

## CRITIQUE OF BIOCHEMICAL EVOLUTION

DUANE T. GISH, *Biochemist*

*Upjohn Co., Kalamazoo, Michigan*

In the field of biochemical evolution, we are in an area where the only debatable question is, could it have happened? There is no historical record available that may be examined to answer the question, did it happen? We must recognize, then, that one's conclusion on this matter will, most likely, be influenced chiefly by one's point of view rather than by the arguments presented. Indeed, we need have no illusion that evidence presented against the theory, no matter how powerful, will influence the conviction of avowed evolutionists that biochemical evolution has occurred. One of these avowed evolutionists, J. D. Bernal, has stated<sup>1</sup> that the earlier studies of the origin of life concentrated on establishing a case for it, but that now the case no longer needs to be made: it can be accepted. He says that what interests us now is not that it could happen, but precisely how it happened. Such statements as this may sound convincing to the uninformed, but even a quick survey of available information reveals how untrue and scientifically unsound such a statement is.

Melvin Calvin, who has engaged in considerable speculation on "evolution before life" has proclaimed "We have no proof of evolution. We can only postulate some possible mechanisms for some of the simple steps that might lead from the chemical elements to chemical compounds that might agglomerate 'just so' and then become basic to life and reproduction processes."<sup>2</sup> In his chapter on evolution and information transfer,<sup>3</sup> which attempts to deal with the evolution of the more complex molecular systems, Alexander Rich is forced to a liberal use of such terms as "we postulate," "we imagine," "we theorize," "we could imagine," "let us imagine" and "we might imagine." Stanley Miller, in a paper<sup>4</sup> widely publicized and acclaimed, described the formation of a variety of organic compounds, including amino acids, in an apparatus containing methane, ammonia, hydrogen and water and energized by an electric discharge. This demonstration has often been cited as evidence that early chemical evolution must have occurred, a chemical evolution that would have led to organic compounds which constituted the building blocks of complex molecules found in the living cell. It may be pointed out, first of all, that the significance of this demonstration is not really very great at all, it might even be termed trivial. Having placed a selected number of gasses in a closed system and supplied a source of energy we would rather be surprised had *not* such a variety of carbon, oxygen and nitrogen containing compounds been formed. Of considerable importance to the significance of this experiment is the answer to the question, did such

a primitive atmosphere ever exist upon the earth? Such a reducing atmosphere has been postulated out of necessity, since it has been realized that reduced chemical compounds, which constitute the building blocks of molecules found in living systems, could not have arisen in an oxidizing atmosphere. It would have been thermodynamically impossible. Philip Abelson, Director of the Geophysical Laboratory, Carnegie Institution of Washington, in his paper<sup>5</sup> on the nature of the primitive atmosphere, has stated that an analysis of geologic evidence sharply limits the areas of permissible speculation concerning the nature of the primitive atmosphere and ocean. According to this evidence, the lowest oxidation state possible for carbon was carbon monoxide, and the evidence indicates further that the primitive atmosphere consisted chiefly of nitrogen and carbon monoxide, with hydrogen, carbon dioxide and water present in lesser quantities. It is evident, then, that the basis for Miller's experiment did not exist.

Even though a basis for the origin of simple organic compounds, such as amino acids, sugars, pyrimidines and purines could be established, the nature of processes that could have led to such complex molecules as proteins, polysaccharides and nucleic acids defies reasonable explanation. Oparin, in his book, "Origin of Life on the Earth"<sup>6</sup> has stated (p. 201) that "our knowledge of the primary formation of the lipids is therefore still scanty and unreliable." On p. 202, he states, concerning the origin of porphyrins, "certainly it is hard to tell at present to what extent analogous processes could have taken place under natural conditions independent of organisms." In reference to nucleic acids, on p. 205, he says "the question of the primary, abiogenic formation of compounds of phosphorus with organic substances is, however, extremely complicated and poorly understood." Finally, on p. 229, he has stated "the problem of the primary development of proteins is extremely perplexing." Since publication of this book, Fox and coworkers<sup>7</sup> have reported the polymerization of amino acids at temperatures of 170° to 180° and Schramm and coworkers<sup>8</sup> have reported the polymerization of nucleotides when heated with a syrup of a polyphosphate ester. It is rather amusing to read these accounts, in as much as evolutionists have always claimed that chemical evolution of the more complex molecules took place in the "primordial soup of the primitive oceans" where such high temperatures and anhydrous conditions must be excluded.

Any natural process that might be imagined for the origin of proteins and nucleic acids would give rise to an infinitely complex mixture, with

almost every conceivable sequence, stereoisomeric mixture, and chain length. Utter chaos would prevail. Any molecular species, once formed, would be subject to a wide variety of further reactions, and it is also certain that the rate of breakdown, such as hydrolysis, would exceed the rate of formation. For example, Howe<sup>9</sup> has pointed out that a pre-biologic earth, without a protective mantle of oxygen and ozone, would have been subjected to heavy doses of ultraviolet radiation in the region of 2700 to 3000 angstroms, radiation which breaks C-O, C-H, O-H bonds and others. Thus, amino acids, proteins and nucleotides, if formed, would have been disrupted by such radiation.

One can imagine the tremendous quantity of a single molecular species that would be required to constitute even a concentration as low as 0.001% in a large body of water. Under these conditions, it is inconceivable how a single molecular species could ever have gained ascendancy, let alone the complex mixture that would have been required for even the most primitive metabolism. The essential key to life is order and specificity. Each nucleic acid has a highly specific primary structure in the sequence of its component nucleotides. This specificity is the key to its function. It may dictate the structure of a protein, such as an enzyme, or it may regulate some biological activity. Before there was such specificity in structure, there could have been no function.

What natural processes could have brought such order out of chaos? What process could have selected a few nucleotides out of an almost infinite number of every conceivable sequence and chain length? What pressures could have forced their selection? In living processes, one way nucleotides express their function is by specifying protein structure, often stated in the terms, "one gene, one enzyme." What function then could nucleotides have had before proteins arose? Assuming that nucleotides arose before proteins, or proteins before nucleotides, presents us with a dilemma. Nucleotides dictate the structure of proteins, but the synthesis of nucleotides is catalyzed by protein enzymes. Which, then, came first? The only reasonable answer is, neither. They both must have been present in their highly specific structure in order to have functioned and survived.

To bridge the gap between the molecular stage of evolution and the cellular, evolutionists have often resorted to the claim that there once existed molecules which "were autocatalytic like the virus."<sup>6</sup> In fact, Lindegren has stated<sup>10</sup> that the possibility that something similar to the viruses we now study was a stage in the evolution of more elaborate organisms is "*the basic hypothesis which directs the scientific activities of most of the foremost geneticists and biochemists of the present time.*" It is utterly amazing to see such widespread acceptance of this view in the scientific community.

It is a shocking display of ignorance concerning the nature and function of viruses and of their replication by the living cell.

Lindegren had the testimony<sup>10</sup> of N. W. Pirie, one of the world's authorities in the viral field, that viruses could never have played such a part. This has also been emphasized by Oparin<sup>6</sup> among others. To say that a virus has the ability to reproduce itself is absolutely wrong. It has no autocatalytic ability whatsoever. Outside of the living cell, a virus is completely inactive, subject only to reactions that lead to its destruction. Even in the environment of the living cell, we cannot say that the virus reproduces itself. *The cell replicates the virus*, using the information supplied by the virus to produce copies of the viral nucleic acid and protein. The replication of the virus requires the action of a complex mixture of enzymes supplied by the cell, and other key components of the cell, such as soluble RNA and ribosomes, must be utilized. The energy required for viral synthesis, of course, must also be supplied by the cell. Since the sole function exhibited by the virus is that of supplying information for its replication, this in itself must presuppose the existence of an entity capable of utilizing that information, *an existence that must have predated the virus*. It is possible that all viruses were at one time normal constituents of the cell, and which later suffered mutations. This mutation may have caused the exclusion of the constituent from its normal metabolic function in the cell, thus at the same time rendering it outside the control mechanism of the cell. Its structure, however, still remained capable of reproduction by the synthetic apparatus of the cell, this function of the cell being less discerning than the metabolic and control mechanisms of the cell.

No molecule capable of autocatalytic replication has as yet been discovered, although, as already mentioned, such a molecule is often postulated by evolutionists. In light of present day knowledge, it can be emphatically stated that no such molecule exists nor has any molecule ever existed. We are now aware, at least in part, of the complex mechanism in the cell that is called into play to synthesize protein. The ultimate source of the information necessary for the replication of a protein molecule is believed to reside in the gene. Information in the gene is used to produce a messenger RNA. This synthesis, of course, requires the cooperation of the appropriate enzyme system and energy sources. The amino acids are activated via an intermediate complex with an activating enzyme, specific for each amino acid, and AMP. This complex reacts with soluble RNA (s-RNA), again specific for each amino acid, to give a complex of the amino acid with s-RNA. The AA-s-RNA complexes move to the microsomes, where they are laid down in the sequence specified by the messenger RNA.

The final step in the synthesis, the release of protein from the template, requires ATP, certain cofactors and an enzyme. The picture outlined here, although a simplified one, gives some idea of the very complex system that must be called into play to synthesize a protein molecule. Furthermore, as Roberts has pointed out,<sup>11</sup> the system is quite sensitive to the spatial arrangement of the cellular structures. Disruption of the cell usually decreases the rate of protein synthesis by a factor of a thousand or more. *The organization of the synthesizing system appears to be of the greatest importance.* The protein synthesis accomplished with the reconstituted systems from *E. coli* and other cells represent only a residual trace of the protein synthesis occurring in the intact cell. These facts emphasize the tremendously complex and highly specific organization required to synthesize a single protein molecule in a living system. The abiogenic synthesis of a specific protein molecule is beyond the pale of our imagination.

The process by which correlated structures of an organism could have arisen by an evolutionary scheme has always been one of the insurmountable roadblocks in the theory of evolution. This roadblock would have been encountered far earlier in the evolutionary development of an organism, however. For on the gene level, itself, we see perfect and necessary correlation. This has been aptly stated by John Cairns<sup>12</sup>: "The bacterial chromosome has been shown to contain regions concerned solely with switching on and off the executive action of other regions; in turn, these 'operator' genes are controlled by 'regulator' genes. *It is the presence of such control mechanisms that converts what might be purposeless or even self-destructive activity into the ordered system we find in every living creature.*" We can see that the old saying, "one gene, one enzyme," can no longer apply, since for each enzyme several genes exist. Here again, as in the case of nucleic acid and protein, we can ask the question, which came first, the functional gene, the operator gene or the regulator gene? How could the function of one be operative without the presence of the others? The conclusion must be that none ever existed independently, and that all must have come into existence simultaneously.

W. R. Hearn expressed his feelings, after attending a symposium on Genetic Mechanisms, that this was a poor time for the opposition to evolutionary ideas on the grounds that they 'are only theories without empirical evidence or plausible mechanisms to back them up.'<sup>13</sup> He pointed out that mutations are getting a lot less mysterious than they used to be and that the structures of biological macromolecules are now being determined. My reaction to recent advances have been just the opposite to that of Hearn's. As we begin to unravel the code of the DNA that constitutes the gene, and see

there the tremendous degree of specificity in each tiny building block and the purposefulness of the overall plan, we see the opposite of Chaos and of purposeless, endless change. Indeed, what purpose, or what excuse for survival could such an organization have had without the presence of the living cell, in which its influence is expressed? And we must always remember that the DNA is not the master of the cell, it is the *servant* of the cell. Though we understand perfectly the chemical or physical basis of mutations, the nature of mutations remains unchanged. That is, as stated by W. R. Thompson<sup>14</sup>, all mutations are either useless, harmful or lethal.

Even evolutionists admit that well over 99% of all mutations are harmful. Even if we were to admit that one out of every thousand mutations were useful, the stability of the genetic material would render the occurrence of a mutation so rare as to be incapable of effecting the change of one species into another. This is emphasized in the paper by W. J. Tinkle<sup>15</sup> in which the work of Muller is cited. His work, based upon experiments in *Drosophila*, permitted the estimate that the mean life of a gene (that is, the average time elapsing without change in any particular gene and its descendants) approximates 100,000 years. One can soon calculate the wait necessary for a favorable gene change, with a mutational rate of that nature, and with a frequency rate of a favorable change being one in one thousand or less!

Whether it be in the cry of a new-born babe, the beautifully correlated structure of the humming bird, or in the marvelously correlated mechanism of functional gene, operator gene, regulator gene, messenger RNA, soluble RNA, ribosomal RNA, and the vast array of enzymes cooperating with them, we are witnesses to the fact that "the firmament showeth the handywork of God." (Ps. 19:1).

#### REFERENCES

- <sup>1</sup>Bernal, J. D., "Horizons in Biochemistry," Ed M. Kasha and B. Pullman, Academic Press, N. Y., 1962, p. 11
- <sup>2</sup>Calvin, M., as quoted in Time Magazine, Nov. 1958.
- <sup>3</sup>Rich, A., "Horizons in Biochemistry," Ed. M. Kasha and B. Pullman, Academic Press, N. Y., 1962, p. 103.
- <sup>4</sup>Miller, S., J. Am. Chem. Soc., 77, 2351 (1955).
- <sup>5</sup>Abelson, P., Abstracts 133rd National Meeting, Am. Chem. Soc., April, 1958, p. 53 C.
- <sup>6</sup>Oparin, A., "The Origin of Life on the Earth," Academic Press Inc., N. Y., 1957.
- <sup>7</sup>Fox, S. and Harada, J., J. Am. Chem. Soc., 82, 3745 (1960).
- <sup>8</sup>Schramm, G., Grotzsch, H., and Pollmann, W., Angew. Chem., Inter. Ed., 1, 1 (1962).
- <sup>9</sup>Howe, G., J. Amer. Sci. Affil., 15, 124 (1963)
- <sup>10</sup>Lindgren, C., Nature, 197, 566 (1963).
- <sup>11</sup>Roberts, R., Ann. N.Y. Acad. Sci., 88, 752 (1960).
- <sup>12</sup>Cairns, J., Endeavor, 22, 141 (1963).
- <sup>13</sup>Hearn, W., J. Amer. Sci. Afil., 14, 87 (1962).
- <sup>14</sup>Thompson, W., Intro., to "The Origin of Species," C. Darwin, E. P. Dutton and Co. Inc., N. Y., 1956, p. 2.
- <sup>15</sup>Tinkle, W. J., J. Amer. Sci. Affil., 15, 15 (1961).