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On the Origin of Life

The possibility of recurring biogenesis and the abiotic origin of optical activity are considered.

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The theory of evolution holds that all living things are interrelated by common descent from an original case of successful biopoesis (*1*). A plausible explanation of how biopoesis may have taken place has been developed over the past two or three decades. Somewhat modified, this explanation can be marshaled in support of the hypothesis that neobiogenesis (*1*) has been a continuing possibility since life first originated. The rejection of this possibility on the grounds that the conditions which established life no longer exist is not entirely justified.

Origin of Organic Compounds

The most productive hypothesis regarding such conditions is that of Oparin (*2*). The gradual origin of hydrocarbons and other organic substances, including amino acids, from a reducing atmosphere of H_2, NH_3, CH_4, H_2S, and water vapor is convincingly detailed, and the subsequent formation of polypeptides and polynucleotides of high molecular weight, colloidal systems, and biochemical pathways ("harmonious correlation of separate chemical processes") leading, eventually, to formation of the first living organisms is logically developed in *The Origin of Life*. Theoretical and experimental support for this hypothesis is already accumulating through the work of Urey (*3*), Miller (*4*), Fox (*5*), Abelson (*6*), and others. The operation of this hypothesis requires atmospheric conditions, levels of radiation, and ocean temperature, sterility, and salinity which no longer obtain. The origin of life under such conditions involving the whole spectrum of the evolution of life, starting from inorganic substances, probably could have occurred in only one stage of the earth's history. Repetitive neobiogenesis, nonetheless, was possible, and still is possible, from the *organic* milieu, enriched in amount and variety by living things.

Oparin's hypothesis calls for the gradual evolution of simple, then complex, organic substances at a propitious time in the history of the earth, until the waters attained an appreciable concentration of a great variety of organic compounds, interacting systems, and coacervates. Life was then supposed to originate from this organic "soup" (*7*). This reasoning holds as well for the continual origin of equally primitive, though not necessarily identical, simple organisms ever since, out of the abundant variety of *organic* substances ever present since the beginning of life.

Arguments against Recurring Biogenesis

The time factor. Several arguments are leveled against this view. The time factor is one. It will be conceded that from an inorganic atmosphere the origin of organic substances of sufficient complexity and concentration to support the establishment of the first living things might have required special conditions and have taken many millions of years. The sterility which existed before the origin of organisms put no premium on time. After the appearance of organisms, it is unlikely that most organic substances maintained their integrity for more than short periods of time. But in the presence of a complex organic milieu, on the other hand, the time required for the transition from highly complex lifeless systems to metabolizing replicating systems (of the nature of primitive living things) is greatly reduced. Given the proper combination of substances and circumstances, neobiogenesis actually may take only a relatively short time.

A complexity of organic compounds and reacting systems exists today almost everywhere. For example, a cell undergoing cytolysis releases into its environment (which may already be rich in organic substances) globules of colloidal material, microsomes, compounds in different stages of reaction with one another, compounds undergoing sequential reactions still in progress, and so on. It is conceivable that out of such surroundings and under specific conditions, a metabolizing system can arise which has the attributes of life. This is not meant to imply that the components released by a disintegrating cell may be regrouped to form another kind of cell. Rather, this is meant to point to the possibility of the existence locally, at times, of circumstances capable of supporting neobiogenesis in a manner similar to that proposed for the first instance from the original mixture of organic substances. Nor is it implied that neobiogenesis, as

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outlined here, was or is a phenomenon of frequent occurrence; rather, it is proposed that there is a distinct possibility that this event has occurred throughout biological time and may still occur today. The frequency of such an occurrence is a matter which at present cannot be readily determined.

Competition against existing organisms. Another line of reasoning against the occurrence of repetitive neobiogenesis concedes, for the sake of argument, that it is a possibility but proceeds to claim that it would be impossible for a primitive living thing thus evolved to survive in the face of fierce competition from the organisms already present and adjusted to the environment. The assumption that an organism, simply because it is newly arisen, will have no adaptive features and will meet insuperable competition in any place and at any time is unwarranted and untenable. The argument has validity only if it can be established that all organisms of neobiogenetic origin would meet with overpowering competition. This reasoning is based on an exaggeration of the concept of the struggle for existence and ignores interspecific compatibility and aid. As long as it is conceivable that a newly arisen organism may be compatible or symbiotic with the existing organisms in its environment, the argument is invalid. In addition, it is possible that through neobiogenesis subsequent to that of the period when living forms first evolved, parasitic organisms may be established—a situation not possible in the first instance. The original organisms had to have a metabolism independent of the existence of other organisms. Since then it has been possible for organisms which lack various functions (for example, forms without the complete metabolism necessary for independent existence) to arise and lead a parasitic or symbiotic existence. If a unit possessing an incomplete metabolism should arise out of the variety of organic compounds existing today, it would be destined to be destroyed in any local environment devoid of living things. In the presence of cells or organisms possessing the requisite complementary metabolism, such a neobiogenetically evolved form would have a chance of survival. Indeed, for such forms, the presence of other organisms, instead of posing the threat of certain extinction through fierce competition, becomes the *sine qua non* of their origin and survival. Thus, a wider variety of simple organisms can originate through neobiogenesis today than was the case when living forms first evolved; the first organisms, perforce, had to be of more specific and limited metabolic scope.

Biochemical similarities among all organisms. Another line of argument against repetitive neobiogenesis points to the similarity in the chemistry of all organisms. This subject has many aspects. For example, all naturally occurring amino acids, regardless of source, are of the L form, with notably few exceptions. It is argued that since D and L forms are mutually antagonistic or require different enzymes, the first organisms could incorporate one or the other, but not both, into their metabolism. The evidence is interpreted as showing that chance favored the L form (*8*). Repeated neobiogenesis, it is argued, would establish organisms which by chance incorporated the D form, and the notable absence of this form is taken to mean a lack of successful instances of neobiogenesis since the period when living organisms first evolved.

Another aspect of this argument is based on the identity of or great similarity between organic compounds found in widely different forms. The same amino acids are found to compose the different proteins in widely different species. Similar metalloporphyrins are the active components of chlorocruorins, chlorophylls, hemoglobins, cytochromes, peroxidases, and catalases, although these compounds may have different biochemical roles. A wealth of other examples exists. Still another argument along the same lines is based on the presence of identical or very similar biochemical pathways in widely different organisms. For example, the ornithine-citrulline-arginine pathway, the tricarboxylic acid cycle, the mechanism for the transfer of electrons in the oxidation-reduction system, and the activity of nucleic acids and "high-energy" triphosphates are found in unicellular and multicellular organisms, plant and animal.

The foregoing observations are taken to mean that the original instance of biopoesis occurred through chance incorporation of specific stereoisomers and specific types of organic compounds. All subsequent organisms, it is claimed, arose by descent from the original form and thus were compelled to utilize the same compounds. Mutation, based on the existing substances, established an increasing variation in compounds, pathways, and species, which were all interrelated, however, through common descent. Organisms descending from separate forms of neobiogenetic origin, it is argued, would be expected to show greater variation, some of these forms having been established, by chance, with opposite antipodes, different organic compounds, and different pathways.

All these observations overlook the probability that, some time after the first organisms arose, the preponderance of biochemically important, optically active, organic substances changed from racemic mixtures to the isomers characteristic of the first successfully established organisms. Whereas the synthesis of organic substances in the absence of living things would usually lead to the formation in equal quantities of both forms of enantiomorphous substances, enzymatic synthesis results in the formation of only one of the antipodes. As the formation of organic compounds shifted from abiotic synthesis to synthesis by living things, there occurred a change in over-all synthesis from racemic mixtures to, preponderantly, the biologically selected isomers. Gradual degradation of the biologically rejected antipodes and their conversion into the biologically accepted ones would result in the shift of emphasis mentioned. Subsequent instances of neobiogenesis would have to occur within such a milieu, and consequently the forms would possess a chemical similarity to pre-existing organisms. Too, subsequent forms of neobiogenetic origin, having as a basis not only existing organic molecules but also existing reacting systems—that is biochemical pathways — would exhibit common metabolic aspects. Such organisms would consequently contain many compounds, develop biochemical pathways, and exhibit reactions characteristic of pre-existing organisms.

Origin of Optical Activity

Intramolecular displacements and conversion of racemates are not the property of living things or enzyme systems only. This problem has been investigated by Winstein, Streitweiser, and others (*9*). In the last few years evidence has also been adduced for stereospecific polymerization in the presence of complex catalysts (*10–17*). Ziegler (*10*) reported the formation of polymers of high molecular weight with complex catalysts under normal conditions of temperature and pressure. These catalysts consisted of a mixture of $TiCl_4$ and triethyl aluminum in heptane. The polymerization of ethylene under these conditions takes place rapidly and is devoid of short-chain branching. Natta and his school expanded these observations with intensive investigation (*12–17*) of modifications of the Ziegler catalysts. They experimented with combinations of $TiCl_3$ and of $TiCl_4$ with aluminum trialkyls (AlR_3) where R equals CH_3 up to C_8H_{17}. Stereospecific polymerization occurred and was highest with the violet crystalline form of $TiCl_3$ and triethyl aluminum, the longer-chain alkyls being less effective (*14*). Other factors which affect stereospecific polymerization are discussed by Natta in a later paper (*16*). Some of these polymers, on crystallographic analysis, appear to have a helical structure and are formed by terminal addition of monomers (*12*); this brings to mind the end-chain addition of mononucleotides to deoxyribonucleic acid primer (*18*) and to ribonucleic acid (*19*). The structure of the catalyst complexes was also studied (*15*). It was found that the active catalytic centers are metallo-organic complexes which exist in enantiomorphous pairs, each member controlling the synthesis of the corresponding antipodal polymer. The result is a mixture of optically active antipodes. This resembles stereospecific synthesis in living forms where each stereoisomer has its corresponding enzyme and differs from the usual abiotic synthesis of stereoisomers, in which both antipodes result in equal numbers from the same catalyst. In the latter case a single mechanism operates, and chance determines the alignment of an asymmetric center in any of its possible positions. It is not possible to separate such a process into different specific stereoisomeric syntheses. In the former case this is conceivable, and as Natta points out, it would be of "remarkable interest" to isolate the asymmetric active centers corresponding to only one of the two enantiomorphous forms, "since it could solve the problem of asymmetric organic synthesis in the field of macromolecules" (*15*). Many important developments can be expected from this new research field. These considerations raise the question whether some resolution of racemic mixtures could already have taken place or optical activity could have already occurred before the emergence of life, the occurrence of specific antipodes in the first organisms thus being not merely left to chance.

Past Controversy

A brief historical survey may be pertinent at this point. Experimental evidence at various times has been brought in support of, and against, the possibility of spontaneous generation. Aristotle's (*20*) belief in spontaneous generation dominated scientific thinking for many centuries. Outstanding among his followers was Needham (*21*) who, two thousand years later, defended spontaneous generation, whereas his contemporary Spallanzani (*22*) held the opposite view. The controversy was once again revived one hundred years after that by Pouchet (*23*), who supported the possibility of spontaneous generation, and Pasteur (*24*), who apparently closed the issue by disproving the contention of his antagonists with his brilliant experimentation. Aside from the fact that, in general, a negative result in an experiment merely tells of the failure of that experiment but does not necessarily preclude success in further experimentation, all experiments testing neobiogenesis have been of too limited a scope to be valid. Contrary to popular belief, Pasteur did not disprove spontaneous generation, as an examination of his reports will show, but rather, he demonstrated the faultiness in design of the experiments of his predecessors who claimed to have shown the occurrence of spontaneous generation. His papers bear titles such as "Experiments relative to generation said to be spontaneous." His central interest was in showing that fermentable mixtures would not ferment if they were not brought into contact with the "germs" present in the air but would do so on exposure to such particles. He successfully demolished the contention of those who claimed to have demonstrated spontaneous generation but did not disprove "once and for all" the possibility that the most primitive microorganisms originated through neobiogenesis. In more recent years, with the technological, biochemical, and philosophical advances that have been made allowing deeper penetration into the problem, the ever-recurring question once again may be raised, but at a more sophisticated level.

Proposed Modification of the Monophyletic Theory of Evolution

Repetitive neobiogenesis, as suggested above, would establish organisms similar in metabolism to known forms. The suggestion that repetitive neobiogenesis may be expected to establish exotic forms of life different from the form of life as we know it may have a place only in science fiction. It may very well be that life as we know it—that is, the complex, interdependent metabolic reactions supported in a structure we recognize as protoplasm—is the only form that matter can eventually take in its evolution toward the origin of organisms. Indeed, it is possible, even though it appears improbable, that life can exist only with the specific isomers which we find associated with it, and that the presence of these isomers was not the result of random choice but of necessity.

One may well ask what is gained by proposing the repetitive origin, in time, of organisms based on a structure and metabolism similar to pre-existing organisms. The answer, of course, is that it does not matter how similar the results of neobiogenesis are to pre-existing organisms. But the idea that neobiogenesis is possible, and may have been taking place ever since life first occurred, does matter. Concretely, it would appear more plausible to accept present-day viruses as units of recent and present origin than to suppose that they descended through some two billion or more years relatively unchanged. Throughout time, viruses either evolved into higher organisms or were eliminated in the process of evolution, being ever re-established through neobiogenesis. The same may be said for bacteria at any period in time, except that bacteria probably represent some degree of evolution from a more primitive progenitor. They, too, are destined for further evolution or elimination, while progenitors, already arisen, continuously evolve into the newer bacteria.

The discontinuities in the paleontological evidence are explained away by the contention that some forms are not subject to fossilization, while many that are did not encounter the conditions favorable for fossilization, and, finally, the conclusion that many discoveries have yet to be made. Some of the discontinuities, however, can be viewed as the result of separate cases of neobiogenesis. The same may be said of the discontinuities in the taxonomic arrangement of existing organisms. The difficulty of placing viruses, bacteria, certain "algae," sponges, and so on, in a fitting place in any taxonomic scheme based on a monophyletic hypothesis may stem from the possibility that the discontinuities are real and represent the existence of separate lines of descent from independent instances of neobiogenesis at different times in the history of the earth down to the present (*25*).

References and Notes

1. *Biopoesis* is used here in the same sense as at the 1957 Moscow conference on the origin of life, to refer to the whole process of the evolution of life from inorganic beginnings, whereas *neobiogenesis* is used to refer to the establishment of primitive organisms *de novo* from a complex organic environment already present from any source. The term *'spontaneous generation'* is associated with theories proposing the spontaneous origin of higher organisms—flies, frogs, rats, and so on—as well as microorganisms from lifeless matter. Its use is avoided in this discussion, except in a historical sense.
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3. H. C. Urey, *Proc. Natl. Acad. Sci. U.S.* **38**, 351 (1952).
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6. P. H. Abelson, *Ann. N.Y. Acad. Sci.* **69**, 276 (1957); lecture before the International Oceanographic Congress, United Nations, New York (Sept. 1959).
7. Recently J. D. Bernal (preprints, International Oceanographic Congress, 1959) restated his hypothesis that small organic molecules —amino acids, purines, pyrimidines, and so on—appearing in the waters were concentrated by adsorption on estuarine and terrestrial clays and there polymerized into molecules of greater molecular weight. The latter were then released and, along with other complex organic compounds in the environment, interacted to form a protoplankton. Under such conditions life could originate, eventually, without requiring the presence of an organic "soup" throughout the hydrosphere. Abelson (International Oceanographic Congress, 1959) called attention to the random interaction of organic compounds in aqueous solution in vitro to form an unusable tarlike mass. Moreover, the presence of adsorbents would, he maintained, prevent the waters from attaining anything like the concentration of a "soup."
8. G. Wald, in his article "The origin of optical activity" [*Ann. N.Y. Acad. Sci.* **69**, 352 (1957)], proposes the view that the first organisms incorporated both enantiomorphous forms of optically active substances, but that the operation of the principle of natural selection on a molecular level established in living things the present isomers which "won the fight" over their antipodes.
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11. F. Eirich and H. Mark, *J. Colloid Sci.* **11**, 748 (1956).
12. G. Natta, *J. Polymer Sci.* **20**, 95 (1956).
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14. G. Natta, P. Pino, G. Mazzanti, P. Longi, *Gazz. chim. ital.* **88**, 219 (1958).
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23. F. Pouchet, "Hétérogénie ou traité de la génération spontanée, basée sur de nouvelles experiences" (Paris, 1859); *Compt. rend.* **47**, 979 (1858); *ibid.* **48**, 148, 546 (1859); *ibid.* **57**, 765 (1863).
24. L. Pasteur, *Compt. rend.* **50**, 303, 674, 849 (1860); *ibid.* **51**, 348 (1860); *ibid.* **56**, 734 (1863); *Ann. chim. et phys.* **3**, 64 (1862).
25. The views expressed in this article have been the result of much pondering over a long period. They could hardly have come to fruition in my mind without the many stimulating discussions on a wide variety of subjects in which I was privileged to participate. Outstanding among these were the lectures and seminars which are the fare every summer at the Marine Biological Laboratory, Woods Hole, Mass., and the many conversations with friends with whom I could confidently discuss these somewhat unorthodox ideas. I wish to mention especially my colleagues B. P. Sonnenblick and G. Panson, my research assistant Paula Gottdenker, and Lionel Luttinger of the American Cyanamid Co. Their friendly but penetrating criticism taxed me again and again and helped me to a better expression of my thoughts. I cannot speak for the extent to which I have convinced those who have heard me, and I must take the responsibility for the ideas expressed in this article.

Somatic Radiation Dose for the General Population

The report of the Ad Hoc Committee of the National Committee on Radiation Protection and Measurements, 6 May 1959

At its meeting in November 1958, the executive committee of the National Committee on Radiation Protection and Measurements undertook to re-examine the problem of exposure of the population to man-made radiations from the point of view of somatic effects as distinct from genetic effects. This review was undertaken because of the widespread public concern over the possible effect of radiation from fallout on the population, and because of the possibility that there might be some new, definitive information regarding the somatic effects of chronic low-level radiation on man.

The NCRP was unaware of any new basic information on somatic effects of radiation, upon which it could with sound reason recommend specific changes in permissible exposures for individuals or for population groups. The NCRP felt that information relative to the question was essentially the same as that outlined in National Bureau of Standards Handbook 59. However, it appeared desirable to make a new and independent examination of the problem for the purpose of affirming the views of the NCRP. For this purpose, the NCRP established an Ad Hoc Committee to examine the question further.

At its inception, the National Committee on Radiation Protection and Measurements centered its activities primarily around the problem of radiation hazards associated with industrial and medical uses of radiation. During succeeding years, it became increasingly apparent that NCRP could not ignore its responsibility for making recommendations concerning radiation exposure of larger population groups. Cognizance was taken of this problem at various times—for example, in NBS Handbook 59 (issued 24 September 1954), on pages 78 and 79, in the paragraphs "Non-occupational Exposure of Minors" and "Number of Ex-