

THE ORIGIN OF LIFE – HOW LONG DID IT TAKE?

LESLIE E. ORGEL

The Salk Institute for Biological Studies Post Office Box 85800, San Diego, CA 92186, U.S.A.

(Received 16 May 1997)

Abstract. We do not understand the steps leading from the abiotic early earth to the RNA world. Consequently, we cannot estimate the time required for the origins of life. Attempts to circumvent this essential difficulty are based on misunderstandings of the nature of the problem.

1. Introduction

Questions of the form ‘How long does it take to get from A to B?’ cannot be answered unless A, B and the route between them are known. We should, therefore, be suspicious of confident answers to the question ‘How long must it have taken for life to get started?’, since we know very little about the route from the Abiotic (A) to the Biotic (B) world. The purpose of this paper is not to provide an answer to the primary question, but to clarify the issues involved.

The identities of A and B depend on the context in which the question is asked. While this has changed from time to time, one context has recently come to dominate the debate. It is generally accepted that the earth was formed about 4.5 billion years ago. The Precambrian fossil record indicates that life was present on the earth at least 3.5 billion years ago (Schopf, 1993). If these were the only limits, they would leave a comfortable billion or so years for the origins of life. Recently, however, persuasive if less certain evidence has been presented for life on the primitive earth as long as 3.8 billion years ago (Mojzsis *et al.*, 1996). Furthermore, recent theoretical studies suggest that large bodies impacted the earth repeatedly early in its history and would have made it uninhabitable until 3.8–4.2 billion years ago (Sagan, 1974; Maher and Stevenson, 1988; Chyba, 1993). This narrowing of the window of opportunity for the origins of life has led to fears that too little time was available and reassurance that there was plenty.

In order to discuss the origins of life in a manner that is relevant to the current context, it is clear that the clock must be started immediately after the last sterilizing impact (Sleep *et al.*, 1989). The time when the clock stops is less well defined. We will choose the time of the first appearance of organisms similar to bacteria or blue-green algae, although it is not clear that the very earliest evidence for life (Mojzsis *et al.*, 1996) is evidence for this kind of life. What, if anything, can we legitimately say about the time for the origins of life, if it is defined in this way? ‘Not much’, will be our conclusion.

The transition from the immediately post-impact world to a world including ‘bacteria’, can be arbitrarily divided into phases in many ways, without changing

the nature of the problem. We will consider an accumulation period during which a supply of organic substrates built up, a pre-organization period during which a first replicating system appeared, and a maturation period during which the first replicating system gave rise to a 'bacterium'. For definiteness, the appearance of the RNA world (Gesteland and Atkins, 1993) could be taken to end the pre-organization period, but this is not essential for our argument. Lazcano and Miller (Lazcano and Miller, 1994), in their discussion of the problem, suggest similar beginning and end points, but introduce an additional boundary between a minimum bacterium-like organism with about 100 genes and a bacterium comparable to *E. coli* with a small number of thousands.

We must next emphasize a logical point which, although self-evident, has sometimes been ignored. The major uncertainty in the sum of a small number of terms comes from the term or terms in the summation that have the greatest uncertainty. If we know next to nothing about one term we know next to nothing about the sum, however precisely we know the values of the remaining terms. Is there a phase in the origins of life on the earth about whose length we know next to nothing?

The sceptical reader will respond by asking whether there is a phase in the origins of life about which we know anything. The implied judgment is perhaps too severe; there is some suggestive experimental evidence that molecular evolution proceeds rapidly once it gets started. Lazcano and Miller have attempted to calculate the time that a bacterium with a minimal genome takes to evolve into one with a larger genome, and have concluded that it is short (Lazcano and Miller, 1994). While there are many uncertainties in their calculation, there is no good reason to doubt their conclusion. It may not be over-optimistic, therefore, to suggest that we know enough about the route onwards from the RNA/protein world to suggest that, once protein synthesis was invented, complex forms of life could evolve rapidly. We will be concerned with the origin of the RNA world and, to a lesser extent, with the transition from the RNA world to an RNA/protein world.

Lazcano and Miller have summarized arguments (Lazcano and Miller, 1994) suggesting that the accumulation of organic compounds on the primitive earth could have led to an adequately concentrated prebiotic soup in a few million years. Even if this were not the case, the accumulation period might not be a major problem. While impacts would have sterilized the earth and presumably destroyed any organized assembly of large polymers, they would not necessarily have destroyed small prebiotic molecules that had already accumulated unless they were large enough to evaporate the oceans to dryness and heat the residues to well above 100 °C. The window for the accumulation of organic materials may, therefore, be somewhat larger than the window for their organization into a 'biological' system. A great deal remains uncertain about this earliest phase in the origin of life, but reasonable arguments suggest that the accumulation of an adequate supply of prebiotic organic molecules was not a major obstacle to the rapid appearance of life, once the earth's environment had become 'friendly' (Lazcano and Miller, 1994). The same conclusion can be reached in the context of

Wächtershäuser's scenario of carbon fixation on transition-metal sulfides (Huber and Wächtershäuser, 1997).

This brings us to the major unknown, the time required for the appearance of the RNA world after the accumulation of a prebiotic soup. Our ignorance in this area is complete (Gesteland and Atkins, 1993). Some authors believe that the RNA world arose *de novo* in a prebiotic soup that already contained nucleotides. Others claim that the synthesis of nucleotides under prebiotic conditions is impossible, no matter how much time is available. In the absence of experimental evidence, one must conclude that no lower or upper limit for the time for the direct *de novo* development of the RNA world is available.

Many other authors have suggested that the RNA world was preceded by one or more organized 'biological' worlds based on a genetic polymer simpler than RNA (Cairns-Smith and Davies, 1977; Cairns-Smith, 1982; Schwartz and Orgel, 1985; Joyce *et al.*, 1987) or on a self-organized cycle of non-enzymatic chemical reactions (Kauffman, 1986; Wächtershäuser, 1988; De Duve, 1991; Wächtershäuser, 1992). Our ignorance of the nature of the materials involved in the first case or on the viability of the cycles in the second is total. It is not possible to estimate how long a process takes before you know what it is. We must, therefore, conclude that it is also impossible to set a lower or an upper limit on the time needed for the indirect origin of the RNA world via some other 'world'.

In the absence of any valid estimate, almost any statement of the form 'On the basis of present knowledge, there is no reason to believe that the RNA world could not have got started in N years' is true. Unfortunately, the claim that 'On the basis of present knowledge, there is no reason to believe that the RNA world could have got started in N years', is also true. There does not seem to be any rational justification for asserting one rather than the other. If we neglect the panspermia hypothesis, we can conclude that life evolved once on the earth, so it must be possible. Since we do not know whether or not 'life' evolved often, we cannot tell whether it was a probable event. Similar considerations apply to estimates of the probability that life originates on other earth-like planets.

It is sometimes said that once the conditions are right life must appear rapidly. This is an obviously cyclic argument. It is true only if 'right conditions' are those that guarantee the rapid emergence of life. There may not be any conditions under which life is sure to emerge rapidly; the emergence of life may always be an infrequent event, like the decay of an atom of a very long-lived isotope. If there are conditions under which the rapid evolution of life is inevitable, there is no guarantee that such conditions existed on the primitive earth at the time that life evolved. The emergence of life may or may not have been a probable event.

A recent attempt to establish a lower limit for the time required for the emergence of life, concludes that 10 million years was enough (Lazcano and Miller, 1994). The authors acknowledge that the major source of uncertainty is the time needed to develop a self-replicating system, but give two arguments suggesting that that time must have been short.

The first argument states that all known prebiotic reactions are fast so the origins of a self-replicating organism must also have been fast. This argument involves a conceptual error which, although apparently recognized by the authors early in their paper, is subsequently ignored. The origin of a self-replicating system cannot be compared to the synthesis of a simple molecule; it requires the fortuitous combination of a large number of synthetic events. An analogous error would be to suppose that it would take only a short time to produce a run of one hundred consecutive heads in a coin-tossing experiment because each toss takes only a short time. This error would lead one to underestimate the time required by a factor of about 10^{30} . One could also speculate that the rapidity of all the known prebiotic reactions has more to do with the acceptable range of extrapolation and the length of postdoctoral fellowships than with events on the primitive earth.

The second argument is more complicated. It begins by noting, correctly, that an informational molecule must have a lifetime at least comparable to the time required for its own replication. Next it notes, correctly, that all known biological polymers have relatively short lifetimes, and assumes, plausibly, that this would also have been true for the earliest informational polymers. The final step is to deduce from the above that the first replicating polymer must have appeared rapidly. This last argument is invalid. The time that elapses before the emergence of a self-replicating system has little if any relation to the time that individual molecules survive, provided only that self-replicating molecules survive long enough to produce descendants. The average time needed to produce a self-replicating polymer molecule clearly depends on the rate at which families of polymer molecules are produced and the probability that a family of polymer molecules is self-replicating. The time that a chimpanzee seated at a typewriter would take to produce the sentence 'Copy this message' would not be changed if meaningless compositions were shredded immediately.

A little more can be said about the time needed to invent protein synthesis and so to move from the RNA world to a world dominated by protein catalysts. Detailed experimental studies, particularly from the laboratories of Szostak (Bartel and Szostak, 1993) and Joyce (Wright and Joyce, 1997), suggest that the chemical evolution proceeds rapidly if an efficient catalyst for RNA replication is available. Other studies, particularly those of Bartel and his colleagues, suggest that RNA catalysts for RNA replication could have emerged from a pool of random oligonucleotides (Ekland and Bartel, 1996). Nothing is certain about the origins of life, but the currently available evidence suggests that progress would have been rapid as soon as an efficient mechanism for generating and then replicating a pool of random oligonucleotides was in place.

A very different argument suggesting that the lifetime of the RNA world was short has been offered by Lazcano and Miller (Lazcano and Miller, 1994). They claim that the RNA world must have been short-lived because the supply of ribose and the nucleotide bases that had accumulated on the primitive earth would soon have been used up. This is difficult to understand. Elsewhere in the same paper

the authors seem to be committed to the idea that RNA was not the first genetic material; Lazcano and Miller also emphasize the difficulty of synthesizing ribose under prebiotic conditions and draw attention to the instability of ribose in aqueous environments. One might therefore have thought that the catalysis of nucleotide synthesis by ‘enzymes’ of an earlier genetic system was part of the Miller-Lazcano scenario; for other authors the difficulty of synthesizing ribose and its derivatives without the help of enzymes has been a main motivation for proposing a pre-RNA world (Gesteland and Atkins, 1993). However Lazcano and Miller clearly do not believe that the supply of ribose and the nucleotide could be replenished by “enzymes” of a pre-RNA world or by ribozymes; they are committed to the unaided prebiotic synthesis at least of the components of RNA. But if ribose, which has a short half-life, was available in the prebiotic soup right up to the time of the emergence of the RNA world why did its synthesis suddenly stop? The logic of the Lazcano-Miller scenario is not self-evident.

In summary: We do not understand how a self-replicating system originated on the primitive earth, so it is impossible, on the basis of chemical arguments, to set upper or lower limits on the time that would be required. Hopefully, further research will clarify the nature of the chemical steps involved. Then we might be able to offer some meaningful estimates about the time needed for the transition from an abiotic to a biotic world.

Acknowledgments

This work was supported by NSCORT/EXOBIOLGY Grant No. NAGW-2881 from the National Aeronautics and Space Administration. We thank Sylvia Bailey for manuscript preparation.

References

- Bartel, D. P. and Szostak, J. W.: 1993, Isolation of new ribozymes from a large pool of random sequences, *Science* **261**, 1411–1418.
- Cairns-Smith, A. G.: 1982, Genetic takeover and the mineral origins of life (Cambridge (Great Britain): Cambridge University Press).
- Cairns-Smith, A. G. and Davies, C. J.: 1977, The design of novel replicating polymers. In *Encyclopaedia of Ignorance*, R. Duncan and M. Weston-Smith, eds. (Oxford/New York: Pergamon Press).
- Chyba, C. F.: 1993, The violent environment of the origin of life – progress and uncertainties, *Geochim. Cosmochim. Acta* **57**, 3351–3358.
- De Duve, C.: 1991, *Blueprint for a cell: the nature and origin of life* (Burlington, North Carolina: Neil Patterson Publishers).
- Eklund, E. H. and Bartel, D. P.: 1996, RNA-catalysed RNA polymerization using nucleoside triphosphates, *Nature* **382**, 373–376; erratum. *Nature* **383**, 192.
- Gesteland, R. and Atkins, J. F.: 1993, *The RNA World. The Nature of Modern RNA Suggests a Prebiotic RNA World* (Cold Spring Harbor, New York: Cold Spring Harbor Laboratory Press).
- Huber, C. and Wächtershäuser, G.: 1997, Activated acetic acid by carbon fixation on (Fe,Ni)S under primordial conditions, *Science* **276**, 245–247.

- Joyce, G. F., Schwartz, A. W., Miller, S. L. and Orgel, L. E.: 1987, The case for an ancestral genetic system involving simple analogues of the nucleotides, *Proc. Natl. Acad. Sci. USA* **84**, 4398–4402.
- Kauffman, S. A.: 1986, Autocatalytic sets of proteins, *J. Theoret. Biol.* **119**, 1–24.
- Lazcano, A. and Miller, S. L.: 1994, How long did it take for life to begin and evolve to cyanobacteria? *J. Mol. Evol.* **39**, 546–554.
- Maher, K. A. and Stevenson, D. J.: 1988, Impact frustration of the origin of life, *Nature* **331**, 612–614.
- Mojzsis, S. J., Arrhenius, G., McKeegan, K. D., Harrison, T. M., Nutman, A. P. and Friend, C. R. L.: 1996, Evidence for life on earth before 3,800 million years ago, *Nature* **384**, 55–59.
- Sagan, C.: 1974, The origin of life in a cosmic context, *Origins of Life Evol. Biosphere* **5**, 497–505.
- Schopf, J. W.: 1993, The earth's earliest biosphere: its origin and evolution (Princeton: Princeton University Press).
- Schwartz, A. W. and Orgel, L. E.: 1985, Template-directed synthesis of novel, nucleic acid-like structures, *Science* **228**, 585–587.
- Sleep, N. H., Zahnle, K. J., Kasting, J. F. and Morowitz, H. J.: 1989, Annihilation of ecosystems by large asteroid impacts on the early Earth, *Nature* **342**, 139–142.
- Wächtershäuser, G.: 1988, Before enzymes and templates: theory of surface metabolism, *Microbiol. Rev* **52**, 452–484.
- Wächtershäuser, G.: 1992, Groundworks for an evolutionary biochemistry – the iron sulphur world, *Prog. Biophys. Mol. Biol.* **58**, 85–201.
- Wright, M. C. and Joyce, G. F.: 1997, Continuous in vitro evolution of catalytic function, *Science* **276**, 614–617.