The Proteinoid Theory of the Origin of Life

And Competing Ideas

SIDNEY W. FOX

The number of requests I am receiving for photomicrographs suggests that we can expect dozens of new textbooks with passages or chapters on the origin of life. Dozens of textbooks of biology with such inclusions have indeed already appeared, most of them since 1971. The first textbook of biochemistry to include a chapter on the origin of life was Albert Lehninger's, published in 1970. Lehninger has explained that armchair speculation was being replaced in the 1960s by serious scientific investigation.

Late in the 1960s, in fact, we had one relatively complete theory (and physical model) of the origin of a reproducing protocell, derived from geologically relevant experiments. During the development of this theory, alternatives for individual component concepts have appeared. I have recently presented elsewhere (Fox 1973a) a comparison of some of the alternative concepts. In responding to the present invitation, I shall again outline the proteinoid theory and then examine competing or alternative concepts in the light of our sequential experimental model.

My view of most of the competing concepts is expressed precisely by Florkin and Stotz (1972):

According to [John] Northrop, there is a common pattern in all controversies . . . . "There is a complicated hypothesis, which usually entails an element of mystery and several unnecessary assumptions. This is opposed by a more simple explanation, which contains no unnecessary assumptions. The complicated one is always the popular one at first, but the simpler one, as a rule, eventually is found to be correct. This process frequently requires 10 to 20 years. The reason for this long time lag was explained by Max Planck. He remarked that 'scientists never change their minds, but eventually die.'"

In the case of the proteinoid theory, as in those cases described by Northrop, we have a relatively simple explanation, with no unnecessary assumptions. The explanation emerged from experiments so simple that innumerable students at all levels have repeated many of them.

Sidney W. Fox is professor of chemistry and director of the Institute for Molecular and Cellular Evolution at the University of Miami, Coral Gables, Fla. 33134. His Ph.D. is in biology (biochemistry) from the California Institute of Technology. He has been U.S.-U.S.S.R. interacademy exchange lecturer with A. I. Oparin (1969), and he is vice-president of the International Society for the Study of the Origin of Life. He has received the Florida Academy of Sciences gold medal, the Priestman lectureship, the Idldles award, and a number of other honors specifically for his advances in the theory of the origin of life, in addition to recognition for his contributions to biochemistry, especially amino acid sequence determination. He was recently presented with a festschrift; the authors include Pauling, Szent-Györgyi, Calvin, Lipmann, Charles Price, and Florkin. Fox is the author or coauthor of more than 200 technical articles and several books. The present paper was given at the 1973 NABT convention.
Fig. 2 is a view of proteinoid. Proteinoid is what is produced in the laboratory; protoprotein is the term for proteinoid that, according to interpretation, originated spontaneously on the Earth. The theory has emerged from the preparation and properties of proteinoid. These polymers have molecular weights, typically, of 5,000–12,000; they contain some proportion of each of the amino acids common to contemporary protein; and qualitatively they have virtually all of the properties of contemporary protein (Fox and Dose 1972). The polymers are usually produced in substantial yield, such as 20–60%, from amino acids. The most striking feature of the process is its utter simplicity—a simplicity imputable to conditions at the surface of the Earth even now.

According to our analyses, the principal reasons that our laboratory is the only one to have presented a comprehensive physical and conceptual model (in 1967) for the origin of life are the following:

1. Life began in essentially only one way, although it may have done so innumerable times.
2. We have studied processes in open systems, comparable to what has occurred in the geologic realm. Closed flasks used in the laboratory by others are far less relevant to the geologic realm.
3. We have discovered for each stage self-ordering phenomena leading to the next stage.
4. The proteinoid microsphere is found to have numerous properties of the contemporary cell and to be evolvable toward the latter. Such emergent functions had to be determined by experiment; they were not predicted.

Some of the experiments, however, began as working hypotheses. The organized body of interpretations is referred to as the proteinoid theory of the origin of life (Florida Academy of Sciences 1968); it is a sequentially coherent conceptualization.

One of the earliest of the competing concepts is that of the famous chemist Emil Fischer (1906), who said (approximate translation):

If today, through a lucky accident, with the help of a brutal reaction, for example, a melting of amino acids in the presence of a water-removing medium, there should successfully be produced a true protein, and if it were further possible, which is still unlikely, to identify the artificial product with the natural material—this would benefit protein chemistry little and biology not at all.

What was indeed true in 1906 is not true today; there is enough additional understanding to produce a true significance. Also, if Fischer had recognized the ease with which material resulting from melted amino acids would easily form a kind of cell, he might have seen a relationship to what is the first problem of biology: the origin of life. But his view must have been in part the understandable myopia of one early chemist. Charles Darwin, however, imagined in a letter to a friend in 1871 “that a protein compound was chemically formed ready to undergo still more complex changes” (F. Darwin

yield huge numbers of model cells. These lack some of the properties of contemporary cells, but they possess others. The properties observed include a content of highly ordered, protometabolically active molecules, ultrastructure, some kinds of selective permeability, and the ability to reproduce by four physical mechanisms. The properties found are those essential for further evolution. Up to the stage of amino acids, many alternative explanations are available (Fox and Dose 1972; Fox et al. 1973). The subsequent two steps are without experimentally developed alternatives. Those above the upper horizontal line in fig. 1 are based on partial experimental demonstration (Fox 1974).
Fischer's view and Darwin's earlier view seem to me to have been truly competitive with each other. However that situation is analyzed, I found, as late as 1963, a number of chemists and biochemists whose views were much like those of Fischer in 1906; in some cases it seemed to me that I was confronting an emotional as well as a dialectic barrier.

The principal advances in the art up to an act of spontaneous generation of a (minimal) cell are seen in Table 1. Also included are competing assumptions that were prevalent at the time the experiments were designed. Had these negative assumptions and others been taken seriously, the experiments would not have been performed.

The idea that synthesis of protein requires a cell is simply one of the later battles with vitalism, this contest having often to be refought. The experimental advance number 1 is one modern equivalent of Wöhler's synthesis of urea in the absence of a cell.

<table>
<thead>
<tr>
<th>Advance</th>
<th>Inhibitory assumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Protein(oid) can be produced acellularly</td>
<td>Synthesis of protein requires a cell</td>
</tr>
<tr>
<td>2. a-Amino acids can be thermally copolymerized</td>
<td>a-Amino acids are decomposed by heating (Carothers and nylon)</td>
</tr>
<tr>
<td>3. Heated a-amino acids order themselves</td>
<td>Disordered polymers would result (E. Fischer, A. I. Oparin, etc.). Nucleic acids were needed</td>
</tr>
<tr>
<td>4. Arrays of enzymic activity result from 3</td>
<td>Matter cannot organize itself</td>
</tr>
<tr>
<td>5. Proteinoids aggregate to form minimal cells upon contact with water</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Principal advances in concept resulting from investigation up to an act of spontaneous generation, with inhibitory assumptions.

Fig. 3. Reproduction of proteinoid microspheres through a budding cycle. M is microsphere; B is bud. Subscript denotes number of generation.
Another conceptual inhibition was that of fig. 2, on the left. Decomposition to tars was the usual expectation from heating α-amino acids. This view was fortified when W. H. Carothers (1936), instead of heating α-amino acids, H₂NCHCOOH, heated ω-amino acids, H₂N(CH₂)₄COOH [n = 5] to produce a first nylon. In many respects, Carothers improved upon silk protein, a polymer of α-amino acids. He indicated, however, the difficulty or futility of heating α-amino acids. The clue to overcoming this difficulty was the copolymerization of mixed α-amino acids in which nonneutral α-amino acids were present.

Emil Fischer, A. I. Oparin (1957), and numerous others since have expected that a primordial polymerization would yield disordered products. Yet others have assumed that nucleic acids would have been needed for such ordering. The idea that amino acids could order themselves comes the closest to being a prefatory assumption of any working hypothesis for our experiments. The concept of self-ordering was, however, not truly an assumption. We observed such action in enzyme experiments we were doing in the early 1950s (Fox et al. 1953).

Once proteinoids had been produced and internal order of the amino acid residues had been demonstrated, the finding of enzymic functions was more easily understood.

The concept of self-organization (table 1) is one I shall take up later.

In accord with the progression of fig. 1, the protocell—the product of "self"-aggregation of proteinoid—is depicted next, in fig. 3. These are proteinoid microspheres reproducing through a budding cycle. They are approximately 15 μm in diameter. Both the first-generation and second-generation (F₁) microspheres are highly uniform in diameter. The growth process is accretive, or heterotrophic.

The main properties found in the proteinoid microspheres are shown in table 2. (The microspheres have many other properties of contemporary cells [Fox and Dose 1972].) They can be subtracted from the

### Table 2. Some salient properties of proteinoid microspheres.

- Limited range of size
- Ultrastructure
- Types of semipermeability
- Ability of immature particles to grow heterotrophically
- Ability to reproduce (four modes)
(Other properties in Fox and Dose 1972)

![Fig. 4. Model protoribosomes composed of basic proteinoid and homopolynucleotide. These are smaller than proteinoid microspheres.](image-url)

![Fig. 5. Synthesis of peptides by models for protoribosomes. System consists of microspheres, ATP, and phenylalanine. I, III, and IV are peptides of phenylalanine. II is unchanged phenylalanine.](image-url)

### Table 3. Experimental advances from reproductive protocell toward contemporary cell.

1. Internucleotide bonds are synthesized by proteinoid microspheres acting on ATP
2. Thermal polyamino acids and homopolynucleotides form complexes (protosomes) selectively, in some cases codonically or anticodonically
3. Peptides are synthesized by nucleoproteinoid microparticles acting on ATP and amino acid
4. Models of photophosphorylation have been demonstrated
functions of the contemporary cell to visualize what was needed for evolution from a minimal cell to a maximal, or contemporary, cell. Progress has been made toward each of these goals (table 3). To treat these advances, we should first look at the models for the first ribosomes, the protein-synthesizing particles of the contemporary cell (fig. 4). This figure shows complexes of basic proteinoid and polynucleotide. These have several properties of ribosomes; we regard them as models for protoribosomes. They have especially the ability to convert ATP and amino acid, in this case phenylalanine, into peptides (fig. 5).

Work by John Jungck in our laboratory (Jungck and Fox 1973; Fox et al. 1974) has indicated how other microspheres of the right sort could convert ATP into small polymers of adenylic acid. This begins to explain the origin of nucleic acids.

Principal processes that need to be understood to bridge the gap from a model of a reproductive protocell to a contemporary cell (to summarize the analysis) are cellular synthesis of protein, cellular synthesis of nucleic acid, a coding mechanism, and energetic coupling of the collective biota with solar energy.

Having completed a description of the unifying proteinoid model, and having discussed some specific inhibiting assumptions for that model, we turn now to assumptions not directly related to concepts of the proteinoid or its evolution. For practical reasons I have selected fewer than all of those premises. What Northrop referred to as "unnecessary assumptions" require only imagination and assertion; such undisciplined concepts can be virtually unlimited in number. Accordingly, I shall attempt to treat, especially, competing concepts that are recent or have been prominent.

One of the oldest of the conceptual conflicts is that represented in table 4. The problem was stated by Pasteur. Although Pasteur held in disfavor the idea of matter organizing itself into cells, he acknowledged the conceptual possibility. Today's biochemist or biologist refers to such a heterotrophic act as self-assembly. What Pasteur needed was an understanding of the nature and origin of matter of the appropriate kind. Now we can say in answer to Pasteur, a century later, "Yes, matter can organize itself into a cell without parents. We can furthermore specify the origin and nature of the necessary matter, plus many of the properties of the organized units."

Many of the conceptual conflicts reflect choices of appropriate experimental approach. Some of this stems from the fact that leading molecular biologists have concerned themselves with how life began. As table 5 proposes, the essential technique of molecular biology is not appropriate even to asking the question (as T. O. Fox [personal communication 1972] was the first to insist), let alone answering it. Studies of assembly of components into systems, however, are in the same direction as evolution itself. The related questions—(i) whether matter can organize itself and (ii) how one can study such processes—are fun-

![Table 4. Biogenesis vs. abiogenesis.](image)

<table>
<thead>
<tr>
<th><strong>Biogenesis</strong></th>
<th><strong>Abiogenesis (and synonyms)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Virchow (1858): &quot;Omnis cellula e cellula&quot; (&quot;All living cells arise from pre-existing living cells&quot;)</td>
<td>Protobiogenesis</td>
</tr>
<tr>
<td>Biogenesis</td>
<td>Spontaneous generation</td>
</tr>
<tr>
<td>Spontaneous generation</td>
<td>Self-assembly of a protocell</td>
</tr>
</tbody>
</table>

"Pasteur (1864): "There is the question of so-called spontaneous generation. Can matter organize itself? In other words, are there beings that can come into the world without parents, without ancestors? That is the question to be resolved."

![Fig. 6. Natural forces vs. vital forces.](image)

![Fig. 7. Panspermia. How did life begin on Mysticus?](image)
Fig. 8. Steps from amino acids to microspheres.

Amino acids $\xrightarrow{\text{Heat}}$ Proteinoid $\xrightarrow{\text{Heat}}$ Protocell

or

Solution of amino acids $\xrightarrow{\text{Heat}}$ Amino acid mixture $\xrightarrow{\text{Heat}}$ Proteinoid

Fig. 9. Chemical reactions involved in the physical steps of fig. 8.

Fig. 10. Peptide-bond synthesis in organisms occurs to a meaningful extent in the presence of ATP.

Fundamental to our entire discussion. I am not an antireductionist, and before I conclude I hope to show that molecular evolution and molecular biology belong together. They need not be in competition.

A very old competing concept, however, is that of vitalism (fig. 6). The feeling that biologic phenomena cannot be fully understood in terms of physics and chemistry appears and reappears in many ways. As stated earlier, vitalism was not simply and finally negated by Wöhler's synthesis of urea, in 1828. I feel sure that the laboratory production of a model protocell was greatly delayed by the blanketing and recurring belief in vitalism.

Fig. 7 deals with panspermia: the concept that seeds of life appeared on this planet from elsewhere. I do not recall who said it, but this view simply "consigns the problem to a conveniently inaccessible corner of the universe." It tells us nothing about how life originated there or here.

In a recent revival of Arrhenius's old idea of panspermia, Crick and Orgel (1973) have suggested "directed panspermia," with an extraterrestrial spaceship as the agent. Crick and Orgel acknowledge the futility of transferring the problem elsewhere, except that another planet may contain a crucially necessary mineral catalyst. In an earlier paper, Crick proposed that a geologically early mineral permitted replication of nucleic acid; prior enzymic
protein was thereby unnecessary. We will return to that problem.

Fig. 8 deals with the recent criticism, allegedly by the late A. Katchalsky (1973), that our view is one that "life began in an oven." Katchalsky's paper was transcribed from a tape of a talk he gave before his untimely demise in the Lod airport; I am doubtful, therefore, that the statement is quite like it sounds in print. However, in earlier years others made similar statements. What is important here is to separate two steps in our flowsheet. In the first, heat does function, ovenlike, to polymerize amino acids. A second step is necessary. In the second step water triggers the aggregation of the special kind of matter, proteinoid, to a special kind of minimal cell. The correct analogy therefore is that molecular precursors of life began in an "oven," and that life itself, by analogy, began in water.

Moreover, we have shown that heat at a constant temperature can promote two steps (fig. 9): (i) the evaporation of water and (ii) the chemical condensation of the dried residues from a solution of amino acids into polymers of amino acids. This sequence meets all thermodynamic requirements (Fox and Dose 1972). Ordinarily, we polymerize dry amino acids above the contemporary boiling point of water. Such temperatures are not necessary, however. Water can certainly evaporate and does evaporate at lower temperatures; we showed, years ago, that the polymerization of amino acids would occur in the presence of phosphates (Fox and Harada 1966) at temperatures well below 100 °C. (Young [1965] accomplished polymerization with phosphate at 25 °C.) An additional point derivable from this scenario is that, at temperatures that would cause fractionation, the first materials to leave would be water and other volatile organic compounds that arose in the synthesis, such as hydroxy acids. Amino acids would be less volatile, and the polyamino acids that would result from them would be even less volatile. Concentration of the initial reactants would therefore be inevitable, and geologic fractionation would favor the reactions of our flowsheet up to the point of a change in phase resulting from the entrance of water, as by rain or tidal wash.

The above explanation applies also to the question of how adequate concentrations of reactants would occur. This question has been asked in several contexts. The answer is simple, as indicated, being related to the need to recognize processes in open systems (Fox 1973b), as in the geologic realm.

Fig. 10 represents a statement that is found in a recently published book on the chemical origins of life (Ponnampemura 1972a). The statement made there is that amino acids are converted to protein by way of the enzymes, which help the molecules over the energy barrier. I find that principles of physical chemistry and knowledge of biochemistry require for peptide-bond synthesis a provision of free energy. In contemporary organisms, as in our models for protoribosomes, the free energy is supplied by adenosine triphosphate (ATP). The thermodynamic constraint is thus overcome, either in our model or in contemporary organisms, by ATP. Enzymes accelerate reactions; they do not of themselves provide free energy for those reactions that require it.

Table 6 mentions a recently publicized idea: the possibility that the first prebiotic proteins arose from precursors that were not amino acids. This idea was originally suggested in principle by Akabori (1959), and it has been pursued by Matthews (1971). I see no reason, basically, to preclude the origin of pro-
replication in evolution. At first glance, molecular replication appears to be simpler than cellular evolution. Operationally, however, primordial cells are seen to have arisen much more simply. Once thermal polyamino acids arose and water was present (as must have often occurred), minimal cells arose by aggregation of the polymer. These cells have been shown to have the ability to reproduce efficiently by budding and accretive growth of the separated buds. Recently, replication of proteinoid microspheres in four protoevolutionary modes has been described (Fox 1973c). Accordingly, the assumption that molecular replication preceded replication of microsystems is not justified and might have interfered with the development of an understanding of the critical primordial sequence.

I would like now to return to competing concepts for earlier stages in fig. 1—especially to the question of the origin of amino acids, with which we begin the considerations that are presented here. In this conflict of concepts, we have experiments that are interpreted on each side of the question. All of the steps in the flowchart of fig. 1 have been carried out in open systems—a kind of situation that, as has been pointed out, is imperative for geochemical relevance. Many syntheses of amino acids and other simple compounds have been conducted in simulation studies in closed flasks (fig. 12). The reactant gases are thus confined, and one can thereby obtain substantial yields of products. Most significant is the fact that reactions that would not go otherwise can be made to occur because of the retention of compounds as fugacious as diatomic hydrogen, methane, ammonia, and water. The historically influential initial result in a closed flask was thus more one of stimulation than of simulation.

This concept was in part put to the test in the Apollo space program during the past few years. Ponnamperuma (1972b) has pointed out that a “bonanza of organic molecules” was expected in advance from the analyses performed on samples from the surface of the Moon. When one traces the basis for the high expectations through the nested bibliographies, he finds that a considerable part of the basis existed in the closed-flask experiments of Miller (1955). At the end of some of those experiments, however, the hydrogen component was as high as 75%. Such concentration could not have persisted for a significant period in the open realm, lunar or terrestrial.

Earlier, I emphasized that our reactions occur in open systems, as does the subsequent aggregation of the resultant macromolecules in the presence of water. Some investigators have taken the position that peptide bond synthesis should occur in aqueous solution. For this purpose they have used various agents, such as cyanamide, and ATP (fig. 13). A reason that has been given for the use of aqueous solutions for such syntheses is the alleged fact that organisms are predominantly aqueous. Of course, organisms are predominantly aqueous, but the sur-
faces at which reactions are carried out are far different from dilute aqueous solution; I refer especially to the surface of ribosomes. Another point that is missed by the proponents of carrying out such syntheses in aqueous solution is that the origin of promoting agents would require even more drastic conditions than those used simply and directly to make polymers of amino acids by moderate heat. The opponents are therefore also pyramiding unnecessary assumptions. Moreover, the thermal proteinoids (see above) have a roster of properties (Fox and Dose 1972) not shown for the products of any of the peptides obtained in aqueous solutions or at surfaces.

L. E. Orgel and associates (Fuller et al. 1972) have recently produced adenosine and other significant biochemical substances in the absence of water. Orgel’s use of solid-state synthesis is equivalent to the use of hypohydrous conditions, as we have long advocated. These are neither competing nor alternative concepts.

As another example of the utility of hypohydrous conditions, Oró and Kimball (1961) produced adenine in aqueous solution from HCN and ammonia, but Wakamatsu et al. (1966) and associates multiplied Oró’s yield by carrying out the same synthesis under anhydrous conditions.

In fig. 14 we come again to what I regard as a most fundamental aspect of molecular evolution and, therefore, of evolution as a whole. This is the concept that molecules react or interact selectively to yield largely ordered products. The competing concept is expressed in various ways: order out of chaos; material arising from a random matrix; and others.

Our experiments in the thermal condensation of amino acids of different types and experiments in several other laboratories have demonstrated most vividly that the amino acids are ordered to a high degree in the resultant polymers. No prior nucleic acid is necessary. As fig. 14 shows, in an oversimplified depiction of these effects, if one arranges three playing cards in all possible orders, he will get six sequences. This is a random array of the possible orders.

The mistake has been to equate types of amino acids to playing cards or to colored beads, each of which is also of the same shape. Random arrangements can result with playing cards or colored beads simply because they are each of the same shape, irrespective of their labeled identities.

Amino acids, however, are of different shapes. In the fig. 14 depiction of three amino acids we have selected shapes that show how three amino acids that are activated to react with each other would assume a configuration that is determined by those shapes. This is a stereochemical effect. The amino and carboxyl groups of the amino acids are represented by the hook-and-eye, in each case, and the coupling is the same as with amino acids. Because the shapes differ, a unique order can result. The specific joining is determined by the superstructures or, for the amino acids, by the side chains. These processes are remarkably selective. The essential result has been established in a number of laboratories (Dose and Rauchfuss 1972), and in fact the ordering and enzymic results from amino acids (Fox and Dose 1972) present by far the largest body of evidence on the consequences of thermal copolymerization of monomers.

In my view, the principle of normal molecular interactions with stereochemical selectivity can now be seen to be of fundamental significance in nearly all of evolution. Such forces underlie the origin of a first informational (protoprotein) macromolecule, and they underlie the origin of the genetic code. Our original expectation of molecular selection was, however, not an assumption. It developed as a working hypothesis from inferences that we drew from

![Diagram](https://example.com/diagram.png)

**Fig. 13.** Polymerizations of amino acids in water, near water, and in relative absence of water.
enzyme experiments involving amino acids and peptides. Inasmuch as we had worked on terminal amino acid assays since 1944 (before Sanger), we were poised to apply Sanger's technique to the first proteinoids. This was the first evidence of nonrandomness within proteinoids; it was followed by many other kinds of evidence from several laboratories.

One of the most crucial concepts for the proteinoid theory is this one of order resulting from the stereochemical individualities of various types of amino acids. It is not apparent to me that this kind of phenomenon could be identified by analytic, or reductionistic, studies. We would not have been able to infer it from sequence studies by us or by others—only by synthetic or constructionistic experiments.

In fig. 15 the relationships of molecular selection are developed further. Darwinian selection operates on generated and evolved biosystems but not on those arising from a random matrix. Studies of molecular evolution have revealed vividly that constraints in molecular possibilities have been dominant. This, then, is the matrix on which Darwinian selection had to operate. We are only beginning to obtain a quantitative evaluation of that matrix, which by extrapolation must extend also into organismic evolution. The lesson of molecular selection, as preceding and lying at the center of Darwinian selection, is a number 1 take-home lesson.

Fig. 16 concerns a comparison between coacervate droplets and proteinoid microspheres as models for the first cell. It would be difficult to find a definition of the coacervate droplet that would answer the question of whether the proteinoid microspheres are or are not themselves coacervate droplets. However, both in the Soviet Union and in this country I have encountered, many times, a question with respect to whether the typical coacervate droplet, as studied by A. I. Oparin and his school, is similar to or different from the proteinoid microsphere.

The type of coacervate droplet that Oparin usually works with is relatively unstable and nonuniform, as fig. 16 shows. The instability is revealed by the fact that a suspension of coacervate droplets will fall apart into two layers on standing for less than an hour. The stability of proteinoid microspheres overlaps the stability range of cells. The crucial difference, however, is that the coacervate droplets do not answer the fundamental question of how cells came into existence when there were no cells to sire them. This failure has its roots in the fact that the polymers used for coacervate droplets are obtained from cells that are already evolved. The proteinoid microspheres, however, arise from polymers obtained in turn from monomers polymerized under geologically relevant conditions. No cellular parent was needed.

Another competing concept is that of the time required for the origin of life (fig. 17). Again, I am using a model primordial reproductive cell as the analog for the first life. I believe the fact that much time was available has been transmutated, in some way, to “much time was required.” Perhaps much time was required to set the stage, but the experiments show that key events were rapid. The experiments suggest to us that these events occurred often, easily, and in many places on the planet.

This view is reflected also in opposing inferences in table 8. I have recently read the argument that creationistic acts occurred innumerable times and at many stages; but this is not the Biblical view, and we can see, in the scientific context, that self-gen-

---

**Fig. 14.** Random association of playing cards (all of same shape) vs. nonrandom association of amino acids (each of unique shape).

**Fig. 15.** Selection from conceptual possibilities vs. selection from physical possibilities.
erating processes were sufficient to generate and maintain a sequence of events. It is easy to believe that natural processes had many repeat performances. If I, for example, had believed that life arose only once, I would not have done protobiogenic experiments.

Table 9 aligns the proteinoid theory against competing concepts in a broader way, and it serves as one kind of summary. Although this presentation has concerned itself with individually competing concepts, the transcendental overview indicates that only one coherent scientific theory exists, and that it is a sequential continuity of steps based on experiments carried out under geologically relevant conditions.

In table 10 we come to the question of criteria of validity. A popular view is to state that our experiments, or those of others, tell us not what did happen but what could happen. However, the view that chemistry is chemistry wherever and whenever it occurs seems axiomatic. Geologically relevant experiments say more than simply that it could have happened. It had to happen wherever the conditions were right. The question of the origin of life has been shown no longer to be imponderable. Analogously, we can now identify criteria of validity.

Another criterion of validity of a total theory is compatibility of the steps in sequence. This in turn does require the premise that evolution is not one random event arising out of another random event. The validity of this underlying premise is judgeable only by overview and is therefore not easy to come by. I believe the internally limited products from heated α-amino acids are only one such manifestation, however dramatic this one is, of internal self-limiting and self-generating processes in either prebiotic or biotic evolution. If this view is correct, the criterion of sequential compatibility of individual steps appears to be a highly valid criterion of what did happen.

With increasing frequency I have been asked if proteinoid microspheres are alive (table 11). In a generally favorable report on my book with Klaus Dose on the origin of life, one reviewer (Sylvestre-Bradley 1973) has pointed out that the units have the properties of feeding, growth, and reproduction, and he asks “Is this not alive?” He then says, “The answer of course is very firmly in the negative,” and he gives as a principal reason the fact that the microsphere does not have any DNA. This reason is of course a reason for its not being alive in a contemporary sense. We have not claimed that the proteinoid microspheres are alive. I believe, however, that one who claims that they are not alive should be required to present a definition of nonaliveness. The experimental results strongly suggest that the protocell arose and has gone through stages of aliveness and that the experiments should construct the definition—not the reverse.

Finally, the experimentally derived concept of the protoribosome, mentioned earlier, provides a con-

![Fig. 16. Concervate droplets (left; × 320) vs. proteinoid microspheres (right; × 450).](http://online.ucpress.edu/abt/article-pdf/36/3/161/31762/4444705.pdf)

| Table 8. Life only once vs. many protobiogenetic occurrences. |
|------------------|---------------------|
| **Life only once** | **Many occurrences** |
| Divine creation   | Natural processes   |
| Fits best with a single event | Not likely to occur a single time |

| Table 9. Proteinoid theory vs. competing concepts. |
|------------------|------------------|
| **Proteinoid**   | **Competing**    |
| Sequential compatibility | Many reactions not disciplined by experiments |
| Geologic relevance; reactions in open systems | Some not geologically relevant |
| Unified theory to protocell | No complete sequence |
| No unnecessary assumptions | Many unnecessary assumptions |
| Unified laboratory model | |

*PROTEINOID THEORY*
ciliatory missing link between concepts of molecular evolution and of molecular biology. In my view, these two areas need not be regarded as competing (fig. 18). The processes of prebiotic molecular evolution properly preceded the processes of molecular biology. More specifically, the phenomena observed in our model protoribosomes are consistent with the central dogma of molecular biology. The protoribosomes require, however, a prior occurrence of proteinoid to supply, for the evolutionary sequence, enzymes when there were no enzymes to make them and to supply a protocell necessary for the formation of polynucleotides as suggested by experiments; and they provide, in their basic form, components essential for the model of the protoribosome.

The studies in molecular evolution have stressed, perhaps beyond all else, the stereochemical nature of the forces and the self-generating quality of the sequence of processes. Such trends can be seen in the evolution of organisms, but not so simply nor clearly as with molecules alone. In the biologic realm the molecular processes operate in the ramified structures and functions of organisms. In my view, the most fundamental argument for not including creationist overviews in biology textbooks is that the science alone is sufficient to explain in outline what is and has been going on, plus the subtle specificities in the vast array of the biologic realm. No additional agent need be invoked to explain an evolutionary sequence that is proving to be self-generating at every stage that has been studied.

Acknowledgments.—My research has been supported by grants NGR–10–007–08 and 10–007–088 from the National Aeronautics and Space Administration. This paper is contribution 265 from the Institute for Molecular and Cellular Evolution.

REFERENCES

Table 10. Criteria of validity for “could” vs. “did.”

<table>
<thead>
<tr>
<th>Geologic relevance</th>
<th>Sequential compatibility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 11. Aliveness vs. nonaliveness.

<table>
<thead>
<tr>
<th>Aliveness</th>
<th>Nonaliveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has not been claimed for proteinoid microspheres</td>
<td>Has been claimed, but nonaliveness mostly has not been defined . . .</td>
</tr>
<tr>
<td>Except that microsystems lacking nucleic acid or phospholipid are sometimes defined as nonalive . . .</td>
<td></td>
</tr>
<tr>
<td>But these characterize contemporary life, are not necessarily typical of original life</td>
<td></td>
</tr>
</tbody>
</table>

Amino acid + ATP Protocell → Protoribosome

Fig. 18. Interdigitation of concepts of molecular evolution with concepts of molecular biology.

Sequence of processes. Such trends can be seen in the evolution of organisms, but not so simply nor clearly as with molecules alone. In the biologic realm the molecular processes operate in the ramified structures and functions of organisms. In my view, the most fundamental argument for not including creationist overviews in biology textbooks is that the science alone is sufficient to explain in outline what is and has been going on, plus the subtle specificities in the vast array of the biologic realm. No additional agent need be invoked to explain an evolutionary sequence that is proving to be self-generating at every stage that has been studied.

Acknowledgments.—My research has been supported by grants NGR–10–007–08 and 10–007–088 from the National Aeronautics and Space Administration. This paper is contribution 265 from the Institute for Molecular and Cellular Evolution.

REFERENCES

Table 10. Criteria of validity for “could” vs. “did.”

<table>
<thead>
<tr>
<th>Geologic relevance</th>
<th>Sequential compatibility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 11. Aliveness vs. nonaliveness.

<table>
<thead>
<tr>
<th>Aliveness</th>
<th>Nonaliveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has not been claimed for proteinoid microspheres</td>
<td>Has been claimed, but nonaliveness mostly has not been defined . . .</td>
</tr>
<tr>
<td>Except that microsystems lacking nucleic acid or phospholipid are sometimes defined as nonalive . . .</td>
<td></td>
</tr>
<tr>
<td>But these characterize contemporary life, are not necessarily typical of original life</td>
<td></td>
</tr>
</tbody>
</table>

Amino acid + ATP Protocell → Protoribosome

Fig. 18. Interdigitation of concepts of molecular evolution with concepts of molecular biology.

Sequence of processes. Such trends can be seen in the evolution of organisms, but not so simply nor clearly as with molecules alone. In the biologic realm the molecular processes operate in the ramified structures and functions of organisms. In my view, the most fundamental argument for not including creationist overviews in biology textbooks is that the science alone is sufficient to explain in outline what is and has been going on, plus the subtle specificities in the vast array of the biologic realm. No additional agent need be invoked to explain an evolutionary sequence that is proving to be self-generating at every stage that has been studied.

Acknowledgments.—My research has been supported by grants NGR–10–007–08 and 10–007–088 from the National Aeronautics and Space Administration. This paper is contribution 265 from the Institute for Molecular and Cellular Evolution.

REFERENCES

Table 10. Criteria of validity for “could” vs. “did.”

<table>
<thead>
<tr>
<th>Geologic relevance</th>
<th>Sequential compatibility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 11. Aliveness vs. nonaliveness.

<table>
<thead>
<tr>
<th>Aliveness</th>
<th>Nonaliveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has not been claimed for proteinoid microspheres</td>
<td>Has been claimed, but nonaliveness mostly has not been defined . . .</td>
</tr>
<tr>
<td>Except that microsystems lacking nucleic acid or phospholipid are sometimes defined as nonalive . . .</td>
<td></td>
</tr>
<tr>
<td>But these characterize contemporary life, are not necessarily typical of original life</td>
<td></td>
</tr>
</tbody>
</table>

Amino acid + ATP Protocell → Protoribosome

Fig. 18. Interdigitation of concepts of molecular evolution with concepts of molecular biology.
easily be replaced, or will he, too, have a meaningful role in the overall plan of the Creator?

Man’s life is a constant process of becoming. A human being is always emerging, and he is emerging from the initial genetic package that is, potentially, all that he ever will be. Man is the body of his soul and the soul of his body.

Man stands now at a doorway. We are all involved with the manner in which he crosses the threshold of science and technology. Beyond this portal, human existence will either ascend or descend, and it is the lot of our generation to make that choice.

Perhaps man’s most profound progress will occur to the extent that he will try to be more humane by refusing to do some of the things he could do.

References


Nicholas J. T. LoCascio

Biology Dept.

State University College at Buffalo

Buffalo, N.Y. 14222

Sister Jean Dominici DeMaria

O.P., Dominican Sisters

St. John the Baptist High School

1170 Montauk Highway

West Islip, N.Y. 11785

Proteinoid Theory . . . from p. 172


et al. 1953. Enzymic synthesis of peptide bonds.

VI. The influence of residue type on papain-catalyzed reactions of some benzoyl amino acids with some amino acid anilides. Journal of the American Chemical Society 75:5539.


General references


Kelson Honored

The National Science Foundation Distinguished Service Award—NSF’s highest honor—has been presented to Keith R. Kelson, acting deputy director for education. He joined the NSF staff in 1954, from the University of Kansas. At the award ceremony Kelson was cited for "creative leadership and devotion in the innovative development and management of the foundation’s programs for education in science."