The Origin Of Life

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The Origin Of Life

Homochirality

Is the origin of chirality solved or unsolved?
The mist of the emergence, in the achiral prebiotic world, of proteins and nucleic acids composed from amino acids and sugars residues of a single handedness, remains still unsolved. One theory advocates that homo-chirality emerged only after the appearance of the first living system (Bada and Miller 1987), whereas another hypothesis maintains that it is imperative to generate first the homo-chiral biopolymers prior to the beginning of life (Avetisov and Goldanski 1996; Ehler and Orgel 1976; Goldanskii et al. 1986; Joyce et al. 1984).

1. Implications for the Origin of Homochirality, By Roni A. Illos, Origin Of Life And Evolution Of Biosphere, 2010, Volume 40, Pages 52

Can studying life on earth give the answer?
We therefore prefer the more agnostic position recently expressed by Quack (2002). In our view, “the jury is still out”, and meanwhile, improved computations, together with new possibilities to actually measure the PVED, promise a bright future for further investigation of the possible role of parity-violation in the origin of life. A verdict can never be reached while the handedness of our terrestrial biosphere remains our one and only data point. The burgeoning interest in chirality detection on space missions and in meteorites raises hope of finding out whether the same enantiomers are used by life on different planets, both within the solar system and beyond: consistent use of the same hand in many different biospheres in different solar systems would lend powerful support to an electroweak origin of bio-molecular chirality. Page 435


The origin of life and chirality is still unknown!
Life is dependent upon bio-molecular spatial asymmetry. Even though the origin of this asymmetry remains unknown (Fitz et al. 2007), it is frequently argued that life could neither exist nor originate without molecular chirality (Bonner 1996). Under this view, the question of the origin of homo-chirality is intrinsic to that of the origin of life: if we want to understand how life first emerged on Earth (or possibly elsewhere), we must understand how homo-chirality emerges from basic chiral building blocks (enantiomers). Page 294

The mystery here may not be so much which chirality but why chirality: although the sugars found in DNA and RNA are right-handed and protein amino acids are left-handed, laboratory syntheses yield racemic mixtures (Blackmond 2004). A pertinent exception is the reaction studied by Soai and co-workers, which demonstrates bifurcation to a single handedness (Soai et al. 1995). Although the Soai reaction has probably little relevance to life on early Earth, it exhibits the features required of a successful model: autocatalysis and enantiomeric cross-inhibition fed by enzymatic enhancement. Page 294

We know little of the prebiotic conditions that led to first life in early Earth and even less about other possible life-bearing planetary platforms in this and other stellar systems. The first amino acids and sugars may have been formed here, or may have been fed from outer-space; in either case, there may have been a net initial chirality in their concentrations, or the initial conditions may have been racemic. The substrate (or substrates) may or may not have supported autogenic production of monomers, with or without a chiral bias. Given these uncertainties, it is important to analyze in detail the polymerization dynamics of different reactor pools in order to compute the final net chirality produced. Page 314


Evolutionists admit that it is impossible to find the verdict:
One exceptionally critical experiment, impossible at this time, would then be to discover life elsewhere than our planet allowing a test of Wald’s view as he expressed it: “If the choice of optical isomers is as arbitrary as proposed one should expect that a survey of life throughout the universe would reveal approximately equal numbers of planetary populations in which the choice of metabolically connected series of disymmetric molecules came out L or D-; roughly equal numbers in which life is based upon L- and upon D-amino acids, and similarly, for the other molecules” (Wald 1957). Page 116

A perhaps more hopeful experiment has been proposed by the possibility that Precambrian sediments might contain evidence of early life forms of the chirality that lost out in the hypothesized competition (Kuhn and Waser 1983b). Page 116

4. Homochirality In Life, By Mark M. Green, Origin Of Life And Evolution Of Biosphere, 2010, Volume 40, Pages 116
Chirality is the essence of living things. Homo-chirality in living organisms is a singular phenomenon. Non-living chemical systems do in general not have a preferred chirality. In the models presented in this paper this is reflected in Figures 3 and 6. The region of the phase diagram displaying homo-chirality is characterized by high fidelity, i.e. high auto-catalytic accuracy. The fidelity is expected to be significantly higher in living systems. When an organism dies the auto-catalytic polymerization stops and as a consequence the fidelity is sharply decreased. The characteristic behavior of the polymerization changes from the chiral to the racemic region of the phase diagram. The relaxation of the system from the homo-chiral to the racemic state is often very slow. Page 240

5. Homo Chiral Growth, By A. Brandenburg, Origin Of Life And Evolution Of Biosphere, 2005, Volume 35, Pages 240

Still an unsolved problem for evolutionists. There is an equal amount of ‘left’ and ‘right’ chiral molecules in inorganic nature, whereas living organisms use only one of the mirror isomers of such biologically important molecules as amino acids and sugars and do not use another. Homo-chirality or ‘chiral purity’ (CP), along with genetic code, which is universal for all living on the Earth organisms, is a distinctive and key property of living. One cannot find a solution to the fundamental problem of life origin without solving the problem of the CP origin (discussion of various aspects of the bio-chirality problem can be found, for example, in papers (Mann and Primakov 1981, 1983; Keszthelyi 1987; Mason 1987; Goldanski 1989; Bonner 1991; Mac Dermott 1995; Avetisov and Goldanskii 1996). Furthermore, CP of biopolymers is a necessary condition for their normal functioning. Therefore, the problem of the CP origin is one of the key problems for understanding processes which lead to creation of self-reproducing biological systems. Page 156

Despite a number of the CP-origin hypothesis, the issue remains open. Among a number of possible physical mechanisms of the mirror-symmetry violation discussed in literature, the ‘radiation’ (or the so-called Vester–Ulbricht) mechanism (Ulbricht and Vester 1962; see also Hegstrom 1982; Meiring 1987) due to interaction of molecules with spiral (helical) particles seems to be the most effective candidate, which could provide an advantage for one of the isomer type. Page 156

6. Of Chiral Influence, By V. I. Burkov, Origin Of Life And Evolution Of Biosphere, 2008, Volume 38, Pages 156

Endless discussion of an unsolved problem. Studies of the origins of life raise many associated fundamental questions. Among these, one is concerned with the origin and propagation of molecular handedness. It is well known that chirality is a signature of life as we know it. Nucleic acids contain only D-sugars while proteins are made only from L-amino acids (although D-amino acids do occur in nature and even occasionally show up in some proteins (Jung, 1992)). What leads to the synthesis of homo-chiral polymers, in which all the constituent monomers have the same handedness? And what is responsible for the evolution of chiral purity, the more or less exclusive dominance of one macromolecular handedness over its mirror image? These are questions of great interest and importance and remain the subject of much discussion. Page 243


A great puzzle to evolutionists. The origin of the single chirality of most bio molecules is still a great puzzle. Page 79

The origin of life is closely related to the problem of the origin of biological homo-chirality (Calvin 1969; Bonner 1994; Cintas 2002). Only one enantiomeric form of amino acids or sugars dominates in the polymeric bio molecules. Did life start with both forms of chiral handedness—with one form becoming extinct? Or did the choice of a single handedness predate the advent of replicating and information-carrying bio molecules? Is nature’s prevailing choice of L-amino acids and D-sugars deterministic or accidental? Ever since the ground breaking work of Pasteur (1848), this conundrum posed tantalizing questions for generations of chemists. Page 79

8. Spontaneous Mirror Symmetry, By Michael Mauksch, Origin Of Life And Evolution Of Biosphere, 2010, Volume 40, Pages 79

Time and chance cannot create optical purity! For prebiotic peptide synthesis no practicable mechanism that leads to the exclusion of the unwanted optical antipodes has as yet been found. Page 165
The evaluation of the results obtained has made it even more difficult to explain the emergence of optical activity during molecular evolution because also mechanisms which completely conserve and even amplify optically active systems are required besides those that lead to their mere selection. Page 166

Whenever stereo selectivity evolved before or after the first living cells emerged, biological systems could only take advantage of stereo selectivity once they were able to overcome racemization, that is, once they were able to selectively convert or destroy the unwanted enantiomers. Page 171


Maybe UFO’s and aliens did it?

Enantio selective extra-terrestrial processes may have contributed to the emergence of biological homo-chirality on Earth. Page 517

Homo-chirality is an important aspect of the origin of life. Page 518

10. **Workshop on Astrobiology, By Gerda Horneck, Origin Of Life And Evolution Of Biosphere, 2010, Volume 40, Number 6, Pages 517, 518**

An unsolved puzzling enigma.

The origin of this selective chirality of amino acids has remained a fundamental enigma since the time of Pasteur, some 140 years ago. Chirality and optical activity are regarded as a principal criterion for life, both on Earth and elsewhere in the universe. The fundamental questions of how molecules of a unique chirality arose in Nature puzzle scientists, thus numerous theoretical and experimental studies addressing these questions have appeared in the last years (for a review see Bonner, 1991). Page 501

11. **Chirality In The Origin Of Life, By Cristobal Viedma, Origin Of Life And Evolution Of Biosphere, 2002, Volume 31, Pages 501**

A very difficult problem for evolutionists.

The origin of homo-chirality of virtually all of life’s building blocks, the same handedness for example in all proteinogenic amino acids, is one of the most difficult to understand problems in the context of the origin and evolution of life itself. Page 210

As we know protein is composed of natural amino acids and it is the most important macro-molecule of the life system. However how the amino acids assembled into peptides and finally formed the protein in the origin of life has been a key problem. Page 250

Origin of chirality is one of the most important problems in a process of chemical evolution. Various predominant hypotheses about the chiral problem have been proposed. Page 279

The origin of nucleic acid has puzzled people for many decades. The key problems lying unsolved are how nucleosides to react with phosphorus reagents and form the long nucleic acid strand in the diluted water solution. Page 302

12. **Conference On The Origin Of Life, By Alan Schwartz, Origin Of Life And Evolution Of Biosphere, 2005, Volume 36, Pages 250, 279, 302**

The origin of the asymmetry of molecules is still an unsolved problem.

In the living systems L-amino acids and D-sugars are found with almost no exceptions. Although all the molecular chirality must have been established prior to the emergence of life, the origin of the asymmetry of molecules is still an unsolved problem. The time of appearance of the asymmetry of molecules, therefore, was quite problematic during chemical evolution. Page 229

13. **Molecular Chirality And The Origin Of Life, By Seiji Yuasa, Journal of Biological Physics, 1994, Volume 20, Pages 229**

The Murchison meteorite may also contain clues to another persistent problem in understanding how life arose: The origin of the handedness, or homo chirality, in many biological molecules. These molecules, including the subunits of DNA, RNA, and proteins, have two chiral forms, or enantiomers. In nature, however, one form always dominates: All of the sugar molecules in the backbone of DNA and RNA are right-handed, or D enantiomers, while the amino acids in proteins are left-handed, or L enantiomers. Exactly what twist of fate caused life to choose one form over the other is a source of often bitter debate (Science, 3 March 1995, p. 1265). Page 871.
Current theories have no experimental proof. Evolutionists admit time and chance would not produce perfect stereo chemistry. Any chemical reaction producing chiral molecules in statistically large numbers that is run in a symmetrical environment yields a racemic mixture, that is, a mixture of equal quantities of right and left handed enantiomers. However, in view of the importance of optical purity in present day life, it is difficult to believe that, at the beginning, a completely racemic life form arose using bio molecules of both configurations simultaneously in the same cell. Page 5

No experiment has convincingly supported these theoretical considerations for the origin of a dominant enantiomer on Earth. Either the results were shown to be artefacts or to be so weak that they are doubtful. Page 6

Unfortunately, the classical electromagnetic interactions, such as circularly polarized light or other fields that can be imagined acting on Earth, would probably never result in a very high yield of optical pure compounds. Page 6

The problem is still unsolved. Despite 120 years of research into the origins of chirality, the problem of how one enantiomer was selected over its chiral pair for use in the origins of life is still unsolved. I suggest that no solution has been found because the assumptions implicit in the problem statement are invalid. An alternative description of the problem is given and demonstrated to be capable of resolution. Two possible resolutions are sketched. Methods and criteria are stated for testing and evaluating the problem statement and its possible solutions. Page 101

Clearly an alternative formulation of problem is required; one that avoids the pitfalls listed above. Five criteria for reformulating the problem can be stated from the logical critique of the previous problem formulations stated above. (1) Something other than asymmetric forces or aggregative chirality must be responsible for differentiating between the enantiomers of a molecule since these two “solutions” to the problem are logically untenable. (2) This “something” must not require asymmetric actions for its own synthesis or else it falls into the same logical flaws listed above. (3) The selection process in which this “something” is involved must concern molecules central to the evolution of life, or else it is impossible to understand how all molecules central to life have become selectively chiral. (4) The process of selection must be a physically viable one, yet one that involves a mechanism common to living organisms and uncommon to the inorganic realm. (5) All of the previous four criteria must be amenable to solution by means of well-established principles and knowledge in such a manner that the solution is testable. Page 103

The pieces of the puzzle are still missing. Experimental observations accumulated over the years have provided evidence leading, either tightly or loosely, to the various theories of the origins of bio molecular homo chirality. They form a jigsaw of which some pieces are missing, perhaps in the form of definitive evidence, but this has not prevented preliminary interpretations of this puzzle being offered. And there have been many. Investigators have proposed a variety of hypothesis, but evidence in favour of each of them is at least fragmentary. Until a deeper level of understanding of the problem is reached and one theory prevails, there is a need to classify the various theories which have been proposed, possibly using different perspectives. Page 6

A vigorous scientific debate

The origin of homochirality in biological organisms has, in fact, originated a vigorous scientific debate. During the last decade, a series of rather simple experiments have demonstrated the feasibility of producing optically active compounds from achiral materials (Avalos et al., 2000). However, there is a large gap between molecular chirality and molecular evolution.

18. Is Life On Earth Accidental?, By Dr. Jordi Llorca, Life as We Know It, 2006, Springer Publishers, Pages 154

The origin of homochirality of virtually all of life’s building blocks, the same handedness for example in all proteinogenic amino acids, is one of the most difficult to understand problems in the context of the origin and evolution of life itself.


But still equally unanswered

These short remarks about the origin of biological homochirality are focused on the questions related to the origin and selection of homochiral polymers and the broken mirror symmetry. They are important questions, but still equally unanswered, since the answers, I believe, closely relate to the evolutionary paradigm we accept. Page 367

Still remains an enigma

In summary, I would like to underscore again that biological homochirality is the macromolecular (not low-molecular) phenomenon, and so the problem of its origin is not reduced to the only question on separation of “left” enantiomers out of “right” enantiomers, say, via enantioselective synthesis, spontaneous resolution of racemate, symmetry breaking far from equilibrium, or enantioselective polymerization. In fact, the problem of the origin of biohomochirality is closely coupled with the basic principles of evolutional paradigm we accept. In this respect, the origin of homochirality is still remained an enigma. Page 370


This statement, however, does not provide an accurate picture of the current status of the problem. Even if we assume that the composition of the primitive atmosphere was favorable for synthesis, and overlooking the fact that entirely convincing syntheses have not yet been described for all compounds sought, serious problems remain. The most vexing of these is the often inescapable production of closely related and chemically similar sets of isomers and homologues; yielding a self-inhibiting set of reactants for stages of assembly to follow. Page 295


Pre Biotic Conditions Unknown

Unlikely to have come into being spontaneously

The origin of life is a grey area of frustrating research, often leading to blind alleys.

Both proteins and nucleic acids are chemically very complex and are considered unlikely to have come into being spontaneously, simultaneously and at the same place on a barren early Earth. Thus the most basic problem in understanding the origin of life is how did such an interdependent system of nucleic acids and proteins evolve and which of these appeared first on the evolutionary path. If only one of them appeared first how did this early life carry out the functions of the other. In other words, if nucleic acid appeared first how did it replicate without protein enzymes or if protein appeared first how did it store genetic information? This chicken-egg dilemma in biochemistry is called the nucleic acid-protein paradox. Page 10

To conclude, the subject of the origin of life is a grey area of frustrating research, often leading to blind alleys. The galloping pace of genome research, resulting in the successful sequencing of human genome, is certain to widen our understanding of life and its origin. But the greatest problem facing researchers today is how to develop genetic coding systems. Experimental polymerisation has, until now, been able to produce strands containing not more than about 100 base-pairs, insufficient to store genetic information. Glen Evans and co-workers (2000) claimed to have developed a technique of first producing short DNA chains and then joining them in a controlled way to achieve up to 100,000 base-pairs long strands, sufficient to produce simpler forms of life. Page 16
1. Early Planetary Environments, By P. V. Sukumaran, Resonance, 2001, Volume 6, Number 10, Pages 10, 16

What was the Earth like back then?
Evolutionists admit there is no evidence or agreement.
There is only limited agreement regarding the probable constituents of the primitive atmosphere. Page 60

Even the 3.8 billion year old Isua rocks in Greenland are not sufficiently well preserved to provide much evidence about the atmosphere at that time. Page 60

There is considerable opinion that strongly reducing conditions were never present on the primitive Earth, but this would mean that the organic compounds would have to be bought in on comets and meteorites, and this assumption has its own set of problems. Page 60

It is a matter of opinion as to what constitutes a plausible prebiotic synthesis. Page 75


There are only a few hard facts on which we can base our research. The quest for an explanation of the origin of life is one of the oldest and most visited themes in biology. The lack of direct evidence from the first ages of Earth, coupled to a still frustrating uncertainty about the precise physicochemical environment at that time, has allowed the development of different theoretical approaches and many speculative theories. There are only a few hard facts on which we can base our research, from which the most important are the chemical feasibility of the scenarios (including the prebiotical synthesis of amino acids and nucleotides) and the knowledge of present day organisms and their molecular biology, which share a common core that can be assumed to stem from the early phases of life's history. Page 314


The original environment is unknown.
Can we re-create this synthesis? The answer is no!
The central challenge facing the students of the origin and evolution of life has been to unravel clues about the nature of the first biota form the ancient [and generally uncooperative] rock record, a record itself modified by processes capable of destroying biological information. Page 843.

A problem arises when we travel back into deep time several billion years. It becomes increasingly difficult, even impossible, to rely on fossils to learn about early life and its environment. Page 843.

While molecular genetics and the fossil record have helped chart the evolution of modern day life, locating geological remains of the origin of life is probably impossible, due to the re working of the Earth’s surface through plate tectonics an erosion. Page 845.

This raises the following questions:
1. How has the earth remained continuously habitable (i.e., retained liquid water) for the past 4 billion years?
2. How did the building blocks of life, such as amino acids and nucleotides, arise from the primitive earth environment?
3. How did these compounds form into molecules that stored genetic information?
4. How did this information make copies of itself (i.e., develop the ability to replicate)?
5. How did membranes evolve to encapsulate this in-formation, and at what stage did membrane-bound life arise?
Page 846.

Can we re-create this synthesis? Unfortunately, the composition of the atmosphere at the time life originated is unknown, although several educated guesses have been made. Page 846.

One of the main problems with investigating them origin of life on earth is the continuous reworking of the earth's surface, which has destroyed any geological traces of an origin-of-life event. In addition, there is no direct record of the composition of the primordial atmosphere. Possible clues to the origin of life might not be found on the earth at all, and the effort to solve this problem has turned to the new science of astrobiology. Page 849.

**Problems Of Making Building Blocks**

There exists a fundamental problem.

A vital point that is usually entirely absent from discussions of life is that nearly all of the catalysts used by organisms are themselves products of the organism. This not only makes the usual distinction between enzymes and metabolites more arbitrary than it seems to be; it also renders any attempt to understand organisms in terms of machine analogies far more difficult than it appears to be. Most authors have not even recognized the existence of a fundamental problem, let alone tried to resolve it. Page 411, 412

This capacity for auto-conservation raises a major theoretical problem, because in present-day organisms the degradation and resynthesis of components involve the action of a series of interdependent macro molecules, which depend in their turn on another series, and so on, so generating a problem of infinite regress. Page 412

However, the major problem of the low concentrations of all available reagents has led to the view that the early organisms were chemoheterotrophic in origin rather than heterotrophic, i.e. They could subsist on purely inorganic sources of carbon and other elements and required no organic molecules from their environment. Page 412

It would be absurd to claim that the simple model illustrated in Fig. 3 provides a full answer to this question, but we believe it may represent a step towards an answer, and in any case we hope we have drawn attention to some problems that a theory of life will need to be able to explain. Page 417


   **No satisfactory explanation as to how the building blocks of life, such as amino acids, were formed.**

   None of the theories provide a completely satisfactory explanation as to how the building blocks of life, such as amino acids, were formed. The difficulty lies in the fact that the composition of the early atmosphere is unknown. It is likely that prebiotic materials (and membranes) were synthesized by more than one route. What these theories lack is a mechanism to account for how replication arose. Amino acids can form proteins, but proteins cannot then make copies of themselves from amino acids. What are required are molecules that can store genetic information and undergo replication. Page 847.


   **Studying undersea thermal vents have not solved anything.**

   There is little consensus regarding the plausibility of organic synthesis in submarine hydrothermal systems (SHSs) and its possible relevance to the origin of life. The primary reason for the persistence of this debate is that most experimental high temperature and high-pressure organic synthesis studies have neglected important geochemical constraints with respect to source material composition. Page 91

   Most aqueous studies use unrealistically short heating times on the order of minutes to hours while in reality, residence times in axial hydrothermal environments range from years (Coumou et al. 2008; Kadko and Butterfield 1998) to decades (Turekian and Cochran 1986), while those in lower temperature off-axis diffuse flow systems may be on the order of thousands of years (Johnson and Pruis 2003). Because these residence times are impractical to model experimentally, the effect of long residence times in SHSs must be extrapolated from shorter timescale experiments. Most experimental studies have used unrealistically high starting concentrations of reduced reactive compounds such as NH₃, HCN, CH₄, and HCHO (e.g. Islam et al. 2001). Page 92

   Even if the prebiotic oceans contained significant amounts of C and N species, the increase in synthetic reaction rates at high temperatures would compete with concomitant degradation reactions and limit the accumulation of organic compounds. Previous measurements of the decomposition rates of amino acids (Bernhardt et al. 1984; White 1984; Miller and Bada 1988; Bada et al. 1995; Ito et al. 2006) appear to show irreversible pseudo-first order kinetics because the equilibria for these reactions are extremely low. Using a high-end equilibrium estimate of 10⁻⁹ M (Shock 1992a), this would become the limiting concentration of amino acids in the ocean due to cycling through SHSs. Page 104
High temperatures in hydrothermal vent systems would then be limiting due to destruction. Although kinetic pathways for amino acid synthesis from reactive compounds exist, extrapolation of these experimental data to geochronomically relevant starting material concentrations and long exposure times within SHSs, suggests it is unlikely that high temperature environments were significant for the synthesis of amino acids, although they may have contributed small amounts of less labile organic material such as acetate to the general pool of organics in the primitive environment. Page 105


We cannot translate lab results to natural settings is valuable.
Although his account lacks the tales of personality and conflict that enliven other works in astrobiology, Deamer’s demonstration that we cannot translate lab results to natural settings is valuable. Because we can get reactions to work in the controlled conditions of a laboratory, he cautions, it does not follow that similar ones occurred on prebiotic Earth. We might overlook something that becomes apparent when we try to reproduce the reactions in a natural setting. This provocative insight explains why the origin-of-life field has been short on progress over the past half century, whereas molecular biology has flourished. Page 30


Geochemically implausible.
It has been proposed that oligopeptides may be formed in submarine hydrothermal systems (SHSs). Oligopeptides have been synthesized previously under simulated SHS conditions which are likely geochemically implausible. Page 109

Problematic.
If amino acid oligomers or polymers (polypeptides) were important for the origin of life, some combination of environmental parameters must have allowed for oligomerization. Based on what is known from physical organic chemistry this may be problematic. Page 110

Geochemically implausible.
Most experiments demonstrating hydrothermal peptide synthesis start with extremely high and geochemically implausible concentrations of amino acids, which ignores their original source, heated for very short periods of time at high temperatures, which neglects the characteristics of the environments where these reactions are proposed to occur. Page 110-111

Although oligomerization occurs under these reaction conditions, the simulation conditions are not geochemically plausible. Much lower concentrations of abiologically synthesized amino acids are likely to be present in hydrothermal environments (Shock 1992a; Islam et al. 2003), as discussed below. Page 111

If all of the nitrogen in the Earth’s crustal, atmospheric, and ocean reservoirs were present as amino acids dissolved in oceans of the present volume the concentration would be 0.2 M (Schwartz 1981). This would be the absolute highest possible amino acid concentration which could have been obtained in the primitive oceans. It is unlikely, however, that all of the nitrogen on Earth’s surface could have been completely converted into amino acids or other water soluble nitrogen species, including ammonia, nitrite or nitrate. Lower amino acid concentrations of 3×10^{-4} M have been estimated based on favourable atmospheric synthesis from fairly reducing atmospheres (Stribling and Miller 1987). The existence of an early reducing atmosphere is presently contentious, suggesting that even these estimates may be somewhat high. For the lower limit, a maximum metastable equilibrium of 10^{-9} M for glycine in HT vent environments has been estimated by Shock (1992a), although it was also estimated that this value could be up to 10 orders of magnitude lower. Thus, the relevant amino acid concentrations for oligomerization studies in hydrothermal systems probably lie somewhere between 3×10^{-4} M and 10^{-19} M. Page 111-112

The environment would destroy bio chemicals rather than creating them.
The long exposure times hydrothermal fluids typically experience would largely decompose most peptides over extremely short geological time scales. Although much remains to be investigated in greater detail, it seems unlikely that minerals or metals could have had a significant impact on this chemistry, but they may serve as true catalysts. Other, cooler environments such as evaporative basins are more likely to be suitable candidates for the concentration, polymerization, and preservation of organic molecules on primitive planets. Page 123

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**The original conditions are unknown.**
A definitive statement cannot be made about the production rates and the concentration of compounds in the primitive ocean because the atmospheric composition, ambient temperature, and ocean size are unknown. Page 76

Although there are attractive features to this theory, there are no relevant experiments to support it. The problems are that organic compounds are not produced from heating the low concentrations of methane found in the vent fluids. Even worse, vent temperatures of 350 degrees Centigrade decompose most organic compounds in a time span ranging from a few seconds to a few hours. In short, submarine vents do not synthesize organic compounds, they decompose them [Miller and Bada 1988]. Page 77


**Thermal vents are not an adequate explanation.**
ABSTRACT. High-temperature origin-of-life theories require that the components of the first genetic material are stable. We therefore have measured the half-lives for the decomposition of the nucleo bases. They have been found to be short on the geologic time scale. At 100°C, the growth temperatures of the hyper thermophiles, the half-lives are too short to allow for the adequate accumulation of these compounds (t1/2 for A and G = 1 year; U = 12 years; C = 19 days). Therefore, unless the origin of life took place extremely rapidly (<100 years), we conclude that a high-temperature origin of life may be possible, but it cannot involve adenine, uracil, guanine, or cytosine. The rates of hydrolysis at 100°C also suggest that an ocean-boiling asteroid impact would reset the prebiotic clock, requiring prebiotic synthetic processes to begin again. Page 7933.


**Geochemically implausible concentrations**
Most experiments demonstrating hydrothermal peptide synthesis start with extremely high and geochemically implausible concentrations of amino acids, which ignores their original source, heated for very short periods of time at high temperatures, which neglects the characteristics of the environments where these reactions are proposed to occur.

Although oligomerization occurs under these reaction conditions, the simulation conditions are not geochemically plausible.


The origin of protein synthesis is one of the major riddles of molecular biology. Page 523


However, the problem with the proteins-first hypothesis is that it doesn’t indicate a clear path to replication and preservation of information, the functions necessary for biological evolution. Page 539

10. The Possible Role of Short Peptides, By Maya Fishkis, Origins of Life and Evolution of the Biosphere, 2007, Volume 37, Pages 537-553

**Probability Calculations**

The probability of life forming by chance is zero!
It has been generally believed that the evolutionary origin of an enzyme from a random sequence of amino acids is exceedingly improbable. The number of different primary sequences of length n = 100 residues, composed at each position of the 20 different amino acids, is 20^{100} = 1.27 x 10^{130}. Hence, the probability that a single protein with a specified sequence would have arisen by random chance through independent selection of a sequence of amino acids is 7.89 x 10^{-131}. This number is so exceedingly small that, as with the chance of producing a Shakespearean play from a monkey dancing on a typewriter, it is essentially impossible. A variation of this argument is that a given protein function is achieved if only a few of the n residues are specified precisely, rather than all of them. On this basis, estimates range from 10^{30}, if 10 residues are essential (13), to 2.1 x 10^{-65}, based on sequence variation in Cytochrome c (refs. 14-16, but see also ref. 17). This general argument has become of some importance as support for the view that proteins could not have arisen from natural prebiotic chemical processes on earth (13) and as support for creationism (18-20). Pages 640, 641.
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1. Theory For Protein Mutability And Biogenesis, By Kit Fun Lau, Proceedings of the National Academy of Sciences, January 1990, Volume 87, Pages 638-642

The overwhelming complexity and difficulty of the origin of life problem.
Given the overwhelming complexity and difficulty of the origin of life problem, the most astonishing thing about it is that life actually has evolved on at least one planet in our universe (1). Indeed, it is entirely conceivable that the origin of life involved a series of highly unlikely events, and a substantial part of the explanation for why there is life on earth comes from the anthropic principle (2), i.e., our planet just happens to be one of the extremely rare parts of the universe where such a series of events was realized (3). The anthropic world view, however, by no means frees the students of early evolution from the obligation to explore all possible ways to decrease the improbability of life by demonstrating plausible paths to one or another of the milestones that need to be reached before life actually takes off. The paper by Baaske et al. (4) in this issue of PNAS seems to do just that by describing a simple abiotic system ensuring striking concentration of mono- and poly nucleotides in inorganic compartments that might be suitable hatcheries for life. Page 9105


The problem of its origin.
The problem of the nature of life is substantially the problem of its origin. Traditionally, the emphasis on an essentially systematic approach is dictated by the overwhelming complexity of living systems, as we know them today, as well as by the plausible assumption that life is one possible branch of material evolution and that, for reasons of “continuity” in such evolution, the early forms of life were divested of those functional and structural complications which are, in a way very often undecidable, not intrinsically fundamental to life itself. Page 489


Mathematically speaking, Totally Impossible!
The human genome consists of about $10^9$ nucleotides, and the number of combinatorially possible sequences attains the unimaginable size of $10^{600,000,000}$. Even the simple case of a bacterium, the genome consists of some 4 million nucleotides, and the number of combinatorially possible sequences is $10^{+2,400,000}$. Page 59, 60

The expectation probability for the nucleotide sequence of a bacterium is thus so slight that not even the entire space of the universe would be enough to make the random synthesis of a bacterial genome probable. For example, the entire mass of the universe, expressed as a multiple of the mass of the Hydrogen atom, amounts to about $10^{80}$ units. Even of all the matter in space consisted of DNA molecules of the structural complexity of the bacterial genome, with random sequences, then the chances of finding among them a bacterial genome or something resembling one would still be completely negligible. Page 59, 60

These striking numerical examples allow us to conclude with Monod that the design of a primitive organism has about the same chance of arising by pure chance, in a molecular roulette, as a general textbook of biochemistry has of arising by the random mixing of a sufficient number of letters. Page 59, 60

In order to understand Stegmüller’s objection, we shall have to rethink critically our statistical arguments [above]. In trying to estimate probabilities, following Monod, we assume tacitly that only of the approximately $10^{2,400,000}$ combinatorially possible sequences encodes the information for the construction of a simple organism, such as a bacterium, so that the probability for the chance synthesis is practically zero. Page 62

Using available experimental data, Hubert Yockey has estimated that the prior probability of the synthesis de novo of a protein structure belonging to the Cytochrome C family is of the order of magnitude of $10^{-65}$. This value is substantially greater than the expectation value for a unique, defined sequence, but is still so low that the spontaneous synthesis of this sequence is practically excluded. Page 62

The RNA sequence that codes for the virus specific sub unit of the replicase complex consists of approximately a thousand nucleotides [See Figure 9.1], so that it already possesses $10^{600}$ alternative sequences [See chapter 2, note 16]. The spontaneous synthesis by the Qb replicase system of a structure corresponding to the replicase gene is therefore extremely improbable. Thus, in contradiction to Popper’s claim, the Qb replicase system does not “suggest” a possible model for a spontaneous origin of life. Page 68

The question of the connection between law and chance in the evolution of life is one of the central philosophical problems in biology. Page 168
However, the issue of the theoretical character of synthetic evolution is a problem in the philosophy of science that possesses a special significance with regard to the more general question of the connection between law and chance in evolution. Page 168

The theory does not claim to be able to reconstruct the process in historical detail. Page 169

The problem of the origin of life is clearly basically equivalent to the problem of the origin of biological information. In accordance with this, the idea of biological information emerges as the fundamental concept in the physicochemical theory of the origin of life. Page 170


The extreme improbability of a self-assembling molecule arising spontaneously.
The problem stems from the unlikelihood that early life replicated in a manner similar to present-day life, owing to the extreme improbability of a self-assembling molecule arising spontaneously. Recognition of this led to the well-known ‘chicken and egg’ problem: which came first, the nucleotides that make up a genetic self-assembly code which through transcription and translation leads to proteins, or the proteins that are necessary to many stages of the transcription/translation process? Pages 443, 444

The problem is more acute: the assumptions that render natural selection applicable to the description of genetically mediated life do not hold for proto cells. Proto cells do not engage in template replication; their replication proceeds without a code through a self-organized autocatalytic process. As a result, there is no definitive distinction between dead and alive, and more importantly, since replication is not code driven, acquired characteristics are inherited. Pages 449


The wonderful problem of the origin of life.
Mathematically speaking, Totally Impossible!

In the next three chapters we turn our attention to the wonderful problem of the origin of life. What more awesome problem could invite our attention? To many recent scholars—Wald (1954), Hoyle and Wickramasinghe (1981), and others—improbable features of current organisms imply improbable origins. If the probability that a protein catalyzes a given reaction is 10^{-20} and if a minimal contemporary organism such as a pneumona-like organism has on the order of 1000 or 2000 enzymes, then the probability of their joint occurrence by chance is, say, 10^{-40,000}. More likely that, as Hoyle says, the whirlwind assemble a 747 from scraps in a junk-yard. Yet here we are, in quite clear contravention to Hoyle's unhappy conclusion. We the lucky, or we the expected? Page 287.


Spontaneous biogenesis is based on faith.
The Darwin-Oparin-Haldane “warm little pond” scenario for biogenesis is examined by using information theory to calculate the probability that an informational biomolecule of reasonable biochemical specificity, long enough to provide a genome for the “protobiont”, could have appeared in 10^{9} years in the primitive soup. Certain old untenable ideas have served only to confuse the solution of the problem. Negentropy is not a concept because entropy cannot be negative. The role that negentropy has played in previous discussions is replaced by “complexity” as defined in information theory. A satisfactory scenario for spontaneous biogenesis requires the generation of “complexity” not “order”. Previous calculations based on simple combinatorial analysis over estimate the number of sequences by a factor of 105. The number of cytochrome c sequences is about 3.8 x 10^{61}. The probability of selecting one such sequence at random is about 2.1 x 10^{-65}. The primitive milieu will contain a racemic mixture of the biological amino acids and also many analogues and non-biological amino acids. Taking into account only the effect of the racemic mixture the longest genome which could be expected with 95% confidence in 10^{9} years corresponds to only 49 amino acid residues. This is much too short to code a living system so evolution to higher forms could not get started. Geological evidence for the “warm little pond” is missing. It is concluded that belief in currently accepted scenarios of spontaneous biogenesis is based on faith, contrary to conventional wisdom. Page 377.

One must conclude that, contrary to the established and current wisdom a scenario describing the genesis of life on earth by chance and natural causes which can be accepted on the basis of fact and not faith has not yet been written. Page 396

**Purely religious not scientific.**

The self organizationist scenarios for the origin of life are examined by means of information theory. It is found that self organization must yield only genetic message ensembles of information content much too low to constitute a genome. It is shown that the statistical structure reflected in “the instructions in the amino acids themselves” is an impediment to the generation of genetic information not a source of it. It is concluded that at present there are no scientifically valid origin of life scenarios. Consequently, belief in little green men in outer space is purely religious not scientific. Page 13

**Science has not the vaguest idea how life originated on earth.**

Since science has not the vaguest idea how life originated on earth, whether life exists anywhere else, or whether little green men pullulate in our galaxy, it would be honest to admit this to students, the agencies funding research, and the public. Leaders in science, speaking ex cathedra, should stop polarizing the minds of students and younger creative scientists with statements for which faith is the only evidence. Research on the origin of life is legitimate and it would be much better off if the effort absorbed by defending scenarios which cannot meet the most elementary criteria for a scientific contribution were directed in a search for new knowledge. It is new knowledge not another clever scenario that is needed to achieve an understanding of the origin of life. This research must be carried out in an atmosphere of the creative skepticism typical of science. In this connection Simpson’s paper (1964) has proved prophetic and is well worth rereading. In the absence of better knowledge of the origin of life the search now being made for little green men and their signals from planets near other stars is based entirely on the evidence of faith and must therefore be regarded as an exercise of religious belief. Page 29


**The problem of the origin of life.**

The problem of the origin of life touches upon quite a different function: the protein produced should possess replicase but not hydrolytic activity. The supposition of random formation of protein with specific activity seems improbable. Page 14


**Far too complex for its chance appearance.**

It is the centre of the problem of the origin of life that an organism seems to be necessarily far too complex for its chance appearance within a reasonable time and locality under any conceivable circumstances: yet a preformed fully functioning organism of some sort seems to be a necessary pre-requisite for organic evolution. In considering one aspect of this problem—the origin of enzymes-Dixon & Webb (1958) have demonstrated the fantastic improbability of even one known protein forming by purely physico-chemical processes. The difficulty is not so much in the appearance of amino acids or of energy, but in the spontaneous appearance of information. (Even if the whole earth had been made of nothing but amino-acids which had rearranged themselves randomly and completely ten times a second for the whole period of the earth’s history, there would have been little chance of producing even once, for a tenth of a second, one molecule of insulin!)

A piece of dynamite, even if left quite alone, will eventually explode. Eventually a chance high energy molecular event will overcome a critical activation energy barrier. The self-propagating process of organic evolution will similarly—in theory—“detonate” spontaneously from an environment containing the necessary components. Here the critical event seems to be the formation of an extremely improbably organized molecular assemblage: here the obstacle seems to be an information barrier of prodigious height. (The insulin example gives some idea of the height of the information barrier between the physico-chemical and the modern biological worlds.) Page 53, 54.


**The RNA World Theory**

Conceptually important problems arise from these controversies.
Chao (1991) also pointed out the connection to problems of the origin of life. He argued that (1) the regular appearance of defective genes would have called for some compartmentation to allow natural selection to keep them sufficiently low in frequency, and (2) that protobiotic compartments presumably needed some form of sex because the error threshold of replication would have been unaltered if there had been no sex, but only haploid sets of asexual genomes. This insight calls for a revision of previous models of the early evolution of genetic systems. This paper reflects on some of the conceptually important problems arising from the above-described controversies. Page 100

This is analogous to the problem of the earliest genomes: functionally coupled RNAs cannot coexist if they are replicated by a common replicase in homogeneous solution (Eigen, 1971). A special kind of activity, i.e. Hypercyclic coupling, can lead to dynamical coexistence (Eigen, 1971), but there is no trace of hyper cycles in segmented viruses. Page 103


RNA are difficult to synthesize under prebiotic conditions.
There is some difficulty reconciling the RNA world with the idea of RNA arising from a primordial soup. Some of the building blocks of RNA are difficult to synthesize under prebiotic conditions. While purines (guanine and adenine) are relatively easy to synthesize under prebiotic conditions, the synthesis of pyrimidines (cytosine, uracil, and thymine) from simple precursors gives very low yields. Another problem with pyrimidines is the difficulty in attaching them to a sugar molecule to form the basic building blocks of the nucleic acid. Page 103


Must grapple with a fundamental problem.
It is widely believed that reactions simpler than but similar to nucleic acid replication and protein synthesis appeared very early in the history of life on the earth. Any attempt to provide a chemical model of the evolution of these coupled processes must grapple with a fundamental problem. Nucleic acids are molecules that seem ideally suited for replication while polypeptides are similarly suited for function. However, at least in contemporary systems, nucleic acids cannot replicate without the help of well-defined protein catalysts, while the synthesis of well-defined protein catalysts is impossible without the direction of replicating nucleic acids. How could a coupled system of proteins and nucleic acids have got started? Page 127

The possibility is remote.
The hypothesis that a pre-enzymatic self-replicating system preceded the present enzyme-dependent system is becoming popular (Cech, 1986; Gilbert, 1986; Darnell & Doolittle, 1986; Westheimer, 1986). If it turns out to be correct, it will not be the final solution to the "origins of life" problem. One will have to ask: Where did the mononucleotide substrates of RNA replication come from? This is now a particularly troublesome question. There is only one plausible prebiotic synthesis of ribose, the polymerization of formaldehyde. Ribose is formed as one of a large number of sugars, and never as the major product. Similarly the condensation of adenine or guanine with ribose leads to complex isomeric mixtures containing a relatively small amount of the natural nucleoside. The prebiotic synthesis of pyrimidine nucleosides is even more difficult. The possibility that the accurate replication of an oligoribo-nucleotide could occur directly in an unfractionated prebiotic soup seems remote (Shapiro, 1986). Page 146

The central unsolved problem of chemical evolution.
At present, the central unsolved problem of chemical evolution seems to me to be the identification of the first informational molecules and the reconstruction of the path from them to DNA, RNA and proteins. There are a number of constraints that must be satisfied by any acceptable theory. Page 147

The central issue of the origin of the genetic code is baffling.
The path from an "RNA only" system to a system involving protein synthesis is also worth thinking about in detail. The central issue of the origin of the genetic code is baffling. Page 147


The evolution of life has been a big enigma.
The evolution of life has been a big enigma despite rapid advancements in the field of astrobiology, microbiology and genetics in recent years. The answer to this puzzle is as mindboggling as the riddle relating to evolution of the universe itself. Despite the fact that panspermia has gained considerable support as a viable
The Origin Of Life

An explanation for origin of life on the earth and elsewhere in the universe, the issue, however, remains far from a tangible solution. Page 267

How that RNA came into being remains unknown.

How that RNA came into being, however, remains unknown so far. Moreover, the “RNA world” hypothesis does not seem to provide a satisfactory explanation to the initiation of mechanism of “self replication” in organisms in the early history of earth, which is so crucial to the understanding of the process of evolution of life on our planet and other habitable bodies in the universe (Orgel 2006). Experiments involving biologically produced RNA have so far failed to provide concrete proof regarding the RNA world being the pathway between non life and life. Moreover, despite development of sophisticated biotechnology tools in the recent years, scientists still have not been successful in transforming inanimate matter into life in the laboratory. Page 277


No definite conclusion.

The evidence that is available at the present time does not support the idea that RNA, or an alternative replicator that uses the current set of RNA bases, was present at the start of life. This conclusion could be reversed if a prebiotic simulation were devised that produced all of the bases in good yield under a single set of conditions, by using a plausible combination of water, atmospheric components, and minerals. In the absence of such a demonstration, more attention should be given to origin-of-life theories that do not require the four RNA bases. Page 4400.


Difficulty of imagining how self organization could create life.

Problems recur with hypotheses for the assembly of the earliest molecules with the properties commonly associated with “life.” These include the unlikelihood that complex self-replicating molecules such as RNA could form by chance encounters even over geological time; the difficulty of protecting such molecules, once formed, from dilution and destruction by high temperatures, hydrolysis and ultra-violet radiation; and finally the difficulty of imagining how self organization alone could lead to the encapsulation of a complex hierarchy of biochemical reactions in a membrane to form the simplest unicellular organism. Page 15173.


None of these paradigms can claim a decisive experimental support.

The early systems, constituting the Last Universal Common Ancestor at the root of the evolutionary tree, were already highly complex. They could not have been the product of regular physical and chemical processes alone and had to be the consequence of evolution. Page 4

How successful are the RNA-first, RNA-later, metabolism-first and, preparatory-metabolism theories in elucidating the emergence of life as an evolutionary process? So far, none of these paradigms can claim a decisive experimental support. Yet, at least in principle, experimental approaches directed by gene-first theories provide a strong potential for achieving their goal. No functioning system of genetic replication has been achieved yet, unless an external protein enzyme has been added to the system (Hanczyc et al. 2009, 121). Page 12

7. The Role of Natural Selection, By Iris Fry, Origin Of Life And Evolution Of Biosphere, 2011, Volume 41, Pages 4, 12

A constellation of problems which has not been fully solved.

The origin of life remains a fascinating and elusive topic. We have even less evidence about it than we have about the origins of photosynthesis or eukaryotes or sex, yet it is the focus of more speculation and debate. It is not a single problem but a constellation of problems, none of which has been fully solved, and different people think of it in different ways. Page 147

We have no direct evidence about this process.

Everything we can say about the origin of life is a mixture of inference and guesswork.

No biologist could believe that life arose from non-life in a single step. We have no direct evidence about this process and there is no consensus about the sequence of events involved. Everything we can say about the origin...
of life is a mixture of inference and guesswork. Even our most basic questions about it invite speculation; we are in no position to argue from incontrovertible fact. The best we can do is to temper our speculations with scientifically informed reasoning. Page 149

The early Earth was well provided with simple organic molecules, but how were these turned into proteins and nucleic acids? How they were polymerised? This remains unanswered. There is an even more contentious question: which came first, nucleic acids or proteins – or, perhaps, cell membranes? Each of these possibilities has been championed. Each entails considerable difficulties. Page 155
But the hypothesis is inadequate.

FIRST
First, it is hard to make key RNA reactions go without external catalysts, and bringing the four bases together for initial synthesis would have been problematic. Page 157, 158

SECOND
Second, RNA molecules are fragile and tend to break up unless RNA is relatively useless both as a repository of information and as an enzyme. Perhaps several short RNA molecules working together could have formed a replicating system, but assembly of a number of short RNAs in the same confined space would have been improbable. Page 157, 158

THIRD
Third, RNA seems unable to catalyse many of the reactions crucial for energy metabolism. Page 157, 158

FOURTH
Fourth, as in the case of amino acid selection for protein manufacture, it is not clear how nucleotides with the correct “handedness” were selected for polymerisation. Fifth, there are major differences in the RNA replication mechanisms of archaea, bacteria and eukaryotes, suggesting that these mechanisms had no common ancestry. This throws doubt on the idea that all major branches of life arose from an “RNA world”. Page 157, 158

FIFTH
Finally, it is not clear how the proto-organisms of the "RNA world" were supposed to manage without membranes. There is no indication of internal state, or responsiveness to environment: autonomously replicating RNA, if it ever existed outside a modern laboratory, was not an organism. Page 157-158


The RNA-World scenario fails a crucial plausibility test. No one yet figured out where the RNA itself came from. And yet, within the small community of origin-of-life researcher so, we can sense a certain unease with that conventional wisdom. The fact is that the RNA-World scenario fails a crucial plausibility test: No one yet figured out where the RNA itself came from. RNA is a very complicated molecule, one that's hard enough to synthesize in a test tube. So how could it have formed spontaneously some 4 billion years when there was nothing on Earth but a kind of random, prebiotic chemical soup? The conundrum is so puzzling, in fact, that most origin-of-life researchers are now convinced that some crucial concept is still missing and a few are convinced that the RNA-World idea is dead wrong. Page 1248

So in the end, says Joyce, the most reasonable assumption is that life did not start with RNA. It must have started with something simpler, something that could have worked out all these problems in advance. The question is, what? The only correct answer is "who knows?" The evidence has been obliterated by 4 billion years of evolution. Page 1249


One particular problem
The origin of the first RNA polymers is central to most current theories for the origin of life. Difficulties associated with the prebiotic formation of RNA have lead to the general consensus that a simpler polymer preceded RNA. However, polymers proposed as possible ancestors to RNA are not much easier to synthesize than RNA itself. One particular problem with the prebiotic synthesis of RNA is the formation of phosphoester bonds in the absence of chemical activation. Page 39
However, wide acceptance of the RNA world hypothesis will ultimately require the discovery of a process by which RNA polymers, or RNA-like polymers, form spontaneously from plausible prebiotic molecules. Page 57


The prebiotic origin of life is still very poorly understood, although there is now widespread consensus that our contemporary life based on the central dogma principle involving the three central biopolymers, DNA, RNA and protein, was preceded by a “world” based solely on RNA (Cech 1993; Joyce 2002; Orgel 2004). It is, however, very doubtful if this RNA world could have developed directly under prebiotic conditions from organic and inorganic components present on the primitive earth. It is both difficult in model prebiotic experiments to find conditions that will produce ribose (and ribonucleosides) in sufficient (relative) amounts, and furthermore, RNA oligomers and polymers are chemically very unstable on a “geological” timescale. Page 323


The possible role of RNA as the initial carrier of catalytic capacity and genetic information faces several difficult problems. The monomers of RNA are not readily synthesized under prebiotic conditions; it is difficult to imagine ways in which they could be assembled spontaneously into polymeric structures of sufficient complexity; and RNA has no ability to capture energy from the environment and cannot readily contribute to organized supra-molecular structures. Page 139


This simplifies the problem of the origin of life in some ways because it is now only necessary to explain the origin of RNA, but it makes inference from biochemistry to prebiotic chemistry more problematical because all biochemicals except RNA may have been invented by RNA. Page 246


The problem with the RNA world hypothesis is that it does not reveal how the initial RNA molecules might have been formed from the relatively short polynucleotides which, at best, had weak catalytic properties. Page 539

14. The Possible Role of Short Peptides, By Maya Fishkis, Origins of Life and Evolution of the Biosphere, 2007, Volume 37, Pages 537-553

Real Truth Unknown

The origin of life on Earth is still a mystery. One of the greatest mysteries in science today. We are surrounded by myriads of life forms—each leaf of a tree in a forest contains billions of living cells, our body contains huge numbers of active microorganisms, we people keep living and growing, incessantly—and we do not yet know how life came about on our planet. Our ignorance about the origin of life is profound—not just some simple missing mechanistic detail. We do not know how the genetic code came about, we do not understand yet how the specific sequences of proteins or nucleic acids came about in multiple identical copies, we do not have a precise idea about the structure and functioning of the first proto-cells. This ignorance stems not only from our experimental difficulties with prebiotic chemistry, but is also conceptual, as we are not yet able to conceive on paper how all these things came about. Page 353

Exceedingly little knowledge.

It seems that the question may be answered, at best, only abstractedly. Because there is exceedingly little knowledge about the actual origin(s) of life, we have reasonably extended to its beginnings the same fundamental evolutionary nature that has been recorded throughout life’s cellular history. Page 378


The original steps are unknown.
We may never know the identity of the first polymer that underwent Darwinian evolution. Even if we knew its chemical nature, we almost certainly would not know the exact sequence of its subunits. Nonetheless, Darwinian evolution provides a frame-work for understanding how such a polymer might have arisen and perpetuated itself in the face of a changing environment.


A major challenge remains in understanding how life might have arisen.

A major challenge, never the less, remains in understanding how cellular life might have arisen. How might a self replicating molecule, even one capable of catalysis, have come to be encased within a membrane and yet continue to proliferate? As a minimum, any such molecule would require metabolic machinery for importing and exporting materials across the cell membrane, for orchestrating cell division or budding, and for insuring that buds were populated by daughter molecules. While a variety of materials display properties that might partially satisfy these requirements [Fox and Dose 1977], it is difficult to conceive of a proto cell acquiring all of properties instantaneously. However, the full suite of functions is surely required for the proto cell to behave as an evolutionary unit.

Chapter: Proto Cell Life Cycles, By Leo W. Buss

Today there are several controversial theories about the origin of life.

Today there are several controversial theories about the origin of life and its early mode of expression on Earth [E.g. Oparin 1924, Change 1983, Woese 1979, Wachtershauser 1988]. Possible strategies of primate life depended on mainly unknown geo physical conditions in the juvenile Earth.

Chapter: The Lesson Of Archae Bacteria, By Karl O. Stetter

Almost nothing is known.

Life is probably much older than these early fossils, but how long did it take for it to appear and become established? Almost nothing is known about the time scales required for the origin and evolution of bacterial metabolic pathways.

Page 66

It is unlikely that the paleontological record will ever provide direct evidence of the transition from prebiotic organic molecules to the earliest cells, nor will it tell us much about the nature of the first biological systems.

Page 66


The most important unsolved problems in modern science.

The origin of life on Earth is one of the most important unsolved problems in modern biochemistry and planetary science.

Page 27

Nevertheless, there still exist serious difficulties in efforts to understand how life began on Earth.

Page 27


Yet fundamental questions remain unanswered.

The origin of life has puzzled molecular scientists for over half a century. Yet fundamental questions remain unanswered, including which came first, the metabolic machinery or the encoding nucleic acids.

Page 14


We still do not know when and how the first living beings appeared on Earth.

A century and a half after Darwin admitted how little was understood about the origin of life, we still do not know when and how the first living beings appeared on Earth. It is difficult to ascertain the earliest traces of life, since most of the rocks from early Archean times that have been preserved have been metamorphosed to a considerable extent. There is no direct evidence of the environmental conditions on Earth at the time of the emergence of life, nor any fossil register of the predecessors of the first cells. Direct information is lacking not only on the chemical composition of the terrestrial atmosphere during the period of the origin of life, but also on
other general and local environmental conditions which may (or may not) have been important for the appearance of living systems (Bada and Lazcano 2009). Cladistic approaches to the origin of life itself are not feasible, since all possible intermediates that may have once existed have long since vanished. Page 664, 665
To write that our understanding of the origin and early evolution of life faces major unsolved problems is an understatement. However, the scientific community recognizes them as intellectual challenges and not as requiring metaphysical explanations, as proponents of creationism would have it. Page 666

Biogenesis is one of the most puzzling scientific problems.
Biogenesis is one of the most puzzling scientific problems. Given life’s biochemical complexity, it is a wonder it ever arose. Even if Panspermia (Hoyle and Wickramasinghe, 1997) is accepted as a way to propagate life, it does not solve the fundamental problem of biogenesis but shifts it from the Solar System to other places in the galaxy.

7. Early Life on Earth, By Stephen Kempe, Astrobiology, Volume 2, Number 1, 2002, Pages 123

The problem of describing the spontaneous generation of the first cells.
For more than a century, now, the problem of the origin of life has been formulated as the problem of describing the spontaneous generation of the first cells in the environment of the primitive earth. Since Darwin’s time there have been shifts of emphasis from one aspect of the problem to another and a substantial increase in paleontological and geochemical evidence, but the essence has not changed. Pages 545

I believe, however, that sometime in the future the technical difficulties which are behind these problems will be solved and experimental tests will be possible. Pages 545

Little progress in 30 years of research.
Modern organisms generally use, with very few notable exceptions, 20 a-amino acids for the synthesis of their ribosomally encoded proteins (Lu and Freeland, 2006) (Fig. 1). This is a small subset of the number of a-amino acids which are structurally possible (Lu and Freeland, 2008). This leads to a variety of questions including:

(1) Why are amino acids used, as opposed to say hydroxy acids, thio acids, or amino sulphonic or amino phosphinic acids?
(2) Why are N-un-substituted a-mono alkyl amino acids used and not b-, g- or d-amino acids, a-dialkyl amino acids or N-alkyl-a-amino acids?
(3) Why are these 20 used, and not some other set of 20? And
(4) Why not more or less than 20?

Some of these questions were the topic of an earlier review paper to which the interested reader is strongly referred (Weber and Miller, 1981). It is rare that authors manage to so completely address a topic in a rapidly changing field such as biochemistry that almost 30 years later there is relatively little to add to the discussion. Page 490


The conditions under which evolution proceeded remain a mystery.
There is still an unfathomable gap between chemical evolution and biological evolution; the former deals with formation of primitive life in prebiotic environments and the latter at present is mostly concerned with evolution after prokaryote-eukaryote divergence. How did metabolic processes evolve in the period when primitive life became sufficiently vital (tentatively called the "pre prokaryote") to evolve toward the prokaryotes and eukaryotes? The conditions under which evolution proceeded from the pre prokaryote to a parent of the prokaryote and eukaryote remain a mystery. Page 3012


The immensity of the problem of the origin of life.
Despite the abundant use of leading questions and tentative terminology in their origin of life discussions, the majority of textbooks exude confidence that confirmation of a naturalistic model of life's origin is inevitable. The treatment in these textbooks stands in marked contrast to a recent review article by Klaus Dose summarizing origin of life research. In this thorough review, a strikingly different picture emerges of the current state of affairs regarding the origin of life. Dose, one of the best known origin of life researchers for the past 20 years, in The Origin of Life: More Questions than Answers (Dose 1988, p. 348) provides the following summary:

More than 30 years of experimentation on the origin of life in the fields of chemical and molecular evolution have led to a better perception of the immensity of the problem of the origin of life on Earth rather than to its solution. At present all discussions on principal theories and experiments in the field either end in stale-mate or in a confession of ignorance. Page 78.

1. Origin of Life & Evolution in Biology Textbooks, By Gordon C. Mills, The American Biology Teacher, Volume 55, Number 2 (February 1993), Pages 78-83

The most vexing issue in biology and philosophy.

The origin of life remains one of the most vexing issues in biology and philosophy. Page 845.

But panspermia did not address the question of where life originated. Modern theories of the origin of life for the most part reject the notion of panspermia and seek to explain how life originated and evolved on Earth. Page 845.


Understanding is clouded.

The conceptual gulf that separates the ‘metabolism first’ and ‘replication first’ mechanisms for the emergence of life continues to cloud the origin of life debate. Page 307


We know almost nothing.

Questions about the origin of life differ from questions on other natural sciences in that their aim is to attempt to reconstruct a past of which we know almost nothing and on which any hope to obtain actual information is quite remote. As pointed out by others [see in particular Wasschtershassuser (1997) in this volume this may be more similar to the processes of historical sciences than most natural science studies]. Page 541

This leads to a dilemma sometimes called Eigen's dilemma: it was necessary to have a high accuracy to obtain long, functionally active macromolecules but to achieve high accuracy, long active controlling macromolecules were needed. There are many chicken and egg problems of that kind for this stage that obscures a direct step by step development. Identification of such perils also gives hints of how functions developed and how the steps shall be interpreted. The RNA world may have been a great achievement, but it could hardly provide in a direct way, the functions that were necessary for the final steps to the first organisms. Page 541

Few problems on the origin of life have been discussed so frequently and in so many and often quite different ways as the onset of protein synthesis and the origin of the genetic code. For the latter see the article by Di Giulio (1997) in this volume. Page 549


Origin of life is a comprehensive research subject with many unsolved problems ranging from the prebiotic synthesis of biologically important organic molecules (like ribose and pyrimidine bases etc.) to the emergence of the first proto-cells including autocatalytic metabolic cycles and replicating information carrier machine. Page 319

The Origin Of DNA And RNA

The evolution of life and the origins of DNA and RNA as the carriers of information are still a mystery. Page 1

There are also no indications that ribozymes with polymerase activity have ever existed since the only naturally occurring ribozymes do not perform polymerization reactions. The transition from ss-RNA as the informational carrier to ds-DNA is also mechanistically difficult since in order to maintain existing catalytic function, the concomitant evolution of a transcription system based on ds-DNA is needed. Therefore, the fundamental molecular mechanisms that underlie the origin of life are still unknown. Page 2

The potential of RNA to perform as both an information carrier and as a catalytic molecule, is at the basis of the RNA world hypothesis. However, it is difficult to imagine ss-RNA to have a dual function since the catalytic properties of RNA depend on the three-dimensional structure, while the informational capacity would require a simple linear structure that can be replicated [13]. The folding of an RNA molecule would prevent its own replication, while for replication a folded ribozyme would be necessary. Therefore, a dual function for the informational and the catalytic functions of ss-RNA seem to be mutual exclusive on a biochemical mechanistic basis. Page 2

1. Modelling Evolution, By Albert D. G. de Roos, Biology Direct, 2007, Volume 2, Pages 1, 2

The idea that such mixtures would spontaneously transform themselves is absurd. Robert Shapiro, a chemist at New York University who studies the molecular origins of life, says that this new system is still a long way from showing that complex molecules such as DNA or RNA could have formed spontaneously from simple chemicals. "It is possible to speculate that a system of this type arose during the course of evolution — though well after life began — as a precursor to RNA and DNA," he says. "At the time when life first began, however, only crude chemical mixtures would be expected on early Earth. The idea that such mixtures would spontaneously transform themselves into the systems of the type described here, without the aid of chemists and laboratories, is absurd."


Numerous unsolved problems.

In an attempt to understand the origin of living systems we encounter the following problems: How can we conceive the origin of the first self-reproducing forms, and by means of what stimuli could a constant increase in the complexity of such forms commence? How can a translation apparatus for genetic information develop? One cannot imagine that such an apparatus for the synthesis of enzymes can function alone without the interference of enzymes themselves, which, however, could only become available after the construction of the apparatus itself. What stimulus mechanism is conceivable that leads to the division of the genetic apparatus into a replication system, and an enzyme-synthesis system? Page 68

3. Consideration for the Origin of Life, By Hans Kuhn, Naturwissenschaften, 1976, Volume 63, Pages 68

Origin of DNA unknown.

Now despite the progress of science and technology, despite perfect knowledge of the structure and composition of DNA molecule, bio chemists have not yet succeeded in recreating the least active gene beginning with a soup of inorganic or gaseous ingredients. At best, they have obtained amino acids, elementary organic molecules that form proteins, normally fabricated according to genetic information. But amino acids and proteins are inert. By themselves they do not yield life. It has been proven only that the sub products common to all life can be produced by chemical reactions independently of life. Page 24.


This stage includes all the steps that led from the basic products of cosmic chemistry to the first replicating RNA molecules. Despite a considerable amount of research, these steps still await elucidation. Page 562

Such an RNA-directed selection process could possibly account for the nature of the 20 proteinogenic amino acids – perhaps including their chirality – whose use does not match their alleged abundance in the protometabolic pool, as deduced from the analysis of meteorites and from prebiotic chemistry experiments. It is tempting to see in such a mechanism the solution to the chirality problem, except that RNA is itself a chiral
molecule. An intriguing question is whether D-amino acids would have been selected if RNA had been made with L-ribose. Page 563

The cell membrane must have been fitted with a variety of transporters and receptors. A cell wall may have been constructed. And, of course, DNA must have taken over from RNA the function of storing replicable genetic information. How this happened is not known but is readily imagined. Page 566


In particular, the problem of the origin of DNA and DNA replication systems is now in the middle of a hot debate. Page 303


**The Origin Of Life Not Observed**

The deep past of the earth is unobservable. Therefore, the problem of the origin of life, the emergence of the first evolvable entity, which is the primordial ancestor of all extant organisms, can only be solved by a theory. Theories on the origin of life are scientific rather than myth, if they have empirical significance: empirical biological significance by providing evolutionary explanations for extant facts of biology and/or empirical chemical significance by predicting unknown but testable chemical reactions. Page 275

The scientific problem of the origin of life can be characterized as the problem of finding the chemical mechanism that led all the way from the inception of the first autocatalytic reproduction cycle to the last common ancestor. All present theories fall far short of this task. While we still do not understand this mechanism, we now have a grasp of the magnitude of the problem. Page 282

1. Origin Of Life, By Gunter Watchershauser, Prokaryotes, 2006, Volume 1, Pages 275, 282

Because of time flow and evolution, primitive life was different from today and only hypothetical descriptions of primitive life can be proposed. Because of the limitations of time, prebiotic chemistry can never be repeated in the laboratory. Therefore, simulations may only represent possible supports for plausible hypotheses from the point of view of historical legitimacy. The only way around this difficulty is to collect clues from different disciplines. Page 459

2. Astrobiology In Europe, By André Brack, Origins of Life and Evolution of the Biosphere, 2001, Volume 31, Page 459

Since the transition from microscopic chemical mechanisms to the macroscopically detectable emergent properties that characterize life remains unresolved, there is little knowledge of what such primitive information-prone mechanism must have been. This is despite the fact that the principles underlying present-day biochemistry and molecular biology are well understood. Page 119

While it is reasonable to assume that the first cellular life forms used amphiphilic molecules for boundary membranes, as well as for other functions, the origin and diversity of amphiphiles on the early Earth remains to be elucidated. Page 123


**Second Law Of Thermodynamics**

**Matter will not spontaneously change from a disorganized to an organized state.**

The spontaneous change is always from organized to disorganize.

The second law has been stated in many ways, verbally and mathematically. A very useful statement of its principle for our present purpose is that matter will not spontaneously change from a disorganized to an
The Origin Of Life

organized state. The spontaneous change is always from organized to disorganized. A change from disorganized to organized will not be spontaneous, and can occur only from the expenditure of energy. Page 168

The concept of the second law which states that matter in a state of given order can change spontaneously only to a more disordered state, is given mathematical expression through utilization of the entropy principle. Page 169

1. Is Life On Earth Accidental?, By Malcolm E. Schrader, Life as We Know It, 2006, Springer-Verlag Books, Pages 168, 169

The spontaneous formation of order from disorder is in contradiction with the common sense, which is expressed in thermodynamic language by the Second Law stating that entropy tends to increase in an isolated system. Then, chemical systems spontaneously evolve toward the equilibrium state in which the concentrations of chemical species are determined by their relative energy levels and statistical rules. Page 24


Bible And Origins

Imagine that you are a well-trained scientist who clearly understands the scientific method and accepts that the fossil record, isotope dating and the phylogenetic tree make a strong case for an Earth 4.5 billion years old, an origin of life 3.8 billion years ago, and an evolutionary process that produced human beings. Now imagine that you are also a Christian who accepts Christ as your savior, the bible as the word of God, and the Book of Genesis as a true account of the origin of life. How could you, a scientist and a deeply religious Christian, possibly rationalize these seemingly diametrically opposed perspectives? Page 201


Panspermia-Hypothesis

In the answer to major questions of astrobiology and chirality, the panspermia hypothesis is often discussed as the only proposal of transportation of life to the Earth. On the basis of the known presence of ionizing radiation in the space, assumed on the level calculated by Clark (Orig Life Evol Biosph 31:185–197, 2001), the hypothesis is rejected as the explanation of origins of life on Earth. In fact, comparatively low doses of radiation sterilize irreversibly all biological material. Sufficiently long sojourn in space of objects containing prebiotic chemical blocks also does not contribute to the origins of life on Earth, because of elimination of homochirality, if any, and of radiation induced reactions of dehydrogenation, decarboxylation and deamination of chemical compounds closing with complete decomposition of organics, leaving elementary nano-carbon and/or minerals like calcium carbonate. Page 351


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