirths the sex difference is even more striking, and it is widely held that this is true also of abortuses (Crew, 1952). It therefore seems likely that the primary sex ratio (males to females) in man is well above unity. Nevertheless, sexing early embryos morphologically presents difficulties (Tietze, 1948), and there seems scope here for cytological study, since human sex chromatin is detectable at 10-12 days (Park, 1957).

The explanations which have been offered for the higher mortality among males both before and after birth need not be discussed in detail. Sex-linked recessive lethal or sublethal genes are likely to be responsible for some of the higher mortality in the heterogametic males, and sex limitation of the expression of certain characters, as a result of endocrine and other physiological differences between males and females, for most of the remainder.

In other species remarkable deviations in sex ratio have been studied. Thus, in certain *Drosophila* stocks it has been shown that the Y-bearing sperm are produced in deficient numbers. Morgan *et al.* (1925) and Gershenson (1928) discovered a gene which has no influence on females but affects males so that the sex ratios of offspring sired by them vary from 85 to 100% females. Later, Sturtevant and Dobzhansky (1936) found this "sex-ratio" gene widespread in different geographical races of *D. pseudo-obscura.* It is located in the right arm of the X-chromosome and is associated with a small inversion. It induces equational division of the X-chromosome at each meiotic division, whilst the Y-chromosome degenerates. The result is that only X-bearing spermatozoa remain available for fertilization.

Another type of deviation in sex ratio is inherited through the cytoplasm. Females of certain strains of several species of *Drosophila* produce progenies that consist mainly or only of daughters, regardless of which males they are crossed with, and this condition is transmitted in turn to all their female offspring. Using micropipettes, Malagolowkin and Poulson (1957) recovered oöplasm from eggs deposited by females with the aberrant sex ratio and injected it into the abdomens of young virgin female flies. After about a fortnight, the recipient females began to develop the aberrant sex ratio; 5 of 16 recipients eventually produced only daughters. Thus the maternally inherited abnormal sex ratio could be infectively transferred, like the CO_2 sensitivity in *Drosophila*

studied by l'Heritier (1958), or like a virus. About half the eggs deposited by "sex-ratio" females degenerated within a few hours, and were presumed to represent dying male zygotes.

A process akin to infective transfer of sexuality itself is known in the bacterium, Escherichia coli. The F^+ character passes from one bacterium to another during mating and confers on the recipient the ability to mate with other individuals (Wollman, Jacob and Hayes, 1956). Whether an infectious element likewise plays a part in sexuality or in the sex ratio of man is beyond the scope of the present discussion.

The main conclusions bearing on natural selection are clear enough. The high primary sex ratio in man is a significant departure from expectation on the basis of random production of gametes and random fertilization. And the elevated mortality of males both before and after birth is an example of unequal survival of different genotypes, in other words natural selection.

As already stated, the reasons for the high primary sex ratio in man are unknown. Some evidence points to the existence of differences between X- and Y-bearing sperm in experimental animals, which might affect their chance of fertilizing ova. Schröder's (1941) claim to have separated X-bearing from Y-bearing rabbit sperm by electrophoresis has received confirmation from Gordon (1957); further experimental work in this important field is greatly needed. Differential participation in fertilization by spermatozoa of different genetical constitution is made more plausible by indications of haploid manifestation in them of certain genes. Beatty (1956) reported that in rabbits heterozygous for a melanic gene some sperm gave a histochemical reaction for the enzyme dopa oxidase, while others did not; in homozygous melanic animals all sperm carried the enzyme. This finding is not quite conclusive, since the enzymes in the sperm cytoplasm could be derived from the cytoplasm of their diploid precursors. In the cells of rabbits heterozygous for the melanic gene there might well be less enzyme than in the cells of homozygotes, with somewhat variable amounts of enzyme carried into the cytoplasm of spermatozoa. Then, since the histochemical technique only demonstrates enzyme in concentrations above a threshold level some sperm cells might appear to have enzyme and others to lack it. More direct evidence of haploid manifestation are the findings of Gullbring (1957) that spermatozoa of males of blood group AB are of two classes, one containing the A antigen and the other the B antigen.

These results suggest that the genetic material is not just pas-

sively carried in the haploid generation of cells, but directly influences their cytoplasmic constitution. They also focus attention on the possibility of some level of infertility in ABO incompatible matings. Matsunaga (1955) has, in fact, obtained evidence—which is not yet conclusive—that the mean number of Japanese pregnancies is greater in matings in which the mother was O and the father A or B than *vice versa*. Other blood group effects before birth have been reported. Thus, there is quite substantial evidence that in haemolytic disease of the newborn due to Rh-immunization the parents are more often compatibly mated as regards ABO blood groups, in the sense that husband could be a donor to his wife, than would be expected (Race and Sanger, 1958). Grubb and Sjöstedt (1955) found, in a series of marriages with two or more pregnancies terminating in intrauterine death for unknown reasons, a highly significant excess of ABO incompatibility in the mating combination Rh positive: Rh positive, but not in other matings. These findings illustrate the interdependence of different blood group systems in the genesis of disease, which is direct evidence that the selective forces acting on one system of blood group genes will be influenced by the presence or absence of blood group genes belonging to different systems, as they doubtless are also by other kinds of genes. This point is noteworthy, since it provides one of the few mechanisms by which polymorphism at several loci can be maintained, and will be discussed below.

Selection at birth

The next great obstacle to be overcome is birth and adaptation of the newborn child to an independent existence. At this time many congenitally abnormal babies perish; and since some of these abnormalities are genetically determined there is appreciable selection against disadvantageous mutant genes. This is also one of the times when haemolytic disease of the newborn takes its toll, and reference will be made below to the effects of this important selective agency on population genetics.

The considerable selection operating at birth is shown by analyses of mortality in relation to one universally measured character, birth weight. Karn and Penrose (1951) and others have demonstrated that unusually light and unusually heavy babies die more frequently at birth or in the first month of postnatal life than those of normal weight. The death rate in all the babies in their sample was about 4½%, that in the group whose weights lay between 7½ and 8½ pounds being about 1½%. Thus, two thirds of all these death were selective

for birth weight, and the total intensity of selection was 3%. Unfortunately, we do not know what fraction of this phenotypic selection is also genotypic, but it is remarkable that by considering a single character, weight, no less than two-thirds of all deaths in a critical period of life have been shown to be selective for it. A large fraction of deaths at some other periods of life may also be selective, but we do not yet know with what measurements or characters to associate deaths at each part of the life cycle. A comparatively high death rate in overweight persons is shown in all available statistics, but since this applies mainly to persons past reproductive age it exerts only slight genotypic selection, even though there is a high intrafamilial correlation of adult weight.

Selection between birth and reproductive age

One set of characters that has been fully investigated is the abnormal haemoglobins of man. Sickle-cell haemoglobin and haemoglobin C are variant forms of normal adult haemoglobin, their formation is controlled by three genes at the same locus, Hb^S, Hb^C and the normal allele, Hb^A (Ranney, 1955). These genes are of particular interest in biochemical genetics because their study has elucidated for the first time the effects of mutations on the protein products of the genes. Ingram (1957) and Hunt and Ingram (1958) have shown that a single negatively charged amino acid (glutamic acid) in each half-molecule of normal adult haemoglobin is replaced in sickle-cell haemoglobin by a neutral residue, valine, and in haemoglobin C by a positively charged residue, lysine. This small substitution has dramatic consequences: the change in over-all charge allows the sickle-cell haemoglobin molecules to aggregate when deoxygenated and so brings about the sickling of erythrocytes, haemolysis and vascular obstruction characteristic of sickle-cell disease in persons homozygous for Hb^S. And the tendency for sickle-cell and haemoglobin-C molecules to form mixed aggregates produces a well-known variant of sickle-cell disease in subjects who are unfortunate enough to inherit a sickle-cell gene from one parent and a haemoglobin-C gene from another parent. This syndrome was described by Kaplan, Zuelzer and Neel (1951) and numerous cases have since been reported from the United States and West Africa. More than 1% of all children born in Ghana have this disease.

The sickle-cell gene is common in many African and some Southern European and Asian populations, despite the fact that sickle-cell homozygotes develop a severe disease from which most die

in childhood. Allison (1954a) recognized that the heterozygous state, the sickling trait, is prevalent only where malaria is or was until recently hyperendemic. He was able to show (1954b) that children carrying the sickle-cell trait are resistant to malignant tertian malaria, so that they stand a better chance of surviving through the dangerous years of first exposure to the disease than children without the trait. There is now substantial evidence that this interpretation is correct (Allison, 1957; Vandepitte and Delaisse, 1958). Hence it is justifiable to conclude that the sickle-cell gene, initially a rare mutant, has been favoured in malarious areas of Africa, Sicily, Greece, southern Turkey, southern Arabia and India, so that it increased in frequency until the advantage of the heterozygote was exactly counterbalanced by the disadvantage of the homozygote, after which the frequency of the gene has remained nearly constant. The incidence of the sickle-cell trait now rises to 40%, but if the environment were to change in such a way that the advantage of the heterozygote was eliminated, it would be expected to fall. This seems to have hampered within three centuries in the Negro population of the United States, among whom the frequency of the sickle-cell gene is now considerably lower than expected from their African ancestry, even when allowance is made for a mixture with White and Indian stocks.

Because of the magnitude of the selective forces acting on the sickle-cell gene, it has been possible to demonstrate selection directly between the time of birth and reproductive age. The main factors concerned seem to be differential mortalities from malaria and sickle-cell disease. Neither of these produces an appreciable mortality before about the fourth month of postnatal life, most of the deaths from both conditions occurring in the age group between five months and five years. Allison (1956) showed that, in a population of infants examined in the field in East Africa, the distribution of the normal and sickle-cell genotypes was very close to that expected from the Hardy-Weinberg law (Table 1). Hence, as expected, there is no indication of selection against any of the genotypes before birth. In a randomly mating population in equilibrium, the fitness of the genotypes *AA*, *Aa*, *aa* with frequencies p^2, 2 pq, q^2 can be expressed as $1 - K q^2$, $1 + K pq$, and $1 - K p^2$, respectively, where K is constant. The expected frequency of genotypes in the zygote and adult populations concerned, assuming equilibrium and a frequency of the sickle-cell gene of 0.1985, are also shown in the table. Again the observed frequencies of genotypes in the parental population correspond with those expected.

TABLE 1.—*Expected and observed frequencies of sickle-cell and normal genotypes in an infant and a parental African population*

GENOTYPE	Expected frequency of zygotes	Observed frequency of infants	Expected frequency of parents	Observed frequency of parents
Hb^A/Hb^A.....	0.6424	0.659	0.611	0.612
Hb^A/Hb^S.....	0.3182	0.310	0.381	0.381
Hb^S/Hb^S.....	0.0394	0.031	0.008	0.008

It can be seen that the frequency of sickle-cell homozygotes has fallen and that the frequency of sickle-cell heterozygotes has increased in the adult population. The significant increase in frequency of sickle-cell heterozygotes suggests that this genotype has a selective advantage of the order of 25% over the normal genotype, due mainly to differential mortality between birth and reproductive age. Confirmatory observation from the Belgian Congo have been published by Vandepitte and Delaisse (1958).

The high frequency of the haemoglobin C gene in West Africa introduces an interesting complication into the population genetics of this area. Allison (1955) postulated that because of the disadvantageous effects of the sickle-cell and haemoglobin C genes in combination, the two genes must tend to be mutually exclusive in populations. This was subsequently found to be the case: Haemoglobin-C is present in all West African territories, the incidence of heterozygotes rising to 29% in northern Ghana, and as the frequency of haemoglobin-C increases that of the sickle-cell trait falls (Allison, 1956; Edington and Lehmann, 1956). Thus powerful selective forces have stabilized the frequencies of all three genes—the sickle-cell gene, the haemoglobin-C gene and the normal allele—in a complex genetic equilibrium. Again, there is evidence that this has occurred through differential mortality between the time of birth and reproductive age (Allison, 1956).

The same sort of situation almost certainly obtains in other human populations in which genes for abnormal haemoglobins are common. Thus, among many Mediterranean people the thalassaemia trait has persisted in frequencies up to 20%, although the homozygous condition is nearly always lethal. And in several southeastern Asian countries, such as Burma, Thailand, Cambodia and Indonesia, the genes for haemoglobin C, thalassaemia and haemoglobin H are all common despite the fact that individuals who inherit any

two of these abnormal genes are liable to haemolytic disease. The most plausible inference is that the possession of a single abnormal gene is advantageous; the selective agencies involved have, however, not yet been investigated.

The study of human populations: Equilibrium between mutation and selection in the case of unfavourable genes

In the preceding sections evidence has been adduced that inequalities exist in the survival of different genotypes at all stages of development up to reproductive age. The resulting selection has effects on populations which will now briefly be considered.

When a major gene mutates, the new allelomorph is generally disadvantageous. The reasons for this are sufficiently evident. Mutations are random changes relative to the needs of the organism, and when these occur in any highly organized system, such as the human body, they are more likely to be harmful than useful.

The spread of disadvantageous mutations tends to be checked at an early stage, since affected individuals often fail to reproduce because they do not survive to reproductive age or because they remain childless. Obviously the check on the spread of unfavourable genes is less rigorous in the case of recessive than in the cases of sex-linked recessive and "dominant" characters. But in every case the population approaches a state of genetic equilibrium, in which the extinction of unfavourable genes is balanced by the recurrence of mutation. As Haldane (1932) pointed out, an indirect estimate of the rate of mutation can be made from the assumption of equilibrium, given the frequency of any disadvantageous trait in the population and the proportion of carriers that reproduce. However, estimates of mutation rates which are wholly indirect are not always reliable in practice. This is particularly true of recessives, where allowance has to be made for inbreeding and where even slight heterozygous advantages will lead to entirely erroneous estimates of mutation rates.

In favourable instances indirect estimates can be compared with directly observed mutation rates. If genes have regular single-dose effects, instances of fresh mutation can be recognized in families where a gene appears in an offspring although it is not present in the parents. Similar techniques can be applied to sex-linked characters manifesting themselves in males. However, such regularity of expression is rarely (perhaps never) found in human genetics, since most single gene effects, especially those manifested in heterozygotes, are subject to modification. Even with the most reliable characters, such as the A and B blood group antigens,

suppression by modifiers takes place (Levine, Robinson, Celano, Briggs and Falkinburg, 1955; Weiner, Lewis, Moores, Sanger and Race, 1956). Events of this kind could easily be misinterpreted as evidence of mutation by the unwary. A further complication arises from the fact that several abnormalities can be confused with one another clinically, from which it is virtually certain that the mutation rates supposed to apply to single genes represent the sum of mutations at several loci. Thus, the published estimates of mutation at the haemophilia locus include mutations at other loci, among them that for deficiency of plasma thromboplastin antecedent. Yet another difficulty is the occurrence of "phenocopies," clinical conditions indistinguishable from those genetically determined but not passed on to the next generation. Vogel (1956) has found these not infrequently in retinoblastoma.

Nevertheless, the estimates of spontaneous mutation rates of human genes—tentative as they are—are of interest in relation to the origin of rare inherited defects and the provision of a baseline for comparison of the effects of artificial mutagens, notably ionizing radiations. The available estimates have been summarized by Penrose (1956). The average value for very deleterious traits manifested in heterozygotes in 14 mutations per million loci per generation, with a range of 4 to 70 per million. The latter figure applies to chondrodystrophy which includes several clinical conditions under the same heading, and is probably much too high. The true spontaneous mutation rates in these conditions are likely to be of the order of 5 per million loci per generation—which is of the same order as commonly found in *Drosophila*, mice and microörganisms. The published figures for mutation rates in the sex-linked characters haemophilia and pseudohypertrophic muscular dystrophy (20 to 95 per million loci per generation) are probably too high for the same reason. Most of the available estimates of mutation to recessive traits are so unreliable as to be merely misleading. The lower estimates, referring to ichthyosis congenita, infantile amaurotic idiocy, phenylketonuria and albinism, are of the order of 11 to 28 mutations per million loci per generation. These are likely to be closer to correct figures than estimates such as 700 per million loci per generation for cystic fibrosis of the pancreas, which may well be grossly in error owing to heterozygous advantage or some other factor. Nevertheless, the excellent studies of Benzer (1957), which have demonstrated considerable differences in spontaneous and induced mutability of different lengths of the coliphage chromosome in the rII region, oblige us to keep our minds open

in case such a phenomenon should occur also in human chromosomes.

Natural selection has been less stringent in man than in most other animals, as a result of the human tendency to protect not only children but also weak members of the species. In spite of this, there is considerable elimination of unfavourable mutations, and, as stated, the development of an equilibrium in which this process is balanced by recurrent mutation. Thus selection tends for the most part to be a stabilizing agency, reducing variability.

The establishment of genetic equilibrium and polymorphism in human populations

It has already been pointed out that the spread of major genes giving rise to even slight disadvantages tends to be checked at an early stage. Occasional mutations are advantageous, and these spread through populations, replacing the original genes at the loci concerned. This process has actually been witnessed in populations of insects and microörganisms. Thus, during the past fifty years melanic forms of many species of moths have become common in industrial areas because they are better camouflaged and less subject to predation than the original forms (Ford, 1956). The spread of insects resistant to DDT and other chemicals, and of bacteria resistant to drugs, has been reviewed by Crow (1957). These are dramatic examples of changes in the genetical structure of natural populations in response to powerful selective forces. It is now generally accepted that resistance is due to preadaptation, in other words, the poison or drug acts as a sieve for concentrating resistant mutants that were present in low frequencies in the original populations.

In polymorphism we are concerned with the fate of initially advantageous major genes. Logically, one should also envisage the situation in which a gene is neutral as regards survival value. However, Fisher (1930) has shown that the balance of advantage between allelomorphic genes must be very exact to produce that situation, and even then there is only a negligible probability that the mutant gene will spread by chance through the population.

Many people find it difficult to accept that seemingly unimportant characters—such as the ability to taste phenylthiocarbamide—may well have survival value. Nevertheless, the genes have multiple effects. It would be difficult to suppose that the chemical processes connecting a gene with a particular character should in no way modify the general development, whether or not the end result by which a gene is recognized is of importance. Thus, all

the genes studied in *Drosophila melanogaster*, though normally identified by their influence upon such apparently trivial features as wing venation or eye colour, have been found to react upon the viability (length of life, vigour, adaptability, or reproductive capacity) of the fly. They must, therefore, affect the physiology of the organism. The characters by which genes are usually recognized may be likened to the small part of an iceberg which is visible above the surface of the sea; most of a gene's effects, like most of an iceberg, are concealed from view.

It follows that if a major gene is found in even a small per cent of a population that gene must have some advantage. This situation is known as polymorphism, which has been defined by Ford (1945) as the occurrence together in the same habitat of two or more forms of a species in such proportions that the rarest of them cannot be maintained by recurrent mutation. The definition has been framed so as to exclude geographical races, rare disadvantageous mutants and continuous variation falling within the curve of normal distribution and controlled by polygenes. In all the animals and plants in which polymorphisms have been investigated, they have been found to be controlled by balanced selective forces (Ford, 1945; 1958). This general conclusion can therefore be extended to the human race, for man is one of the most polymorphic animals known.

With these considerations in mind, Ford (1940) suggested that the blood group polymorphisms in man might be controlled by selective forces arising through inequalities in the susceptibility of persons possessing different blood groups to specific diseases. In the same year haemolytic disease of the newborn was shown to be due to Rh-incompatibility. This phenomenon produces a direct selective effect on the blood group genes. Inevitably it acts against heterozygous offspring, which—as Haldane (1942) and Wiener (1942) pointed out—would lead to an unstable equilibrium in which the less common (Rh-negative) gene should be eliminated from populations. No convincing explanations for the persistence of the Rh-negative gene in Western Europe have been advanced. It seems likely that persons heterozygous at the Rh locus possess some advantage which more than counterbalances the disadvantage of susceptibility to haemolytic disease (Allison, 1955).

There is now abundant evidence that Ford's thesis is correct. The data on susceptibility to disease of persons possessing different blood groups have been reviewed by Fraser Roberts (1957). The evidence is overwhelming that patients with carcinoma of the

stomach have a higher incidence of group A, and patients with peptic ulcer a higher incidence of group O, than control populations from the same areas. The evidence is also quite strong that diabetes mellitus and pernicious anaemia are about 15% commoner in persons of group A than controls of other groups. No definite association has been found between blood groups and carcinoma of the bronchus, colon and rectum, hypertension, and toxaemia of pregnancy, which demonstrates the adequacy of the controls and emphasizes the significance of the positive results. It is therefore certain that the possession of particular blood groups influences susceptibility to disease and probable that the resulting selection has stabilized the frequencies of the several blood groups at different levels in different human populations. The mechanism by which stabilization is achieved is still far from clear. The possibility of heterozygous advantage will be difficult to assess until it is possible to identify such heterozygotes as A_1/A_2, A_1/O and Dd without having resort to genetical data.

The polymorphism of the abnormal haemoglobin genes in man has already been discussed. They provide one of the best known examples of heterozygous advantage at a single locus. Evidence is accumulating that other traits for which man is polymorphic are subject to natural selection. Thus, the haptoglobins, a group of genetically controlled serum proteins analysed by Smithies and Walker (1955), are absent in about 30% of West Africans (Allison, Blumberg and ap Rees, 1958). The lack of haptoglobins may well be disadvantageous since the haptoglobins normally prevent loss of haemoglobin and iron from the body by way of the urine. Why the trait remains common in Africans is unknown, but its incidence suggests that there may be some compensatory advantage in possessing a single dose of the recessive gene responsible for the suppression of haptoglobins.

Also common in Africans is a sex-linked trait in which there is a deficiency of glucose-6-phosphate dehydrogenase and reduced glutathione in erythrocytes (see Childs, Zinkham, Browne, Kimbro and Torbert, 1958). The defect renders affected subjects liable to haemolysis from therapeutic doses of the antimalarial compound primaquine, sulphonamides and other drugs. It seems also to be the defect leading to favism, a haemolytic diathesis that quite commonly follows ingestion of fava beans in susceptible individuals in Mediterranean populations. Why this apparently disadvantageous trait should also persist in high frequencies is unknown.

Even a seemingly trivial character, ability to taste phenylthio-

carbamide, may be associated with susceptibility to disease. The chemical relationship of phenylthiocarbamide to several giotrogenic compounds led Harris, Kalmus and Trotter (1949) to investigate the incidence of tasters in patients with thyroid goitre. A significant excess of patients unable to taste phenylthiocarbamide was found, as compared with the general population, and this has recently been confirmed by Evans and Kitchin (1958).

Effects of natural selection on polygenic characters

The effects of selection on quantitative characters such as height, skin colour and intellectual capacity are difficult to analyse and predict. In each case there seems to be a zone of optimum fitness, depending upon local conditions. Skin colour is darkest in the tropics, lightest in temperate regions like Scandinavia and intermediate in the arctic. This could well be adaptive; one factor worth consideration is that light skins may have been advantageous and become common in populations living in areas of limited sunlight and therefore liable to vitamin D deficiency (rickets having been in the past an important cause of maternal mortality in childbirth).

Wright (1935) and Haldane (1957) have argued that it is difficult to see how selection for a metrical character as such would preserve heterozygosis at more than one locus. However, Fisher (1930) and Kimura (1956) have analysed the situation where two pairs of linked genes interact in such a way as to alter one another's selective values (*e. g.*, with genes Pp, Qq, where P is advantageous to p in combination with Q but not with q, whereas p is advantageous with q). Then if one pair of genes is fixed by heterosis, the other pair will also remain fixed. This argument can be extended to give fixation of several pairs of genes, the distinction between polymorphism at two or more loci and polygenic control being arbitrarily defined.

As pointed out above, different genetical hypotheses regarding the control of human metrical characters cannot yet be tested. The number of genes, gene frequencies, degree of dominance and strength of interaction or epistasis are all indeterminate. The effects of environment are usually imperfectly understood. To argue from phenotypic to genotypic selection, we need adequate data, but, as Haldane (1957) points out, there are many pitfalls. In the first place, if any environmental influence simultaneously alters a metrical character and raises fitness, there is phenotypic selection in the direction in which the character is altered. Thus, if an adequate diet promotes growth in stature there is phenotypic selection

for stature. If education raises the score in intelligence tests but at the same time results in reduced fertility, there is phenotypic selection for a low score in the tests. Secondly, even if a metrical character were wholly determined genetically, phenotypic and genotypic selection could act in opposite directions. It is probable that when measured over long periods, phenotypic and genotypic selection would be almost always in the same direction, but they certainly need not be so over a short period such as a few human generations.

It seems likely, as Haldane (1949) pointed out, that during the last 5,000 years the main agents of natural selections in man have been infectious diseases. As soon as the inventions of agriculture and cities had made relatively dense human populations possible, selective agencies such as vertebrate predation ceased to be important, and diseases facilitated by overcrowding took their place. A man who can outwit a mammoth or if necessary escape from it by climbing a tree is likely to be mentally and physically superior to a man who cannot. But there is nothing to suggest that a man who can resist tuberculosis is superior in other respects to a man who cannot. Infectious diseases probably spread a great many previously rare genes through human populations. The fact that they were rare means that in general they lowered the fitness of our ancestors. They probably lower our own, except in environments where the organism against which they confer resistance is common. This is certainly true of the sickle-cell gene.

The abolition of infectious diseases, which is now a possibility and may be a reality in a few decades, should lead not only to an immediate improvement in human physique but to a progressive improvement through many centuries. Alarm has been expressed that in civilized societies disadvantageous genes (*e. g.*, those for a diabetes mellitus and retinitis pigmentosa) tend to accumulate owing to medical care of affected individuals. The opposite trend is equally likely. As diseases like malaria cease to be important, genes like the sickle-cell gene will gradually disappear from populations.

Even rather short term trends cannot be predicted with confidence. In hygienically advanced countries, selection by death has been replaced to a large extent by selection for differences in family size. Very little is known of the correlation of measurable characters with family size, except as regards intelligence, and even this is changing quite rapidly. At present there is a negative correlation between intelligence and family size down to low levels of

intelligence, when infertility becomes common. Phenotypic selection is favouring moderately low intelligence and acting against very high and very low intelligence. As Penrose (1956) has shown, this is compatible with stabilizing selection, although there is probably some directional selection—a slight downward trend of intelligence in the population.

The diminished fertility of persons with extremely high or low intelligence has often been the subject of comment. Fertility is the second major component of fitness or survival value. The low fertility of extreme types presumably results from their being homozygous at a large number of loci. It would be of interest to know whether the fertility of other extreme types is significantly impaired.

To sum up, although we know more about natural selection in man than in any other species in its natural habitat, our information is still very scattered and incomplete. I have attempted to show different ways in which natural selection might take place in man, and have quoted examples where it is reasonably clear that natural selection has been operating. But in order to have a clear picture of how selection will act in other instances, especially on polygenic characters, we need much more information analysed with great precision.

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The Development of Evolutionary Thought

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Without any doubt the greatest event of all times in the development of biological thought was Darwin's theory of Evolution. It is now 100 years since the theory was presented in brief form to the general public in a joint article by Charles Darwin and Alfred R. Wallace and ninety-nine years since the publication of Darwin's definitive work "The origin of species by means of natural selection or the preservation of favoured races in the struggle for life."

For the first time biologists were provided with a grand rationale for their studies. The student of comparative anatomy was more than a cataloguer of bones and other parts. The structure of organisms was seen to be a product of evolution, and the apparently irrational diversity of living organisms became a means of finding the interrelations of all creatures. The embryologists found that there were many paths from fertilized eggs to adults and that these paths seemed to reflect in some mysterious way the evolutionary history of the species. All biologists were, in one way or another, students of evolution.

The general contribution of Darwin was really a double one. First, he suggested that the species of today are not immutable or the result of special creation but are the product of descent with change from different species that lived in the past. Second, he proposed that evolution occurs as the result of an interaction between variability and natural selection. If some individuals in a population, because of their hereditary endowments, are better able than others to survive and leave offspring, these better adapted types increase in frequency and eventually supplant the less well adapted types. This was the mechanism he proposed for evolution. Darwin offered a model situation of how this could come about that

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was familiar to all, namely, the effects of selection by man of the numerous types of domesticated animals and plants. Horses could be selected for speed or for great strength. Sheep could be selected for better wool or better meat. Could not nature achieve similar results by selection? Darwin's answer was 'yes.'

The two aspects of Darwin's theory suffered different fates. By the end of the 19th century those willing to replace emotion with reason were fairly unanimous in believing in the fact of evolution: the existing diversity of species could be best understood as a consequence of descent with modification and differentiation. Darwin and those following him had made their point. With respect to the mechanism of evolution, however, there was far less agreement. As time went on it seemed more and more difficult for evolution to be accounted for by the interplay of variation and natural selection. Was there sufficient variability, even in the entire horse population, to produce a cow by careful selection? It seemed most unlikely, yet the Darwinian mechanism would have to have done even greater things.

It is of interest to recall that criticisms of this sort forced Darwin to retreat from his original beliefs regarding the mechanism of evolution and to adapt a point of view close to that of Lamarck—a name often regarded as the antithesis of Darwin's. In retrospect we realize that, at least theoretically, this retreat need not have been made. The early Darwin was far nearer the truth than the later Darwin. In due time the data of genetics were to provide the necessary information about the variability needed as a basis for Darwinian evolution. Genetics, however, is a 20th century science, and Darwin was a 19th century man.

The aspect of the problem that was so difficult for Darwin to account for was the origin of variability. All species, domestic and wild, are variable. Yet, how could evolution continue, once the supply of existing variability was exhausted? It was possible for man to increase the size of sheep or chickens by repeatedly breeding from the largest in the flock, but no one produced a sheep the size of a cow or a chicken as large as a turkey. Once a certain size had been reached, selection seemed to have little or no additional influence.

Darwin was indeed vague on the question of the origin of new variations. He had to be: the answer was more than half a century in the future. Nevertheless, at least in the beginning, he held that new variants could arise spontaneously and that the type of

variant had no direct relation to the environment. This is precisely what we believe today.

Many of the questions were resolved when the data of genetics were available. It is necessary therefore to review briefly the findings of genetics that are essential for an understanding of modern evolutionary theory.

The science of genetics had its effective birthday in 1900 when the earlier work of Gregor Mendel became generally known to biologists. In the matter of a few years the origin, nature, and mode of inheritance of variations became well known. The essential points were these:

First, the material basis of inheritance is almost exclusively the chromosomes within the nucleus. Specialized areas of the chromosomes are known as genes. Currently we believe that the genes are composed of a complex compound, deoxyribose nucleic acid.

Second, the origin of new variability is a consequence of changes in the chromosomes themselves. Collectively these changes are known as mutations. Mutations can involve small changes in the chemical make up of chromosomes—we call these gene mutations —or grosser realignments and modifications of the chromosomal material that are known as inversions, translocations, duplications, and deficiencies. There can also be changes in the number of chromosomes.

Third, the genetic material is extraordinarily stable, both in time and in the presence of other genes. On the average, even the most changeable of genes can be expected to mutate not more than once in a million generations. Once a change has occurred, moreover, the gene in the mutated state is about as stable as it was before.

Another aspect of the stability is this: in most organisms that reproduce sexually, the majority of genes are in a double dose. Thus, if our eyes are blue, it is because every cell in our body has two genes for blue eyes. In man this gene exists in two main states, one necessary for blue eyes and one necessary for brown eyes. The blue-eye and brown-eye gene have an interesting relationship. If an individual has one blue-eye gene and one brown-eye gene his eyes are brown, and just as brown as if he had two brown-eye genes. Such an individual with two forms of the same gene is said to be heterozygous. We speak of brown as a dominant gene and blue as a recessive gene. The point of greatest importance for Darwinian evolution is this: a dominant and a recessive gene can coexist in the same cell and neither will be modified or con-

taminated by the other. Thus, if two brown-eyed individuals of the sort having one brown-eye gene and one blue-eye gene produce children, about one quarter of the children will have blue eyes, and the eyes will be just as blue as if both parents possessed blue eyes. Recessive genes can be masked by dominant genes for generations and then, in the proper cross, they can be extracted and found to be wholly unaltered.

If Darwin had realized this, namely, that inheritance is particulate and not a matter of blending, he would have been saved much torment, since a most damaging argument against Darwin's views involving blending was presented in 1867 by Fleeming Jenkin, a Scottish engineer. Let us suppose, said Jenkin, that a single individual with a favorable variation does appear in the population. This individual will have to mate with some other not of the favorable sort. The offspring of the favorable individual and the ordinary individual would be intermediate, if inheritance was a matter of blending. Further matings would result in an increased dilution of the favorable character until it was totally swamped by the more abundant unfavorable character. The chance appearance of a favorable variant hardly seemed a sufficient basis for evolutionary changes. Darwin could not answer this argument. Mendel had known the answer for two years but the community of biologists was not to know of Mendel until another 33 years had elapsed.

Fourth, the individual structures and physical processes of an organism are usually controlled by many genes. An eye may be blue or brown but there is more to an eye than a thin layer of pigment. It is a complex structure, and its formation is controlled by the action of many different genes. Features such as height in man have a similar complex control. Each individual has many genes controlling height, some tending to make him a little taller and others tending to make him a little shorter. The actual height is a balance of the action of all these genes. There are several important aspects of this notion. For example, two individuals—each 5 feet 11 inches tall—might have a different genetic basis for their heights, and thus two such individuals may have a child that stops growing at 5 feet 4 inches. This would be a "sampling error" of inheritance. The parental germ cells would have contained a superabundance of the genes for short stature. Not only is every structure or physiological process under the control of many genes, but, in addition, genes have manifold effects. Any one of them may affect many different structures in seemingly unrelated ways. We should emphasize the "seemingly," for there is

much evidence to indicate that each gene does have one primary effect—the production of a specific protein or enzyme. The manifold effects are derivative.

Fifth, when a mutation occurs it has no specific relation to the environment in which it occurs. Thus, among mammals, it might be of selective advantage for individuals living in the north to have long hair. So far as we know, however, a mutation controlling long hair would occur with equal frequency in a warm climate or a cold climate. In a warm climate it would be at a disadvantage and hence selected against. In a cold environment, however, it would result in better adaptation and be selected for, and would increase in frequency. This has been an extremely difficult hypothesis to test. In fact, it was not until geneticists began to work with microorganisms that adequate evidence was available. Now, to the very best of our knowledge, we can say that mutations are spontaneous and the type of mutation is not the result of a directing environmental stimulus. In his early days Darwin held a similar view. It was, in fact, the main way he differed from Lamarck. Lamarck would hold that the mutation to long hair was stimulated by the cold environment. Lamarck's belief certainly seems the more logical and aesthetically satisfying: unfortunately it is wrong. The very beginning and basis of all evolutionary change, as we now see it, is an indeterminate event.

We now know many ways of artifically causing mutations: by X-rays, ultra violet rays, mustard gas and, of course, the products of atomic disintegration. These agents increase the rate of mutation. They cannot be used to produce *specific* mutations at will. Our inability to induce specific mutations at the present time is no final verdict. Gene mutations are changes in chemical molecules. The day will come when we know enough about the chemistry of the process to control these changes. It is inconceivable that it be otherwise.

Sixth, as a final major contribution of genetics to evolutionary thought, we should list the fact that heterozygous individuals are frequently superior to homozygotes. This term, heterozygous, was first mentioned in reference to the brown-eye and the blue-eye genes. If an individual has one of each he is heterozygous. In some instances it can be shown that a heterozygous individual is superior to either of the pure or homozygous types. A most interesting case is known for man.

In some parts of the world there occurs a disease known as sickle-cell anemia. It is so named because the red blood corpuscles take

on abnormal shapes under some conditions. The disease is caused by a mutant gene we can call Sk. The normal form of the gene will be called +. There are three possible combinations:

+ +. This person is homozygous for the normal gene and the blood cells are normal.

+ Sk. This individual is heterozygous, having one normal gene and one Sk gene. These individuals have a mild anemia.

Sk Sk. This individual is homozygous for the Sk gene. The anemia is severe and frequently results in death.

With the data so far given, it may seem strange that there are any Sk genes in the human population. A double dose in a homozygous individual is most deleterious, and even the heterozygotes are at some disadvantage. The adaptive relation would be: ++ > + Sk > Sk Sk. In some populations however, the Sk gene is fairly common. Why has not natural selection eradicated it from the human species?

The answer is most interesting. The gene is common only in areas where malaria occurs. Here the adaptive relation of the three genetic possibilities is altered. The heterozygous individuals, + Sk, have a marked superiority to the other types in resistance to malaria. The adaptive relation then becomes + Sk > ++ > Sk Sk. The advantage of the + Sk genetic constitution in combating malaria offsets the slight disadvantage of the anemia. The Sk Sk individuals, however, still suffer and usually die early in life. Yet, the Sk gene remains in the population because of the advantage it confers in heterozygous individuals.

It is well to note the remorselessnes of evolution in this case. The superior individuals in a malarial region are the heterozygotes. Yet one quarter of the offspring of such individuals will inevitably have sickle-cell anemia and die early in life. One must now begin to think of evolution in terms of the population as well as of the individuals. There are some situations, such as the one just described, where a few individuals will die in order that the genetic health of the group will be better.

There is now a tremendous amount of data showing that the heterozygous state may be superior. This has helped to explain many difficult facts. Why, for instance, is there so much seemingly useless variability? Part of the answer is now known to be the adaptive superiority of heterozygotes. Some genes exist because they are advantageous when they are coupled with other genes. (Another reason for frequency of seemingly useless variability is

this: genes have many effects—most of the effects being invisible. Some of the effects might be most important but unnoticeable and others be unimportant but noticeable.)

So much for the building stone of evolution, variability, and our understanding of it as provided by genetics. The second component of evolution is natural selection. The study of natural selection has been hindered by the fact that it seemed to many a self-evident truth. It is to be expected that the fit will survive better and have more offspring than the unfit. In fact, by definition the fit are the ones that survive and leave more offspring. There is more to the problem than a tautology, however.

It is quite easy to study selection under laboratory or artificial conditions but extremely difficult to do so in nature. The reason for this is clear. When studying the effects of selection one measures the change in frequency of genes or adapted individuals. In the course of time the population changes from less fit to more fit. Under natural conditions we would have to wait for the appearance of a favorable mutation and its increase in the population, or for the slow increase in frequency of a favorable mutation that is already present.

The odds against our being able to observe the mutation when it first occurs are enormous. It was mentioned before that mutation is a rare event: the chance that any specific gene mutates is generally no more than once in a million generations and usually much less. Looked at in another way, however, if the population consists of a million individuals, then in one of them the gene in question will have changed. In a large population, therefore, mutations are occurring constantly, and selection will preserve what is better and abolish what is not. But how does this effect our observations? Simply this: if any mutated state of a gene is superior, this mutation will have occurred and will have been preserved repeatedly in the past and hence become part of the normal hereditary makeup of the species. At any one time the genetic makeup of a species is the best that mutation and selection have been able to accomplish. Other things being equal, it is most improbable that we would be conducting our experiments at that rare moment when some absolutely new mutation of adaptive superiority would occur.

It should be mentioned in passing that once this fact was realized a seemingly serious argument against gene mutations being the basis of evolutionary change could be answered. The argument was this: since most mutations result in an individual that is less

fit, how can mutations be of importance in leading to increased adaptation, which is the whole point of evolution? The answer is that mutation is the basis of evolutionary change but the good mutations are rapidly incorporated into the genetic makeup of the species. Most mutations, therefore, would be to less favorable states of the gene and this is exactly what is found.

This discussion may seem like an excuse for confessing an inability to study natural selection. This is not the case. The difficulties that I have presented refer to the near impossibility of observing an improvement in the adaptation of a species living in its normal environment. If, however, we study the events occurring when a species encounters some new environmental or stress situation, we can obtain clear evidence of the working of natural selection. I will give several examples: industrial melanism in moths, resistance to insecticides in insects, and resistance in drugs in bacteria.

During the past century a dramatic change has been observed in many species of British moths. The change has occurred only in the industrial regions, and it involves body coloration. Originally the moths were light colored; now they are nearly black. The genetic basis is simple: the dark form differs from the light form by a single gene. The dark form is protectively colored in the industrial region where the trunks of the trees are dark—due largely to the absence of lichens. Birds, the principal enemies, find it difficult to discover the dark moths. The original pale form is conspicuous and is readily seen, caught, and eaten. The pale form is by no means extinct. It occurs rarely in the industrial areas but it is the common form in rural England. Here the selective forces are reversed. The dark form is conspicuous and is easily captured by birds, but the pale form is protectively colored against the lichen-covered tree trunks.

The events are easy to reconstruct. Before industrial fumes had killed the lichens on the tree trunks, the pale-colored forms were typical of the entire species. The mutation to the dark form occurred rarely, but when it did birds would destroy the dark forms rapidly. Following the industrial revolution, however, the environment changed markedly. The lichens died, and the pale individuals were exposed to predation. At this time any dark individuals that appeared as rare mutants would be at a distinct advantage. Their chances of survival would be greater, and they would consequently leave more offspring. The fit would survive

and the unfit would not. In a few decades the species had evolved from a light to a dark phase, in the industrial areas.

An equally dramatic example of natural selection is occurring in our own time. When the insecticide DDT was first used against the house fly, it proved an effective means of control. In a few years, however, house flies all over the world have become resistant to this substance. Mutations that result in the flies' being better able to withstand the DDT have occurred, and these have, of course, a tremendous selective advantage.

There is a similar story for the strains of bacteria that are resistant to various drugs, such as the antibiotics. When these drugs are used in treating diseases, not infrequently a mutation occurs that confers resistance. Now many hospitals are greatly concerned because of the occurrence of strains of bacteria that are resistant to the commonly used antibiotics.

In each of these examples a species has been confronted with an environmental challenge. Either it must change its color to lessen its chances of being eaten by birds or change its physiology so that a previously lethal chemical becomes tolerable. The alternative is extinction. To the biologists who have studied these events it seems little short of miraculous that the species have responded so rapidly and effectively to challenges never encountered in the prior history of the species. Evolution is usually very slow but, when the selective forces change, it may be very fast.

It is well to emphasize once again the lack of a determining relation of the environment to the change. The bacterial genes did not mutate because of the drugs. The genes were mutating in the same ways long before the drugs were discovered. The mutant state was never "better," however, until the drugs were present in the bacteria's environment. In the new environment individuals with the genes conferring resistance could survive and others could not.

One hundred years after Darwin's theory was proposed, we feel some confidence in our understanding of the nature of variation and of the mode of action of natural selection. These two phenomena are the basis of organic evolution. We should not, however, leave the subject at this level. It would be as unsatisfactory as telling a person who had never seen a house that the basic elements of a house are wood and bricks.

When we attempt to see how variability and natural selection actually operate to result in evolution, we find that there are many patterns. In some patterns a new species can evolve in a day, in

others in a million years. There does seem to be one very common pattern, however, and this is evolution by geographic speciation. This is common in many organisms but especially in the higher animals.

As the name implies, space is an important element in geographic speciation. In a model situation we can consider a population of normal variability spreading over a large area. Let us further suppose that the area has a variety of climates and that it is divided by barriers, such as high mountain ranges or other inhospitable zones that the individuals of the species rarely cross. For purposes of simplicity let us suppose that one of these semi-isolated areas is warm and another cool.

Throughout the range of the species mutations will occur but not as a specific response to heat or cold. Any mutation that adapted an individual to cold would be at a selective advantage where the climate was cold but either neutral or disadvantageous in the warm area. Its frequency would increase, therefore, only in the cold zone. The reverse situation would hold for mutations that adapted the species to the warm environment.

Evolution would involve the selection of mutations that occur spontaneously and the direction would be towards the ever increasing adaptation of the semi-isolated populations. The divergence might become so great that the individuals of the hot and cold zone could no longer interbreed and produce fertile offspring. When this occurs we have two species.

I should like to give an example of this process and, to save time, use the example for two purposes, first to show geographic speciation, and second to answer the question: 'If evolution occurs, why do we not observe some cases where one species seems to be dividing into two?'

The meadow frog, *Rana pipiens,* occupies a tremendous range in North America, far more than any other species of its genus. That this species is doing something interesting is indeed suggested by this extensive range of geographic distribution. How is *Rana pipiens* able to exist under such a great diversity of temperature conditions? An analysis of the situation shows that this species has achieved this extensive distribution by evolving a number of temperature races. Thus, individuals from the Gulf Coast states can tolerate much higher temperatures in the embryonic stages than can individuals from Canada or New England.

A parallel study of the possibility of hybridization of these frogs has revealed a fascinating situation. Of course, if they all belong

to the same species they should cross perfectly. It is not surprising, therefore, that if the cross is Quebec x New York, New York x New Jersey, New Jersey x Louisiana, or Louisiana x Florida, the offspring are normal or show exceedingly slight deviations from normal. With more extreme crosses such as Vermont x Florida, or Wisconsin x Texas, or Vermont x Mexico, the hybrids show severe defects. In fact, in the Vermont x Mexico cross, the hybrids are so defective that they all die. When this degree of cross incompatibility is observed, we generally say we are dealing with two species.

This is certainly a paradox. If we study adjacent populations of *Rana pipiens* in nature there is every indication that we are dealing with a single species. Adjacent populations intergrade, and there is no evidence of genetic incompatibility between them. We would say they belonged to a single species. When we test widely separate populations in the laboratory, however, we see that a tremendous amount of divergence has occurred. The New England and Mexico populations behave as separate species.

This paradox is really of our own making. If evolution is occurring, we should find some populations in an intermediate state between one species and two. *Rana pipiens* is one of these. We have caught it in the act of speciating.

I have tried to show you in a very brief way where we stand after a century of Darwinism. As we see it now, Darwin was much closer to the truth than he had any right to be; in fact, only a genius could have analyzed in so penetrating a manner the meager amount of data available in 1858.

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Genetic Functions of Viruses

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The purpose of this paper is to illustrate the thesis that viruses function as genetic elements in their host cells and that most recognizable manifestations of a viral infection can ultimately be traced to the action of specific genes introduced by the virus into the cells. The examples used come from the study of phage-bacterium interaction, which has been analyzed more thoroughly than other viral infections. Recent discoveries, however, on the apparent action of rabbit papilloma virus in determining the production and specificity of a cellular enzyme (Rogers, 1959) and on the effects of mutations of the Rous sarcoma virus on the morphology of its host cells (Temin, 1960), forecast major advances in a similar interpretation of animal virus infection in terms of viral gene action. Such advances are especially desirable because the animal viruses include ribonucleic acid (RNA)-containing viruses, and infection with RNA viruses, or with the RNA isolated from them, is the main approach available for the study of the genetic function of RNA.

The types of interaction between a phage and its host bacterium are classified according to the outcomes of infection, which include either the destruction of the host cell, with the production and release of a new crop of viral particles, or the establishment of a more or less stable relation in which the viral genome persists in the host cell as an added genetic element (*prophage*). The outcome of infection is determined, on the one hand, by the intrinsic compatibility or incompatibility between cellular and viral genome and, on the other hand, by genetic and physiological conditions. Thus, *intemperate* phages can follow only the destructive path because the first result of their penetration is an irreparable disintegration of the nuclear apparatus of the bacteria (Luria and Human,

1. Professor of Biology, Massachusetts Institute of Technology. Lecture presented on 5 February 1959.

1950). With *temperate* phages, instead, both destructive and persistent types of infection are possible. The penetration and vegetative multiplication of the genome of a temperate phage may be followed by the establishment of a system of controls, which prevent both the irreparable steps to cellular destruction and the formation of mature virus particles (Lwoff, 1953). Once these controls have become operative, the infected bacterial cell can continue to multiply; there is then an opportunity for the viral genome to become established, as prophage, in some of the descendants of the surviving infected cell. These descendants give rise to lysogenic progeny (Zinder, 1958; Luria *et al.*, 1958).

The determining role of phage genes over the activities of the infected bacterium can be recognized in all the various phases of the phage-host interaction. The functions controlled by phage genes fall into three main classes: (1) the synthesis of specific components of the phage, such as the proteins of the phage particles; (2) the establishment of the machinery needed for the synthesis of phage materials, as well as for the regulation of alternative outcomes of infection; (3) the synthesis of new cellular products, such as toxins or surface polysaccharides, whose role appears to be completely unrelated to the viral functions of the phage.

The role of a specific phage gene in the determination of a cellular function can be ascertained if the function is altered by mutations at a mappable locus in the phage genome. The control mechanisms that prevent lysis and permit the establishment of lysogeny are determined by a set of phage genes, whose mutations can increase, reduce, or suppress the capacity of a temperate phage to lysogenize (Levine, 1957; Kaiser, 1957). The same group of phage genes also controls immunity, that is, the suppression of vegetative multiplication and maturation of the prophage and of related phage genomes entering a lysogenic bacterium (Jacob, 1959). The nature of the gene products responsible for immunity has not yet been determined.

In other instances, the nature of the substances controlled by viral genes is known. Thus, individual proteins of the phage particles are determined by specific genetic regions in the phage. Gene-controlled changes in these proteins are recognized as changes in the properties of the phage particles, such as host range or antigenic specificity (Brenner, 1959). Phage mutations also can suppress or alter the lysozyme-like enzyme that leads to bacterial lysis (Streisinger, personal communication).

Mutations that suppress the synthesis of an essential phage com-

ponent or that render it nonfunctional act, of course, as lethal mutations. Yet, mutants of this kind can be detected if the mutation occurs in the prophage state, giving rise to a defective prophage. The presence of a defective prophage can be recognized by appropriate tests on the lysogenic bacteria; and its genetic defects can be analyzed by complementation and genetic recombination between the defective prophage and a superinfecting related phage (Jacob and Wollman, 1956).

A peculiar group of phage-initiated functions is the appearance of new enzyme activities after infection with intemperate phage, including some enzymes needed to synthesize specific constituents of the phage nucleic acid, such as the hydroxymethylcytosine of certain coliphages (Flaks and Cohen, 1959). While it is likely that these enzymes are determined by phage genes, it is difficult to prove that this is so because phage mutants unable to produce these essential enzymes are obviously difficult to obtain.

In general, it may be assumed that a phage includes in its genome all the genetic determinants needed for its own replication and for the production of the viral particles. One of the basic problems concerning viruses is that of the process that has brought or held together into one genetic element those genes that are concerned with the persistence, multiplication, and maturation of the virus—in other words, the problem of viral origin. Whether the viral genome is a remnant of a once independent genetic system, evolved through parasitism, or a fragment of a cellular genome that has acquired a certain degree of independence, at least as far as transfer to other cells is concerned, remains to be seen. Probably both processes have been at work at various stages of viral evolution. There are other classes of genetic elements that share some of the independence of viruses. In bacteria, several examples have been found of genetic elements, collectively called *episomes,* that share with phages the properties of being dispensable, able to multiply as extrachromosomal fragments, and capable of a reversible association with the chromosomal portion of the cellular genome (Jacob *et al.*, 1960). Phages are episomes which also possess the genetic capacity to determine the formation of specialized, cell-free agents of transfer, the phage particles.

Some of the episomal factors of bacteria, for example, the sex factor F in *Escherichia coli,* can become associated with fragments of the bacterial chromosome, which thereby become capable of multiplying extrachromosomally as part of the episome (Jacob and Adelberg, 1959). Similar mechanisms probably account for the

presence in some phages of genes that control cellular properties unrelated to phage functions. For example, *Salmonella* phage ϵ^{15} contains a gene that controls the formation of somatic antigen 15, probably a specific portion of the polysaccharide on the bacterial surface (Uetake *et al.*, 1958). The new antigen appears within 2 to 3 minutes after infection with the phage and is formed only so long as the phage is present in the bacterium. The function of the phage gene that controls antigen 15 can be altered or abolished by mutation, without recognizable effects on the phage's own functions. Such a gene may have remained in the phage genome accidentally as the latter evolved from a bacterial ancestor. More likely, it may have entered the phage genome from some of its previous hosts.

One process by which host genes can enter a phage genome is illustrated by phage-mediated transduction (Zinder and Lederberg, 1952). Here a phage particle acts as a vehicle for the transfer from cell to cell of genetic traits and, more specifically, of small fragments of the bacterial chromosome (Lennox, 1955). In at least two instances, those of phages λ and P1 of *E. coli*, the transferred host genes are associated in a stable, composite genetic element with a portion of the phage genome. Phage λ can transfer a group of host genes that control galactose utilization (the *gal* genes) (Morse *et al.*, 1956). These genes become associated with the λ prophage by replacing a part of the phage genome, which thereby becomes defective (Arber *et al.*, 1957).

The case of transduction by phage P1 provides additional information on the transfer of bacterial genes to a phage. This phage is capable of transferring any group of genes among strains of *E. coli* and of various Shigellas (dysentery bacilli). In most cases, no association can be demonstrated between the transferred genes and any phage genes, as though the phage particles acted purely as a vehicle for chromosomal fragments. But, using appropriate donor and recipient strains and appropriate genetic markers, it is possible to show at least in some instances, notably for the transfer of the genetic region that controls lactose utilization (the *lac* genes), that the transferred genes are associated with a portion of the phage genome (Luria *et al.*, 1960). The combined elements are defective phages. When a defective phage carrying the *lac*$^+$ genes enters a *lac*$^-$ bacterium, it may either become a defective prophage or act as a donor of the *lac*$^+$ genes to the host chromosome. Which process will occur depends, on the one hand, on the activity of the phage genes, which determines the ability to become prophage, and, on the other hand, on the degree of genetic homology between donor

and recipient bacterial strains, which controls the possibility and frequency of integration of the transferred genes into the chromosome of the recipient bacterium. If neither prophage establishment nor gene integration occurs, the transduced genes may be transmitted unilinearly in functional state to only one of the products of cell division at each generation (abortive transduction).

Thus, transduction gives evidence of a process by which bacterial genes and phage genes become associated. The occurrence of such association with a phage such as P1, which apparently can transfer any chromosomal fragment, indicates that the formation of transducing phages is capable of giving rise to a whole variety of new genetic complexes. Admittedly, this process does not throw any light on the origin of phages as viruses, that is, as genetic elements which possess genes needed for performing the viral cycle. Yet, the fact that many phages are capable of performing transduction suggests that this process may have played a significant role in bacterial evolution.

It is conceivable that at some stage of bacterial evolution the production of particles containing chromosomal fragments in a protein shell may have been a common function of many bacteria, providing an important mechanism for gene transfer. If so, there would probably be a distinct selective advantage if the genes concerned with the various steps of the synthesis and release of the protein shells were brought together into a single genetic element that could itself be included in the particle. This, on the one hand, would insure that the recipient bacteria became in turn potential donors for genetic transfers, and, on the other hand, would permit the establishment of regulatory mechanisms controlling the expression of the shell-producing genes. Once the shell-producing genes had been linked together, all that was needed to create a phage was the acquisition of the ability to multiply autonomously without association with the bacterial chromosome. In the absence of supporting evidence, such an interpretation of the origin of phage must remain, of course, pure speculation.

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Recent Advances in Systematic Botany

DAVID D. KECK [1]

Each scientific discipline is a synthesis of many kinds of knowledge, theory, and method. The discipline of taxonomy, or systematics, is the science of classification of organisms, and it is built upon the fields of morphology, physiology, ecology, and genetics. Its potentialities and its limitations are largely those of the basic fields whose raw materials it utilizes. Of course, taxonomy, in turn, is of fundamental importance to all other fields of biology. Whenever the biologist is studying an organism, whether fossilized, preserved, or alive and growing, his concern should be to know exactly *what* it is—its true identity. Sometimes this information is not easy to obtain.

The lecturer touched upon the current trends in systematic studies; the development of experimental methods; the contributions from other disciplines including biochemistry, biophysics and mathematics; improvements in instrumentation, as in the newer optical equipment (phase, ultra-violet, and electron microscopes); the stress on previously little used characters, such as the fine structure of pollen grains, vascularization of the inflorescence and flower, leaf-traces, peel-techniques in paleobotany; and the chemical constituents and methods for their determination. The major portion of this lecture appeared under the title, "The Future of Systematic Botany," in *Systematic Zoology*, 8(2):76-82, June, 1959.

1. Program Director for Systematic Biology, National Science Foundation. Summary of lecture presented on 19 March 1959.

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Darwin and Paleontology

ALFRED S. ROMER [1]

It was without question his experiences on the voyage of the *"Beagle"* which stimulated Charles Darwin to begin the evolutionary studies which were to culminate in the publication of "The Origin of Species." But what aspects of these experiences were the important ones? The curious nature of the Galapagos fauna first comes to mind, and that this was highly influential on his thinking is indicated by the statement in the opening sentence of the "Origin" that he was "struck with certain facts in the distribution of the organic beings inhabiting South America." But in this same sentence is named a second important stimulus—that of "the geological relations of the present to the past inhabitants of that continent." The voyage of the "Beagle" was not planned for natural history exploration, and it was only because of the scientific interests of the ship's highly intelligent if highly eccentric commander, Captain Robert FitzRoy, that Darwin was signed on as naturalist. During the nineteenth century, Britannia definitely "ruled the waves" and felt a responsibility for furnishing aids to shipping of all sorts, commercial as well as naval. Coastal charts were of primary importance for safe navigation, and the *"Beagle's"* major mission was charting the coasts of South America, principally Patagonia and Chile. There was relatively little to engage Darwin's interest aboard; but fortunately the nature of the *"Beagle's"* work was such that the ship often remained in a given region for long periods, and he was consequently able to spend much time ashore and pursue biological and geological investigations to his heart's content.[2] Nearly two

1. Alexander Agassiz, Professor of Zoology, Harvard University. Lecture presented on 16 April 1959.

2. The proposal was made a few years ago that funds be raised to "repeat" the voyage of the *"Beagle"* in commemoration of the centennial of the original voyage. As one of the referees on an application for funds for the project, I gave it a very low rating. If the purpose of the project had been solely to support further research in the areas in which Darwin worked, this would have been meritorious. But why repeat the sea voyage itself? One has only to read Darwin's diary to see that, for him, the actual sea passages on the *"Beagle"* were merely a highly disagreeable mode of transportation from one region to another. His principal occupation aboard was the enjoyment of seasickness.

years were spent by the "*Beagle*" off the Argentinian coast, and Darwin was ashore for much of this period. Still another year was spent on Chilean shores, and Darwin was at liberty to explore the region of the great chain of the Andes.

Darwin had, up to the time of the "*Beagle*" voyage, spent his life amid the mature and settled landscapes of England, where one gains little impression of geological change. He had, to be sure, studied geology at Cambridge and knew that much change had occurred in earlier ages in that peaceful countryside. But this had been long ago, far away in time, and his knowledge of such events was academic and made little impression on him. In Chile, on the contrary, he found himself in a region where major geologic changes were going on before his eyes. The rise of the Andes is a relatively recent geologic happening, one which is still going on today. Vulcanism is active; earthquakes, associated with mountain building, are of frequent occurrence. One major earthquake (as well as other minor ones) occurred during Darwin's stay in Chile. This was on February 20, 1835, while he was at Valdivia, in southern Chile. (It was fortunate that he was not farther north, toward the center of the disturbance, else, with hundreds of Chileans, he might have lost his life.) "An earthquake like this," said Darwin, "at once destroys the oldest associations; the world, the very emblem of all that is solid, moves beneath our feet like a crust over a fluid; one second of time conveys to the mind a strange feeling of insecurity." Further striking evidence of recent geologic change lay before his eyes, in Chile, in the presence of raised beaches, which lay far above the present sea level but in which the sea shells often presented so fresh an appearance that no great antiquity could be attributed to them.

In some ways the most notable impressions of geologic change forced upon him by his American experiences were those of which he wrote in his "*Beagle*" diary on March 30, 1835. He had left the ship in Chile and had crossed the Andes to Mendoza on the Argentinian side of this mountain chain. Returning, by a second (and more usually travelled) route, via Villavicencio and Uspallata, he had climbed to the summit of the precordillera. There, among the ancient sediments were (and still are) the remains of an extensive "grove" of fossil trees of Triassic age. Both in his day-to-day diary and in the "Journal of Researches" compiled from the diary, Darwin reflects upon the startling environmental changes brought about by the major geological events clearly seen here. "It required little geological practice to interpret the marvellous

story, which this scene at once unfolded; though I confess I was at first so much astonished that I could scarcely believe the plainest evidence of it. I saw the spot where a cluster of fine trees had once waved their branches on the shores of the Atlantic, when that ocean (now driven back 700 miles) approached the base of the Andes . . . This dry land, with its upright trees, had subsequently been let down to the depths of the ocean. . . . And I now beheld the bed of that sea forming a chain of mountains more than seven thousand feet in altitude."

A few days later, on April 4th, Darwin had crossed the precordillera, descended into the Valley of Uspallata and, toiling up the main range of the Andes, had reached Puente del Inca, high up under the shoulder of Aconcagua, mightest of all American mountain peaks. And in his diary entries here we see, perhaps, the first faint dawn of the thoughts which were presently to emerge into his beliefs in natural selection correlated with environmental changes, as a *modus operandi* in evolution. Here, in a high mountain valley, were numerous ruins of Indian dwellings. Why were such structures built in these desolate mountain valleys? Not for miners' dwellings, for there are no mines; not for farmhouses, for the country is absolutely barren today; not as travellers' shelters, when found well off any travelled trail. Consideration of this problem, combined with the thoughts on geologic change impressed on him a few days before by the fossil forest, led to the concept that climatic change—very probably associated with changes in elevation due to the gradual rising of the Andes—would account for the presence of these dwellings in a now barren land. "If the Andes were lowered till they formed a mere peninsula with outlying islands, would not the climate probably be more like that of the South Sea Islands, than its present parched nature? At a remote geological era, I can show that this grand chain consisted of Volcanic Islands covered with luxurious forests . . . If the mountains rose slowly, the change of climate would also deteriorate slowly; I know of no reason for denying that a large part of this may have taken place since South America was peopled."

Climatic change, then, may be responsible for the contrast between the present distribution of the inhabitants of South America and that of the past. And Darwin's meditation here in this high Andean valley gave an approach to the wording of the significant first sentence of the "Origin"—"the geological relations of the present to the past inhabitants of that continent." To be sure, at this earlier time Darwin was thinking of "inhabitants" only in terms of

man. But a spark had been struck which, after smouldering a bit, was to burst into clear flame. Darwin's earlier experiences on the eastern coasts of South America had been such that it was easy for him to expand the concept of change in the "inhabitants" of South America from man alone to embrace the fauna as a whole. For he himself had been one of the first to collect representatives of the strange series of mammals, now mostly extinct, which populated that continent during the Cenozoic Era, the Age of Mammals.

The story of this fauna is now rather adequately known. South America, we now know, became separated from the rest of the world almost at the very beginning of the Cenozoic, and at the time of this separation only a few groups of mammals had reached that continent. As a result the story of mammal evolution in South America over some 70 millions of years or so was very different from that of the other major land masses of the world. Surviving there today are special groups of monkeys and of rodents (of which the guinea pig is a familiar representative). Other groups, however, developed in unfamiliar patterns. No true flesh-eaters of the order Carnivora had reached that continent; in their absence, marsupials, descended from opossum-like forms, developed to occupy the carnivores' place in nature. During the Cenozoic there developed pouched mammals paralleling the wolves, weasels and felids of other continents—even a marsupial sabre-toothed "tiger" paralleling in startling fashion the placental sabre-tooths which had arisen in northern continents. Developed in South America were the members of the Xenarthra, the so-called edentates. Representatives of modest size still persist in the form of numerous armadillos and a few ant-eaters and little tree sloths. During the Tertiary, however, two spectacular branches sprang up from the xenarthran stock: glyptodonts and ground sloths. The glyptodonts were giant armadillo relatives whose bodies were protected by a solid-domed carapace of bony armor; the ground sloths were a varied series of giant, clumsy, terrestrial relatives of the tree sloths, represented by such forms as *Megatherium* and *Mylodon*. Equally unfamiliar to the non-paleontologist are the groups of ungulates, or hoofed mammals, which swarmed the plains of South America during Tertiary times. A few hoofed forms had reached South America before its separation, but these few included no representatives of the familiar groups which in other continents developed into such forms as horses, rhinoceroses, deer, cattle and the like. Instead there arose a number of hoofed orders of strange character, now entirely extinct. One such order was that of the Litopterna. Among the litopterns

some forms paralleled the horses of other continents, paralleling them in, among other features, toe reduction to the degree that one fossil litoptern, in attaining the monodactyl condition, shows even greater reduction of the side toes to slender splint bones than is true of the most advanced true horses. Another group, of which *Macrauchenia* was a late-surviving example, paralleled (as the name suggests) the camels and llamas to a considerable degree, although not related in the slightest to these familiar forms. Greatest of all South American mammal groups was an ungulate order termed the Notoungulata, which branched out into scores of genera and species, all now extinct. They were exceedingly varied in nature, and for the most part difficult to compare with mammals of other regions, although we may gain some crude idea of the appearance of *Toxodon*, a large late form whose remains are well-known, by suggesting that it somewhat resembled a cross between a hornless rhinoceros and a hippopotamus.

These varied members of the native fauna flourished throughout the length of the Tertiary period, which occupied most of the extent of Cenozoic time. But with the oncoming of the Pleistocene period, the so-called Ice Age, the South American faunal picture changed rapidly and in startling fashion. The Panamanian isthmus emerged, and North America became connected with the south. Travel across this isthmus could, of course, take place in both directions and some of the South American natives ventured north. The porcupine, armadillo and opossum are successful survivors of northward migration; numerous ground sloths and even glyptodonts plodded into North America and, although now extinct, became "United States citizens" during the Pleistocene.

For the most part, however, migration went in the other direction, north to south. Series of more progressive ungulates, such as deer, llamas and tapirs, developed in the Northern Hemisphere, invaded South America. The native ungulates, it would appear, were unable to compete with them. They became reduced in numbers and variety during the Pleistocene and today have completely vanished. Still more crucial, however, we may believe, was the fact that there poured into the south a great array of true carnivores—wolf- and dog-like forms, mustelids, "cats" large and small, to say nothing of raccoon relatives and bears. Not improbably the arrival of these carnivores (against which Nature had not provided any adequate defense) may have been the crucial event which brought about the utter downfall of the native ungulates, as well as of the glyptodonts and ground sloths, and the reduction of their flesh-

eating predecessors, the carnivorous marsupials. The spectacular chapter in mammalian history shown by the Tertiary fossil record of South America came to a disastrous end.

A *Megatherium* skeleton from the Argentinian pampas had been brought back to Madrid some decades before, but otherwise almost nothing of this story was known when Darwin sailed for South America, and he himself was one of the first to bring back fossil representatives of extinct South American mammal groups. During the two years spent by the "*Beagle*" mapping the Patagonian coast, he spent much of his time ashore and collected a considerable suite of specimens, almost all of them of Pleistocene age. Some of his material was gained during journeys overland, but a considerable part of his collection was made early in his voyage. After passing down the east coast of South America, with stops at Bahia, Rio de Janeiro, Montevideo and Buenos Aires, the "*Beagle*" made for Bahia Blanca, then a little Argentinian outpost in northern Patagonia, as a headquarters from which to begin the serious work of charting the Patagonian coast. Darwin lost no opportunity of escaping from the ship, and presently he ran upon a good fossil locality.

"September 22nd, 1832. Had a very pleasant cruise about the Bay with the Captain and Sullivan. We staid some time on Punta Alta about ten miles from the ship; here I found some rocks. These are the first I have seen, and are very interesting from containing numerous shells and the bones of large animals."

"September 23rd. A large party was sent to fish in a creek about 8 miles distant . . . . I walked on to Punta Alta to look after fossils; and to my great joy, I found the head of some large animal imbedded in a soft rock. It took me nearly three hours to get it out. As far as I am able to judge, it is allied to the Rhinoceros [actually it was a ground sloth]. I did not get it on board till some hours after it was dark.

"September 25th. I walked to Punta Alta and again obtained several fossils.

"October 8th. After breakfast I walked to Punta Alta, the same place where I have before found fossils. I obtained a jaw bone which contained a tooth; by this I found out that it belongs to the great ante-diluvial animal the *Megatherium*. This is particularly interesting as the only specimens in Europe are in the King's collection at Madrid, where, for all purposes of science, they are nearly as much hidden as if in their primaeval rock.

"October 16th. Again I walked to Punta Alta to look for fossil bones."

Darwin returned to England in the fall of 1836. The following year he began the evolutionary researches which were to culminate, some 23 years later in the publication of "The Origin of Species." Everyone interested in the history of science is familiar with the stirring and often heated discussions which took place in England, on the Continent, and in this country before organic evolution became accepted as a well-grounded fact in earth history. Darwin's fossil collections are associated with a curious quirk in this story. As is well known, his major scientific opponent in England, in 1859 and after, was Sir Richard Owen, then a major figure in British scientific circles, an accomplished anatomist and paleontologist (and also very much of a "stuffed shirt"). The reasons for Owen's opposition to Darwin's thesis were complex in nature, but were in part, at least, due to the disruption which acceptance of evolution would cause in the orderly scheme of things as he, Owen the great authority, conceived of them. His attitude (to oversimplify it in rather crude fashion) was that (*a*) evolution wasn't true and (*b*) anyway, he had discovered all this years ago.

Amusingly, Owen was himself unwittingly responsible in considerable measure for Darwin's interest in evolution and the development of his epoch-making theory.

As may be read in Owen's biography, Owen and Darwin met one another only a few weeks after the "*Beagle*" had finished her voyage, in the home of the geologist Sir Charles Lyell. Owen was then an able and energetic young man at the start of his scientific career. What was more natural than that Darwin should turn over his fossils to this rising scientist? Owen promptly set to work on these specimens with enthusiasm, and presently produced a report on them which was published, to the extent of 110 pages and 32 quarto plates, as a section of "The Zoology of the Voyage of H. M. S. *Beagle*."

Darwin was obviously stimulated by Owen's work. In his diary for the following year appears the decisive entry: "In July opened first notebook on 'Transmutation of Species.' Had been greatly struck from about month of previous March on character of South American fossils—and species on Galapagos Archipelago. These facts origin (especially latter) of all my views." It may well be that in later years Owen realized (and regretted) the impetus he had given in his youth toward starting Darwin on the path that was to lead to such a scandalous invasion of his sacred domain!

But although fossils played a major part in initiating Darwin's studies, they play a disappointingly small role in "The Origin of

Species." Today any elementary work expounding evolutionary facts and theories includes a series of chapters marshalling the evidence for evolution from a variety of fields, such as anatomy, embryology, zoogeography and paleontology. In the last area, emphasis is generally laid on such well-known evolutionary series as that of the horses, elephants and dinosaurs, as well as the general paleontological record, demonstrating that the theory of evolution fits all the known facts, and that any other interpretation of the vast amount of paleontological knowledge which we possess is difficult if not impossible.

In Darwin's classic, many areas of possible proof are adequately and convincingly treated. Not so the paleontological story. The treatment given in two chapters on "The imperfections of the geological record" and "The geological succession of organic beings," is essentially a negative one, defensive in nature. The reason for this type of discussion is obvious if we contrast our present knowledge of fossils with the state of paleontological knowledge a century ago. Even today we must rely primarily on the story of vertebrate evolution, for the antiquity of many of the invertebrate phyla is so great that their origins are still buried in pre-Cambrian obscurity. Today we still have gaps in the history of vertebrates, but much of the story seems clear in broad outline, and in many areas there is abundant detailed evidence. We have vast accumulations of material from a wide variety of geological horizons and a wide variety of continental areas, in addition to those of western North America, which have long yielded a magnificent array of fossil forms. Far different was the situation in 1859. Practically nothing was known of fossils from areas outside western Europe. The great western fossil fields of the United States were known only by few and fragmentary remains brought back by early travelers. And even in Europe relatively little work had as yet been done on the available deposits. In the absence of the abundance of materials available in later times, early opponents of evolution could, and did, ask highly embarrassing questions. If there has been gradual evolution instead of successive distinct creations, why are not the fossil-bearing strata filled with missing links? Evolutionary theory, its opponents said, would lead us to expect that known fossils would show a well-arranged phylogenetic pattern—which in Darwin's day they did not. Still further, various groups appear suddenly, abruptly, in certain geological formations, contrary to what would be expected under the evolutionary theory of gradual transformation.

These and many other arguments based on the fossil record were brought against evolutionary beliefs. Darwin answered these objections, and answered them ably, with the imperfections of the geologic record as the reason for many of the apparent contradictions between evolutionary theory and paleontological facts, and our imperfect knowledge of this imperfect record as a source of further difficulty. He argued ably, but had, of necessity, to argue defensively; and decades were to elapse before the then scattered pieces of fossil evidence could be welded together to give the present coherent story.

To make matters worse, the paleontologists of Darwin's day were almost to a man opposed to any evolutionary interpretation of the fossil evidence. Vertebrate paleontology had been essentially founded by the great French scientist Cuvier, half a century before. The fossils known in his day gave him no reason to abandon belief in a series of successive distinct faunas, separated by natural "revolutions," and he had argued ably (and generally justly) against evolutionary theories propounded by Lamarck and Geoffroy Saint Hilaire. Owen, Darwin's major English opponent, was in great measure a disciple of Cuvier and saw no reason to depart from the Cuvierian point of view. No more did Agassiz, a second major figure in paleontology a century ago, who was Darwin's major American opponent and was like Owen very much a Cuvier disciple.

This was the situation at the time of the publication of "The Origin of Species." But later decades were to see a marked reversal. In the 1870's there began extensive exploration of the western Tertiary beds of this country. Not too many years were to pass before Marsh could present a convincing series of forms showing the evolution of the horse. (*Hyracotherium*, the most primitive member of the series, was known in Darwin's day, but in the absence of connecting forms its ancestral position was not recognized.) Cope, Marsh's brilliant rival, likewise found the western American fossil beds to present convincing evolutionary evidence. In Europe, too, such work as that of Kovalevsky showed that restudy of existing materials, added to newer discoveries, led almost inevitably to evolutionary interpretations. By the time of Darwin's death the situation had changed radically and approached that seen today, in which paleontology gives the strongest support to the fact of evolution and in which work in paleontology without belief in evolution is unthinkable.

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Linnaeus and Darwin

L. R. C. AGNEW [1]

I have an impossible task to perform this afternoon. Think of it, gentlemen—to say something original or even memorable about two of the most distinguished figures in biology, and this in a matter of forty or fifty minutes at the tail end of a year which has seen a spate of commemorative volumes, papers and addresses in this and many other countries. But this is a cowardly way to start a lecture—by firing distress signals before my ship, so to speak, has even left safe anchorage. Let me, however, proceed, albeit at the risk of boring you with what has been said many times before.

Carolus Linnaeus (1707-1778).

Carolus Linnaeus was born in 1707 in South Sweden. His names, of course, are Latinized. He could have been called Carl Ingemarsson, but his father, Nils Ingemarsson, went into the Church and (following an old custom) took a Latinized name; he called himself Linnaeus supposedly after a large lime-tree (called *Lind*, in Swedish), and after he had saddled his son with this surname it seemed appropriate to give him a Latinized Christian name as well, so the simple-sounding Carl was transformed into the more formidable Carolus. Now the point of mentioning this quaint tale is to show that even as early as his christening, botany was involved, and botany was to remain the dominant interest of his life. Linnaeus's biographers all mention his keen interest in flowers and plants in early childhood, and when the choice of a career later came up, the Church—his father's calling—was a non-runner. Linnaeus wanted to study medicine, for botany in those days was part, and a large part at that, of the medical curriculum; most of the drugs and of course all the remedial herbs were of plant origin. One could also make a living as a doctor, whereas a professional botanist would have needed private means to exist.

1. Professor of History of Medicine, The University of Kansas. Seminar presented on 8 October 1958.

Linnaeus got some good premedical instruction, so to speak, in high school where, bored with the usual school subjects, he was lucky enough to find a teacher—a Dr. Rothman—who encouraged him to read the botanical and physiological texts of the day. After leaving school he had a year at Lund University, where his botanical studies continued under the expert eye of Kilian Stobaeus, a well-known doctor and naturalist. After this, in search of wider botanical experience, he went to Uppsala, which used to have a fine and famous botanical garden, which, however, he found, to his horror, in a shocking state. There appear to have been two aged medical professors there as well, and they were also in a shocking state—so young Linnaeus was left pretty much on his own, and this was probably the best thing that could have happened, in view of his passionate love of botanical observation. After a year or so, indeed, at the age of 23—in 1730—he wrote a brief thesis entitled *Introduction to the Floral Nuptials*, and this really excited the local faculty. In this work we find Linnaeus enunciating the doctrine of plant sexuality. Others—for example, Nehemiah Grew in England, Camerarius in Germany, and Vaillant in France—had suggested that plants have sexual organs (stamens and pistils), but it was Linnaeus's great distinction not merely to confirm this but to utilize these organs in a practical system for classification of the plant world. On the strength of this precocious work, the Director of the Botanical Garden—Professor Rudbeck—quickly made Linnaeus his deputy, and let him teach the medical students botany. During the summers of 1730 and 1731 he taught hard and worked harder, and built up a backlog of wonderful material for his new sexual system of plant classification.

In 1732—now 25—he sought further specimens and made a famous trip to Lapland; the diary he kept during this five-month tour of almost unknown territory is still preserved and is packed with all manner of observations and written in an engaging fashion. It has even been described as "one of the treasures of Swedish literature." Various other trips followed, and in the course of one of these he picked up an interesting non-botanical specimen in the shape of his future wife, and later, faced with the need to support this lady, he had to get a medical degree as quickly as possible in order to practice somewhere. Holland was an obvious choice; the great universities of Leiden and Utrecht were there. But like great universities the world over, they were expensive, so he dropped by the University of Harderwijk, and within a week he had taken an examination, printed and defended his thesis, and obtained the

coveted degree of Doctor of Medicine. He did not, however, rush home to Sweden after this happy event. His work was already known in Holland, and the Dutch urged him to stay a while. He met the Dutch botanist and zoologist, Johan Frederik Gronovius, and showed him the manuscript of a projected book, the *Systema Naturae*—the system of nature. Gronovius, along with a friend (a wealthy Scottish doctor named Isaac Lawson) agreed to meet the publication costs, and thus this famous work appeared in the year 1735.

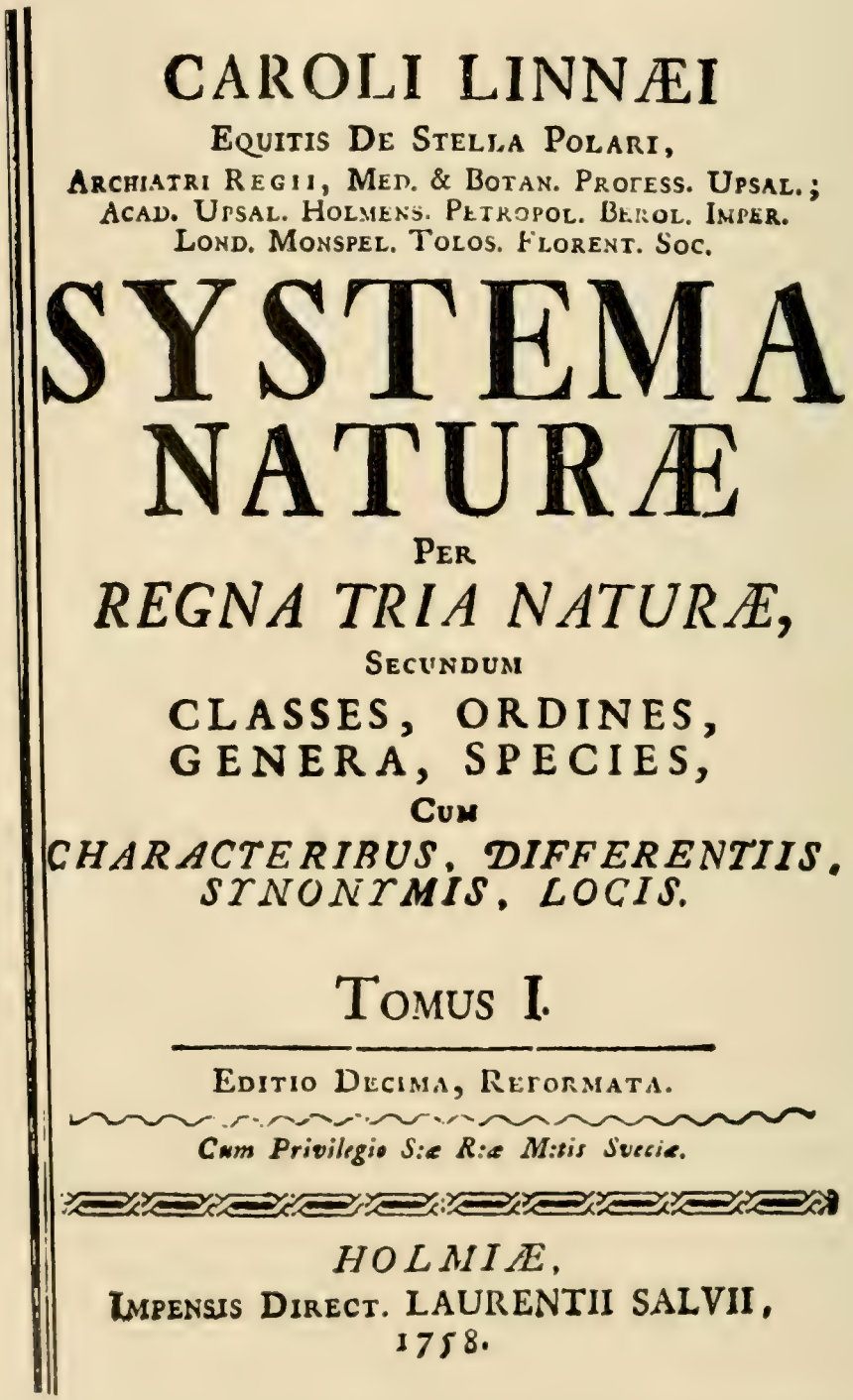
Let us discuss this book for a few moments—indeed, at this point let me remind you that what we are commemorating this year is the bicentenary of the appearance of the tenth edition of this very work. Why? Well, the tenth edition of the *Systema Naturae*, which appeared in 1758, is regarded by biologists as the permanent basis for the scientific names of living things. Here we find the so-called binary or "binomial nomenclature"—that system of defining every known living thing by two Latin names, the first being that of its *genus* and the second that of its *species*. For example, man is *Homo sapiens*, and the two common hookworm parasites that infest man are *Necator americanus* and *Ancylostoma duodenale*. That last parasite reminds me of a famous rhyme. Human infestation with *Ancylostoma duodenale* (ancylostomiasis) was very common many years ago in England in the Cornish tin-mines; so much so, that prayers used to be offered for relief, and the rhyme went:

We pray to the Lord in all our Diocese,
To help us get rid of ancylostomiasis!

The first edition (1735) of the *Systema Naturae* consisted of only seven sheets in extra large folio. By the time we reach the twelfth edition, which came out in three volumes in the years 1766-68 and was the last edition to be supervised by Linnaeus himself, we find it running to some 2,300 pages. It is worth noting that some five years before the famous tenth edition of the *Systema Naturae* appeared, Linnaeus had provided around 6,000 plants with appropriate descriptions and designations, using his system of binomial nomenclature, and that this did for the vegetable kingdom what the *Systema Naturae* was later to do for the animal kingdom; this particular book, published in 1753, was called the *Species Plantarum*. There are two sure ways of appreciating the magnitude of this remarkable tidying up of the plant and animal kingdoms: have a look at the confused state of biological nomenclature before Lin-

naeus's time, and if that doesn't convince you, become an entomologist and see how far you can go without binomial nomenclature.

While we're on this subject of Linnaeus's great book, the *Systema Naturae*, it might be worth recalling that it was hailed by many non-scientific men. For example, Thomas Gray—the English poet who wrote the famous Elegy—had a copy of the tenth edition. Gray bought it in London in 1759 and "almost immediately he



CAROLI LINNÆI

EQUITIS DE STELLA POLARI,

ARCHIATRI REGII, MED. & BOTAN. PROFESS. UPSAL.;
ACAD. UPSAL. HOLMENS. PETROPOL. BEROL. IMPER.
LOND. MONSPEL. TOLOS. FLORENT. SOC.

SYSTEMA NATURÆ

PER

REGNA TRIA NATURÆ,

SECUNDUM

CLASSES, ORDINES,
GENERA, SPECIES,

CUM

CHARACTERIBUS, DIFFERENTIIS,
SYNONYMIS, LOCIS.

TOMUS I.

EDITIO DECIMA, REFORMATA.

Cum Privilegio S:æ R:æ M:tis Sveciæ.

HOLMIÆ,
IMPENSIS DIRECT. LAURENTII SALVII,
1758.

FIG. 1.—Title page of the tenth edition of the *Systema Naturae.*

FIG. 2.—An interleaved page from Thomas Gray's copy of the tenth edition of the *Systema Naturae*, showing his annotations and drawings.

began to annotate its margins with the English names of animals and plants, adding to them the equivalents in several foreign languages, particularly French, Italian, Swedish, German, Latin, and Greek. Other marginalia, nearly all in English, describe the size or appearance of some particular species, whether from observation or reading it is difficult to say."[2] He also made many deft pen and ink sketches of various specimens, and Fig. 2 gives some idea

2. C. E. Norton, *The Poet Gray as a Naturalist* (Goodspeed, Boston, 1903).

of their quality. These fascinating volumes are now in Harvard's Houghton Library.

But let us return to Linnaeus himself—we left him in Holland, as he arranged for publication of the first edition of the *Systema Naturae* in 1735, when he was only 28 years old. He was to remain in Holland some three years, until 1738, working hard and publishing something of the order of fourteen major works. Many of these were from manuscripts he had taken with him from Sweden, and some were based on fresh material. For sheer stupendous output of first-class work these three Dutch years are hard to beat in the history of science; indeed, the only thing that can equal them—or perhaps even surpass them—is the fantastic year and a half that the young Newton spent at his country home during the year (1665) of the Great Plague of London, some seventy years before Linnaeus was to arrive in Holland for the first time. But that's another story, although mention of Newton is perhaps not out of place here. After all, in terms of systemization of a disorderly biological world, Linnaeus could be dubbed the Newton of eighteenth century biology, just as our next candidate for discussion—Darwin—is assuredly the Newton of nineteenth century biology, if not, indeed, of all biology.

Linnaeus left Holland in 1738 and had a few sticky months in Stockholm as a doctor before the tide turned completely favorable, in that he obtained one of the two professorships of medicine in the University of Uppsala, after a pamphlet fight with another candidate by the name of Wallerius. Linnaeus taught botany, and he was in charge of the botanical garden. The publications kept flowing from his pen; students from many different countries came to work with him; his own country ennobled him, and he was now styled Carl von Linné; and many other countries gave him all kinds of formal recognition for his great achievements. Throughout it all he remained the same enthusiastic, hardworking, gentle, naïve, religious man he had always been, although in the closing stages of his life failing health gave him a somewhat grimmer outlook on life. He died in 1778 after a series of strokes.

After his death an astonishing thing occurred: his son succeeded him (unworthily) and promptly sold all his father's collections and manuscripts to an English medical student named James Edward Smith. Smith later founded the Linnean Society of London, and presented it with his Linnean collection in 1828; and this wonderful material—which would doubtless have remained in Sweden (and

rightly so) had it not been for the shortsightedness of Linnaeus's son—is now in the Society's premises in Burlington House, London.

I hope you don't get the impression from all I have said that Linnaeus was a dull pedantic fellow, ploughing a dreary systematic or taxonomic furrow, or, if you prefer it, an obsessional classifier and nothing else. He was a superb naturalist, whose major interests were of course botany and classification and whose well-roundedness we do well to remember today. He had blind spots, to be sure (what scientist doesn't?). For example, as Eric Nordenskiöld has pointed out, "he never formulated any elaborate theory of the phenomena of life in their entirety . . . nature is created by God to His honour and for the blessing of mankind, and everything that happens happens at his command and under His guidance." This was probably a good thing in that it kept him out of philosophical squabbles. It was bad in the sense that on the matter of the nature of species we find him writing that "there are just as many species as there were created in the beginning," and also "there is no such thing as a new species." Clearly, Linnaeus was no evolutionist. Not so, however, our next candidate for commemoration —Charles Darwin.

Charles Darwin (1809-1882).

Why are we also celebrating Darwin's name today? After all, he was born in 1809 and died in 1882; and you will remember Linnaeus' dates were 1707-1778, so we have a century between them. So why Darwin this year? Why don't we wait until the centenary of his death, and have a big celebration in 1982? The answer is similar to the one I gave you about why we commemorate Linnaeus this year—the publication of a famous piece of work. Not, however, the *Origin of Species,* although this, of course, is Darwin's masterpiece—but it was published in 1859. No, we commemorate this year the centenary of the so-called Darwin-Wallace papers which were presented to the Linnean Society on July 1st, 1858. These papers were formally transmitted to the Secretary of the Society (J. J. Bennett) on June 30th, by the leading geologist of the day, Charles Lyell, and by one of the leading botanists, Joseph Hooker. The title of this communication was "On the Tendency of Species to form Varieties; and on the Perpetuation of Varieties and Species by Natural Means of Selection." Now let us go further and examine the text of the letter that Lyell and Hooker sent to the Secretary of the Society along with the Darwin-Wallace papers:

On the Tendency of Species to form Varieties; and on the Perpetuation of Varieties and Species by Natural Means of Selection. By CHARLES DARWIN, Esq., F.R.S., F.L.S., & F.G.S., and ALFRED WALLACE, Esq. Communicated by Sir CHARLES LYELL, F.R.S., F.L.S., and J. D. HOOKER, Esq., M.D., V.P.R.S., F.L.S., &c.

[Read July 1st, 1858.]

London, June 30th, 1858.

MY DEAR SIR,—The accompanying papers, which we have the honour of communicating to the Linnean Society, and which all relate to the same subject, viz. the Laws which affect the Production of Varieties, Races, and Species, contain the results of the investigations of two indefatigable naturalists, Mr. Charles Darwin and Mr. Alfred Wallace.

These gentlemen having, independently and unknown to one another, conceived the same very ingenious theory to account for the appearance and perpetuation of varieties and of specific forms on our planet, may both fairly claim the merit of being original thinkers in this important line of inquiry; but neither of them having published his views, though Mr. Darwin has for many years past been repeatedly urged by us to do so, and both authors having now unreservedly placed their papers in our hands, we think it would best promote the interests of science that a selection from them should be laid before the Linnean Society.

Taken in the order of their dates, they consist of:—

1. Extracts from a MS. work on Species*, by Mr. Darwin, which was sketched in 1839, and copied in 1844, when the copy was read by Dr. Hooker, and its contents afterwards communicated to Sir Charles Lyell. The first Part is devoted to "The Variation of Organic Beings under Domestication and in their Natural State;" and the second chapter of that Part, from which we propose to read to the Society the extracts referred to, is headed, "On the Variation of Organic Beings in a state of Nature; on the Natural Means of Selection; on the Comparison of Domestic Races and true Species."

2. An abstract of a private letter addressed to Professor Asa Gray, of Boston, U.S., in October 1857, by Mr. Darwin, in which

* This MS. work was never intended for publication, and therefore was not written with care.—C. D. 1858.

FIG. 3.—First page of the Darwin-Wallace papers presented to the Linnean Society. (*J. Linn. Soc.*, 1858, vol. 3, p. 45.)

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2. An abstract of a private letter addressed to Professor Asa Gray, of Boston, U. S., in October 1857, by Mr. Darwin, in which he repeats his views, and which shows that these remained unaltered from 1839 to 1857.

3. An Essay by Mr. Wallace, entitled "On the Tendency of Varieties to depart indefinitely from the Original Type." This was written at Ternate in February 1858, for the perusal of his friend and correspondent Mr. Darwin, and sent to him with the expressed wish that it should be forwarded to Sir Charles Lyell, if Mr. Darwin thought it sufficiently novel and interesting. So highly did Mr. Darwin appreciate the value of the views therein set forth, that he proposed, in a letter to Sir Charles Lyell, to obtain Mr. Wallace's consent to allow the Essay to be published as soon as possible. Of this step we highly approved, provided Mr. Darwin did not withhold from the public, as he was strongly inclined to do (in favour of Mr. Wallace), the memoir which he had himself written on the same subject, and which, as before stated, one of us had perused in 1844, and the contents of which we had both of us been privy to for many years. On representing this to Mr. Darwin, he gave us permission to make what use we thought proper of his memoirs,

* This MS. work was never intended for publication, and therefore was not written with care.—C. D. 1858.

etc.; and in adopting our present course, of presenting it to the Linnean Society, we have explained to him that we are not solely considering the relative claims to priority of himself and his friend, but the interests of science generally; for we feel it to be desirable that views founded on a wide deduction from facts, and matured by years of reflection, should constitute at once a goal from which others may start, and that, while the scientific world is waiting for the appearance of Mr. Darwin's complete work, some of the leading results of his labours, as well as those of his able correspondent, should together be laid before the public.

We have the honour to be yours very obediently,

Charles Lyell,
Jos. D. Hooker.

You can see what happened. Darwin had been working away steadily for some twenty years amassing a huge body of facts relevant to his slowly maturing—like fine old wine, if you like—theory of the origin of species by natural selection. His friends urged him to publish, but no, he wanted to wait until he was quite, quite satisfied. He talked of the book he would write when he was good and ready, but meantime he accumulated fact after fact. He made a rough sketch of this work in 1842, and enlarged it into a long essay in 1844, which Hooker saw and Lyell knew about. But nothing appeared in cold print. His proposed book on the whole business became larger and larger, but still he withheld his hand. There were rumbles, uneasy rumbles, when, as early as 1855, he found a paper by Alfred Wallace in the *Annals of Natural History* in which the ideas expressed were close to his own thoughts; and in a letter dated May 3, 1856, he confided to Lyell "I rather hate the idea of writing for priority, yet I certainly would be vexed if any one were to publish my doctrines before me." Surely this is one of the greatest understatements in all science—nearly twenty years of work on the problem of evolution, and he "would be vexed"; it is safe to say that a less phlegmatic man would have verged on a stroke at the thought of being beaten to the tape. The screw turned a bit more the following year (1857), when Darwin received a letter from Wallace (who was then in Celebes) asking questions about varieties and the breeding of domestic animals. Darwin fenced back gamely, and replied "I can plainly see that we have thought much alike and to a certain extent have come to similar conclusions." He mentioned that he had been some twenty years in this research work. And again, in December of the same year, Wallace asked more questions, and again Darwin replied, once more mentioning his twenty long years of work. And finally, Wallace's next letter was the killer—for he enclosed with it his paper "On the Tendency of

Varieties to depart indefinitely from the Original Type." Darwin was obviously shaken, but carried the thing off in gentlemanly fashion. "Do you not think his having sent me this sketch ties my hands?," he asked Lyell, and then went on to say that "I would far rather burn my whole book, than that he or any other man should think that I have behaved in a paltry spirit." But nobody involved in the whole affair, which culminated in the famous communication to the Linnean Society, behaved in a paltry spirit, and what might have been a sordid affair was resolved in admirable and exemplary fashion. Wallace, of course, knew that Darwin had had a head start, and Wallace, gentleman that he was, gracefully resigned himself, as Professor Irvine puts it, for a lifetime of being the moon to Darwin's sun. But Darwin had learned his lesson—he would write a brief paper on evolution, he thought; but as the months rolled by the manuscript rose higher and higher on his desk until, in the year (1859) after the Darwin-Wallace communication, his *Origin of Species* was finished and published.

What can we say of the *Origin of Species?* It is his masterpiece, but why is it a scientific masterpiece? Listen to Sir Julian Huxley on this very question:

"First of all, because it convincingly demonstrates the fact of evolution: it provides a vast and well-chosen body of evidence showing that existing animals and plants cannot have been separately created in their present forms, but must have evolved from earlier forms by slow transformation. And secondly, because the theory of natural selection, which the *Origin* [*of Species*] so fully and so lucidly expounds, provides a mechanism by which such transformation could and would automatically be produced. Natural selection rendered evolution scientifically intelligible: it was this more than anything else which convinced professional biologists like Sir Joseph Hooker, T. H. Huxley and Ernst Haeckel." [3]

What does Darwin mean by "natural selection"? Well, after he had read Malthus' *Essay on Population* (1798), he agreed with Malthus that the reproductive powers of animals are far greater than needed to maintain their numbers. Thus only if a large proportion of the offspring are destroyed will animal populations remain constant, as they normally do. But if lots of individuals are being destroyed, there must be a struggle for existence, and in this struggle for existence the favorable variations will survive and the unfavorable ones be exterminated. These favorable variations will accumulate, and this "natural selection" will lead to gradual change in the characters of a species towards better adaptation.

3. Huxley, Julian. Introduction (p. x) to the Mentor edition (New York, 1958) of Charles Darwin's *The Origin of Species.*

This gradual change, when it has gone far enough, will result in the origin of a new species. This, then, is the gist of Darwin's theory, and his book contains a wealth of evidence to support it. Nowadays one has to view this theory in the light of our knowledge of embryology, genetics and mutations—knowledge which Darwin lacked—but the old bucket, so to speak, still holds water, despite a few leaks here and there.

Evolutionary thought before Darwin cannot be considered here; suffice it to say Darwin was by no means the first to suggest that species were subject to change, and that he readily acknowledged this fact. Among those who had earlier mentioned the possibility of species change were Marchant, Montesquieu, Buffon, Maupertuis, Diderot, Erasmus Darwin, Geoffroy St. Hilaire, Goethe, Lamarck and Moritzi. For various reasons—imperfect formulation of the problem and insufficiency of evidence being the main ones—all these claims for priority are far less strong than Darwin's.

Now I talked a good bit biographically about Linnaeus, and it might be worthwhile to say something of Darwin's own life and professional background. Whence came, for example, those wonderful planks, those biological facts that shore up the *Origin of Species* so solidly? Those of you who know the story might say—and you'd be right—that the famous five-year voyage of the *Beagle* was the main source of his material. Darwin set off in December, 1831, as naturalist on this ship, and by his return in 1836 he had made an enormous number of new discoveries. One thinks of the Galapagos Islands, off the coast of Ecuador, where "the landscape not only suggested evolution, the facts demanded it." [4] His son, Francis, writing years later in the *Dictionary of National Biography*, records how "it is impossible to overrate the influence of the voyage on Darwin's career: it was both his education and his opportunity. He left Engand untried and almost uneducated for science, he returned a successful collector, a practised and brilliant geologist, and with a wide general knowledge of zoology gained at first hand in many parts of the world. And above all he came back full of the thoughts on evolution impressed on him by South American fossils, by Galapagos birds, and by the general knowledge of the complex interdependence of all living things gained in his wanderings." Some ten years after he left the *Beagle* we find Darwin spending several years working on the morphology and classification of barnacles (and eventually, in 1851 and 1854, publishing

4. Irvine, William. *Apes, Angels, and Victorians* (New York, McGraw-Hill, 1955), p. 50.

his findings). How Linnaeus would have liked this part of Darwin's activities!

What of his philosophy, particularly his biological philosophy? When did he first get infected, so to speak, with the evolution virus? Evolution—or talk of it—was fashionable in Darwin's youth, and indeed the Darwins had a family interest in it. Old Erasmus Darwin, Charles' grandfather, in his *Zoonomia* (1794-96), had hinted broadly at the matter, but Charles ". . . was much disappointed, the proportion of speculation being so large to the facts given." [5] What about school? No, there's not much here except a general interest in natural history. Is college perhaps the answer? Well, let us examine this possibility briefly.

In 1825, a few months before his seventeenth birthday, Darwin and his elder brother, Erasmus, enrolled as first-year medical students in the University of Edinburgh, possibly because their father, Robert Waring Darwin (1766-1848), was himself a physician. Young Charles disliked most of his formal studies, and his *Autobiography* gives us some of his reactions. For example, as regards materia medica: "Dr. Duncan's [Andrew Duncan, 1773-1832] lectures on Materia Medica at 8 o'clock on a winter's morning are something fearful to remember." [6] Chemistry at 10 a. m. was a little better because "the instruction at Edinburgh was altogether by Lectures, and these were intolerably dull, with the exception of those on chemistry by Hope" [7] [Thomas Charles Hope, 1766-1844]. But anatomy at 1 p. m. resumed the *status quo*, for "Dr. Munro [*sic;* Alexander Monro, 1773-1859] made his lectures on human anatomy as dull, as he was himself, and the subject disgusted me. It has proved one of the greatest evils in my life that I was not urged to practise dissection, for I should soon have got over my disgust; and the practice would have been invaluable for all my future work." [8]

Darwin appears to have been fairly studious in his first year at Edinburgh and to have participated little in the corporate life of the University. Records are available of the books he borrowed from the University Library, and Boswell's *Life* of Johnson appears to have been one of his favorites. The following academic year (1826-27) Charles returned to Edinburgh without his brother Erasmus. He was more gregarious this time and—possibly indica-

5. Darwin, Charles. *The Autobiography of Charles Darwin, 1809-1882* (London, Collins, 1958), edited by his grand-daughter, Nora Barlow; p. 49.

6. *Ibid.*, p. 47.

7. *Ibid.*, pp. 46-7.

8. *Ibid.*, p. 47.

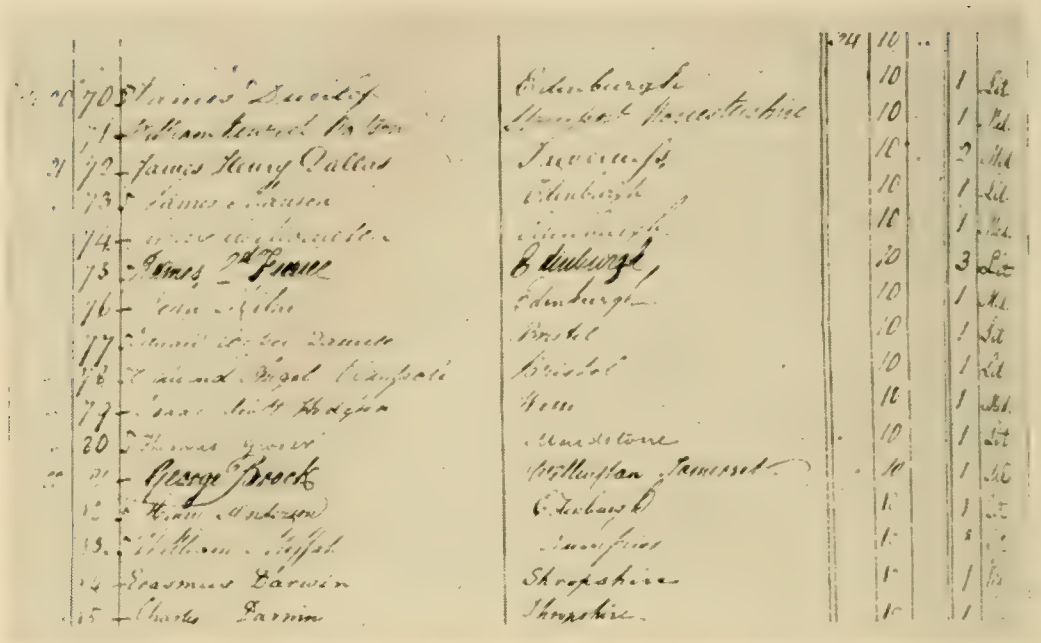

FIG. 4.—Matriculation register of the University of Edinburgh showing the enrollment (October 22, 1825) of Charles and Erasmus Darwin as first-year medical students.

tive of this—did not borrow any books from the Library. He became very friendly with Robert Edmond Grant (1793-1874) who at that time lectured on the comparative anatomy of invertebrates. Darwin accompanied Grant on many specimen-hunting trips and records how on one occasion Grant ". . . burst forth in high admiration of Lamarck and his views on evolution." Darwin goes on to say that "it is probable that the hearing rather early in life such views maintained and praised may have favoured my upholding them under a different form in my *Origin of Species*." [9]

Of particular interest was Darwin's membership in the Plinian Society, an undergraduate group which "met in an underground room in the University for the sake of reading papers on natural science and discussing them." [10] The minute book of the Society has been preserved, and Darwin's first formal scientific contribution is gravely recorded in the minutes of the meeting of March 27, 1827 (not 1826 as erroneously mentioned in the *Autobiography*):

Mr. Darwin communicated to the Society two discoveries which he had made:

1. That the ova of the Flustra possess organs of motion.
2. That the small black globular body hitherto mistaken for the young Fucus lorius is in reality the ovum of the Pontobdella muricata.

9. *Ibid.*, p. 49.
10. *Ibid.*, p. 50.

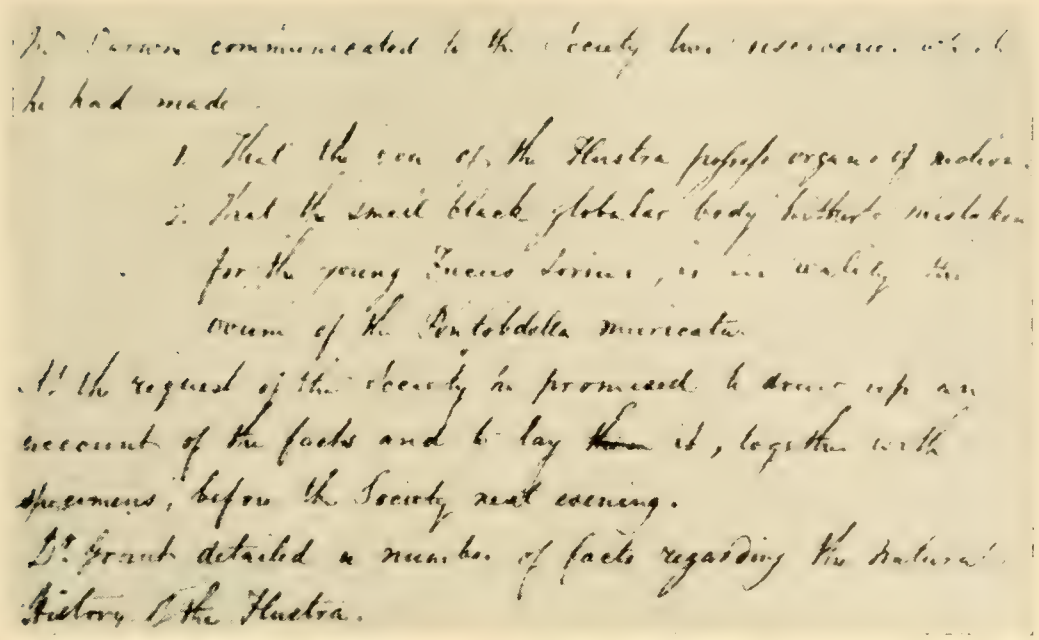

FIG. 5—Extract from minutes of the Plinian Society (March 27, 1827) recording Darwin's first formal scientific contribution.

At the request of the Society he promised to draw up an account of the facts and to lay it, together with the specimens, before the Society next evening.

Dr. Grant detailed a number of facts regarding the Natural History of the Flustra.

Darwin also attended with Grant meetings of the Wernerian Natural History Society and heard, among others, Audubon who spoke at the meetings in December, 1826, and January and February, 1827. He also attended, as a guest of the geologist Leonard Horner (1785-1864), a meeting of the Royal Society of Edinburgh at which the famous novelist Walter Scott presided. He went to classes held by Robert Jameson (1774-1854) who was Professor of Natural History, but records that his lectures on geology and zoology "were incredibly dull." [11]

All in all, apart from his many fine extra-mural experiences and the obvious stimulation of his friend Grant, Darwin was clearly disappointed in Edinburgh, and after his second year he resolved to abandon medicine and to study at Cambridge instead, with the idea of becoming—of all things, in view of his later beliefs—a clergyman. But he found Cambridge little better than Edinburgh, bluntly observing that "during the three years which I spent at Cambridge my time was wasted, as far as the academical studies were concerned, as completely as at Edinburgh and at school." [12] He be-

11. *Ibid.*, p. 52.
12. *Ibid.*, p. 58.

came interested in music and hunting, "but no pursuit at Cambridge was followed with nearly so much eagerness or gave me so much pleasure as collecting beetles." [13] At Cambridge, as at Edinburgh, he was much influenced by a member of the faculty, and in the *Autobiography* he gratefully recalls ". . . a circumstance which influenced my whole career more than any other. This was my friendship with Prof. Henslow [John Stevens Henslow, 1796-1861; Professor of Botany, 1827-61] . . . and during the latter half of my time at Cambridge [I] took walks with him on most days; so that I was called by some of the dons 'the man who walks with Henslow'; and in the evening I was very often asked to join his family dinner. His knowledge was great in botany, entomology, chemistry, mineralogy, and geology. His strongest taste was to draw conclusions from long-continued minute observations. His judgment was excellent, and his mind well-balanced; but I do not suppose that anyone would say that he possessed much original genius." [14]

What are we to deduce from this account of his student days at Edinburgh and Cambridge? Perhaps just this—that the tiny acorn of Darwin's thinking on evolution was stimulated to grow by Grant at Edinburgh, and possibly by Henslow at Cambridge, and from all this (aided, abetted and accelerated by the *Beagle* voyage) eventually sprang the mighty oak, his majestic *Origin of Species.*

Linnaeus and Darwin were giants of their times, as indeed they are of ours. Each was a superb naturalist, each had a sort of unorthodox, more or less independent education, each made protracted voyages in search of the raw materials—biological facts—for his fine publications. They were both simple men in the best sense of the word. If a sort of communal epitaph is in order for them today, I would suggest the quotation that Linnaeus himself put on the front of one of his own pamphlets—that quotation from Virgil which runs *famam extollere factis, hoc virtutis opus*; and this, as you know, means simply that it is the duty of a man of worth to increase his fame by deeds. This, I submit, is precisely what Linnaeus and Darwin did in the course of their illustrious careers, and is excellent advice for any who would follow in their footsteps today.

13. *Ibid.*, p. 62.
14. *Ibid.*, p. 64.

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I am grateful to Mr. William Jackson of the Houghton Library, Harvard University, for permission to reproduce an illustration from Thomas Gray's copy of the tenth edition of the *Systema Naturae,* and to the Keeper of Manuscripts of the University of Edinburgh for permission to reproduce illustrations of Darwin's matriculation record and the extract from the minutes of the Plinian Society.

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The Chemical Basis for Evolution

DAVID PARETSKY [1]

"It is better to ask some of the questions
than to know all of the answers."
The Scotty Who Knew Too Much, J. Thurber.

From ancient days Man has been curious about his origins and his ancestors. The mythologies of cultures present and past are replete with legends of cosmogeny and anthropogeny. Until relatively recent times, the theory of spontaneous generation neatly explained biogenesis: complex living forms arise spontaneously from non-living organic matter. Residual mud from the flooding of the Nile produces vermin; soiled linen stored in closed rooms gives rise to mice; maggots arise from rotting meat, and so on. When Pasteur established his germ theory of disease, he simultaneously destroyed the concept of spontaneous generation with all its implications. Left unanswered was the question, "If life does not arise *de novo*, what was the origin of life on Earth?"

Arrhenius' *panspermia* hypothesis proposed that life came to earth as spores, originating extraterrestrially and carried through space by means of light pressure. Ignoring the problems of survival among the hazards of temperature and radiation of outer space, the *panspermia* theory merely shifts the problem of biogenesis from Earth to another spatial body; the fundamental question remains unanswered.

Attempts have been made in the laboratory to obtain an understanding of conditions under which the first bit of living material, to which we will refer as the "protobiont," could have appeared. At this point an examination of the attributes of living material is necessary in order to appreciate the problem more fully.

1. Professor of Bacteriology, The University of Kansas Seminar presented on 29 October 1958.

Properties of Living Systems:

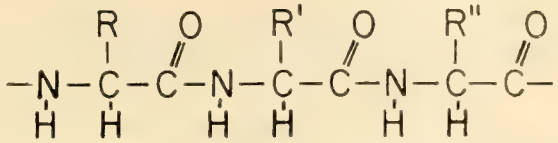
Probably the most remarkable property of a living system is the ability of self-replication. In contrast to crystal growth, the replication of cellular constituents is the result of altering *dissimilar* components in the environment to a state of cellular similarity. The growth of a $CuSO_4$ crystal occurs in a solution which contains $CuSO_4$, but the synthesis of *Nitrosomonas* cytoplasm occurs in a solution containing NH_4^+, HCO_3^- and certain inorganic salts. Since synthesis of cell or cell-like material is an endergonic process, energy for bio-synthetic reactions must be made available as useful energy. That is to say, the living system must be able to convert heat, light or electrical energy into a form of chemical energy capable of driving energy-requiring reactions. The net result of the energy conversions and couplings is the formation of new biological material. The new material must be sufficiently like the old so that the already established energy mechanisms are retained, and yet the living system must have a degree of plasticity to ensure modifications to permit the cell to survive in altering environments. By what universal mechanisms do presently known living system accomplish such difficult tasks? What insight to biogenesis may be gained by examination of answers to this question?

Chemical reactions conducted by the living system occur under fairly mild conditions of pH, temperature and pressure. Chemical equilibria *in vivo* are attained generally at pH ranges between 5-8 at 20°-40°C. The rates are far more rapid than comparable reactions occurring *in vitro* at pH extremes and at elevated temperatures. It is quite apparent that known living systems would be readily destroyed if their hydrolytic activities had to occur in *N* acid or alkali at 100° C. Rapid replacement or addition of cytoplasm essential for the maintenance of cellular integrity is accomplished by the extraordinary reaction rates. The catalysts which mediate cytochemical reactions are the enzymes whose chemical and electronic configurations enable the lowering of the energy of activation necessary to initiate a chemical reaction, and enormously decrease the time required for reactants to attain equilibrium.

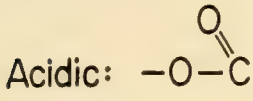
Proteins and Enzymes

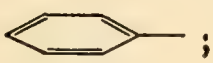
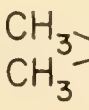
All known enzymes are either wholly or in part proteins. It is impossible to examine seriously the physical and chemical properties of the proteins in a limited discussion. Suffice it to note that proteins consist of amino acid residues (most often in L-configura-

tion, and with the $-NH_2$ group α-to the carbonyl group) linked by the peptide bond, -CONH,



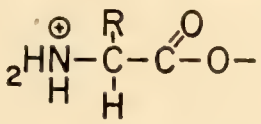
While the backbone of the protein is essentially a repetitive structure, the R group is of diverse nature:

Acidic:  ; basic, $-CH_2-NH_2$;

aromatic,  ; lipophilic,  ;

hydroxy- or sulfhydryl-ended, $-CH_2OH$; $-CH_2SH$.

It is the R groups of the proteins which are most responsible for intramolecular and intermolecular bonding, for solubility characteristics and other specific properties which differentiate proteins among themselves. The polyfunctional groups of amino acids



are retained by the oligo-peptides, the polypeptides and the proteins, and are not lost during polymerization. Indeed the macromolecule is more than the sum of its parts: in addition to retaining the polyfunctional character of the amino acids, the polymer now has the properties of a lyophilic colloidal micelle, including surface energy, relatively long range electrostatic forces and reactive loci resulting from the contributions of the R groups.

Proteins contribute not only to the special nature of biocatalysis and to cell structure but to the specific differences among cells. A protein or proteinoid molecule must have participated in the chemical activities of the protobiont.

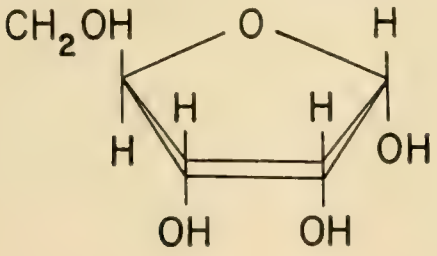
Nucleic Acids and Coding

Recognition of the contributions of the protein polymer to living systems logically poses another question: How was the protein peculiar to a protobiont replicated so that necessary vital protobiontic functions could continue? While the picture of protein replication is as yet not completely clear, an increasing body of information has revealed the interpendence of the protein system and the replicating device. Enzymes (proteins) catalyze the synthesis of species specific replicating mechanisms which in turn direct the synthesis of species specific proteins. The evidence which has accumulated clearly indicates that the replicating mechanism resides in another macromolecule, the polynucleotide. Just as the protein consists of amino acid residues in peptide linkage, so the polynucleotide consists of purine, pyrimidine, pentose and phosphoric acid residues, existing in ribosyl and phosphoryl linkages:

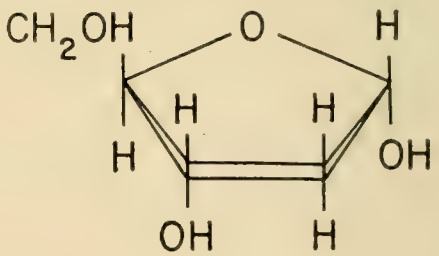
Base—pentose—orthophosphate

Base—pentose—orthophosphate

The pentose is of two kinds: D-ribose and 2,D-deoxyribose

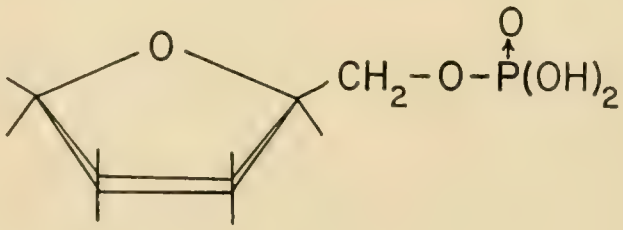


D-ribose

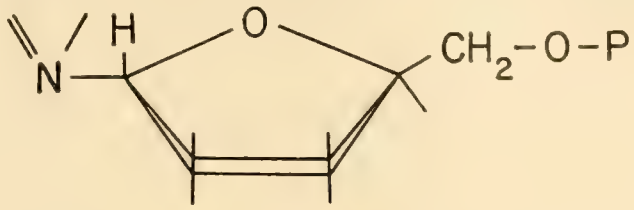


2, D-Deoxyribose

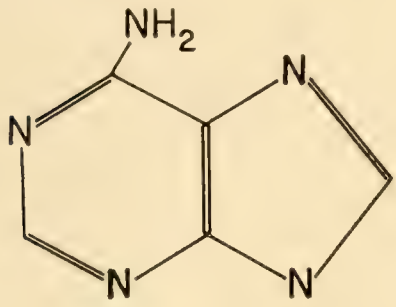
The orthophosphate is esterified on the 5′ position of a pentose moiety.



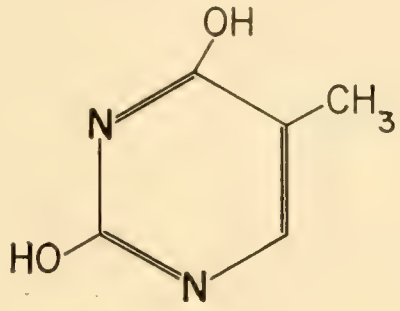
In turn the pentose is linked to the base by a glycosidic bond on the 1′ carbon:



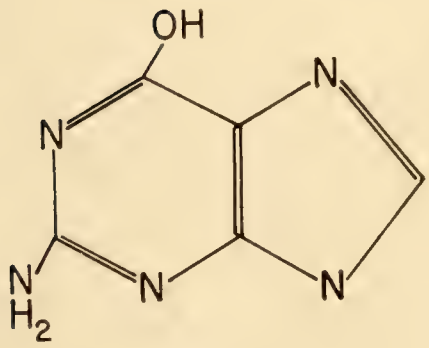
The base-pentose moiety is termed a nucleoside; the base-pentose-phosphate is a nucleotide, or nucleic acid. As is now well known, the coding mechanism resides in a polynucleotide twinned helix with the sugar as 2,D-deoxyribose.[2] The deoxyribonucleic acid (DNA) contains 4 characteristic bases. The purines adenine and guanine, and the pyrimidines thymine and cytosine:



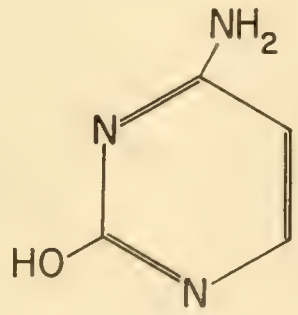
Adenine



Thymine



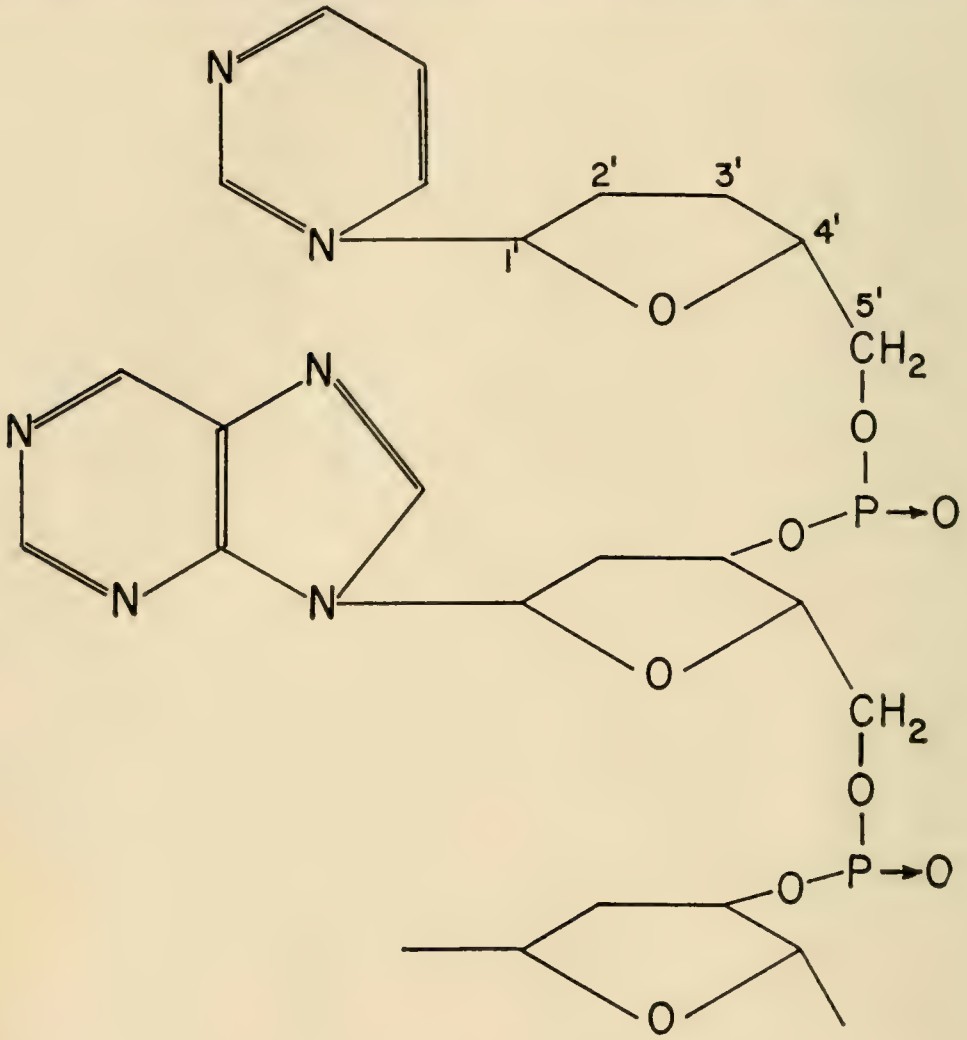
Guanine



Cytosine

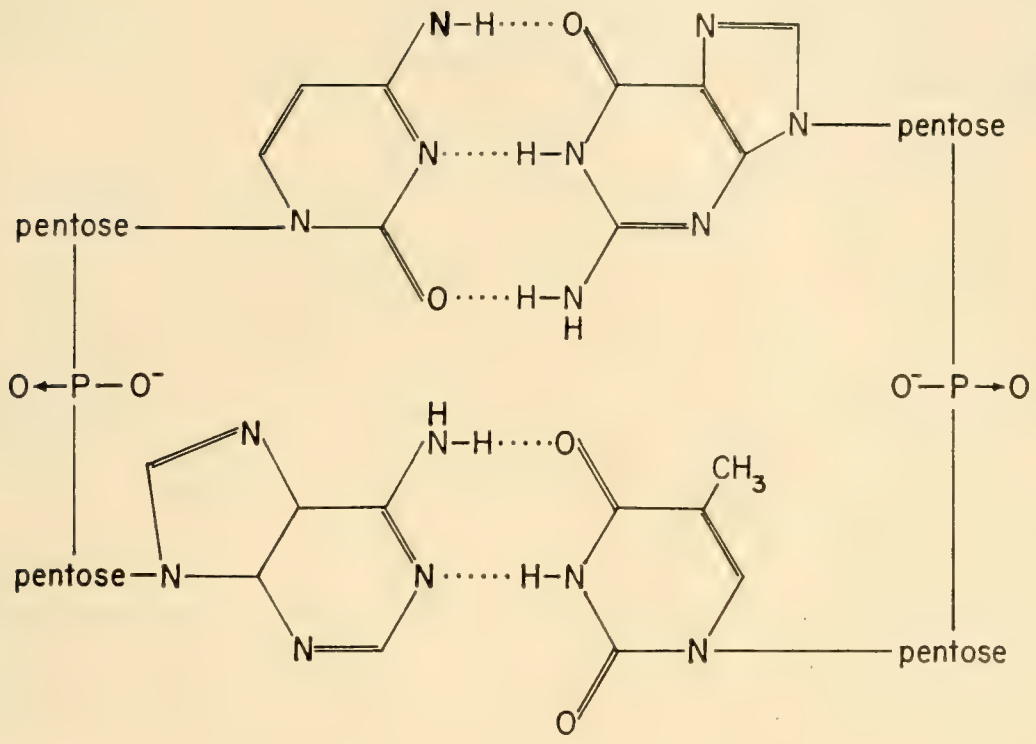
2. The notable unexplained exceptions are the RNA-viruses which apparently lack DNA and yet are precisely replicated.

The nucleotide residues are joined by the orthophosphate moiety, from the 5′ position of one pentose to the 3′ position of the other:

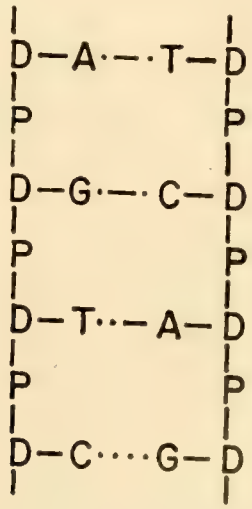


Thanks to the brilliant insight of Watson and Crick, and the groundwork of Chargoff, Mirsky and others,[3] it is believed that two single helix strands are held together by hydrogen bonding between adenine of one chain and thymine of the other; between guanine of one chain and cytosine of the other:

3. An excellent account of the physical, chemical and biochemical properties of the nucleic acids is presented in Chargoff and Davidson's "The Nucleic Acids" (1955).



A simple representation would be:



where D = 2, deoxyribose and P the phosphoryl group.

It is the *sequence* of base arrangement which determines what type of RNA and what type of protein will be synthesized. The "gene" is the operational term describing a given sequence of nucleotide residues. Alteration of base structure by nitrous acid on the *molecular level* will be reflected as a mutation on the *organism*

level; alterations in sequence by radiation or by introduction of base analogues into the polynucleotide chain will be expressed as mutations. The minimal chemical species requirements of a protobiont are (1) protein for catalysis and (2) polynucleotide for replication.

Energy

The conservation and storage of energy was one of the most formidable problems solved by the successful protobiont. Abundant sources of radiant, thermal, chemical, electrical and light energies which were available had to be transformed into a state usable when needed to drive the endergonic processes of synthesis, replication, diffusion against a concentration gradient, etc. The chemical energy associated with substances can readily be converted to heat, which is immediately dissipated. In biological systems this energy is converted into chemical energy of molecules, in which it can be stored. In a more basic analysis, when the reaction: $A \rightleftharpoons B$, $\Delta H < O$, is performed in a biological system, additional components are coupled to the system, and no demonstrable heat may obtain, although $\Delta F < O$. This is in contrast to the *in vitro* purely chemical reaction, in which heat is evolved.

(a) $CH_3CH_2OH \xrightarrow{(O)} CH_3CHO + H_2O$ (with evolution of heat)

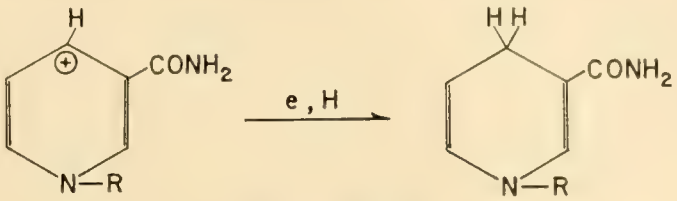
(b) $CH_3CH_2OH + DPN^+ \xrightarrow[\text{dehydrogenase}]{\text{alcohol}} CH_3CHO + DPNH + H^+$ (with evolution of ΔF)

The significant energy producing reactions of the cell are biological oxidations. Energy is stored in energy-rich bonds in such compounds as carbamyl phosphate, arginine phosphate, guanidyl phosphate, adenosine triphosphate (ATP), creatine phosphate, certain mixed phosphoric-sulfuric acid anhydrides, onium compounds such as adenosyl methionine, thiamin, etc. In existing living systems, the universal mechanism for biological oxidations is by electron transfer; loss of H or gain of O are special cases. The energy made available by such transfer may be calculated by the equation.

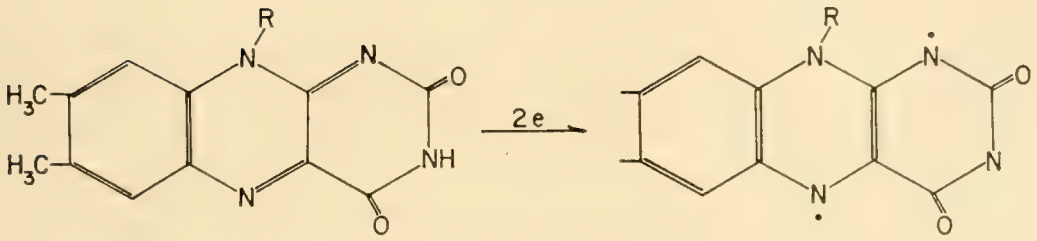
$$\Delta F = -n \mathcal{F} \Delta E'_0$$

where n is the number of electrons transferred in the reaction, F the Faraday constant (23,068 calories per volt equivalent) and E'_0 the charge, expressed in volts, of the oxidation-reduction potential

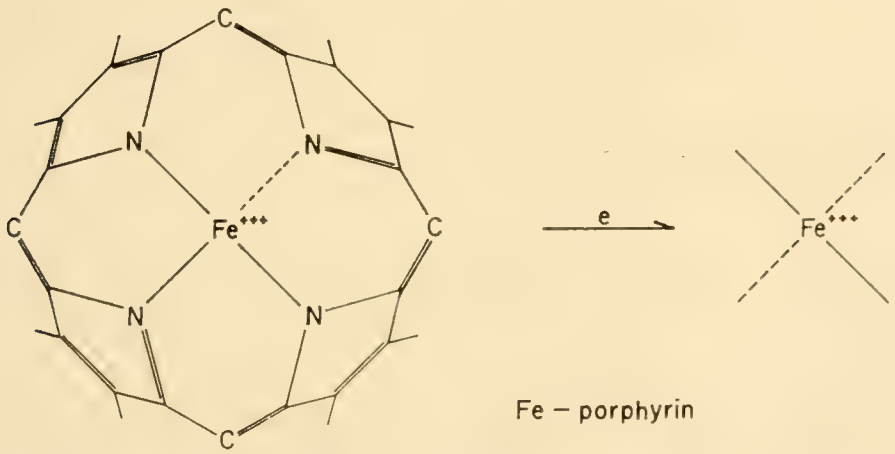
at pH other than 0. The most ubiquitous prosthetic compounds involved in electron transport include the pyridinium, isoalloxazine



Pyridinium reduction



Isoalloxazine reduction



Fe – porphyrin

and porphyrin species. The Fe-porphyrin structure is found in all aerobic as well as many anaerobic organisms, and is directly involved in electron transfer.

The Primitive Earth

We may now consider the events which perhaps 3000 million years ago produced a system capable of self-replication, with novel types of catalysis and energy conversions. We shall assume an earth of fairly moderate temperatures (60-200° C.), with a reducing atmosphere containing, among other things, water vapor, methane, ammonia, carbon monoxide and hydrogen sulfide. Either dissolved or present as solids were nitrides (Fe_4N), which react readily with water forming NH_4^+. Free oxygen was absent. Ultraviolet light of the shortest wave lengths, unabsorbed by ozone, penetrated the

atmosphere, producing molecular photoactivations. Enormous supplies of thermal, electrical and radioactive energies were available.

Free radicals were formed and underwent numerous combinations and decompositions. New species of compounds were formed which did not absorb the very short ultraviolet waves, and so retained some stability. The soluble materials dissolved in the oceans and were adsorbed by clays—kaolin, montmorillonites and bentonite compounds.[4] Adsorptions set up a locus of concentration and provided surfaces where molecules were placed in the juxtaposition necessary for reactivity. Phosphorus compounds were present in the reduced state, as hypophosphites and phosphites, and in the reduced state the salts were far more soluble than the corresponding phosphate. Their solubility made available the reduced phosphorus compounds for further reactions. The classic experiments of Miller and Urey show that glycine, succinic, formic, acetic, aspartic and glutamic aids, as well as formaldehyde, urea and other organic compounds, may be formed from the supposed primitive atmospheres of CH_4, NH_3, H_2 and H_2O. The synthesis of the chemical species required for the synthesis of the protobiont may now be pictured.

I. *The Proteins*

A. *Synthesis of Amino Acids*

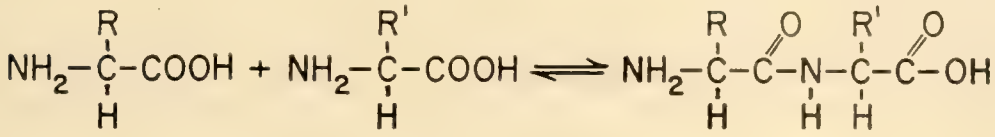
$$RCHO + HCN + NH_3 \rightleftharpoons \left[H\text{-}\overset{\overset{R}{|}}{\underset{\underset{NH_2}{|}}{C}}\text{-}CN + H_2O \right] \rightleftharpoons H\text{-}\overset{\overset{R}{|}}{\underset{\underset{NH_2}{|}}{C}}\text{-}CO_2H$$

This is the well known Strecker synthesis, which is probably responsible for amino acid synthesis in the Miller-Urey experiments. In pre-biontic time it likely occurred on the surfaces of clays on primitive shores, and the reaction was driven by electrical, thermal and radioactive energies. Laboratory synthesis of amino acids and the Miller-Urey experiments produce racemic mixtures. No satisfying hypothesis has yet been advanced to explain the selectivity for the L-isomer. Was the L-isomer selected because of differences in physical properties (many of the amino acids have different solubilities for the D- and L-isomers)? A polypeptide of D- and L-isomers will suffer considerable distortions and should not have the stability of the L-isomeric or D-isomeric chain. The formation of the α-helix is also hindered by opposite isomeric residues (Wald,

4. It is of more than passing interest to note that certain montmorillonites have helical structures, with surface charges enabling adsorption of ionic compounds on the helix surface. These helices are L- or D- pitched, with intercoil distances of 10-180 A° (Dekeyser). The possible role of these helices in determining the steric isomerism of natural products at prebiontic times awaits experimentation.

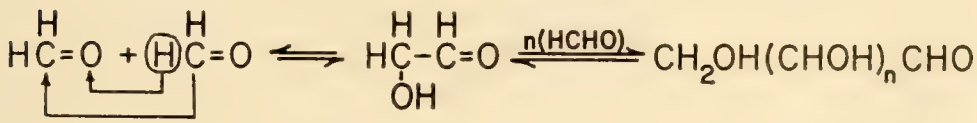
1957). This would explain selection of a non-racemic polymer, but does not account for the survival of the L- rather than the D- form.

B. *Synthesis of Peptides*

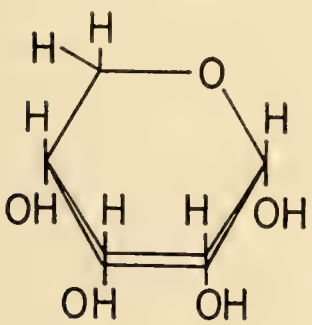


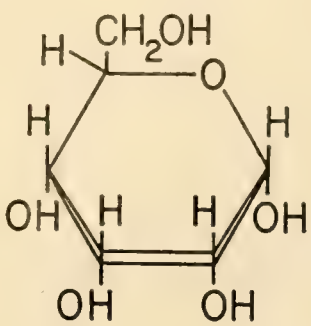
This reaction is endergonic, requiring about 3,000 calories. It is interesting to note that the energy required for peptide bond formation decreases with increasing chain length, representing a type of catalysis; that is, the product of the reaction favors the formation of more product from reactants. Furthermore, with increasing molecular size, the product begins to acquire properties not held by the reactants. Significant amounts of surface energies, van der Waal's forces and Heitler-London forces appear as the polymer approaches colloidal dimensions. The colloidal polymer is able to exert these forces on a reactant, catalyzing transformation of the reactant, or substrate.

II. *The Carbohydrates*



This reaction is exergonic, and will proceed rapidly in an alkaline medium. The reaction can be terminated by ring closures. The stability of the 5- and 6-membered structures undoubtedly favored the formation of the pentoses and hexoses as intermediates in the aldehyde polymerization.

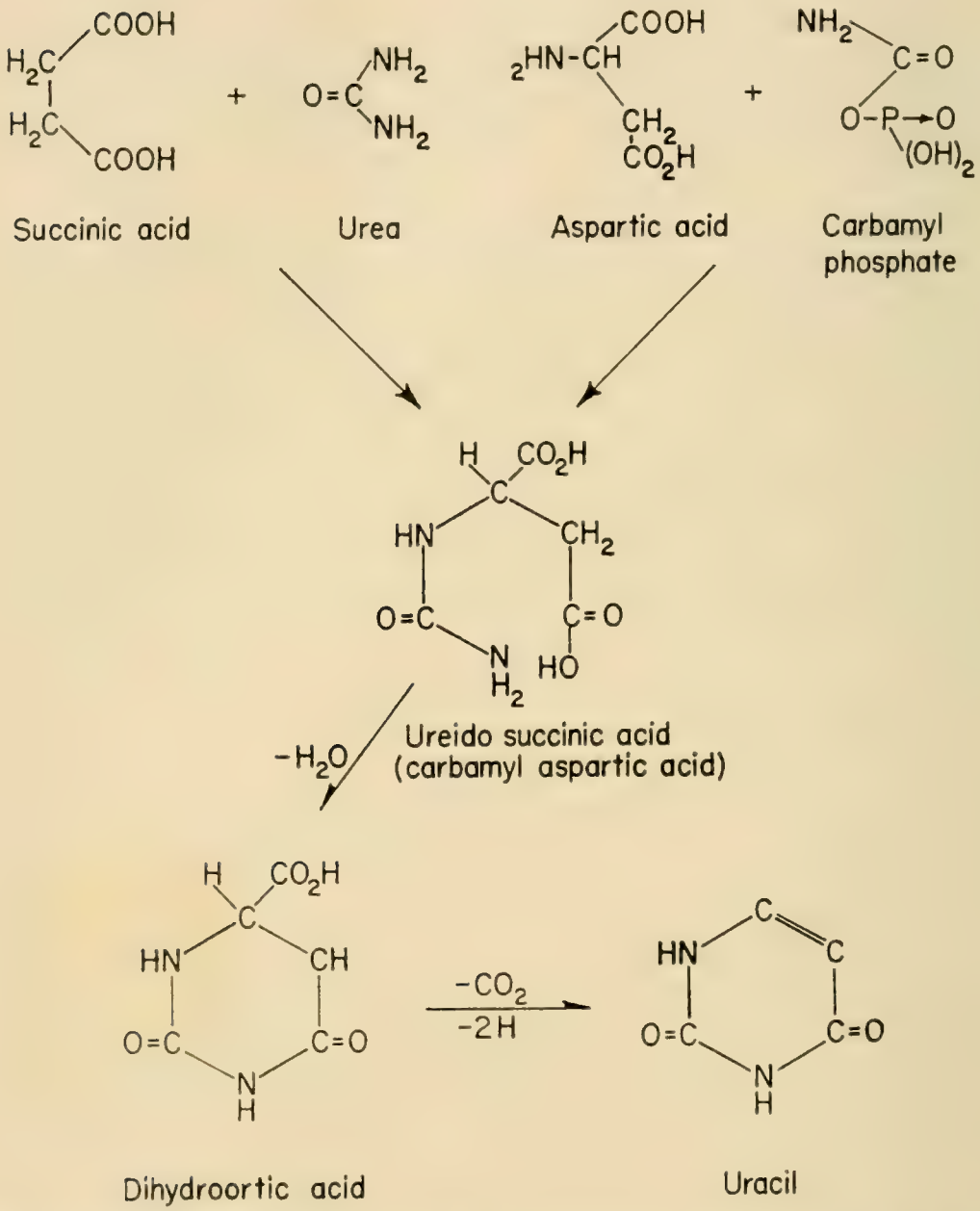




III. *The Nucleic Acids*

A. *The Purines and Pyrimidines:*

1. *Pyrimidine*



Succinic and aspartic acids as well as urea are produced in the Miller-Urey model. Carbamyl phosphate is readily formed from KCNO and K_2HPO_4. Again, the clay surface or a similar colloidal surface is proposed as the site of ureido succinate formation, with subsequent cyclization and decarboxylation. If Fox's thermal origin hypothesis is additionally invoked, the formation of uracil is more plausible yet. It is now known that uracil may undergo transformylation (with active "HCHO") to produce thymine, and amination to form cytosine.

2. *Purine*

The case for spontaneous generation of purine is not as strong as for the other species discussed. We can only speculate at this time that *in vitro* reactions similar to those found *in vivo* took place: HCHO + glycine + glutamine + aspartic acid + CO_2 + fumaric acid + ribose pyrophosphate → purine mono-nucleotide. It has been recently shown that -CN can condense to form adenine (Oro and Kimball, 1961).

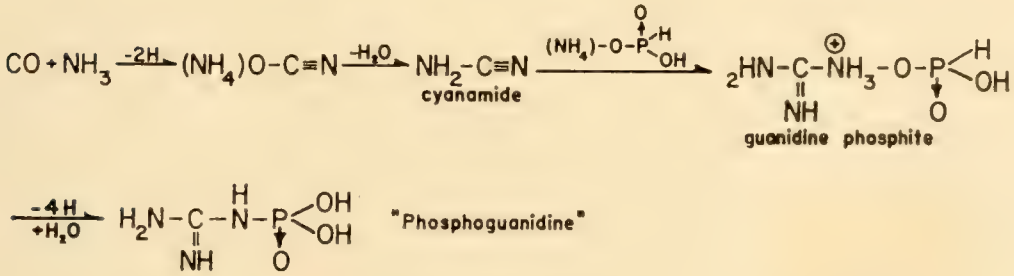
3. *Polynucleotides*

$$n(XDP) \rightleftharpoons (XMP)_n + nP_i$$

The Ochoa-Kornberg reaction is enzyme catalyzed, with $\Delta F < O$, indicating that under the appropriate conditions the reaction will occur "spontaneously."

IV. *The Energy-rich phosphate bond*

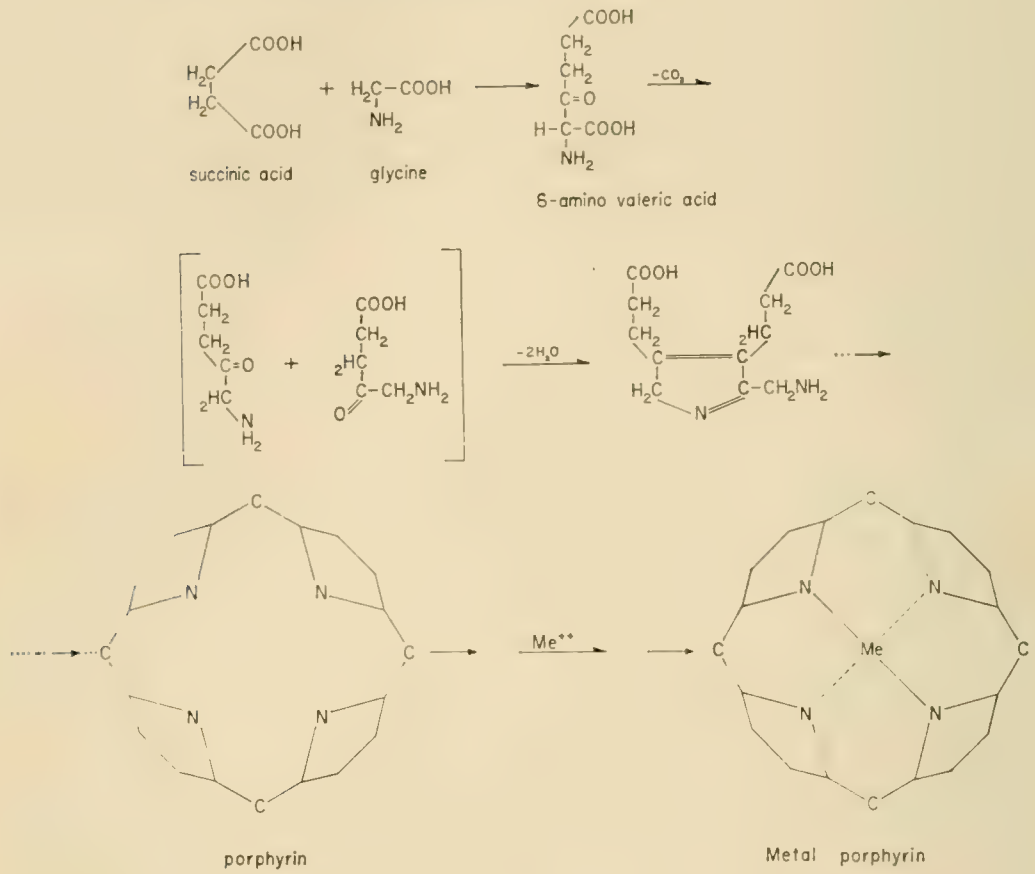
A. *Phosphoguanidine*



This series of reactions was proposed by Gulick (1955) and makes feasible the synthesis of the energy-rich bond in phosphoguanidine. Taken into account are the CO and the phosphate present in the primitive reducing atmosphere. The high solubility of the phosphite salts (as compared to phosphates such as the Ca, Ba and Mg salts) made them available for chemical reactions.

V. *Electron Transport Systems*

A. *The metallo-porphyrins*



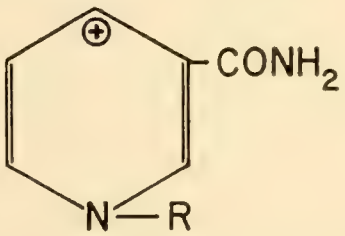
The iron ion serves as an electron shuttle:

$$Fe^{++} \underset{+e}{\overset{-e}{\rightleftharpoons}} Fe^{+++}$$

Coordinated with the porphyrin structure, the Fe ion is 10^3-fold more active in electron transfer than it is in aqueous solution. As Calvin (1959) points out, since electron transfer is involved in iron-porphyrin synthesis, as the iron-porphyrin structure was formed it increased the rate of its own formation by virtue of its greater catalytic effect. This positive-feedback mechanism, whereby the product of a reaction increases the rate of its synthesis from precursors, is comparable to the situation encountered in protein synthesis, in which, by virtue of its physical and chemical properties, the protein product catalyzes its own synthesis from amino acid and peptide precursors. The virtually equivalent structures of the iron porphyrins of catalase and the cytochromes and of the magnesium porphyrins of the chlorophylls indicates either common origin or an evolution of one porphyrin system from the other. It might be tempting to speculate that since the cytochromes function as electron donors to oxygen the cytochromes or catalase did not evolve

until photosynthesis had made oxygen available. In such case one would suppose a prior appearance of the chlorophyll pigments, which subsequently evolved to the iron porphyrin pigments. The presence of porphyrin pigments in some anaerobic bacteria challenges such a concept. On the other hand, the chemical evolution of a metallo-porphyrin pigment which emitted an electron on photoactivation created a situation in which an efficient terminal electron acceptor system would be a favored metabolic state. The iron porphyrin may well have evolved almost immediately after the magnesium porphyrins. With increased oxygen in the environment, aerobic systems evolved, losing in many instances the chlorophyll-like pigments.

B. *Pyridinium compounds*



The ubiquity of the pyridinium nucleotide makes it likely that this species represents one of the oldest electron transport systems. Although its chemical derivation is still obscure, the points of similarity between pyridinium nucleotide synthesis and the Kornberg polynucleotide synthesis cannot be overlooked as following a successfully established pathway.

Summary:

While the questions attending the chemical origin of a living system are as yet largely unanswered, a few pieces of information are now available which shed some light on the problem. We now are fairly certain of the fundamental constituents of all known life. We are constantly obtaining more information on the roles of proteins and nucleric acids, electron transport systems and energy-rich compounds in the maintenance of living cells. We have some insight into how these compounds can be made in the labortory, *in vitro*. It seems certain that the earliest living systems were anaerobic, later acquiring an ultra-violet-stable pigment which participated in photochemical reaction. Aerobiosis appeared on the scene at a more recent time. Bearing witness to this are the anaerobic chemotrophic bacteria, the anaerobic phototrophic bacteria, the aerobic phototrophs and the aerobic chemotrophs. There are as yet many un-

answered questions: Why the virtually exclusive occurrence of the L-isomer of amino acid residues in proteins, or of the D-isomer of ribose? What are the molecular advantages of these isomers, that they should represent the most favored state for cellular reactions? Did the protobiont have a multiplicity of enzyme-like systems, enabling it to compete more advantageously for the abundance of inorganic compounds and paucity of organic compounds in the medium, or did it possess but few catalytic systems with utilization of more complex organic compounds? Lithotrophy or Organotrophy? At what point did a membrane appear, permitting the establishment of a concentration gradient?

Enzymes are protein and proteins are required for nucleic acid synthesis. Yet nucleic acids are the sites of protein synthesis and carry the hereditary information. Did proteins antecede nucleic acids, or were nucleic acids the first to appear? Did the reactions occur on clays on which molecules had been adsorbed, or were the Oparin coacervates the protobiontic precursor?

Some of the questions can never be answered, but many will be resolved in the laboratory. The solution to the chemical basis for the origin of life remains one of the most exciting challenges to scientific imagination.

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Biochemical Evolution

PHILIP NEWMARK [1]

Biochemistry formulates the phenomena of biology in chemical terms. The tools of the present-day biochemist enable him to examine at the molecular level both structure and function in biological systems. In the past ten years, especially, the biochemist has been much concerned with the properties and reactions of the biological macromolecules, particularly the proteins and nucleic acids. In some respects the tremendous stimulus that contemporary biochemistry has thereby given to biology parallels the stimulus provided by Darwin's work a century ago.

Although we are far from fulfilling J. B. S. Haldane's prediction (1937) of some twenty years ago that ". . . our final theory of evolution will see it largely as a biochemical process," the advances in biochemistry during the past few years make it feasible now for us to begin to document this statement.

The fact, among others, that all living things on the earth together comprise only 0.00003 percent of the total mass of the earth (Mason, 1958) leads us to an essentially deterministic view of living matter. Although we must admit with Pirie (1957) that life could exist in ways other than those with which we are familiar (especially on other planets in the universe), the essential correctness of Henderson's (1958) thesis that the relative abundance and unique properties of the chemical elements on the earth are of central importance in all living processes remains unshaken. One example will illustrate this point.

The porphyrin ring systems of the chlorophyll and cytochrome molecules (Fig. 1) possess, respectively, unique chemical properties essential for the capture of light energy from the sun and for the conversion of this energy into the chemical bond energy required

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for the performance of work by all living systems (Kamen, 1958; Lemberg and Legge, 1949). Of the seven most abundant metals in the earth's crust, only magnesium and iron are found complexed

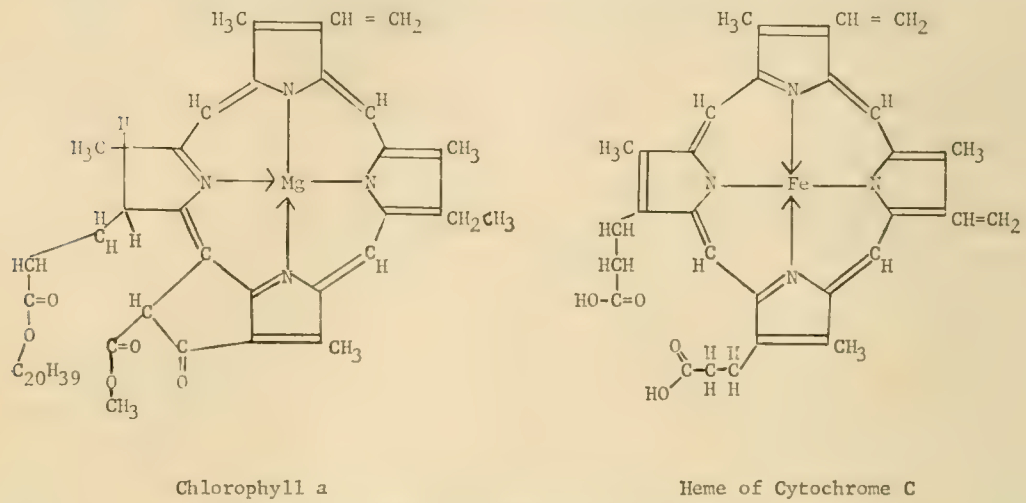


FIG. 1.—Porphyrins

in the porphyrin rings of chlorophyll and the cytochromes, respectively. The other metals—aluminum, titanium, potassium, sodium and calcium—are chemically unacceptable; they cannot form complexes with the porphyrin rings that possess the required chemical characteristics. Only a relatively light metal like magnesium gives a photoactive complex with porphyrin. Porphyrin complexes of the heavy metals like iron or copper are not photoactive (Gaffron, 1957).

As a consequence of this view we must conclude that were the evolution of living matter on a terrestrial planet such as the earth to be repeated, at a comparable time after the start of the process we would find life much as it exists on earth today.

The previous speaker in this series dealt with what may be called chemical evolution—the series of changes leading from inorganic compounds to organic compounds of sufficient complexity and organization to be called "living." In discussing biochemical evolution I shall be concerned primarily with those molecular changes occurring in living matter with the passage of time that produced the existing morphological and physiological differences among the various organisms inhabiting the earth.

Molecules in Living Matter

After two billion years of life on this planet, what kinds of molecules are found in living things? We are at once impressed with the conservatism inherent in the basic biochemical similarities among all forms of life.

Subunit Molecules. First let us consider the groups of relatively simple organic molecules that are universally distributed and are the principal building blocks of the functioning macromolecules. Two groups, the monosaccharides, or simple sugars, and the fatty or carboxylic acids (Fig. 2), are composed of carbon, hydrogen and oxygen. Whereas there is considerable diversity in the kinds of sugars and fatty acids that are found in the polysaccharides and complex lipid structural components of living cells, there is a remarkable unity in those compounds that are involved in the energy producing reactions of metabolism. For example, the six-carbon sugar, glucose, and the two-carbon fatty acid, acetic acid, are used as metabolic fuel almost universally by the predominant living species. The carbon skeletons of these two compounds are oxidized eventually to carbon dioxide and water, and the energy released

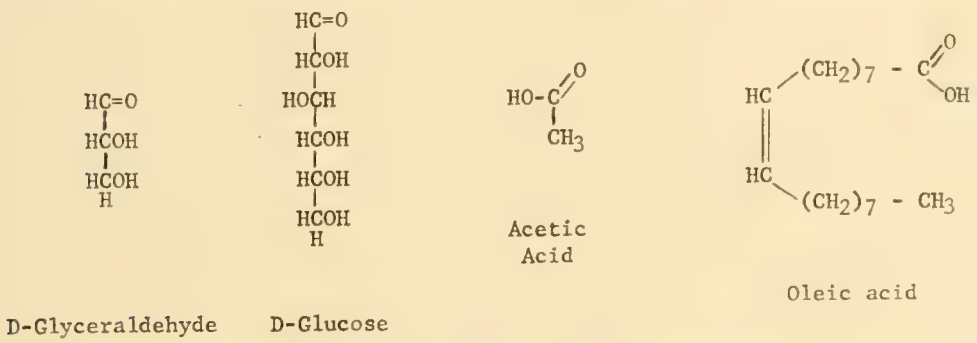


FIG. 2.—Simple Sugars and Fatty Acids

during this combustion process is conserved in part for synthetic purposes in the form of reactive anhydride chemical bonds (see section on Energy Transferring Molecules).

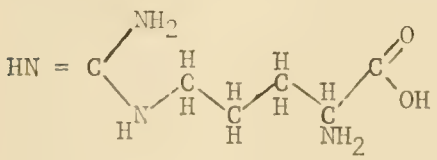
A third group of building blocks, the amino acids, contain nitrogen and also sulfur in some cases (Fig. 3). Some twenty amino acids appear in varying proportions in the different proteins found in living cells. However, the proteins of some organisms are distinguished by containing one or two additional amino acids, or by having an unusually high percentage of one or several amino acids.

The fourth group of monomeric molecules, the pyrimidine and purine mononucleotides (Fig. 4), contain still another element, phosphorus, as well as the five-carbon monosaccharides, ribose or 2-deoxyribose. The nitrogen in these molecules is all in the heterocyclic pyrimidine and purine moieties. All nucleic acids are composed of these mononucleotides in varying proportions.

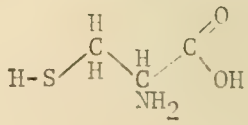
Energy Transferring Molecules. As with the energy fuels we find a conspicuous unity in the kinds of molecules functioning in

energy transfer in living cells (Fig. 5). Note that these compounds are very closely related in structure to the mononucleotide subunits (see Fig. 4). The energy reservoir in the pyrophosphate bonds of adenosine triphosphate (ATP) is utilized to drive most of the living cell's synthetic reactions. Molecules like diphosphopyridine nucleotide (DPN) are called coenzymes. They function as electron carriers in energy yielding oxidation reactions and in energy requiring reduction reactions. A number of the vitamins required in the diets of higher animals are components of the coenzymes. In DPN the pyridine ring portion of the molecule is the vitamin nicotinamide (niacin). DPN-like coenzymes are closely associated through relatively weak secondary bonds with the protein portions of the enzymes that catalyze the oxidation-reduction reactions.

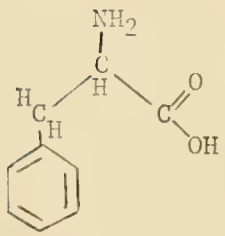
I indicated earlier that the porphyrins (Fig. 1) also play a vital role in energy transfer, but in order to function in this way they have to be bound through covalent bonds to special proteins, the cytochromes. The porphyrins provide many examples of biochemical unity as well as diversity in different biological forms, of



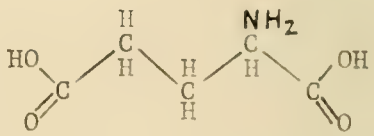
Arginine



Cysteine



Phenylalanine



Glutamic acid

FIG. 3.—Amino Acids

the conservatism as contrasted with the innovations in structure that have been an essential feature of the evolutionary process (Kamen, 1958; Lemberg and Legge, 1949; Gaffron, 1957).

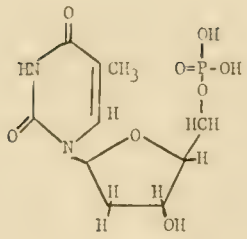
Chemical Bonds. The various subunit molecules discussed previously are usually present in living cells in the form of macromolecules. The chemical operation common to the synthesis of all of the macromolecules is the elimination of a molecule of water for every covalent bond formed between two of the monomeric units.

In polysaccharides a glycosidic bond is formed when the aldehydic or ketonic group of one monosaccharide interacts with one of the hydroxyl groups on the second monosaccharide. The amino acids in proteins are linked by amide bonds between the α-amino group of one amino acid and the carboxyl group of the second. Mononucleotides in the nucleic acids are joined by phosphodiester bonds between the ribose or deoxyriboses moieties. In the lipids (not usually considered macromolecules) the fatty acids are esterfied with the glycerol or other alcohol moiety; or, as in the steroids, complex fused ring molecules resembling phenanthrene are built up by the condensation of many molecules of acetic acid (Fig. 2).

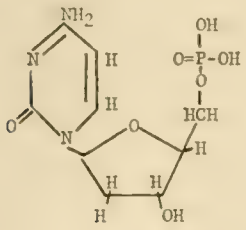
Optical Activity and Stereospecificity. One of the most strikingly invariant features of the molecules in living systems is their isomeric specificity. Almost all of the commonly found sugars belong to the D-series of optical isomers; they are directly related to D-glyceraldehyde (Fig. 2). It is solely the difference in stereochemical configuration around the glycosidic carbon of the D-glucose subunit that produces the difference in macromolecular architecture between the fibrous cellulose and the amorphous starch. In the mononucleotide subunits of the nucleic acids (or indeed in the energy transferring molecules ATP and DPN (Figs. 4, 5) the glycosidic bond between the ribose or deoxyribose and pyrimidine or purine moieties is always in the beta configuration. And the amino acids in proteins are always found as the L-isomers (Fig. 3).

Macromolecules. It is in the biological macromolecules—in the polysaccharides, nucleic acids and proteins—that we find the most abundant examples of the results of evolutionary variation in chemical composition, structure and function, of analogy and homology at the molecular level. A number of experimental techniques for studying these variations are available to the biochemist. These include determination of chemical constitution, physico-chemical properties, immunochemical reactivity and biological or enzymatic activity. I shall illustrate with examples of proteins only because they have been the most intensively studied and because they appear to show the greatest spectrum of individualities in structure and function.

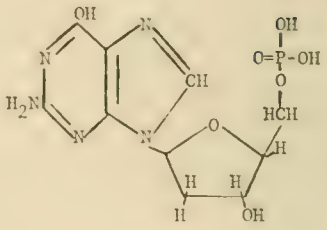
Historically, the immunological technique was one of the first to be employed in assessing the relationships among the proteins of various animal species. In a classic study made over fifty years ago, Nuttall (1904), at Cambridge University in England, compared the precipitates obtained when blood sera from a variety of animals



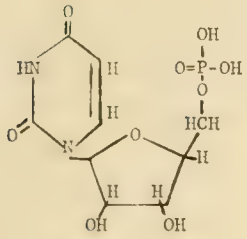
Thymidylic acid



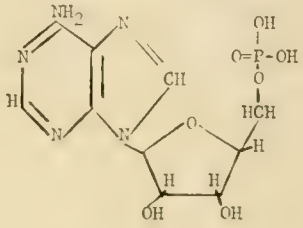
Deoxycytidylic acid



Deoxyguanylic acid



Uridylic acid



Adenylic acid

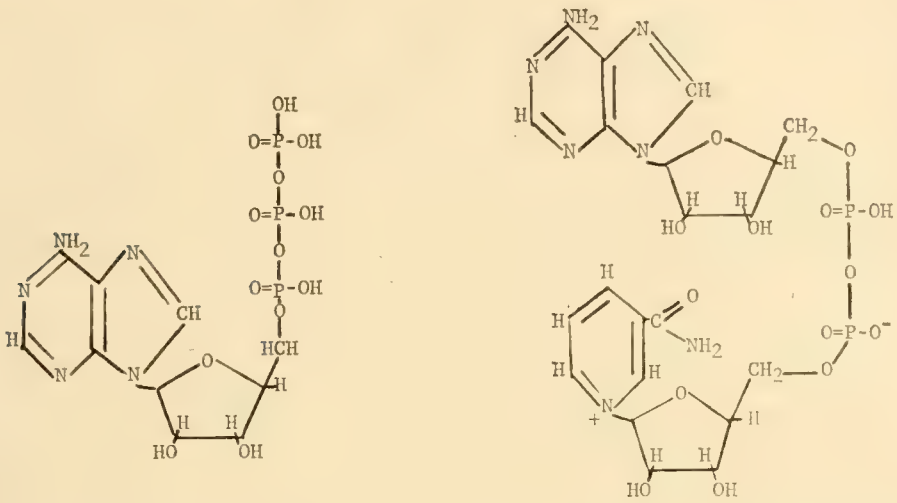
FIG. 4.—Pyrimidine and Purine Mononucleotides

were mixed with anti-human serum obtained from rabbits that had been immunized by periodic injections of the human serum. Some of his results are summarized in Table I. It is evident that the

TABLE I.—Immunological Cross Reactions in Blood Serum Proteins

Animal Serum	Percentage Precipitated by Rabbit Antibodies to Human Serum
Primates	
Human	100
Chimpanzee	130
Gorilla	64
Mandrill	42
Spider monkey	29
Carnivores	
Dog	3
Cat	3
Tiger	2
Ungulates	
Ox	10
Sheep	10
Reindeer	7
Goat	2
Horse	2
Swine	0
Rodents	
Guinea pig	0
Rabbit	0
Marsupials	
Wallaby	0
Kangaroo	0

greatest amount of cross-species interaction occurred with the sera from the most closely related phylogenetic group, the other primates. Landsteiner (1936) studied the likenesses and differences among the blood sera proteins in man, and from this derived the universally used four main blood group types. Dr. Charles Leone (1947) of



Adenosine triphosphate (ATP)

Diphosphopyridine Nucleotide (DPN)
or Nicotinamide adenine dinucleotide (NAD)

FIG. 5.—Energy Transferring Molecules

the University of Kansas used this approach to study the relationships among a large group of invertebrates.

With the development during the past decade of improved chromatographic techniques for separating amino acids, and of powerful chemical and enzymatic methods for determining the sequence of amino acids in partially hydrolyzed proteins (the peptide fragments), it has become feasible to determine the complete amino acid sequence in proteins. To date this has been achieved for several polypeptide hormones: insulin, ACTH (adrenocorticotropic hormone), vasopressin and oxytocin.[2]

In figure 6 we have examples of the types of differences in amino acid composition that have been observed in the same hormones isolated from different species of animals. Note that beef and pig insulin differ only in two amino acids, and that the vasopressins differ in a single amino acid. In both instances, though, the same chemical type of amino acid is involved in the substitution, viz. both lysine and arginine (in the vasopressins) are basic amino acids, and both valine and isoleucine (in the insulins) are neutral amino

2. In the months since this talk was given the complete amino acid sequences have been deduced for several proteins in the 13,000 to 18,000 molecular weight range. These include the enzymes ribonuclease and mammalian cytochrome c, and the protein subunit of tobacco mosaic virus.

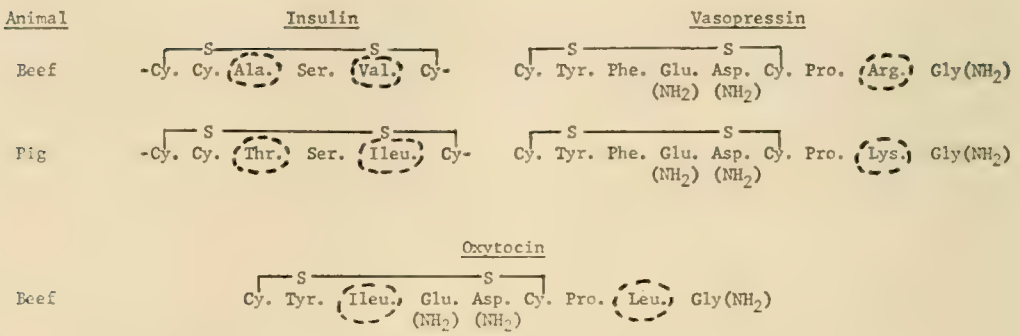
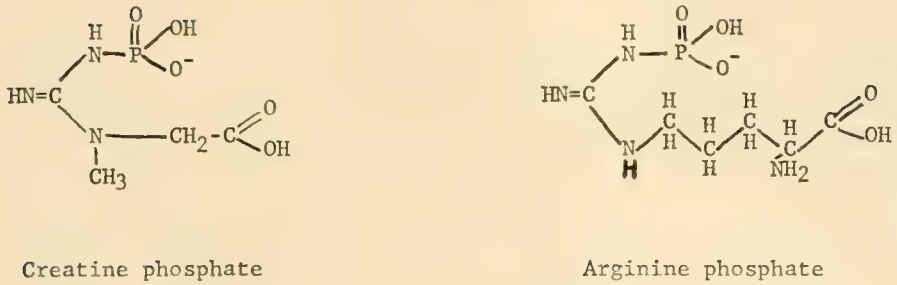


FIG. 6.—Amino Acid Sequences in Polypeptide Hormones

acids. Now note that vasopressin and oxytocin, which have markedly different physiological properties, differ only in two amino acids. In oxytocin the neutral aliphatic amino acids, isoleucine and leucine, are substituted for the neutral, aromatic and basic amino acids, phenlyalanine (or lysine) of vasopressin.

One might ask whether proteins have always been as they are now, and whether the evolutionary process has always involved the same complement of amino acids. The answer would appear to be, yes. In a beautiful series of studies, Abelson and his colleagues at the Geophysical Laboratory of the Carnegie Institution of Washington have recently detected and identified about eight common amino acids from fossils of a variety of geologic ages (Abelson, 1957). The oldest of these fossils—identified as blue-green algae and molds—were obtained from pre-Cambrian gun flint stone on the northern shore of Lake Ontario. Their estimated age is one to two billion years. At first thought it might seem incredible for organic compounds like amino acids to survive for a billion years, yet by examining the rates of degradation at 180° to 450° C. for those amino acids found in the fossils, Abelson and his colleagues showed that it was reasonable to expect about half of the original amounts of these amino acids to survive for three billion years at room temperatures. And as might now be anticipated those amino acids that were degraded most rapidly in the elevated temperature experiments were not found in the fossils. It would appear that—at least during the billion or two years of the fossil record—nature has been obtaining all the diverse proteins from the same group of 20 to 25 amino acids.

The physico-chemical characteristics (such as migration rate in an electrical field) of the hemoglobins obtained from humans having the genetically-linked sickle cell anemias differ significantly from the characteristics of the hemoglobins from normal individuals. Similar differences have been observed between fetal and adult



Creatine phosphate Arginine phosphate

FIG. 7.—Phosphagens

hemoglobins in man. These kinds of differences have been correlated with slight differences in amino acid composition (Itano, 1957).[3]

Molecular Evolution in Action

All the examples of protein singularity and heterogeneity show us only the results of the evolutionary process. Are there any more direct examples of the process at work? Are there any examples at the molecular level of ontogeny recapitulating phylogeny? Yes, I shall mention several (from Wald, 1952; Florkin, 1949).

Phosphagens are phosphorus containing amino acid derivatives found in muscles (Fig. 7). They serve as reservoirs of chemical bond energy. The energy of their phosphoamide bonds is exchangeable through enzymatic transfer of the phosphate group to form the terminal pyrophosphate bonds of ATP (see Fig. 5). Arginine phosphate is characteristically found in invertebrate muscles, whereas creatine phosphate appears in vertebrate muscles. Some echinoderms contain both phosphagens, whereas others of this phylogenetic group contain one or the other. The muscles of the shark embryo contain arginine phosphate, while those of the adult shark contain creatine phosphate.

Evolutionary changes in enzyme systems are very well illustrated from studies—largely by the English biochemists (Baldwin, 1948)—on the patterns of catabolism of nitrogen containing compounds in vertebrates. The chemical form of the final excretory products (Fig. 8) is always well adapted to the environment in which the animal lives. In fish the principal excretory product is ammonia, which is very soluble in water. Amphibia and turtles excrete principally urea, whereas birds excrete the highly insoluble uric acid.

3. In the past few years Kaplan and his colleagues (Kaplan et al., 1960) have been studying the possible evolutionary relationships among dehydrogenase enzymes possessing the same catalytic function but derived from a wide variety of animals and microorganisms, and from different tissues in the same organism. By examining the effects on catalytic rate of varying substrate concentrations, and by using a series of coenzyme (DPN) analogs, they detected marked heterogeneity in the enzymes. This technique promises to be very useful for comparative biochemical studies.

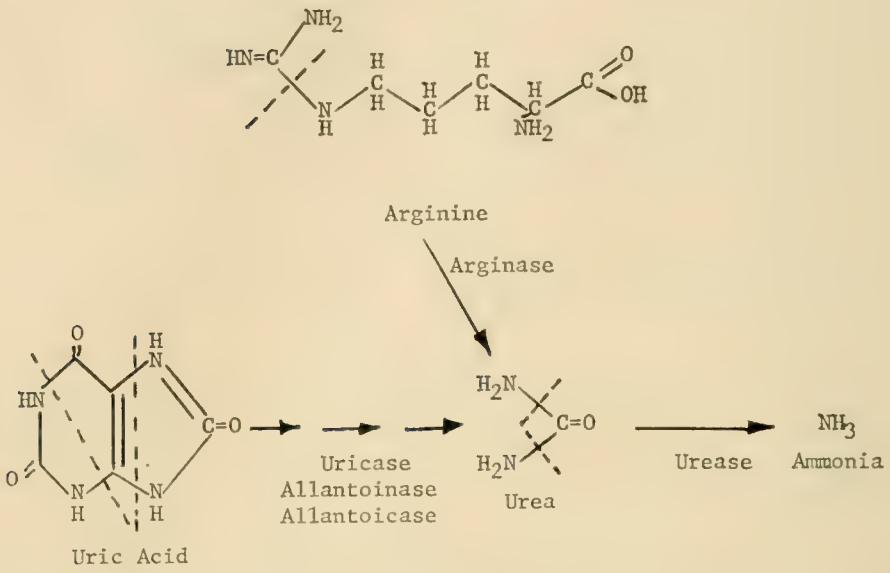


FIG. 8.—Nitrogen Excretion Pathways in Animals

A comparable series of changes occur in invertebrates. Marine crustacea contain the enzymes required to degrade uric acid to ammonia, whereas the enzymes are absent in the insects.

An ontogenetic change that parallels the phylogenetic change is observed in the metamorphosis of the frog (Munro, 1939; Needham, 1942). Ammonia is the sole nitrogenous excretory product in the tadpole. Urea appears coincident with emergence of the fore-limbs, atrophy of the tail and widening of the mouth; and the arginase level in the liver increases at the same time (arginase is the enzyme that catalyzes the hydrolysis of arginine to ornithine and urea.) During embryonic development in the chick or duck, ammonia is in highest concentration at about the fourth day of embryonic life and declines rapidly in amount thereafter. Urea first appears at low levels about the third day, increases to a maximum about the ninth day, then declines. The adult excretory product, uric acid, first appears after urea (about the fifth day) but does not become the principal nitrogenous excretory product until the eleventh day, after the level of urea has begun to decline.

One last example: In frog metamorphosis it has been shown, largely by Wald and his colleagues (Wald, 1945-1946), that the types of vitamin A visual pigments in the eyes of the tadpole are the same as those found in fish that spawn in fresh water. By contrast, the visual pigments in the eyes of the adult frog are the same as those found in other land vertebrates.

Mechanism of Biochemical Evolution

My talk till now has been discursive. I have not yet offered any explanations on a molecular basis of how the observed evolutionary changes occur.[4] For this we must turn to genetics, specifically to biochemical genetics. In recognition of pioneering developments in this field, Beadle, Tatum and Lederberg were recently awarded the Nobel Prize in Medicine. The most exciting recent advances have come from work on viruses.

The simplest plant and animal viruses consist of only nucleic acid and protein, yet they possess two of the primary attributes of living matter: They can induce their own replication in suitable host cells, and they can mutate.

In a classic study about 15 years ago, Avery, MacLeod and McCarty (1944), at the Rockefeller Institute, reported that DNA (deoxyribonucleic acid) isolated from one strain of *Pneumococcus* bacteria could produce a hereditable transformation in the growth characteristics and virulence of a second strain of *Pneumococcus*. Other types of transformations have since been observed with other bacteria. In 1952, Hershey and Chase, from the Cold Spring Harbor Biological Laboratory, demonstrated clearly that the DNA moiety of a bacterial virus (bacteriophage) was the infectious entity that entered the bacterial host. The role of the protein portion of the bacteriophage was to protect the infectious DNA and to mediate the attachment and attack on the host cell wall. Three years ago Fraenkel-Conrat and Williams (1955), from the Virus Laboratory of the University of California in Berkeley, proved conclusively that the infectious principle of tobacco mosaic virus was the ribonucleic acid (RNA) moiety. More recently the isolated RNA's of several plant and animal viruses, completely free of their protein coats, were found to be capable of infecting susceptible host cells. The infected hosts produced whole virus containing both nucleic and protein portions. It has also been shown that changes in viral nucleic acid structure induced by ultraviolet and X-ray irradiation, by incorporation into the nucleic acids of unnatural analogs of the purine and pyrimidine base components (see Fig. 4), or by reaction of the nucleic acids with chemical mutagens like nitrous acid, can be perpetuated as hereditable genetic changes both in the virus structure and in its biological properties.

The accumulated experimental evidence points in the same direction. The storehouse of genetic information and the raw ma-

4. An excellent recent exposition of material covered in this section is found in the small monograph by C. B. Anfinsen, The Molecular Basis of Evolution, John Wiley and Sons, New York, N. Y., 1959.

terial of evolutionary development is nucleic acid. In cellular organisms the DNA of the nucleus appears to be the principal director of the cell's metabolic and developmental potential. Since all DNA molecules are long, linear polymers composed almost entirely of the same four deoxyribonucleotides (Fig. 4), it appears most reasonable that the genetic information is coded in the linear sequences of the nucleotides. It follows that mutations can arise when the sequences of the nucleotides are altered by a reshuffling of the existing sequences, or by loss or change of one or more nucleotides.

Thus, the DNA of the nuclei of the germ cells of higher forms appears to have the role of "queen bee." For humans it is this DNA that must be so zealously guarded for the future of the species. In the long view, if man is to live out his evolutionary life span on this earth, it is this genetic material that must be protected from those deleterious environmental hazards that man himself makes—the radiations produced from peaceful as well as potential wartime uses of nuclear energy.

This, then, is the message of the biological molecules, "Guard the nucleic acids if you value life, because that's the stuff life's conserved in."

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Morphology and Evolution—The Concept of Homology

BYRON S. WENGER [1]

A few moments reflection are all that is required to convince one of the futility of any attempt to give even a smattering of the information relating morphology and evolution since essentially all of the earlier and most of the recent information pertaining to evolution is derived from morphological studies. For this reason the present seminar will be limited to a discussion of a morphological concept pertaining to the theory of evolution. The concept to be considered is that of homology.

Apology is definitely in order to a number of authors, only a few of whom can be mentioned here, who have presented excellent discussions of this subject. Already in 1894, E. B. Wilson (1896) drew essentially the same conclusion that will be drawn here today—all that will be added will be some more modern evidence and interpretations. More recently, Oppenheimer (1940) has discussed many of the problems in her excellent review of the germ layer concept, and Zangerl (1948) has discussed homology from the point of view of methodology in morphological research. Finally, particular recommendation should be made for the discussion of the subject by de Beer (1958) in his book on recapitulation, a concept which is in many ways related to that of homology.[2]

With all the excellent papers that are already available, the main justification for the present discussion is to bring the subject into focus with the current series, and to add a little personal interpretation.

While Richard Owen is credited with having been the first to use the term homology in its present sense, recognition of the same structure in different organisms had certainly been made well be-

1. Associate Professor of Anatomy, The University of Kansas. Seminar presented on 17 December 1958.

2. A paper by Källén (1959) which appeared since this paper was presented should be mentioned as the author makes some similar points.

fore his time. Aristotle, in his classification of beings, necessarily recognized corresponding structures in different organisms, and early in the sixteenth century Leonardo da Vinci correctly interpreted correspondence of parts between the human leg and the hind leg of the horse, while Belon made a surprisingly sophisticated comparison between individual bones of bird and human skeletons (Singer, 1950). Certainly success at rational classification such as that achieved by Linnaeus and those who followed had to be predicated upon recognition of varying degrees of sameness between different forms.

With the rise of comparative anatomy, such comparison became commonplace, but it was Owen who formalized it with the term homology and shortly thereafter expanded the concept to include three types of homology, general, special and serial. These were defined by Owen (1848, p. 7) as follows: "Homology: The same organ in different animals under every variety of form and function." With the recognition of the three types of homology, this definition, *i. e.*, dealing with comparison of an organ between different animals, becomes the definition of "*special homology.*" If, on the other hand, the comparison is made between a structure and a hypothetical ideal type, demonstration of sameness indicates a case of "*general homology.*" Finally, if the sameness of structural patterns is demonstrated between successive parts of the same animal, *e. g.*, the fore and hind limbs of tetrapods, the latter is considered to be an example of "*serial homology.*"

The recognition of change in homologous structures with time was one of the important lines of evidence leading to formulation of the theory of evolution. The latter in turn has added enormously to the concept of homology, giving it meaning in terms of genetic continuity through evolution rather than in terms of relationship to some idealized type. In the most generally accepted interpretation of the concept, homology is determined by comparing structures found in different organisms. Such demonstration of homology is taken as evidence of genetic affinity of the organisms, and degree of homology is considered as one index of genetic relationship. In this sense it is impossible to avoid either a genetic implication in the concept or recognition of genetic continuity through evolution as the basis for homologies recognized in morphological studies. Thus Owen's "special homology" becomes the main sense in which the term homology is used, while general de-emphasis of the archetype as the basis for comparison in comparative anatomy has left little use for Owen's term, "general homology." A

strong implication of "general homology" is, however, present in the interpretation by some morphologists (see Zangerl, 1948) of homology as determined only by comparison with an arbitrarily constructed hypothetical type and carrying no implication of genetic relationship or evolutionary change.

Well before the appearance of Owen's papers on homology, the value of embryological investigation in determination of correspondence of parts had been recognized by comparative anatomists, and Owen himself used such material in his studies on homologies of the vertebrate skull. Following Owen, a great deal of use was made of embryological evidence to determine homology. This approach, especially in the hands of men like T. H. Huxley, turned out to be so fruitful that sameness of embryological development became generally accepted as another necessary criterion of homology and is included in most definitions currently encountered.

One can hardly object to the embryological criterion in general; it would be difficult to imagine two structures homologous by the usual morphological criteria that do not have some developmental patterns in common. Legitimate objections have, however, been raised to attempts at extending this criterion of homology to early embryonic primordia. This practice, along with extrapolation of the concept of recapitulation was carried to an absurd extreme in the latter part of the 19th century, particularly by Haeckel and his followers.

It was apparently in reaction to this trend that E. B. Wilson (1896) presented his paper at Woods Hole, emphasizing the pitfalls inherent in attempts to use correspondence of early embryonic origin as a necessary criterion of homology. His point of view (p. 114): ". . . it is the prospective and not the retrospective aspect of development that is decisive. . . . Comparative anatomy, not comparative embryology, is the primary standard for the study of homologies, and hence of genealogical descent."

In spite of the admonition by Wilson, the practical successes of embryological investigation in clarifying problems of homology have kept it in the foreground as one of the important, if not the most important, criteria of homology. With this background, it is not surprising that the great strides made in experimental embryology during the first half of the present century should have led a number of workers to look to this field for a more definitive determination of homology. Holtfreter (1936) proposed similarity of inductive relationships as a criterion of homology, pointing out as an advantage the possibility of experimental confirmation. Al-

though this criterion is valid in many cases, as for example in the apparently universal induction of medullary plate by chordamesoderm in the vertebrates, it has not justified the hopes once held for it. On the contrary, a large volume of experimental data has accumulated demonstrating conclusively that homologous organs are not always induced by comparable structures.

Only a very few of the pertinent experiments can be cited here. The classical experiments on development of the lens of the eye (Willier, Weiss and Hamburger, 1956, p. 402 ff.), which are almost universally cited, should be mentioned. It is well known that in a wide variety of vertebrates most of the ectoderm of the body is capable at some time of forming a lens under the inductive influence of the optic vesicle. Furthermore, in some salamanders even the differentiated margin of the optic cup is capable of producing a lens if the normal lens is removed. On the other hand, while certain species of frogs of the genus *Rana*, like most vertebrates, normally require induction by the optic vesicle for development of the lens to take place, in other members of the same genus differentiation can take place in the total absence of the optic vesicle. Such lenses are all homologous in any reasonable sense of the concept.

Another very fruitful experimental approach to the problem is that of xenoplastic transplantation used in the classic experiment of Spemann and Schotté (1932). In this experiment, ectoderm representing prospective flank epidermis of a urodele embryo was grafted over the prospective mouth area of an embryo belonging to an entirely different order, Anura. The reciprocal experiment was also performed. Results of these experiments are clear cut: belly skin transplanted to the mouth region of another embryo differentiates into typical mouth structures, but these structures *always bear the characteristics of donor mouth parts; i. e.*, salamander belly skin transplanted to the frog jaw region differentiates typical salamander teeth while frog belly skin transplanted to the salamander jaw region differentiates into the horny jaw plates characteristic of frog larvae. Baltzer (1950, 1952) and his students have repeated and expanded this type of experiment in a beautifully executed series designed to elucidate questions of homology. Though these experiments are more elaborate than those cited above, the results are essentially the same, and Baltzer concludes that three grades of homology may be recognized between structures differentiating under the influence of a given inductor. First is the case of complete homology, as exemplified by the inner ear differentiated from prospective frog epidermis grafted to the ear

region of a salamander. This ear is considered to be completely homologous to the normal ear of the salamander. Incidentally, even though functional in the salamander host the grafted ear retains those detailed characteristics by which the frog ear differs from that of the salamander. Second, Baltzer recognizes cases of partial homology between the larval "suckers" of anuran embryos and "balancers" of certain urodele embryos. Finally, the third degree of homology is illustrated by the horny "teeth" of the frog larva cited above, for which no recognizable homologue can be found in the salamander.

It is interesting to note that degrees of homology are recognized also by investigators who rely wholly upon morphological evidence. Further, it is highly probable that a purely morphological investigation of Baltzer's material would lead to essentially the same conclusions as to the extent of homology of these structures.

Briefly, we may conclude that similarity of inductive relationships as well as location of structures in the early embryo can be eliminated as necessary criteria of homology since homologous structures can differentiate under the influence of different inductors in different animals, and, conversely, the same inductor can initiate differentiation of very different (non-homologous) structures. The experiments cited above do, however, introduce a new point of view in the study of the development of homologous structures.

It is apparent that while in normal development of different organisms (as well as under varying experimental conditions) a given structure may arise from different regions of the embryo or under the influence of different inductors, *once it is determined, by whatever means, to develop into that structure it will go ahead and differentiate the characteristics peculiar to that structure in the particular species.* It is these characteristics that are of value in deciding the homologies of the structure and, *furthermore, it is the developmental processes leading directly to expression of these characteristics that are useful in determining homology.*

A similar conclusion can probably be drawn with regard to Owen's third type of homology—"serial homology." This refers to similar patterns of structures in the body of the same animal, *e. g.*, the common pattern of appendages in successive segments of arthropods or the fore and hind limbs of vertebrates. While the best examples of serial homology can probably be found in invertebrates, the following example is selected from vertebrate material because of personal familiarity.

Balinsky (1933, 1935) has shown that supernumerary limbs can be induced in the salamander embryo by non-specific stimulation from one of a number of materials implanted in the flank at an appropriate stage of development. The responsive area is a band along the side of the embryo extending from the normal forelimb area to the normal hind limb level. As the experiment is performed at successively more caudal levels, the frequency of forelimb inductions falls off, and a point is reached where hind limb inductions appear, increasing in frequency as the experiment is performed closer to the normal hind limb level. The point to be made is that over a distance of several segments either forelimbs or hindlimbs can be induced. Unfortunately these induced limbs are frequently imperfect and their positive identification as fore, hind or intermediate may be open to some question. However, the induced limbs can be identified clearly as either fore or hind limbs in a sufficent number of cases to warrant the conclusion that the genetic endowment of these animals contains "blueprints" for forelimbs and for hindlimbs—not for an indifferent form to be modified by its position in the embryo.

A similar conclusion may be drawn from the experience of Holtfreter (1955), in which induced tails have been observed to regenerate limbs. Obviously, we cannot conclude that these tails are homologous to limbs—only that the particular circumstances of the experiment were such as to call forth expression of the potentialities of the cells for limb development rather than those for tail development.

Since the final pattern of an organ is determined neither by the inducing system, which merely chooses one among a number of possible directions for development, nor by special properties of the particular group of reacting cells, which prior to determination are still capable of differentiating in any of a number of different directions, it (the final pattern) must be determined by other factors. These factors are *included along with many alternative pattern determinants in the total genetic make-up of all parts of the embryo capable of such differentiation.*[3]

In spite of the contention of some workers (Zangerl, 1948) that common descent is not necessarily implicit in our concept of homology, it would be difficult to find a case of the latter that could not best be interpreted in terms of common genetic background. In the cases cited by Zangerl, the apparently independent appearance

3. The total genetic pattern has been specified to include cytoplasmic as well as nuclear genetic factors and so avoids digression into this area.

of similar structures in related species of fish, the phenomena can probably best be interpreted in terms of similar selective (or other evolutionary) factors acting upon a genetic pattern common to all members of the group. De Beer (1958, p. 146) mentions this type of phenomenon, to which the term "latent homology" is applied.

In view of the above implication of common ultimate genetic background of homologous structures and the well recognized dependence of morphological characters upon genetic determinants, one might be led to expect that the ultimate decision regarding homology might rest upon demonstration of control by similar (homologous) genes. Although at present homology of genes and chromosomes can be demonstrated only in closely related species, the far off day when all genetic information might be decoded could conceivably bring the possibility of deciding homologies on the basis of common genetic control.

While a decision regarding the above suggestion cannot be made at the present time, examination of such information as is currently available would tend to indicate that realization to be unlikely. In his discussion of this matter de Beer cites the case of an eyeless mutant in *Drosophila*. Suitable selection for an alternative gene pattern results in normal expression of the eyes even in the continued presence of the eyeless gene. Certainly this "reconstituted" eye is homologous to the eye of a normal individual.

Although this experiment deals with only one or a few among probably many thousand of genes controlling various aspects of eye development, the principle can be extended to a hypothetical situation. Regardless of the total number of genes involved, over the long period of time concerned with evolutionary history, all could be replaced similarly, one by one; yet one need postulate only a strong selective pressure in favor of the eye in its original form to account for an eye completely homologous to the original by morphological standards yet under the control of a totally different set of genes. This type of genetic change might well underlie the variation from species to species in location of organ primordia in the embryo or of differences in inductive relationships cited earlier.

It is apparent, as it was to Wilson (1896), that each species has within its total genetic make-up the "blueprints" for all its morphological (as well as functional) characteristics, with no connection to past forms or other present forms except that which has by chance been retained in this genetic material. That we can recognize homologies between different forms can be considered as a fortu-

nate "break" for comparative anatomists as well as a direct consequence of the mechanics of evolution, which might be characterized in the following way: the more complex a structure (or an organism) becomes, the less likelihood will there be of the occurrence of a major change in pattern without creating a disharmony that would be incompatible with survival. Thus we get the frequently apparent conservatism of evolution, involving the persistence throughout a wide variety of organisms of common morphological patterns which we call homologous. As just mentioned, a drastic change in pattern of a complex organism probably would not survive; however, if on rare occasion it did and if the resulting new pattern were sufficiently harmonious to permit survival and perpetuation, we would find it difficult to recognize homologies with the original stock and would speak of it in terms such as "macroevolution."

SUMMARY

Historical development of the concept of homology is discussed, together with some of the various criteria that have been suggested for resolving questions of homology. While common genetic background is implicit in our current concept of homology, it is not generally suitable as a criterion; rather the reverse is true—demonstration of homology is usually accepted as evidence of common genetic background.

While homologous structures usually follow similar developmental patterns, especially in terminal stages of development, location of primordia within the embryo or inductive relationship to other parts of the embryo cannot be used as absolute criteria of homology.

It is concluded that, although other lines of investigation may yield supporting evidence, homology is primarily a morphological concept, and the methodology of morphology is the most appropriate for resolving questions of homology.

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The Nature of Physiological Adaptation

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It is my purpose this afternoon to explain the nature of physiological adaptations and to discuss the role of adaptation in biological evolution. Most of the things I will say are not new and, particularly, some of them have been expressed in an elegant manner by Dr. P. Weiss of the Rockefeller Institute. Perhaps it would be as well, first of all, to try to make out what is meant by the word adaptation and in particular, physiological adaptation.

A living system is an aggregate of some 10^{10} atoms in the smallest independently living things to about 10^{32} atoms in the largest living things. The individual constituent atoms themselves are not considered as living, but the whole constellation is regarded as living because of certain peculiar properties it possesses. The actions of individual molecules seem to be the same whether the molecules make up a living system or not. This means that the properties which characterize a living thing are the properties of an aggregate of molecules situated with respect to one another in such a way that the resultant of their interactions gives the material form and properties of a living thing. The property which seems to characterize best a living system is this: A living system organizes new atoms from the surrounding environment into the constellation which is recognized as the particular living system.

Another property of living systems is the topic of our discussion this afternoon: During the course of its existence, the pattern of the constellation changes in a manner to give stability to the continued existence of an average pattern. These changes are called "physiological adaptations."

One of the great resources of a species for survival is the physiological adaptation of its individual members.

1. Associate Professor of Physiology, The University of Kansas. Seminar presented on 14 January 1959.

Right here, one position must be made clear: The environment of living creatures is not made suitable for them, but rather they change to be suited to it. As environments change through time, poorly fitted combinations simply do not survive to reproduce and do not perpetuate their kinds. Further, it is obvious that no living system can escape the continuous and rigorous tests of fitness.

But these continuous tests, which countless generations have managed to pass successfully, can never have been completely identical in any two cases. No two organisms are faced with precisely the same conditions in space and time. Now, if organisms were rigidly pre-adapted to fit precisely only one particular detailed course of life, their chances of ever encountering just that one expected course, hence of surviving, would be practically zero.

Physiological adaptation, then, is the fitting of the living system into its own unique environment. Such fitness is a requirement for endurance. There is an approximate fitness conditioned by the evolutionary history of the system which then is adjusted by the physiological adaptations to make a better fit. Such on-the-spot adjustments give the precision of fit that no rigidly set system could achieve, and it is clear that rigidity can be a property of living systems only so far as environments do not change.

It is evident that the physiological modifications themselves are not inherited. They act without committing the future progeny. This brings us to one of the important characteristics of physiological adaptations: The younger the animal, the greater the capability to adapt. That is to say, as an animal lives out its life and undergoes particular modifications as the environmental situations demand, certain other modifications are by necessity excluded. Thus, each change has an element of commitment in it. Indeed, the greater capacity of the young is not only in the magnitude of the possible modifications but the variety as well. But I see something further in this: In a new animal, the genetic material has a greater number of possible environments in which it can survive than has the genetic material in an old animal. This means that one of the gains from reproduction, in both mono- and biparental reproduction, is the production of a young animal with a greater flexibility for the manifestations of the genetic material. That is, the genetic material works in "less committed" protoplasm.

Physiological adaptations are generally changes in the velocity of an existing reaction rather than formation of a completely new reaction. This is not to say that the variety of patterns is small. Although the physiological changes themselves may represent only

new velocities, the possible permutations and combinations of changing velocities in a very large number of reactions are almost infinite in number. The degree of the response, of course, bears some relationship to the intensity of the environmental disturbance. Adaptations are not all-or-none. The response in a given animal is a function of the disturbance and although it is not generally a simple function, we can say that the stronger the disturbance the greater the response. With an increasing environmental change the response approaches some limit and usually approaches this maximum value in an asymptotic manner.

The response, then, is graded and the disturbance is any change in the environment which moves the concentration of a critical compound from its usual physiological range. Since there are an infinite number of possible disturbances in the environment, we see an almost infinite number of adaptations. Adaptation to changes in the salt content of the environment is seen in most aquatic animals; adaptations to temperature changes are seen in practically all forms of life—even protozoa adapt to temperature changes. Adaptations to changes in substrates have been shown in practically all kinds of animals from bacteria to mammals.

The disturbance may be the introduction of a completely new agent into the environment of the animal. By new I mean that the agent need not have been in the environment of any ancestor of the animal. For example, adaptation to the repeated administration of a newly synthesized drug is so common that it can even influence the economy of the pharmaceutical industry. The diminishing effect from a given dosage of a drug with repeated use occurs with almost every known drug.

We must not generalize from what I have said, however, and conclude that all damaging agents induce protective adaptations. They do not. For example, to my knowledge, there is no effective adaptation to increasing dosages of radio-activity.

When a system adapts, a particular reaction may go faster, or some other reaction may go slower, and either response may achieve an almost equally successful adaptation. When the environment changes in a way completely new to an individual organism, the response will be predictable only to the extent that knowledge is available about how other living systems responded to a similar change.

In any given environmental change, several different kinds of responses always result. That is, an "adaptation" consists of several physiological responses. Detailed examination of the different modi-

fications shows that they run dissimilar courses. Recently, E. F. Adolph (1961) compiled information on fifty different responses in the rat to an atmosphere of low oxygen. He found that each of the fifty different responses had an individual time course. For example, during the adaptation to a low partial pressure of oxygen by rats the time courses of some responses were as follows:

> (1) The increase in the red cell volume was exponential until about the 10th day, and then it levelled out at 170% of the control level. (2) The rectal temperature rose quickly in the first 2 days and then remained constant at 20% above the control. (3) The plasma volume showed a completely different pattern, rising the first 5 days and then falling to 70% of the control level at ten days and remaining steady at that level. (4) The testis weight showed a slow decline until the 19th day at which time it fell abruptly from 80% to only 50% of the control level.

In the reactions to any given disturbance, analysis reveals that each response in turn is a result of sub-patterns of reactions, and further analysis leads to sub-sub-patterns and so on. Just how far down toward the molecular level the changes in an adaptation take place would be difficult to answer at this time since no physiological reaction has yet been studied in such complete detail that the entire chemical sequence of events is known. However, we might expect that, like any analysis, the response can be traced as far as the tools and operations will allow, and as the tools improve with time the trace of the response undoubtedly will be followed to the molecular level.

There have been several attempts to find common denominators in all adaptative responses. The question is this: is there some organ or tissue response or biochemical reaction which is common to all adaptations? My own feeling is that it is a meaningless question, but as a working hypothesis it has stimulated work yielding much valuable information. A better question would be: how much cross-adaptation in particular environmental disturbances actually occurs? That is, having adapted to one kind of disturbance to what extent will the creature be able to adapt to some other similar disturbance?

The evidence indicates that there is little cross-adaptation. When rats were adapted to such things as cold air, low oxygen or water excess, there was apparently no cross-adaptation whatsoever. The adaptations were more specific than general. It is clear, I think, in view of this rather specific nature of adaptations, that the question

of cross-adaptation is one of overlap. To the extent that the properties of two different environmental disturbances overlap, there will be cross-adaptation.

All adaptations outlast the disturbance which induced them. However, there is a strong tendency for the adaptation to disappear when the stimulus is absent. It can be argued that the disappearance of the disturbance is in itself a disturbance to which the animal must adapt. But from the observer's point of view, we can say that "deadaptation" occurs with a tendency to return to the initial state. As one might expect, the pattern of the deadaptation is different from that of the adaptation. Indeed, in none of the reactions examined by Adolph (1961) did the pattern of the deadaptation resemble the experimental response.

Every organism, indeed every organ and tissue, shows a pattern of compromises in adaptation because of the conflicts from different basic physical requirements. Thus, for example, an increased thickening of the human skin provides better protection to mechanical abrasion but reduces the effectiveness of the sensory nerve endings. Perfection is ruled out because conflicts are not resolved in perfections.

In summary, all living creatures have the machinery to adjust to changing environments and to adjust in such a way that their major component parts have stability and retain their identity. These adjustments are super-imposed on what might be considered the average pattern. They are not "all-or-none" but are graded and specific responses to the particular environmental change. Thus, physiological adaptations are the power of adjustment to changes in a unique environment possessed by the individual organism within the boundaries set by heredity.

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Some Stages in the Development of the Concept of Natural Selection [1]

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Introductory Remarks

It would be difficult to discuss adequately the many implications of the theory of natural selection in present-day biology, let alone describe in any detail whatsoever its development since the days of Darwin and Wallace. Rather than merely adumbrate the entire field and leave the audience with a mass of undigested generalities I prefer to limit myself to several specific aspects of the Theory of Natural Selection and to try and trace their development from Darwin's time to our own. I shall say little that is new to those of you who are familiar with the subject, but in talking to colleagues I find that there is a considerable time lag between discovery of new facts and reformulation of principles on the one hand and the diffusion and assimilation of such knowledge by related disciplines on the other. Although my college days passed really not so very long ago, I find that my knowledge of bacteriology or embryology, acquired as an undergraduate, is thoroughly outdated when compared to actual progress and present-day issues in these fields. While I do not wish to infer similar lacunae in the general biological education of my colleagues, I hope they may still find it of interest to review with me the changes which the concept of natural selection has undergone since the time of Darwin and particularly the views on the subject held in recent years when the emphasis has changed considerably.

Natural selection can be examined from many angles. The morphologist looks to natural selection to explain the many and

1. Contribution No. 1099 from the Dept. of Entomology, of the University of Kansas, Lawrence. Seminar presented on 18 February 1959.

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often intricate morphological structures which organisms have evolved in pursuance of their activities or which, occasionally, have no easily discernible function. The physiologist studies the nature of acclimation, a phenomenon which by itself appears to be adaptive and the existence of which can only be explained in terms of natural selection. To the systematist natural selection appears to have assisted in, if not dominated, the production of the many groups of organisms of high rank and low which he wishes to describe and relate. It would be simplest if organic diversity could be ascribed entirely to that omnipotent force, natural selection; much tortuous dialectic is expended on showing how differences between various groups are likely to be adaptive. While armchair biology of this type has fortunately become unfashionable in recent years, I hope this will not lead systematists to accept the efficacy of natural selection without further thought or concern about its mode of operation!

The topic which I wish to discuss in my Darwin-Linnaeus Lecture does not involve the complicated concepts and problems above. I shall address myself to two points only: Does natural selection actually occur and if so, what are the laws that make it operate? The first would seem an idle question. One hundred years of Darwinism should have established natural selection as a fact. Few reputable biologists today would wish to question its existence. Yet when called upon to cite clearly substantiated instances of natural selection, we are left with a mere handful of cases, most of them observed under what might be called semi-controlled conditions. When this scant body of knowledge is viewed in relation to the vast field of application of the theory of natural selection, it becomes apparent that now, as 50 years ago and also in the time of Darwin, the preponderance of the evidence is deductive rather than observational. There are historical as well as epistemological reasons for this state of affairs which are adequately detailed elsewhere (Robson and Richards, 1936; Huxley, 1943).

It is, of course, well known that theories of the *modus operandi* of natural selection have undergone marked changes which have paralleled our changing concept of heredity. I hope to review some of these theories here.

Darwin's views

Let us start our consideration of natural selection with the views of that one of its co-authors who has had the major influence on succeeding writers and observers. It is well known that Darwin's theory as formulated in the Origin of Species is largely deductive. He states three facts of nature, which to this day have remained

undisputable, and draws from them two important deductions. The facts of nature are: (1) the potentially geometric rate of increase of animal and plant populations; and (2) the fact that, despite occasional major fluctuations in population size, the numbers of a species remain fairly static; *i. e.*, that when considered over substantial periods of time population size of a species is a reasonably constant quantity. From these two facts he deduces that a struggle for existence must take place. This struggle is not necessarily an active one ("nature red in tooth and claw"), but Darwin himself considered this term ". . . in a large and metaphoric sense including dependence of one being on another and including (which is more important) not only the life of the individual but success in leaving progeny." That a struggle for existence occurs has been taken as a tenet of biological thought until the present day, with perhaps a minor eclipse at the turn of the century. However, while the basic idea is still as valid today as it was in Darwin's time, recent re-evaluation and reformulation of theories of control of animal populations necessitate a corresponding new interpretation of the struggle for existence. (3) Darwin's third fact of nature was the existence of continuous variation for most characters of wild as well as domesticated populations. Given a struggle for existence, it seemed obvious then, as it does now, that selection would take place favoring those individuals best adapted to succeed in the struggle for existence. Spencer's term "survival of the fittest" still appears as a *bon mot* although liable to misinterpretation, particularly in relation to human affairs.

The subject of artificial selection must not be neglected in discussing Darwin's views, although it shall not be considered in the present essay, except insofar as it sheds light on natural selection. The intensive and important work of recent years would require lengthy and thorough discussion to do it justice. We must not forget, however, that almost the entire body of evidence for the efficacy of selection was obtained by Darwin by analogy with the phenomenon of artificial selection as practised by animal and plant breeders.

We might conclude our statement of Darwin's ideas with several important qualifications made by himself to which we shall have to return later in the discussion. Darwin realized that while artificial selection will affect only those characters which the animal breeder can perceive, natural selection will work on all the characteristics of the organism and that most of these properties would be hidden to the scientific observer. A second idea of Darwin's, which is still

much in evidence, is the development of characters of seemingly non-adaptive value as the result of organic correlation. Selection for a desirable trait will bring about the development of a correlated character of neutral adaptive value.

Furthermore, in response to comments and criticisms on his earlier editions Darwin recognized that much of the loss of animal and plant life included under the general heading of "struggle for existence" is of the nature of catastrophic destruction of organisms and that much of such destruction would be likely to be random, eliminating adapted as well as non-adapted organisms. He nevertheless claims, and we shall examine the modern view of this claim later on, that if this destruction is random the normal amount of variation would be undiminished and selection would still act on the survivors, weeding out unfit ones and preserving the offspring of the fitter creatures.

We do not have time to enter upon a thorough discussion of the criticisms leveled at Darwin and his theory. Many of them are of no more than historical interest. I would like to single out comments by only one man, whose criticisms Darwin himself titled "the most valuable ever" (Francis Darwin, 1892, reference 1958, p. 289). In an article published anonymously by F. Jenkin in the North British Review (Anonymous, 1867), the author criticises Darwin on several points. Jenkin states that selection cannot transcend the normal variability of species. He feels, therefore, that, however much time is assumed by Darwin and the Darwinists in trying to account for the differences existing between species and higher categories, it is unlikely that we shall be able to select beyond the normal range of variability as exhibited within a species at the moment. He states: "A given animal or plant appears to be contained, as it were, within a sphere of variation; one individual lies near one portion of the surface, another individual, of the same species, near another part of the surface; the average animal at the center. Any individual may produce descendants varying in any direction but it is more likely to produce descendants varying towards the center of the sphere, and the variations in that direction will be greater in amount than the variations toward the surface." This is a serious question which, while no longer considered a stumbling block for evolutionary theory, still has not been unequivocally solved.

The second of Jenkin's objections which we shall review is no longer valid in the light of modern genetic theory. However, it merits discussion since it appears to be the first attempt at a quan-

titative treatment of the phenomenon of natural selection and thus a forerunner of the direction which the theory has eventually taken. Jenkin distinguished, with Darwin, between continuous, minute variations and occasional, major, discontinuous variations, also known as sports. The author shows how improbable it would be for these sports to survive in a large population of normal individuals, even on the assumption that the advantage of the sport is twice that of normal individuals. Assuming a reduction each generation from one million young (or eggs or seeds) to ten thousand at maturity, the odds against survival of a normal individual are 100:1, while even in the sport the odds are no less than 50:1. This line of reasoning presages Fisher's (1929, reference 1958) estimate of the probability of extinction of a single mutant gene, although the basic assumptions of the two computations are necessarily quite different. On the other hand, Jenkin shows the high probability that when two types are present in almost equal proportions both will be maintained in the succeeding generation in spite of the drastic reduction in numbers.

Jenkin then proceeds to argue that even in the unlikely event of a sport's surviving and mating this will not result in a gradual increase in the percentage of sports. Here his position rests on the then prevalent view of blending inheritance, the pitfalls of which Darwin recognized without being able to substitute a more satisfying hypothesis, ignorant as he was of Mendel's results. Since the offspring of the sport were expected to be intermediate in advantage between it and the normal form (*i. e.*, of fitness value 1.5 in modern terminology), Jenkin conceded that they in turn would have more offspring than the normal. However, since the difference in fitness between the hybrids and the normals was halved in each generation (Jenkin considered and rejected as improbable the idea of their mating among themselves), the increase in number of the descendants of the sport soon reached an asymptote at which, while 2.38 times as numerous as before, they were in effect indistinguishable from the normal type. The author points out correctly that if the offspring of the sport retain in full vigor the peculiarity constituting the favorable sport then the descendants will undoubtedly replace the other population, although he states "it is a stiff mathematical problem to calculate the number of generations required in any given case." This alternate assumption, rejected as unlikely by Jenkin is in fact particulate inheritance, although based on a single dose of heritable matter per individual. The "stiff mathe-

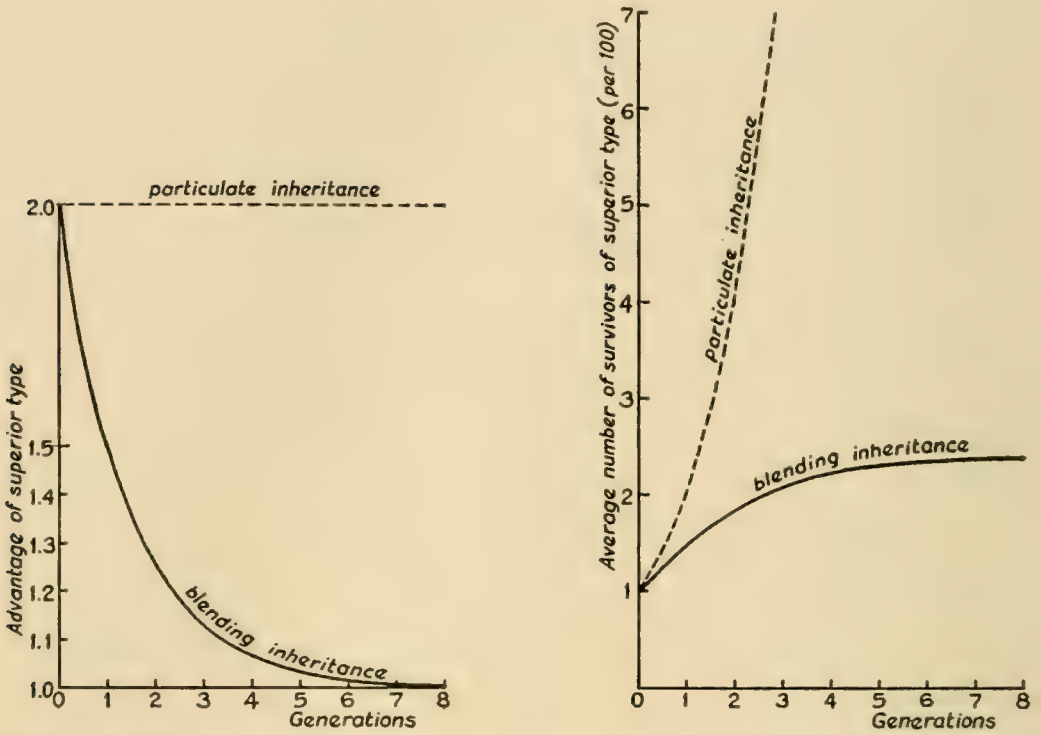

FIGURE 1.—Graphs illustrating Jenkin's argument against natural selection. Shown on the left is the advantage of the superior type (assumed to be 2.0 for a newly-arisen sport) during successive crossing with the normal type. The advantage is reduced almost to that of the normal type (1.0) in eight generations when blending inheritance is assumed; under particulate inheritance the advantage remains constant. The average number of survivors of the superior type (per 100 organisms) is shown on the right. Assuming blending inheritance, an initial survival of one sport of advantage 2.0 and a 100-fold increase of the population in each generation, followed by mass-mortality with one percent survival, we note that the population of superior types increases but has reached an asymptote near 2.38 per 100 by the eighth generation. At this time the descendants of the sports are practically indistinguishable from the normal type. Compare this curve with that for particulate inheritance (analogous to clonal selection in modern work), where selection is very efficient in increasing the percentage of sports. The various curves represent the equations $A = 2$; $N = 2^n$ for particulate inheritance and $A = 1 + (\frac{1}{2})^n$, $N = \prod_{j=1}^{n} (1 + (\frac{1}{2})^j)$ for blending inheritance, where A is the advantage of the superior type, N is the number of survivors of that type per 100 individuals, and n is the number of generations since the original appearance of the sport. The assistance of F. J. Rohlf in the preparation of these graphs is acknowledged.

matical problem" was solved by Haldane fifty years later, in the entirely analogous case of clonal selection.

Figure 1 illustrates the changes, for successive generations of the selective advantage of a superior type and of the average number of survivors (per 100) of this type under the two alternate hypotheses: particulate and blending inheritance. The graphs show clearly how blending practically eliminates any selective advantage in eight generations.

His various arguments led Jenkin to the following well-phrased but, in the light of subsequent developments, somewhat premature conclusion: "What can we believe but that Darwin's theory is an ingenious and plausible speculation, to which future physiologists will look back with the kind of admiration we bestow on the atoms of Lucretius, or the crystal spheres of Eudoxus, containing like these some faint half-truths, marking at once the ignorance of the age and the ability of the philosopher. Surely the time is past when a theory unsupported by evidence is received as probable, because in our ignorance we know not why it should be false, though we cannot show it to be true. Yet we have heard grave men gravely urge, that because Darwin's theory was the most plausible known, it should be believed."

The Post-Darwinian period

When we turn to the successors of Darwin, we encounter the period of the great flowering of evolutionary doctrine and the theory of Darwinism. The names of Haeckel and Weismann are known to all. The major establishment of evolutionary theory was grounded in the fields of comparative morphology, comparative embryology and systematics. Much of the discussion of natural selection centered on its ability to explain diverse phenomena in these fields. A quantitative formulation of natural selection proved impossible since the basic element of such a theory, namely a sound theory of variability and heredity, was lacking. Thus much of the work was deductive and speculative and need not concern us here.

It is well known, of course, that the early biometricians, Galton, Weldon and Karl Pearson, were engaged in setting up models which might explain the nature of continuous variation and the changes in continuously varying characters when subjected to natural selection. In retrospect, the importance of their works seems to lie in the methodology which they established and which today is of primary importance in investigating the study of selection, rather than in the results which they achieved.

Two developments in the decades preceding the turn of the century require our attention. The first is a systematization of the types of selection which could exist in nature. While much of this is simply careful thought about well-known phenomena of natural history, it did enable biologists to delineate the problems involved more precisely than before. A useful and quite modern looking classification is given by Plate (1908), whose review of the theory of selection, while published subsequent to the rediscovery of Men-

del's work, still gives a very excellent survey of the state of Darwinism at the end of the nineteenth century. Plate discusses the form of the struggle for existence under the following headings: (1) *catastrophic elimination.* By this he understands the simultaneous mass destruction of many individuals by great physical force such as floods, cloudbursts, storms, tides, earthquakes, prairie fires, etc., or by organisms of overwhelming powers compared to the organisms which are being destroyed, such as a whale or an elephant. He includes destruction of eggs or juvenile forms, which seems to be non-selective and which occurs as part of the life cycle of many species. The argument is presented by some opponents of natural selection that after massive, non-selective elimination of individuals has taken place the remaining few have ample food and shelter and therefore are no longer subject to natural selection. Plate adequately attacks this idea by stating that there are still many factors other than the two above necessary for the life processes of these organisms and that some of these factors were bound to be marginal at times. Therefore a struggle for existence would still take place even in the absence of limitations of food and space. He approaches a stochastic idea by saying that if it is possible that in any one year 98% of the organisms died, there must surely be some years in which 100% of the organisms will die. He considers this improbable, however, since he does not know of species which have died or become extinct all of a sudden. He notes that, from the cases where extinction is known, it appears to have been a gradual process. Present-day ecologists are not troubled by these facts. In most cases total destruction would be a local phenomenon and individuals lost would be replaced by others from surrounding areas, thus maintaining the species in numbers.

In relation to catastrophic elimination Plate quotes Gulick (1905), who advanced an early view of random changes in genetic constitution. He states that if by chance only one or two reproductively capable individuals remain after a catastrophic destruction they would give the species a new appearance since their offspring retained only a part of the original active or latent hereditary qualities of the original population. This same result would occur if some individuals were segregated from the main mass of the population and isolated in a new area. In this way one could explain how two neighboring islands could have two clearly distinct races of the same species.

(2) The so-called *constitutional struggle* is selection by changes in physical factors leading to differential survival of favored types. This type of selection is said to be independent of population density of the organisms, a view which was held until the recent challenge by Andrewartha and Birch (1954).

(3) *Interspecies or intervariety struggle* and

(4) *Intraspecific struggle.*

In Plate's day such concepts were still handled almost entirely in a qualitative manner and consisted largely of natural history type reports, such as the introduction of new organisms into an area, resulting in the displacement of the native population.

While the definition of the types of selection by Plate encouraged precise thinking on the problem, an extension of his type of approach led to a futile and quite ridiculous overclassification of the selection process, complete with a cumbersome, albeit linguistically correct Graeco-Roman terminology. It is to the credit of evolutionists that the sterility of this approach was quickly perceived.

The first attempts at demonstrating natural selection under natural or semi-natural conditions are a second development of which we should take note. Plate's review lists six researches into the subject, which is not an impressive record for more than four decades of research after the publication of Darwin's work. It would be well at this point to include such work not only up to the end of the 19th century but up to approximately 1930, since no major improvement in technique is evident in these studies over this span of time. Only in the 1930's and subsequently did the development of population genetics improve studies and interpretations of natural selection. An excellent review of the various papers up to 1930 can be found in the book by Robson and Richards (1936), and no point would be served here in trying to reproduce their accounts. Of interest are the criteria set up by Pearl (1930) for proof that natural selection has altered a race. These are:

(1) Proof of somatic differences between survivors and eliminated.
(2) Proof of genetic differences between survivors and eliminated.
(3) Proof of effective time of elimination.
(4) Proof of the somatic alteration of the race.
(5) Proof of the genetic alteration of a race.

In reviewing the literature of natural selection until 1930 we find that very few studies would measure up to modern experimental standards, particularly as regards statistical significance of

the results. In the zoological literature only four studies can be considered as of any consequence: (1) A study by Crampton (1904) analyzing morphological characteristics in moribund and live pupae of the moth *Philosamia cynthia*, in which of eight characters measured, five differed significantly in size between the two kinds of pupae. It was also shown that, at least for one character, variability was less in the survivors than it was in the dead pupae. Similar studies were made on the adults. Unless we suppose that physical factors or perhaps a biotic agent which brought about the death of the pupae would be simultaneously responsible for a change in its morphology (not an entirely unreasonable assumption), it must be believed that these changes in morphology are related to changes in physiology of such aberrance that death resulted in these organisms. We may even be dealing here with so-called phenodeviants of which much has been made in recent years both by Michael Lerner and by C. H. Waddington. (2) A study by Thompson, Bell and Pearson (1911) and (3) a similar one by Kellog and Bell (1904) measuring variation and correlation in the wasp *Vespa vulgaris*, the ladybird beetle *Hippodamia convergens*, as well as the honey bee *Apis mellifica*, show that some characters change in their means as well as in their variability from season to season. These phenomena may represent natural selection. (4) In the fourth study, Bumpus (1898) measured nine characters in 136 English sparrows which had been killed during a hurricane. He compared them with survivors and found that individuals deviating from the average type in either direction were more numerous among those who succumbed than among the individuals who survived. Thus, individuals with the greatest and longest wing span and those with the greatest and smallest head were eliminated. If these data could be substantiated we would have an interesting example of selection toward a central type, so-called stabilizing selection in modern terminology. While the differences given are statistically significant, the samples themselves are so small and the general situation so relatively artificial that one should hesitate to base any far-reaching conclusions on them.

The Mendelians

The rediscovery of the Mendelian principles of heredity and the concomitant eclipse of the Darwinian hypothesis of natural selection has been often told, and I could not improve upon the published accounts. The early Mendelians, such as Bateson, Saunders and

T. H. Morgan, were impressed by the particulate and discontinuous nature of the genetic material and relegated natural selection to secondary status. In the rush to enter the new disciplines of genetics, cytology and chemical and experimental embryology, natural selection, which had been the central problem of much of biology, was for a time ignored.

Nordenskiöld (1929) in his history, conceived in 1916, states the following: "As a result of exact heredity research the theory of evolution has itself been directed along other lines; pylogenetic speculations have for the most part been abandoned, at least for the time being. Natural selection is certainly retained in principle by some students of heredity (by Bower, for instance) but it is really of no practical importance; the phenomenon cannot be observed and it is therefore not possible to fit it into a subject of research that is based on exact observations."

At the end of the second decade of the 20th century, however, three men appeared on the scientific scene whose biological genius and mathematical ability enabled them to combine the findings of the biometrical school with Mendelian heredity and to construct the first workable models of evolutionary processes. If quantification is the yardstick of the maturity of science, the appearance of the writings of Fisher, Wright and Haldane heralded the coming of age of evolutionary biology. It is well known, but should probably be added for the record, that these men were not the first to investigate the statistical properties of Mendelian heredity. As early as 1908 the famous English mathematician Hardy and a German physician named Weinberg had independently arrived at the fundamental postulate that zygotic frequencies for a single Mendelian locus, after one generation of random mating, are retained in equilibrium proportions and that consequently the frequency of the alleles at this locus remains constant. This very simple principle which on the jubilee of its discovery had finally appeared in some elementary biology textbooks and is already being taught to beginning biology classes in a few enlightened colleges, is the point of departure for much of the sophisticated work in population genetics, as the science came to be called. Mention should also be made of the work of H. S. Jennings, who, during the years of the first World War, developed the mathematical consequences of inbreeding in a Mendelian system to a considerable degree. To list separately in chronological or other order the monumental contributions of Fisher, Wright and Haldane would require far more time than is at our dis-

posal here. The interested reader is referred to the book by Li (1955) which covers this subject extensively.

Haldane (1924 *et seq.*) in a series of important papers developed the mathematical description of selection in a great variety of genetic situations for single pairs of alleles, multiple alleles at a single locus, and the like. Similar results were obtained by Wright in a later paper (1931). Wright also developed a general formula for discussing selection, which has turned out to be of great value in handling a variety of situations. The utility of a selection formula is self-evident. For example, it can be shown quite clearly why selection against recessives as envisaged in many eugenic programs becomes quite inefficient once the frequency of the deleterious recessive has been reduced below a certain point. Formulae were generated which permitted the estimation of the number of generations required for selection to proceed from one gene frequency to another and conversely of the selection intensities necessary in order to achieve a given result in a given amount of evolutionary time.

Concurrently with an increased understanding of the method of operation of natural selection came an awareness and a quantification of other evolutionary factors; mutation, the action of which had of course been known since the turn of the century and suspected much earlier, migration, and departures from random mating were each incorporated into formulae predicting changes in gene and zygotic frequencies. A number of interesting situations were shown to lead to equilibria of gene or zygotic frequencies. Among them we may list selection for heterozygotes, various types and degrees of assortative mating, and the balance struck by various evolutionary forces acting against each other. Selection in favor of heterozygotes turned out to be an uncommonly useful concept, able to explain the occurrence of balanced polymorphisms in populations, including cases where one allele is quite deleterious when homozygous. An example of the latter instance is sickle-cell anemia, discussed by Dr. Allison in an earlier talk of this series.

The mathematical theories acquired an elegance and sophistication far ahead of any possible verification of their results by field and laboratory methods, but the results were not seriously questioned by evolutionary biologists since they were merely logical consequences of the generally accepted Mendelian model. Evolution during the 1930's and early 40's was conceived of as changes in gene frequencies, and the problem of natural selection and its recognition was framed in these terms. Several studies in the

1930's reflect this interest. L'Heritier and Teissier (1934) showed that in *Drosophila* populations the frequency of wild type *Drosophila* was increased at the expense of the mutant, Bar, and that similar results were true for other mutant characters. Analogous results have been obtained by Reed and Reed (1950) on white eye in *Drosophila* and by Kollros (1944) on pearl eye in *Tribolium castaneum*.

Of particular importance was the addition by Wright of a stochastic element to the quantification of the evolutionary forces affecting the genetic composition of a population. A probabilistic model of this sort appears to be a necessity in the present state of our knowledge, as long as we are unaware of the causes of climatic and other environmental changes, as well as of fluctuations in population size. It is necessary that such fluctuations, if their direction cannot be predicted, at least be accounted for in terms of the magnitude of their variation. The change from a deterministic to a stochastic model has brought about a considerable complication in the mathematics. The appearance on the scene of a brilliant young Japanese geneticist by the name of Kimura has resulted in a dramatic expansion of the model but has also moved it very definitely into the sphere of higher mathematics, so that there are probably no more than a handful of biologists today able to appreciate Kimura's arguments, while the rest have to take his conclusions at face value.

The earliest treatment of evolutionary mathematics rested of necessity on simple assumptions, *i. e.*, the action of evolutionary forces on one or at most two loci. However, during the development of the science the theory of continuously varying characters, the continuous fluctuations of the early Darwinians, was not neglected. Following the pioneering work of Nilsson-Ehle and Johannsen, the ground was laid for a genetics of quantitative characters based on many factors of small and, on the simplest assumption, additive effects. Here again the mathematical groundwork was laid by Wright and Fisher, while Lush extended and popularized the theory for animal breeders. Quantitative genetics, as the science has been called, has profoundly affected animal and plant breeding and a comprehensive body of very technical literature has evolved. On the other hand, until very recently its influence on general evolutionary theory has been negligible, and only the recent influence of Lerner (1958; Lerner and Dempster, 1949) and several of the geneticists of the Edinburgh group has tended to cross-fertilize evolutionary ideas with concepts from quan-

titative genetics. Most if not all the characters that ordinarily are considered to be components of fitness in a population are quantitative characters. These include fertility, fecundity, duration of the immature stages, length of reproductive life, life span and similar measures. Natural selection should affect these more than any other characters, and they are expected to and have been shown to respond rapidly and vigorously even to minor changes in environmental conditions. It is therefore surprising that not more attention has been paid by workers in the laboratory or in the field to natural selection for such characters.

Recent Evidence from Field Work

Recent work on demonstrating natural selection under field or simulated field conditions have still centered on the "major gene" (or at least "discrete character") approach. I shall mention only a few, although probably more could be found. The by now classic case of industrial melanism in moths has recently gained considerable clarity through Kettlewell's (1958) beautiful demonstration by a series of critical experiments of the differential predation of the exposed form on a contrasting background.

The European garden snail, *Cepea nemoralis*, has been the subject of considerable inquiry and controversy in recent years. The evidence for natural selection through differential predation by thrushes seems to be clearly established (Cain and Sheppard, 1950). The controversy revolves around the relative importance of natural selection for establishing the genetic differences among local populations of the snail.

An interesting demonstration of natural selection in a living population was provided recently by two members of the Entomology Department here at the University. Drs. Camin and Ehrlich (1958) have been able to show differential survival of offspring of water snakes *Natrix sipedon* on islands in Lake Erie off the coast of Ohio. The selecting agent has not been identified in this case, although it is suspected to be differential predation of the snakes by birds.

One of the most dramatic cases of natural selection in the field has been the development of resistance to DDT and other insecticides by numerous species of insects (Crow, 1957). While it is difficult to obtain carefully controlled field data showing the intensity of the selective stimulus, the mortality of the insects in the field, as well as the achieved levels of resistance, similar experiments have been performed in the laboratory, which make it very

probable that the laboratory conditions simulate the field conditions closely. We have carried out such studies in our laboratory here (Sokal and Hunter, 1954; Sokal, 1959). DDT-resistance, although a poor character, since the phenotype can only be measured by exposure of the insect to the poison, does provide a very dramatic illustration of the Darwinian principle of natural selection.

An impressive and voluminous body of literature has been accumulated by Dobzhansky and his school. The work consists of analysis of frequencies of chromosome inversions in *Drosophila pseudoobscura* and other species of *Drosophila*. While we are here not strictly dealing with a single gene effect, we are at least dealing with a block of genes prevented from crossing over by the inversions present in the chromosome. Dobzhansky's findings have demonstrated clearly the maintenance of adaptive polymorphism by the superiority of the heterozygote. We have here experimental proof of a mechanism postulated much earlier by the mathematical geneticists. Different inversion frequency equilibria have been shown to be the result of different conditions of food, crowding, temperature, etc., in the population cages which Dobzhansky uses to simulate the natural environment of these flies. Results are deterministic in that the outcome is repeatable. On the other hand subtle factors which *a priori* might not have been considered to be significant can appreciably affect the outcome of the competition among the various genotypes. For example, selection for a given inversion type is affected by the presence of other inversion chromosomes in the population.

In discussing this subject I have deliberately slighted the botanical literature. Studies such as those of Sukatschew (1928) on the dandelion, *Taraxacum officinale*, and of Harlan and Martini (1938) on mixtures of barley seed correspond more to competition experiments among different species of animals, since these plants do not normally interbreed.

Integration of the Genotype

It has already been stated that while population geneticists have built up an extensive quantitative science based on deductions of the consequences of Mendelian heredity there has as yet been little verification of the theory either in the laboratory or in the field. However, recent work has shown that an approach based simply on changes in gene frequency is grossly oversimplified. Interactions of various kinds between genetic units appear to be a common means to the production of optional phenotypes and must therefore play an important role in natural selection.

Interaction may take place between different alleles at a single locus. The superiority of heterozygotes for many components of fitness (heterosis) has been known for a long time, and recent work appears to indicate near-universality of the principle. An important aspect of the fitness of heterozygotes appears to be their buffered responses when subjected to a fluctuating environment during development. Lerner (1954, 1958) has called this phenomenon developmental homeostasis, Waddington (1957) preferring canalisation or homeorhesis. Lerner thinks that the occurrence of developmental homeostasis in the individuals of a population is likely to lead to genetic homeostasis of the population for the genes controlling the characters under consideration. By genetic homeostasis he means the tendency of a population to maintain a genetic composition which will provide a maximum number of individuals near the phenotypic optimum.

Interaction between genes at various loci has been well known for some time, but inferences regarding its consequences in population structure are quite recent. In view of these interactions the gene pool of a population can no longer be considered as merely the sum of all the genes of its members, but it is organized in the sense that the presence of one gene has an effect on the selective values of various other ones. Thus a genotype has to adapt not only to the environment but also to the frequency and distribution of other genes in the population; the various components of the gene pool thus have to be coadapted. This term was introduced by Dobzhansky, who showed that chromosomes carrying a given type of inversion will differ markedly in their response to selection depending on their geographic origin and that the outcome of selection in a given environment depends on the background of coadapted genes and chromosomes.

It has been shown by Wright some time ago that multifactorial phenotypes have so-called adaptive peaks and valleys. While a given adaptive peak assumed by one population may not be the most desirable one, it may be difficult to leave this adaptive peak to move onto a higher one in view of the fact that the change in genetic pattern would move it through an undesirable combination (an adaptive valley). Except by random genetic drift such shifts could occur only if the adaptive landscape itself changes. It is, indeed, generally assumed that environmental change is a regular feature of the environment, although we have little systematic study to support this belief.

Yet another impediment to a simple formulation of the selection process is the manifold correlations of characters shown in recent experiments on artificial selection (see Lerner, 1958). Intensive selection in a given direction almost always carries with it the correlated response of several other characters, among them usually components of fitness, such as fertility and fecundity. A number of hypotheses have been advanced to account for these phenomena; in fact, the explanation is likely to differ with each case and may well be composite in nature. The computation of selection effects must therefore take into account the advantages and disadvantages of various correlated characters.

We cannot pursue these recent shifts of emphasis in the investigation of natural selection any further here. It should have become apparent by now that evolutionary mathematics will have to consider many more parameters before it can even approximately deal with the problems raised above. It is doubtful whether our present mathematical tools permit such extension; even if complex models could be constructed, it may be next to impossible to verify them experimentally.

Outlook

What are some of the important problems which scientists must solve in relation to natural selection in the near future? There has been an almost complete lack of attention on the part of geneticists to the study of the selective agent and its mode of action. This agent is the environment, considered in the widest sense. Traditionally it has been subdivided into physical and biotic factors, but Andrewartha and Birch (1954) have made a cogent argument for a subdivision of limiting factors into weather, food, a place in which to live, other organisms of the same kind and organisms of different kinds. This subdivision of the environment appears to me to make a satisfactory framework for classifying selective agents, although probably another category would have to be added to refer to the intraorganismic selection to which gametes are probably subjected. Perhaps yet another class for intracellular selection of genetic material may be required.

The actual process of selection should have been the province of the ecologists, but, regrettably, ecologists to date have not been very evolutionarily minded. They have applied certain mathematical models involving the struggle for existence, such as those of Gause, Volterra, Lotka and Pearl. These models, however, did not consider genetic variability, and we have yet to develop a theory

which will simultaneously consider genetic variability as well as ecological parameters in a population. Andrewartha and Birch (1954) have probably been among the first ecologists to consider genetic variability within populations, although their interest has remained largely theoretical. Fine work along these lines has recently been done by Wellington (1957), who demonstrated behavioral differences related to an apparently genetic polymorphism in tent caterpillar larvae. Mention of this work raises the entire isssue of the distribution of tolerances and responses to environmental factors in populations and of the separation of genetic and environmental components of these distributions. This is a challenging problem, particularly when confounded by the spatial distribution of the members of the population relative to the field of environmental forces acting on them. It seems to be a generally accepted fact that the environmental preferenda of animals are identical to their optima, yet there seems no necessity that this is so. If such relations exist, selection is likely to have brought them about. The above problems would appear to outline a very fruitful field for inquiry.

It is important for us to know to what degree changes in population size will affect the genetic composition of a population. If these changes can be ascribed to definite environmental forces, the selection process can probably be described fairly simply. If, on the other hand, fluctuations in population size take place which are either entirely or largely random in direction and time of occurrence, the genetic consequences are much harder to define. If population fluctuations are random, it does not necessarily follow that the genetic response will also be non-directed. On the contrary, it may be expected that populations subject to frequent and drastic changes in numbers have acquired mechanisms for safeguarding their genetic variability. Only in very small populations are we likely to note genetic drift. It is important and urgent to study various populations in the field over an extended period of time in order to learn the magnitude of fluctuations in numbers and from it deduce the number of individuals contributing to the gene pool of the next generation. Evolutionists could then begin to evaluate the importance of the role of genetic drift in these populations. Many of the studies of drift up to now have been largely deductive, in the sense that genetic drift was assumed to explain changes which could not otherwise be accounted for. By the very nature of the problem, positive proof of genetic drift in natural populations is unfortunately difficult to obtain.

We are aware of some cyclical microevolutionary changes which represent natural selection in the field. The classical studies are by Timofeeff-Ressovsky on *Adalia bipunctata*, a ladybird beetle polymorphic for elytral pattern, and by Dubinin on various populations of *Drosophila funebris* polymorphic for chromosome inversions. In both species, changes in the proportions of the various types occurred during certain seasons in a more or less cyclic manner. Similar phenomena have also been shown by Dobzhansky and his group in this country.

We know very little about the effects of repeated selection or of cyclical fluctuations in selection intensity on a population. Populations that are repeatedly subject to identical selective forces must have a method of maintaining some sort of homeostasis, otherwise they would become quite ill adapted at times and liable to extinction. Polymorphism seems to be one such method of adaptation. However, a scheme which permits the extinction of the local population and its replacement by better adapted individuals from surrounding populations would seem to be another mechanism of species survival.

Similar reversible genetic changes may occur in populations as they grow and decline. As a population of genetically variable individuals grows and the struggle for existence intensifies, there is selection for certain components of fitness. Thus presumably the means and very likely the variances of some characters are likely to change. As density is decreased through catastrophic reduction of the population, exhaustion of the food supply or colonization of a new food source, selection is likely to be in a direction other than that in the dense population. It may well be that certain species exhibit some regularity in the genetic changes accompanying population cycles and that these genetic differences in turn determine observed variations in the demographic parameters. We are at present working on experiments in our laboratory to investigate the possibility of such phenomena in *Tribolium*.

The general problem of the limitation of numbers in animal populations has recently received much attention. Dissatisfaction has been expressed with Lotka's and Volterra's equations for population growth, which while being reasonably descriptive are based on questionable assumptions. Considerable controversy about the relative importance of their theories has engaged the supporters of a deterministic self-limiting system which relies on some density-dependent, negative feedback and those propounding an essentially stochastic model in which the temporary scarcity or severity of var-

ious limiting resources or factors keeps the population in check. Those interested in the details of this argument should consult the Cold Spring Harbor Symposium Volume No. 22 for 1957. Much additional field work is necessary to obtain the information on which these issues may some day be resolved. It should be interesting and profitable for geneticists to investigate the genetic consequences of these two hypotheses.

A considerable literature has accumulated on laboratory experiments testing the outcome of competition between related species for a limited supply of food or space. A general result of these experiments seems to be the replacement of one species by another under a given set of environmental conditions. The superiority of the one species is not absolute; given a different set of environmental conditions the relationships may be reversed. Studies of this sort have in the past not considered the genetic constitution of the two populations, each individual being considered identical to any member of the same developmental stage of its species.

Under environmental conditions intermediate between those producing either of two determinate results, the outcome of competition experiments must be variable, favoring at times one species, at times the other. Such conditions must exist frequently in areas of overlap between the ranges of related species, and it is probable that when they occur considerable selection must take place in the successful species. It may well be that the determining factor in such experiments is the efficacy and speed of selection for a type able in some way to better its competitors. While I know of no competition experiments involving studies of selection, other interspecies relations, specifically host-parasite relations, have been studied from this viewpoint. There is a considerable literature on the genetics of plants resistant to insect attack, as well as to fungus infection. Much profitable work remains to be done along these lines in epidemiology and medical entomology.

Turning briefly to another topic, I would like to stress the importance of studying cases of selection in nature. Are populations kept near optimal values for components of fitness and for other characters? Or is selection mainly for changes in the variability and perhaps for modifying genes which manage to canalize developmental patterns? Careful study in the field will be required to secure information on this topic.

Our knowledge of selection coefficients in nature is still woefully inadequate. We have no idea, except in a few isolated cases and by deduction in some human populations (see, for example, Clarke,

1959), what the magnitude and stability of such coefficients are likely to be. Much of the argument between the adherents of natural selection and genetic drift could be removed if only we had reasonable estimates of effective sizes of breeding populations, as well as magnitude of selection coefficients in nature. To what degree do the selection coefficients change with changes in the population density? This problem has already been treated theoretically to some degree by Haldane, who showed as early as 1924 that very intensive competition in a population is likely to select the most variable individuals, rather than select for lines showing the greatest increase in a given character.

We have learned much in the last two decades about the expression of the genotypes in different environments. Much work has been done on genotype-environment interaction, and any theory of selection has to take it into consideration. Selection normally operates on the phenotype, and therefore we have to know the way in which the genotype will be expressed. Natural selection is blind in the sense of selecting those phenotypes which are satisfactory to it regardless of whether the particular level of expression of the phenotype rests on a genetic or environmental basis. In the long run, however, selection can remain effective only if there is some genetic variability underlying the variation of the characters. Since fluctuations in environmental conditions are prevalent in nature, gene-environment interactions should be frequently observed. It would be useful to know whether environmental fluctuations resulting in changes of the phenotype slow down selection appreciably, also whether a character selected for an optimum in one environment will retain its high level of performance in another one. Some recent evidence on this from artificial selection has been obtained (Falconer and Latyszewski, 1952).

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THE UNIVERSITY OF KANSAS
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Taxonomic and Biological Speciation

RONALD L. MCGREGOR [1]

Taxonomists during the two centuries since Linnaeus have been most successful in describing species, in exploring widely to discover new species, and in distinguishing and naming groups of species. Much of this work has followed a species concept ably presented by Linnaeus in his Philosophia Botanica, of 1751, when he said, "We number so many species as were created of diverse form in the beginning."

With the appearance of Darwinism, taxonomists experienced a rude shock, and it took a number of years before Darwin's ideas were really put to good use. These ideas have resulted in the development of biosystematics, with its emphasis on genetical and cytological methods, population and ecological studies, and a concept of species defined on the basis of gene exchange and arranged along phyletic lines.

In recent years an increasing number of plants have been studied by biosystematic methods. Still, the mass of species has to be dealt with by orthodox taxonomic methods. It thus becomes clear that the species concept of the biosystematist cannot be directly used in much of plant taxonomy. The experimental approach has not brought a revolution in taxonomy but has demonstrated that the characters of gross morphology, which taxonomists have of necessity used, really are significant.

Any concept of species must be fashioned on the criteria of practical expedience in the interpretation of biological phenomena and the application of a standard system of nomenclature.

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Taxonomy of the Higher Categories

BYRON LEONARD [1]

The aim of the systematist is an understanding of the natural evolutionary interrelationships of organisms, and the convenience of being able to place groups of animals in systematic categories (the "pigeon-hole effect") must be regarded as a valuable earned dividend rather than a principal goal in itself. Within this framework of thought, each of the several categories in the hierarchy of a taxonomic arrangement has logical reality and is not to be regarded as artificial. It must be admitted, of course, that often there exists wide disparity between the ideal of taxonomic arrangement and the actual practice of taxonomy by the individual investigator. The tremendous vacuities in detailed knowledge of organisms all too frequently make it virtually impossible to establish natural relationships. For example, although most systematists agree that the species may be conceived of as a group of animals or of populations of animals that maintain a high degree of genetic isolation in nature, in practice it is often well-nigh impossible to confirm a premise of genetic isolation, in the case of any specific group of organisms. Nevertheless, as new techniques of attacking such problems increase in number and come closer to assaying fundamental attributes of animals, there is reason to have faith that dedicated investigators will approach the ideal of establishing taxonomic systems that accomplish the desire of attaching names to organisms and at the same time reflect evolutionary interrelationships among them.

Whether or not there actually exists an evolutionary interrelationship among the known phyla is a question that may never receive a definitive answer. But within a phylum, the various taxa certainly can be arranged in a system reflecting true evolutionary re-

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lationships, if sufficient knowledge is intelligently applied to the problem over a sufficient interval of time. Meanwhile, the large increment of artificiality now necessarily a part of almost all our taxonomic systems should not engender cynicism toward the higher categorical taxa. These can, and we must hope will, constantly be adjusted to reflect more nearly the natural evolutionary stages in the differentiation of a group of animals within a phylum.

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The Significance of the Geological Succession of Organic Beings: 1859-1959

ROBERT W. WILSON [1]

It is appropriate that in any series of papers concerning the doctrine of organic evolution, and dedicated to Charles Darwin, we pay attention to the fossil record and what it reveals. The fact that evolution is no longer a theory, as it was when Darwin championed it, but a major tenet of the biological and geological sciences is owing in large measure to paleontological work of the past hundred years. Moreover, Darwin himself carried on researches in geology, collected fossils, and was greatly influenced by his first-hand contact with vertebrate paleontology. It is not possible, however, in any reasonable space, to review even briefly the entire role of paleontology in evolutionary studies: here I propose to place the emphasis on vertebrate paleontology and to be further selective in discussing only such topics as have been of interest to me. In so doing, I hope that they prove also of interest to others. First, I will discuss the state of the paleontological record in Darwin's day, what it meant to him and his contemporaries, and second, I will review certain aspects of the record in the light of present-day information.

In the "Origin of Species," as is well known, Darwin presented five lines of evidence for his theory of descent with modification, or of evolution. These lines were: (1) variation of plants and animals under domestication, (2) comparative anatomy (morphology), (3) embryology, (4) geographic distribution of plants and animals, and (5) paleontology. However much we have come to believe in these lines of evidence as "proof," it still is true that all lines save perhaps paleontology offer only circumstantial evidence, and will always do so. Darwin clearly recognized the fact that the fossil record

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was, and would continue to be, the least circumstantial of the several lines of evidence offered in the argument, perhaps in time affording direct proof or disproof. Thus, although an ordered succession of fossils would not necessarily prove descent with modification, a completely random record in an orderly succession of rock layers would disprove it.

The first edition of the "Origin of Species" was published a hundred years ago, and the fossil record considered by Darwin was that of the period preceding 1859. It was even then a considerable record, for paleontology had already been something of a science for fifty years, but its observations were essentially limited to western Europe.

Parenthetically, I might observe that interestingly enough Darwin was first influenced by an extra-European record. In the opening paragraph of the introduction to the "Origin of Species," Darwin relates (1859, p. 1) that, "When on board H. M. S. *'Beagle'* as naturalist, I was much struck with certain facts in the distribution of the inhabitants of South America, and in the geological relations of the present to the past inhabitants of that continent. These facts seemed to me to throw some light on the origin of species—that mystery of mysteries, as it has been called by one of our greatest philosophers." I cannot resist quoting also the remainder of this opening paragraph. "On my return home, it occurred to me, in 1837, that something might perhaps be made out on this question by patiently accumulating and reflecting on all sorts of facts which could possibly have any bearing on it. After five years' work I allowed myself to speculate on the subject, and drew up some short notes; these I enlarged in 1844 into a sketch of the conclusions, which then seemed to me probable: from that period to the present day I have steadily pursued the same object. I hope that I may be excused for entering on these personal details, as I give them to show that I have not been hasty in coming to a decision."

Especially in regard to fossil vertebrates, the record of Darwin's day was a defective one, and Darwin himself recognized this. He spent considerable time pointing out the incompleteness of the record. In so doing he gave an extremely penetrating and revolutionary analysis of the record—revolutionary because, contrary to established theory of the day, he argued that the geologic record was a discontinuous record of a continuous process rather than, as most geologists thought, a continuous record of a discontinuous process. It has been said that such an eminent geologist as Adam Sedgwick was horrified at Darwin's position (H. E. Wood, 2nd, oral com-

munication, 1958). In this Darwin was, of course, making a virtue of necessity for it was obvious to him that the fossil record as it was then known hardly furnished positive support for his theory. In fact, leading vertebrate paleontologists of that period were chiefly of a school opposed to descent with slow modification (Cuvier, Hugh Miller) and some (Richard Owen) never were convinced even long afterward.

As an example of what the paleontological record meant to most of them, I cite the Scotch paleontologist, Hugh Miller, who in 1852 gave as his address, when taking the chair for the first time as president of the Royal Physical Society of Edinburgh, a discourse on "Geological Evidences in favour of Revealed Religion." In referring to the plants and animals of the last three Eras of time, Miller (1859, p. 311) asked the worthy gentleman present "whether, at those grand lines of division between the Palaeozoic and Secondary, and again between the Secondary and Tertiary periods, at which time the entire type of organic being alters, so that all on the one side of the gap belongs to one fashion, and all on the other to another and wholly different fashion,—whether they have not been as thoroughly impressed with the conviction that there existed a Creative Agent, to whom the sudden change was owing, as if they themselves had witnessed the miracle of creation?" Further, Miller (*ibid.*) continued, "may we not hold that the acquaintance with bygone creations, each in succession of a higher type than the one which preceded it, which geology enables us to form, must soon greatly affect the state of arguments employed on the sceptical side, which, framed on the assumption that creation is but a 'singular effect'—an effect without duplicate,—have urged, that from that one effect only can we know aught regarding the producing Cause." The prose is a bit cloudy, but here Miller is arguing against both descent with slow modification and a single, special creation. Darwin later (1859, p. 280) could only counter by saying, "Why then is not every geological formation and even stratum full of . . . intermediate links? Geology assuredly does not reveal any such finely-graduated organic chain; and this, perhaps, is the most obvious and serious objection which can be urged against my theory. The explanation lies, as I believe, in the extreme imperfection of the geological record." This imperfection, Darwin then discussed in considerable detail.

The fossil record of vertebrates has improved tremendously since 1859. Indeed by comparison with the present one it can almost be said not to have existed in 1859. Of extinct fossil mammalian

genera, less than 10 per cent of the current number were then known, and none of them had been studied, of course, from an evolutionary point of view. The most complete historical record of mammalian life now known is that of the Great Plains area during the last forty million years of the "Age of Mammals." This area was barely becoming known in 1859—likewise the well-known fossil fields of South Africa and South America. Eastern Asia was a paleontological void.

Darwin seemingly was not able to cite a single evolutionary sequence among fossil groups. His nearest approach to giving such a sequence was in comparing the relationship of geologically late fossil types from particular regions with those now living in the same region. He wrote (1859, p. 339), for example, "Mr. Clift many years ago showed that the fossil mammals from the Australian caves were closely allied to the living marsupials of that continent. In South America a similar relationship is manifest . . . clearly seen in the wonderful collection of fossil bones made by MM. Lund and Clausen in the caves of Brazil. I was so much impressed with these facts that I strongly insisted, in 1839 and 1845, on this 'law of the succession of types'—on 'this wonderful relationship between the dead and the living.'" He then pointed out how difficult it was to explain this relationship on the basis of then current theories, and that it was "at once explained"—by the theory of descent with modification.

The first proposed family tree or evolutionary record based on fossils was that of the horse. It was not, however, until 1872 that Thomas Huxley suggested that a sequence in Europe of *Palaeotherium-Anchitherium-Hipparion-Equus* might represent an example of evolution over a long period of time. In 1873 the paleontologist Kowalesky, with a more extended study, came to the same conclusion. Of course, *Palaeotherium* is not a horse and the other fossils represent side-branches of the tree. These gentlemen dealt with the fossil horses of Europe, and the ones available to them were no more than a very approximate series. The direct record was to be found in North America, a fact first announced by O. C. Marsh in 1874, as the American evidence rapidly came to light following the Civil War, especially from the Great Plains area.

Before leaving Darwin and his day, it might be mentioned that another point which worried him greatly was the element of time. Physicists of the 19th Century thought the history of the earth to be considerably shorter than Darwin believed it should be under his theory. Protesting on Darwin's part did no good. Lord Kelvin,

for example, simply stated that physics was an exact science which geology and zoology were not, and theory must be altered to fit the facts. As a matter of record, Darwin's views on the duration of geological time disturbed even Charles Lyell, the great English geologist whose geological work had influenced Darwin so much in reaching his theory of organic modification (H. E. Wood, 2nd, oral communication, 1958). (One suggestion of Darwin was that the time from Late Mesozoic to Recent might be on the order of 300 million years.) Backed to the wall by the physicists, Darwin (1878, p. 409) made this prophetic statement: "With respect to the lapse of time not having been sufficient since our planet was consolidated for the assumed amount of organic change, and this objection, as urged by Sir William Thompson [Lord Kelvin], is probably one of the greatest yet advanced, I can only say, firstly, that we do not know at what rate species change as measured by years, and secondly, that many philosophers are not as yet willing to admit that we know enough of the constitution of the universe and of the interior of our globe to speculate with safety on its past duration."

In the hundred years since 1859, thousands of specimens of fossil vertebrates have been collected from over a large part of the earth. The improvement in knowledge is very great indeed. These specimens arranged stratigraphically, or in temporal sequence, show a strong sequential order (even as they did in Darwin's day) in which gradual approach in anatomical structures is made to those found in existing species. Even under casual inspection it is obvious that only two interpretations of this record are possible: (1) that repeated special creations have occurred in complex and irregular fashion which tend ever more toward existing life, or (2) that descent with slow modification has occurred. The older ideas of repeated special creation with complete obliteration of the older creations are untenable because both larger and smaller groups do pass across boundaries of geologic periods, and frequently across Era boundaries as well. Figure 1 shows the known Permo-Triassic orders of terrestrial vertebrates and their ranges with respect to the Paleozoic-Mesozoic boundary. Only 12 per cent of the orders end with the Permian (close of the Paleozoic Era), 25 per cent across the Paleozoic-Mesozoic boundary, 31 per cent are first known in the Early Triassic, and 31 per cent are not known until Late Triassic time. This is hardly the type of boundary pictured by Hugh Miller. Further, the range of taxonomic units, even as small as genera, is frequently not consonant with these boundaries. The Mesozoic is

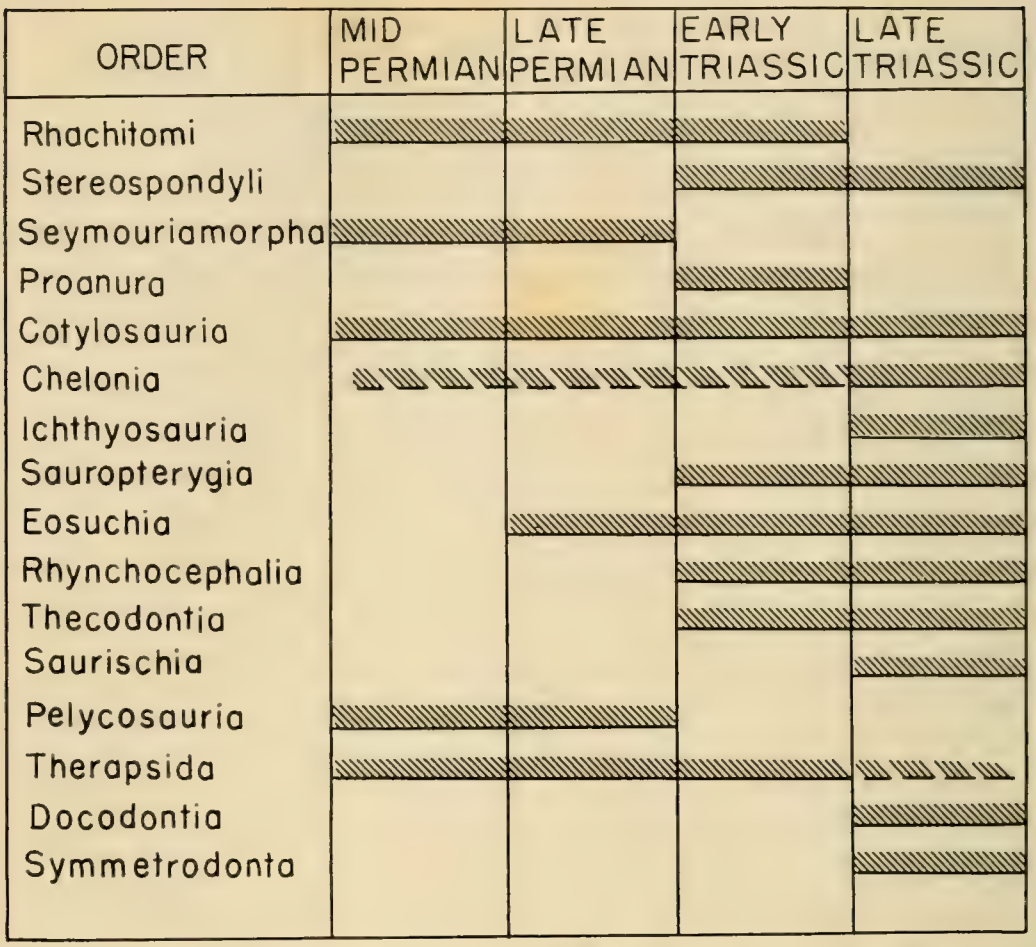

FIG. 1.—Temporal ranges of Permo-Triassic orders of terrestrial vertebrates.

popularly called the "Age of Reptiles," and the Cenozoic the "Age of Mammals," but the genera of reptiles listed below failed to hear the announcement on extinction.

REPTILIA KNOWN FROM BOTH LATE MESOZOIC AND EARLY CENOZOIC OF NORTH AMERICA

Eosuchia	Chelonia
Champsosaurus	*Compsemys*
Lacertilia	*Basilemys*
Iguanavus	*Adocus*
Exostinus	*Peritrisius*
Peltosaurus	*Plastomenus*
Harpagosaurus	*Platypeltis*
Crocodilia	*Caretta*
Leidyosuchus	
Crocodylus	

Likewise, morphological distinctions between major classes of animals are obliterated in the fossil record. Thus, there are known intermediate species between Osteichthyes and Amphibia (*Ichthyostega*), Amphibia and Reptilia (*Seymouria*), Reptilia and

Aves (*Archaeopteryx*), and Reptilia and Mammalia (*Tritylodon*, or even the living *Ornithorhynchus*). Moreover, for the Osteichthyes-Amphibia and Reptilia-Mammalia we have a series of transitional steps. These steps were covered in a relatively short span of time for the fish-amphibian transition (Mid-Late Devonian, 30 million years), and a much longer span for the reptile-mammal "transition" (Late Pennsylvanian-Late Triassic, 75 million years). The longer time for the latter results from a difference in concept as to what is meant by transition in the two cases.

The evolution of the vertebrates is recorded almost entirely by step-like series of fossils, with each step representing a structural break of considerable magnitude in terms of ordinary mutations. This record is best interpreted as a record of evolution although it is not possible to rule out absolutely the idea of a complicated pattern of special creations (unless ruled out on the grounds that special creation of any kind, in the ordinary meaning of the term, involves belief in a force which cannot be accepted into the world of scientific theory). Hence, there is considerable importance in demonstrating the occasional existence of series of fossils in which successive steps in the chain match more exactly the changes anticipated from a study of modern genetics. Such a series now exists in the classic case of the horse, and also in a number of other groups of fossil mammals such as camels and oreodonts.

Various detailed sequences within the horse series cover morphological changes of greater magnitude than the breaks usually present in the fossil record of vertebrates, and so finally it may be stated that the present record of fossils (fossil mammals at any rate) is sufficiently good to demonstrate the reality of evolution to the satisfaction of all who would accept the idea under any circumstances.

The fossil record is also now sufficient for us to obtain a fair picture of the pattern of evolution—some parts more detailed than others—and it is with some phases of this pattern that I now want to deal. Unfortunately, although the paleontologist can observe this pattern, he can only deduce explanations of it from theories developed by the neozoologist, and hence "proof" for many conclusions in the sense familiar to experimental scientists is not present.

In modern vertebrate faunas, we have few animals that are intermediate or transitional between categories of a higher sort. This is so because those that existed were eliminated long ago, along with the ancestral members of the categories. As a result of the absence of any examples on which to base an opinion, we might imagine these transitional kinds of animals to have had characters each neatly

intermediate between those of an ancestral category and those of its supposed descendant group. The living monotremes might or might not furnish us a warning in this regard. They show characters that are strikingly reptilian (the shoulder girdle) mixed with strictly mammalian ones (such as the structure of the middle ear).

Clearly, in many fossil annectants, as in monotremes, rather than intermediate characters as such, a mosaic is present of "nearly static ancestral and evolving descendant characters" (Schaeffer, 1956, p. 201). De Beer (1954), the English anatomist, has called this phenomenon "mosaic evolution," and considers it characteristic of the transition phase in the evolution of higher categories. The transitional form has structures altogether typical of the ancestral group combined with progressive structures which are usually definitive of the new category. The animal has feet in both camps as it were, a condition which probably has survival value. An example may be cited of a Triassic fish group known as the Subholostei. These fish as a group bridge the gap between primitive Paleozoic palaeoniscoids (living relatives are sturgeons), and the more advanced fish of the Holostei (with living representatives such as the gar pike), but in mosaic fashion. For instance, the maxilla in some has a primitive, palaeoniscoid shape and articulation (Fig. 2); the tail in some has the short axial lobe typical of higher Holostean (Jurassic) fish. Another and perhaps more familiar example is the earliest known bird, *Archaeopteryx;* although typical feathers are present, having a pattern of distribution quite like that of modern birds, they are associated with a typical reptilian tail and forelimb. The therapsids, those reptiles leading toward the mammals, have long been noted also as an example of this kind of evolution. In them, several lines of descent lead toward the primitive mammals, each line ex-

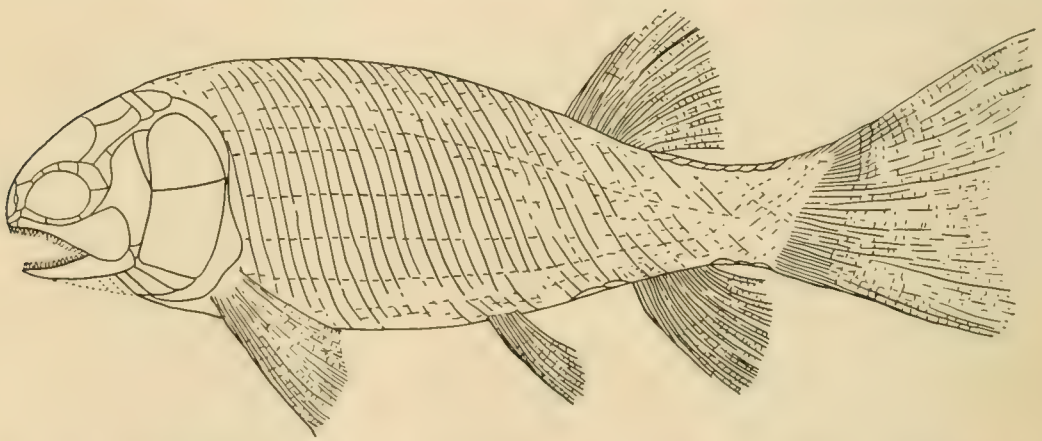

FIG. 2.—The subholostean fish, *Mendocinia.* (After Schaeffer, 1956, fig. 2)

hibiting different combinations of reptilian and mammalian characteristics. The platypus is a survivor of one of these lines.

Almost all biologists are agreed, I think, that the evolutionary process is chiefly one of adaptation between organism and environment. Some would, in addition, ascribe a role of varying importance to non-adaptive evolution; others, however, would deny any such evolution. In regard to the fossil record, the vertebrate paleontologist, A. S. Romer, has stated (1949, p. 103), "Evolution as seen in the fossil record is in its entirety a study of continual adaptive processes, for any feature of mutational nature which becomes well enough established in a group to appear in the fossil record is surely sufficiently advantageous to be considered an adaptation or is associated genetically with adaptive features in other structures or functions." It seems possible to think of structures accidentally appearing once in a great while, which neither have functional importance nor harmful quality to the organism. These might be conserved because of their neutral aspect. Nevertheless, I would suppose that conservation of energy would operate, and selective pressure would be exerted to prevent these structures from developing far and to eliminate those that ceased to be adaptive (*i. e.*, functional). Let us consider some examples of adaptation taken from the fossil record.

The mammalian order Rodentia contains about one-third of all living genera of mammals. At any lower taxonomic level, including individuals, rodents are as abundant as all other mammals together. They are also common as fossils although not so abundant relatively as their Recent relatives.

Figure 3 shows abundance in rodents as represented by number of genera plotted against time. For comparative purposes the Insectivora and Carnivora are also shown. Insectivores and rodents are both groups of small mammals about equally difficult to collect as fossils. The difference in shape of these two ordinal plots shown in the figure suggests that collector's predilections, amount of surface exposure of rocks of different ages, and other factors have not influenced the record unduly. It may also be said that rodents, although extremely rare numerically in the late Paleocene when they first appear, are thereafter abundant as specimens regardless of the extent of their taxonomic differentiation.

Taken at its face value, this record shows rodents originating sometime in the Paleocene, and thereafter differentiating at a relatively steady rate. An increase in diversification is suggested for the Oligocene, a slight recession in the middle Miocene, and in the late Miocene-early Pliocene an acceleration that continues to the

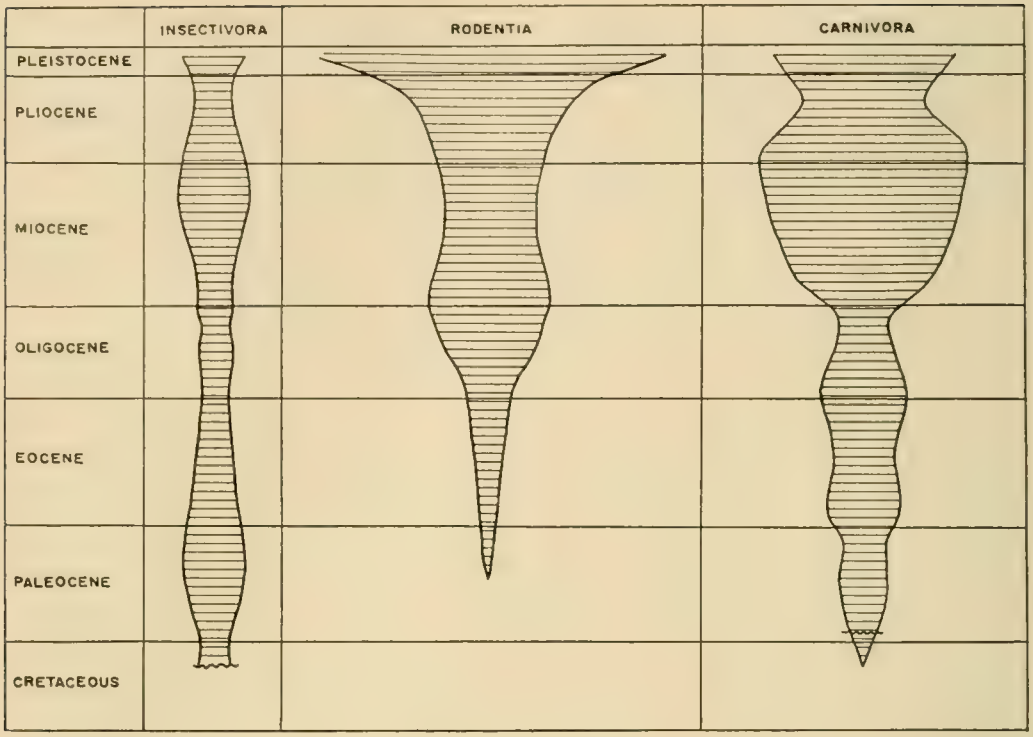

FIG. 3.—Numbers of known genera of rodents, insectivores, and carnivores plotted against time.

Recent. The recession in the middle Miocene may be real or an artifact of the record; the picture otherwise seems probable to me. The expansion from late Miocene to Recent seemingly is to be associated with the origin and rapid differentiation of the Muridae, the most abundant of living mammals. Broadly, however, the record of the rodents is that of continuous diversification within the framework of a major adaptive feature—gnawing.

There have been, in the history of rodents, two periods of rather rapid development of the structures concerned with gnawing. The first period was in the Paleocene, at which time the gnawing habit was rapidly acquired (Wilson, 1951). (This "rapid acquisition" is based on several lines of evidence—all inferential, but convincing to me.) Following initial development of gnawing incisors, there was only slow increase in ability to gnaw over the next twenty million years or so (Eocene), during which time the rodents underwent their primary taxonomic expansion. The second period of rapid development was near the close of the Eocene, when several different lines of rodents developed specializations of the jaw musculature, simultaneously but somewhat differently, which permitted really heavy gnawing among later Tertiary members of the order. This development probably accounts for the Oligocene bulge in Figure 3. Since that time further improvement in gnaw-

ing has been slow, adaptive modification centering on other anatomical features.

These periods of rapid development seem characteristic of the fossil record, when development of a major adaptive feature is concerned. The vertebrate paleontologist, G. G. Simpson (1953, p. 335), has discussed this phenomenon of rapid evolution at some length and has stated that it occurs while populations are shifting from one major adaptive zone to another, and especially when a "threshold" is crossed. The term threshold may be used when several correlative trends reach such a point that a major change is possible. For example, in rodents it occurred when development of strong masseter muscles in connection with oblique grinding action of the molar teeth, together with development of the incisors as forceps, as in many insectivores, set the stage for genuine if feeble gnawing. Animals with such features, the mixodectids, were in existence in mid-Paleocene time, although none of the known ones seem involved in the ancestry of the rodents. Rapid evolution also occurred later (late Eocene) when several developments combined to make strong gnawing possible for the first time.

We do not know what environmental stresses in rodents were involved in the changes just mentioned. Comparable changes are seen, however, in the feet and teeth of horses in Miocene time, and in the development of limbs in the earliest tetrapods of the Devonian. Here we can speculate with some assurance as to what these environmental pressures were: spread of open grasslands, in the first case, which opened the way for a new mode of life on the prairie and restricted the old mode, and periodic failure of the local water supply, in the second case, which put a premium on ability to migrate overland at times.

Acceleration in evolution is not restricted, however, to major break-through into new environments and new modes of life. Figure 4 illustrates a case of simple, accelerated increase in size in one line of fossil beavers, the Castoroidinae. An approximate growth curve of anteroposterior length of cheek-teeth against time has been plotted. Selective factors in this particular case are not known. During the earlier part of the history of this line, the constituent forms (*Monosaulax, Eucastor, Dipoides*) increased in average size slowly and apparently almost steadily, but did not show any tendency toward giantism. Indeed, the mid-Pliocene (Hemphillian) *Dipoides* was smaller than the contemporary true beavers. *Procastoroides* of the late Pliocene-early Pleistocene (Blancan) was larger than modern *Castor*, and the rate of size-change had

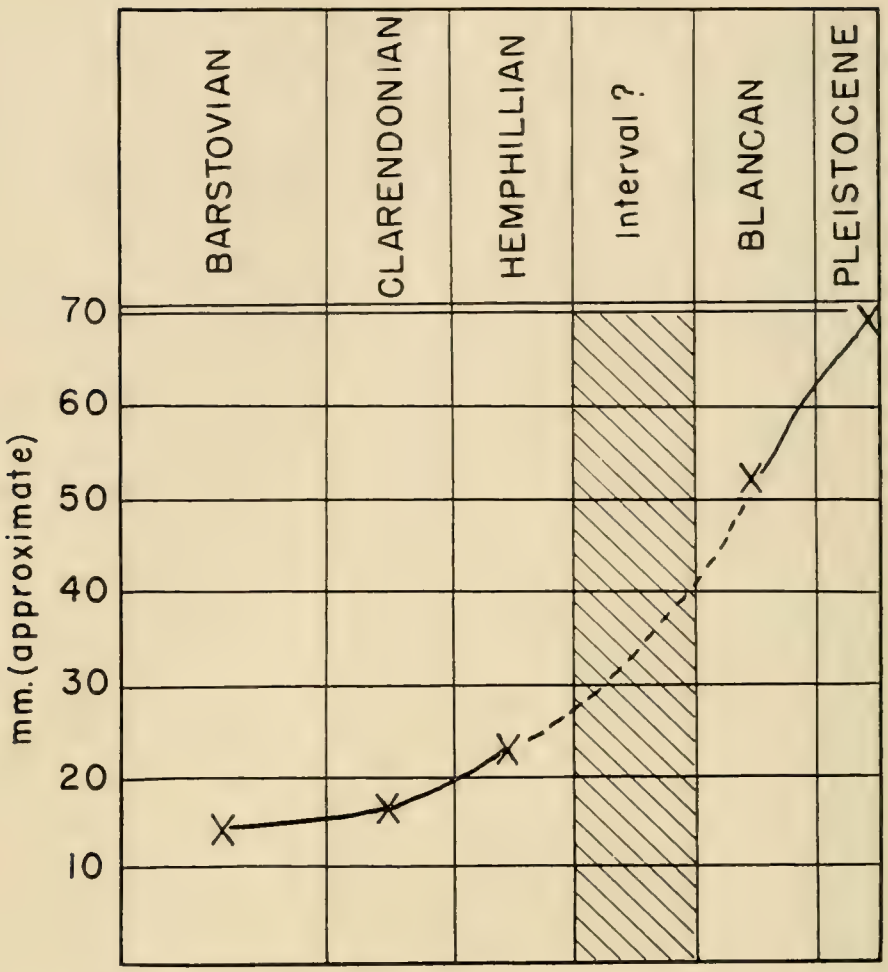

FIG. 4.—Rate of change of length of cheek-teeth ($\underline{P4}$-$M\underline{3}$) in Castoroidinae. (After Wilson, 1949, fig. 11)

by that time obviously increased. The Pleistocene *Castoroides* had a tooth-row twice as long as in *Castor*, and the animal itself was many times the size (probably of eight to nine times greater bulk) of any living beaver (Wilson, 1949, pp. 147-148).

Let us turn to some secondary phenomena of adaptation. Orthogenesis means different things to different biologists and philosophers. One common meaning, however, is that "variations and hence evolutionary change occur along certain lines impelled by laws of which we know not the cause" (Lull, 1929, p. 151). Or we might say that natural variability is such as to force evolution (adaptation) along certain paths only (Butler, 1946). Some would have it that the cause is within the organism (*elan vital*, limited direction of genetic variability), others that it is the result of the guiding hand of the Supreme Creator. In any case, orthogenesis is opposed to the factor of natural selection stressed by Darwin as an explanation of adaptation.

It is frequently thought that paleontologists developed the theory of orthogenesis, that most believe in it, and that the historical record of the horse proves it to them. That the paleontological record suggests orthogenesis to some investigators, not necessarily paleontologists, is probably partly owing to the difficulty, in most cases, of determining environments and environmental change, and partly because the more incomplete the record of a group, the more rectilinear the family tree appears to be—as for example, when only a single fossil is known for some existing animal. Moreover, orthoselection seems certainly involved in simplifying the record. That is to say, "once a group has become to some extent specialized, it is more likely to continue along the same path by the selection of suitable mutations as they arise, than to become adapted to a different mode of life" (Butler, 1946, p. 218). Whatever else may be said for the idea of orthogenesis, the geologic history of the horse certainly does not prove or even suggest it. But, as Simpson has pointed out, although students of fossil horses know this, almost no one else does. The non-specialist is in some ways hardly to be blamed. Figure 5 is a lineage of the horse from Lull's famed textbook, "Organic Evolution" (1929). Note how the eye is led up from *Eohippus* (equals *Hyracotherium*) to *Equus* and that only two North American side-branches are shown. Contrast this with Figure 6, a "simplified" version of what probably did happen (Simpson, 1953, p. 261). Furthermore, there is not a single character of the horse, so far as known, which shows a steady trend from *Hyracotherium* to *Equus*. Figure 7 (after Simpson, 1953, p. 265) shows how some principal features of the Equidae really were modified during the long, fifty-million-year history of the group. Moreover, several of these features (hypsodonty, for example) can be correlated directly with environmental modification.

A frequent, secondary effect of adaptive evolution is convergence. This is a phenomenon in which there is considerable morphological resemblance in unrelated animals because of similar modes of life. The resemblance of the ancestral types is distinctly less. There are frequent examples from the records of both living and extinct animals. Figures 8-10 show some typical cases. Figure 8 is an example of convergence in dentition among extinct allotheres, both living and extinct marsupials, and extinct primates. The dentition, in each case, has shearing premolars followed by multituberculate molars and seems adapted to shearing through fibrous or tough outer layers of vegetable matter, followed by crushing or grinding

of the pieces by the molars. The end results of convergence in the several lines depicted are sufficiently alike to have misled some taxonomists in the past. A second example, Figure 9, is between sabre-toothed cats (which are true cats) and sabre-toothed marsupials, both groups now extinct. Several other sabre-toothed

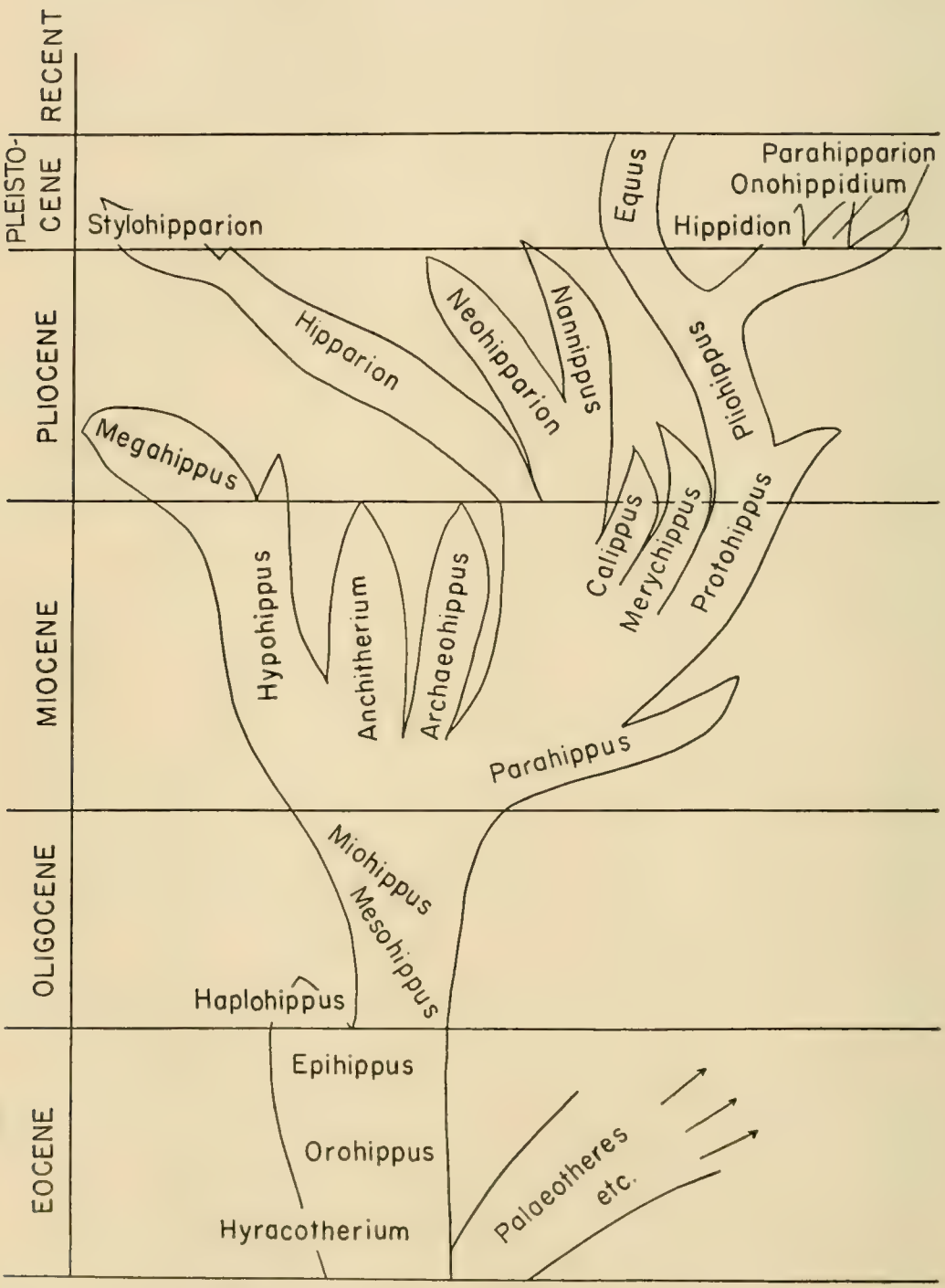

FIG. 5.—Phylogeny of the Equidae according to Lull. (After Lull, Organic Evolution, 1929, p. 591: reproduced by permission of The Macmillan Company)

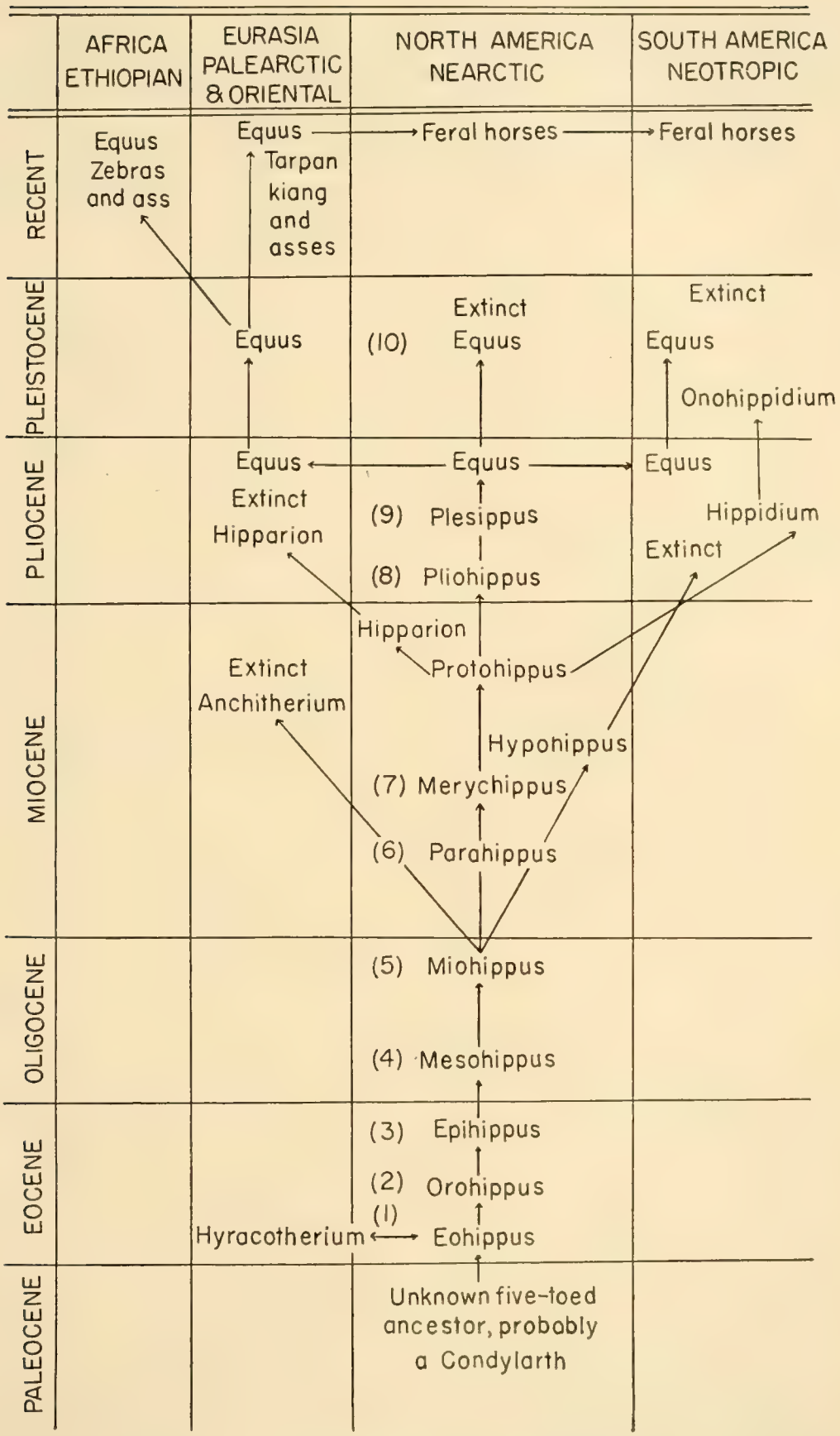

FIG. 6.—Phylogeny of the Equidae, greatly simplified. (After Simpson, The Major Features of Evolution, 1953, fig. 33: reproduced by permission of Columbia University Press)

mammals from different sections of the Mammalia could also have been figured. The similarities are startling, but no prolonged analysis is necessary to demonstrate the lack of close relationship involved. Lastly, Figure 10 is an example obviously affecting the entire animal to a considerable degree—convergence between a por-

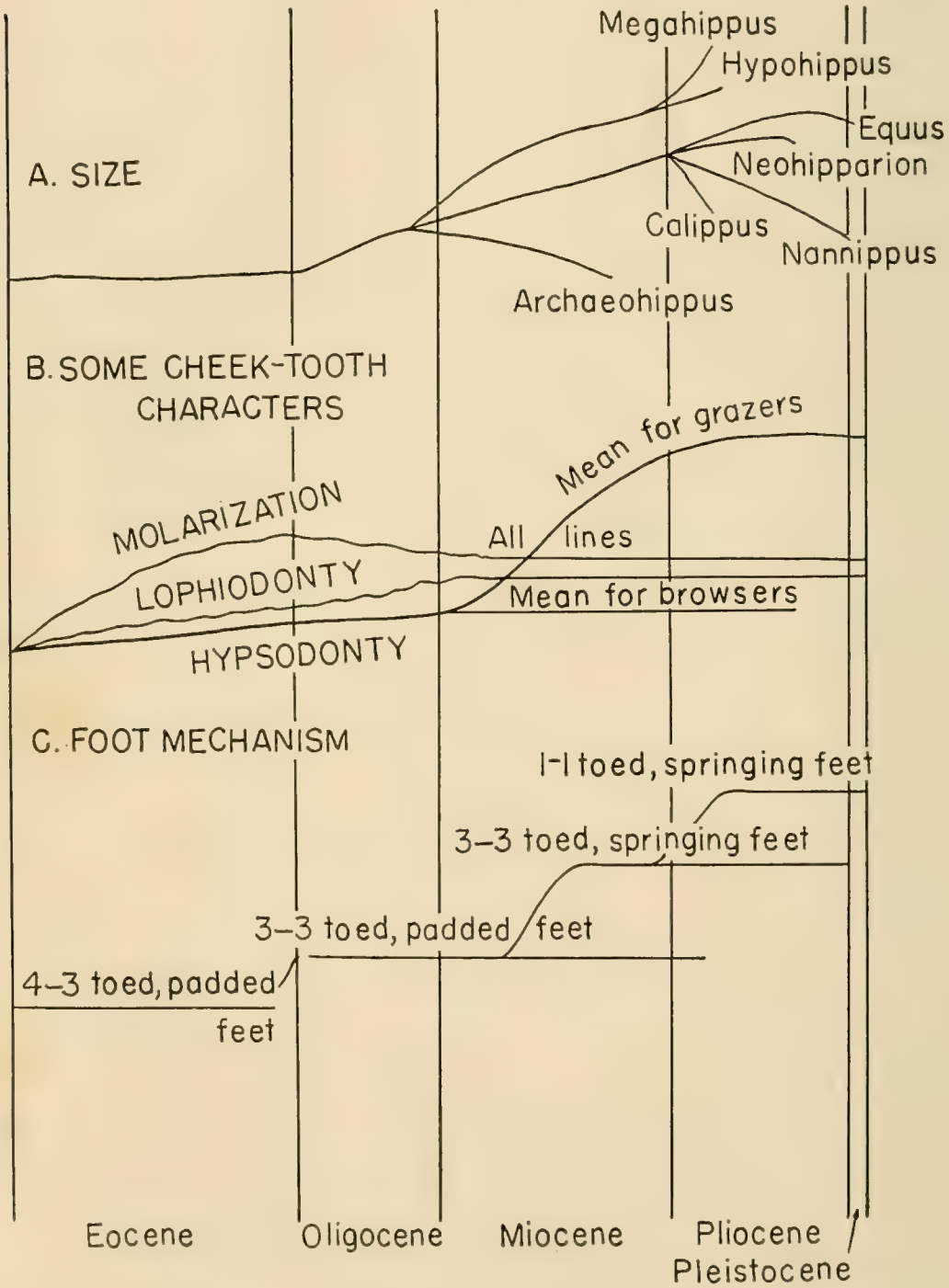

FIG. 7.—Evolution of characters in the Equidae. (After Simpson, The Major Features of Evolution, 1953, fig. 34: reproduced by permission of Columbia University Press)

poise (mammal) and an ichthyosaur (reptile). Both have converged toward fish, but even more toward each other.

Parallelism, often confused with convergence, is a phenomenon in which forms closely related to each other possess characters in common which are lacking in their common ancestry. Habitus and heritage are both similar. Examples are extraordinarily abun-

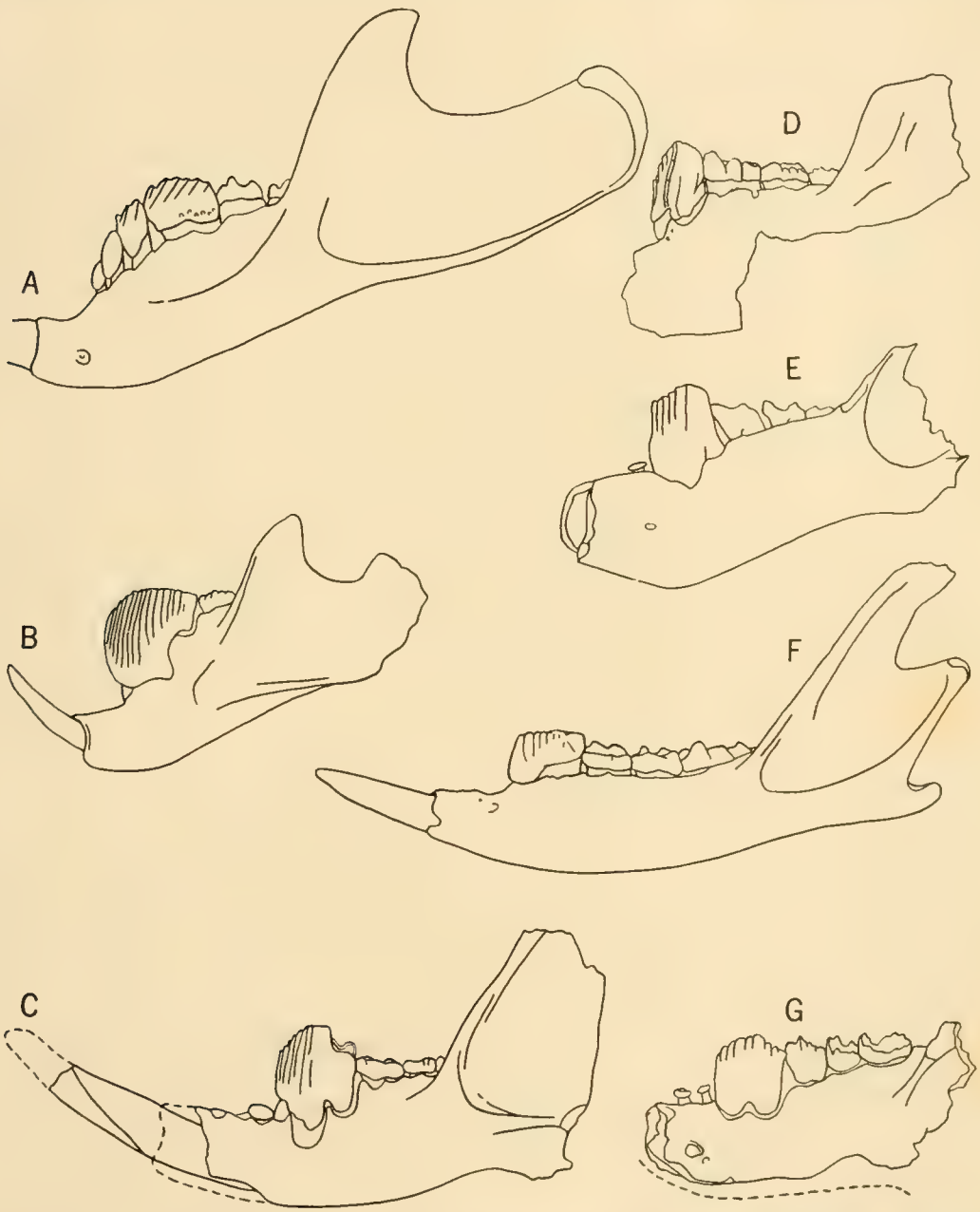

FIG. 8.—Dental convergence in some mammals. A, *Ctenacodon* (multituberculate); B, *Ptilodus* (multituberculate); C, *Abderites* (extinct South American marsupial); D, *Polydolops* (extinct South American marsupial); E, *Burramys* (extinct Australian marsupial); F, *Bettongia* (Recent Australian marsupial); G, *Carpolestes* (extinct primate). (Modified after Simpson, 1933, Journ. Mammalogy, p. 100, fig. 1)

dant. Figure 11 is of New and Old World porcupines. The quills and a number of other structures are parallelisms.

In parallelism, the complex of genes in the several forms under consideration is the same, or nearly so. In convergence, the gene complex may be quite different. The two phenomena are kept sep-

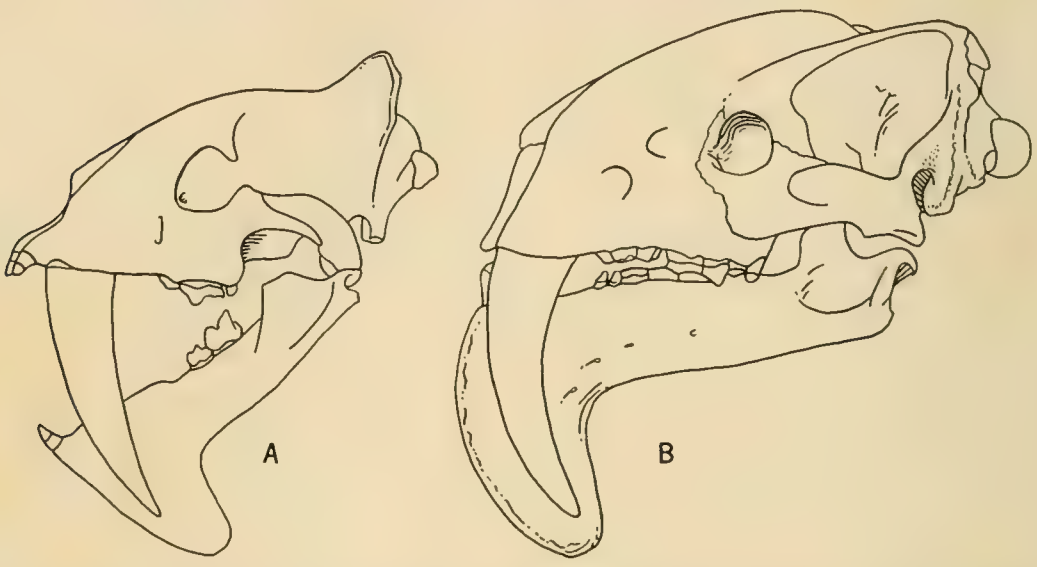

FIG. 9.—Convergence in skull and dentition between A, sabre-toothed cat (*Eusmilus*), and B, sabre-toothed marsupial (*Thylacosmilus*). (After Riggs, 1934, Trans. Amer. Philos. Soc. (n. s.), vol. 24, pt. 1, fig. 4.)

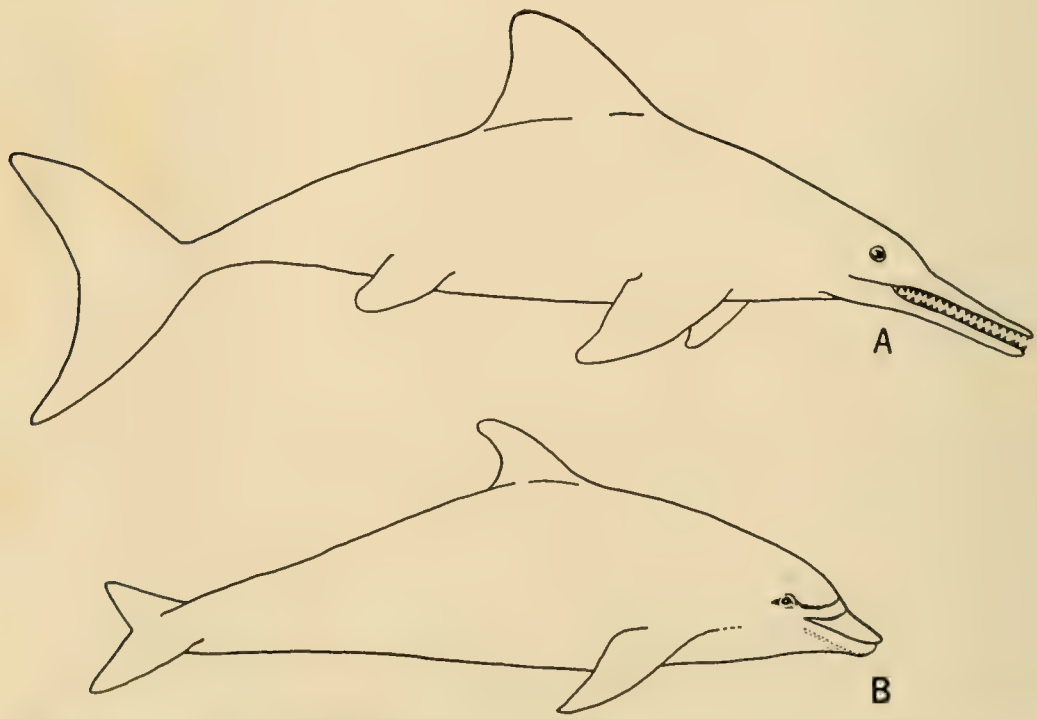

FIG. 10—Convergence between A, an aquatic reptile (ichthyosaur), and B, an aquatic mammal (porpoise).

arate by most paleontologists. Nevertheless, from the standpoint of morphology, the difference is largely one of perspective. The sabre-tooths just mentioned did have a common ancestor in the Mesozoic. True, they diverged for some time before converging, but splitting of a stock into two or more lines, with some initial divergence of morphology, must take place if parallelism is to be a later phenomenon.

Lastly, something should be said about extinction, which may be viewed as failure to adapt. This is a phenomenon which is largely a geological one, although we can learn a certain amount about the mechanisms of extinction by studying the relatively minor Recent examples available to us.

Romer (1949) has remarked that extinction is the common lot, survival is the exception, and he has suggested that not more than one per cent of Middle Mesozoic tetrapods have living descendants. Moreover, since the earth can support only so much total organic life, and since the existence of certain groups in certain situations prevents other groups from moving into these situations or developing offshoots that can, extinction must be extensive if progressive evolution is to go on (Simpson, 1953, p. 281). It would seem that extinction is as important a process as origination. Much less attention, of course, has been given to it and its causes.

In addition to the fact that extinction is the common lot, it also

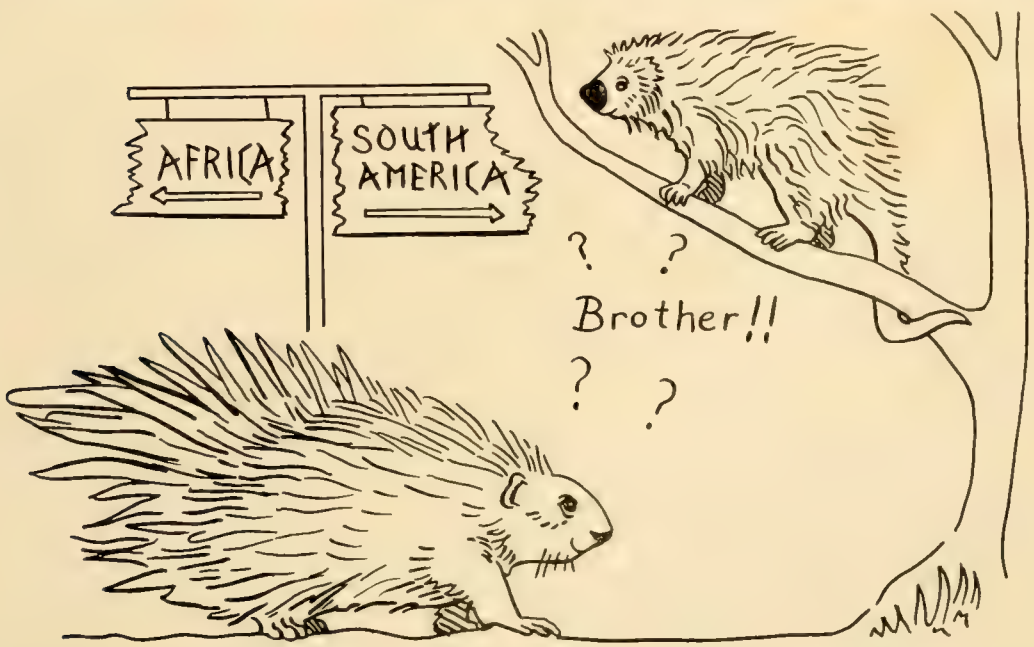

FIG. 11.—Parallelism between Old and New World porcupines. (After Simpson, 1953, Evolution and Geography, fig. 4. Oregon State System of Higher Education, Eugene)

seems true that at times in the history of the world there has been more than the average amount of it—as for example among vertebrates at the close of the Mesozoic. It is on these peaks that most of our attention has been focused. What caused the extinction of the dinosaurs is a question answered with a new explanation by someone almost yearly.

It may be said straight off that no single factor yet advanced seems adequate to explain the extinction of dinosaurs, or of any other major group of animals. At present, we simply do not know, in specific terms, what causes these sweeping extinctions. We do know in general terms that a group which becomes extinct does so because it failed to adapt to changing environments, but that is all. Yet certainly any animal group, such as the dinosaurs, which had survived to the end of the Mesozoic had done so by being able to meet all environmental changes for a very long time. Finally, however, the rate of adaptive response fell behind the rate of environmental change. How difficult it is for us to study the phenomenon of extinction may be seen by the fact that there is no evidence of any significant environmental change in the area during the time when dinosaurs were becoming extinct in the Rocky Mountain region. All we can show of change at this time is that climates were becoming slightly drier, slightly cooler. Such factors as increased pressure from mammals, changing food supply, meteoric showers, and the like, seem, at least when taken singly, to be ineffective.

Some other explanations of extinction are: (1) momentum in evolution, that is, that groups evolve themselves out of existence by "overspecialization"—a sort of suicide, and (2) racial old age, that is, that groups, just as individuals, pass through infancy, youth, maturity, and old age, finally dying of old age. The first of these two theories has more respectability, but neither seems built on more than a few cases in which orthodox solutions are not readily apparent.

Perhaps man, in his wisdom, has introduced another, as yet only potential, factor in extinction. He has for a long time been able to control his immediate environment to a certain extent. He is now able to modify it somewhat over larger areas. If he cannot already do so, at least the possibility exists that he will be able shortly to modify it greatly and rapidly over large areas via atomic explosions. If the worst does happen, he will be the only organism in the earth's history that became extinct because of its ability to control the

environment. We have come a long way since the dawn of earth history. We have come a long way even since 1859.

I have been reviewing, briefly and inadequately, a number of topics. What has been said may be summarized now in the statements which follow.

The geological succession of "organic beings" shows beyond all reasonable doubt that evolution has occurred. This succession can demonstrate phylogeny, and actually does so in some groups. The fossil record shows in at least some cases that morphological gaps of considerable size are bridged by innumerable steps of small size. The fossil record demonstrates that transitional species frequently exhibit a mosaic of characters of both ancestral and descendant species, rather than a mean for each character. The record by itself cannot interpret evolution. If we are permitted a reasonable amount of deduction from our data—and relying strongly on the work and observation of biologists working with modern plants and animals—we can think of the fossil record and of evolution as a phenomenon of adaptation. There seems nothing in this record that casts doubt on the efficacy of natural selection in producing adaptations, and in special cases there is evidence in support of it as opposed to other factors. Perhaps in any case, it is sufficient for the paleontologist to show what did happen, if he can do this, and leave the why and the wherefore to his colleagues in other biological disciplines.

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