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CHEMICAL EVOLUTION — SOME DIFFICULTIES

Dr Peet, who is the Head of Science Section & Science Coordinator, Guildford County College of Technology, examines the theories which have been advanced to explain the origin of life from inorganic matter. He shows that the difficulties are far greater than often supposed.

As the study of biology has shifted to the realm of the molecular, it has required an understanding of, and an explanation in terms of, chemistry.

In approaching the subject, it would be helpful to clarify certain assumptions and principles behind my reasoning. First of all, I am concerned to identify the facts on which the prebiotic evolutionary theory is based. On these we will agree. Then, we must be clear on our extrapolations from facts into theories. The scientist is wary of far-reaching extrapolation, yet this is common, in evolutionary theory. Limited range extrapolation is of course permissible — without it observable facts can rarely be tied together to give a coherent picture. Science is based on the assumption that such a coherent pattern exists; we have no quarrel with this. But, theories of unification may start with differing sets of presuppositions, and these can cause us to link facts in different ways.

In this paper, I am asking whether the path used by the materialistic evolutionist to link chemical observations is valid and in accord with his own rules. We will test his claims and examine their relevance to the debate on the origin of life. In contrast to the Biblical claim, "In the beginning God created..." (Gen.1:1), Prof. Fox has said, "In the beginning, life assembled itself."[1] Does the evidence — experimental and theoretical — give any substance to that claim?

We shall consider amino acids and proteins in detail. This is primarily because this is the area which has been the most extensively evaluated by the chemical evolutionist. Other biochemical systems will be examined as we progress but, as we shall see, the evidence is even weaker for these.

Two evolutionists have recently set the stage for us. Prof. M. Eigen has said, that the origin of life "never can be repeated by us, but we could ask proper questions, knowing the problem."[2] Prof. Ponnamperuma writes: "To the chemist, prebiotic synthesis appears as a two-part problem:

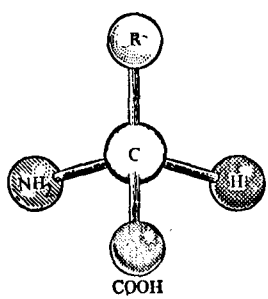
(i) to make small molecules necessary for life;

(ii) to combine the small molecules under similar conditions into the polymers, the polypeptides and oligonucleotides, which are the precursors of nucleic acids and proteins."[3]

We have no quarrel with these statements; have these colleagues, or others, found a reasonable answer?

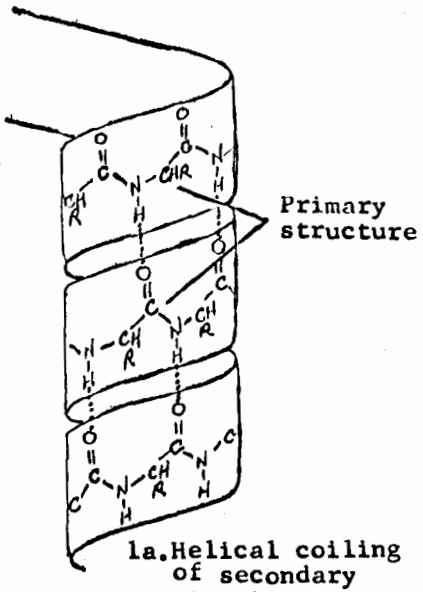
Amino acids — their Nature and Occurrence

Most extensively studied, in terms of prebiotic synthesis, are the proteins. We will consider these in detail, knowing that the problems for other compounds (e.g. carbohydrates, nucleic acids, etc.) are probably even greater. Proteins are important to life — they are the basis of structural materials (hair, muscles, wool, skin, nails etc.) and of enzymes. They are produced by the polymerisation of α-amino acids, of general structure:

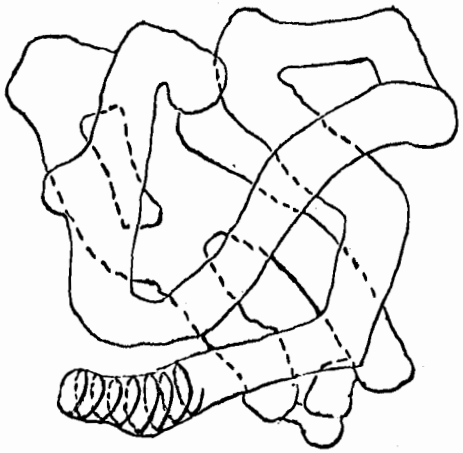


There are about twenty amino acids known in nature which form the building blocks of proteins. The order in which these are linked in proteins is known as the primary structure (figure 1a) Then part or all of the chain may coil up on itself to give the helical secondary structure (figure 1a). This then folds up on itself to give the overall tertiary structure (figure 1b). The secondary and tertiary structures are held in place by linkages (through hydrogen or sulphur) between parallel amino acids (figure 1a). The manner of folding of the chain determines the biological activity and is, in turn, determined by the nature and order of the amino acids in the primary structure.

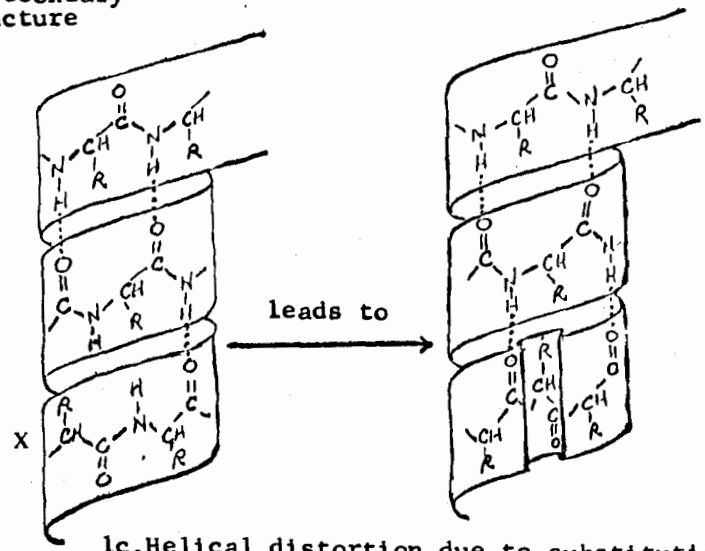
Figure 1. Protein Synthesis



1a. Helical coiling of secondary structure



1b. Folding of tertiary structure



1c. Helical distortion due to substitution of a D-amino acid in a L-chain at X

The Raw Materials of Abiotic Synthesis

In attempting any chemical synthesis, we must first ask the nature of our raw materials. Immediately we are faced with a problem: we do not know what was available. In general terms, we assume that the substances are present in simple chemical forms which were converted to more complex structures, the compounds of life. The primeval chemicals would be gaseous (being small molecules) but could be, in chemical terms, either reducing or oxidising in nature. Our present atmosphere is oxidising. But organic compounds, the "compounds of life", are chemically unstable in an oxidising atmosphere. The primitive atmosphere must be anaerobic. If oxygen were present organic compounds would simply end up in combusion[4] and so are unlikely to be found in such conditions. So, it is postulated, the primeval atmosphere would have to be a reducing one — ammonia, methane and water being proposed. A similar one — ammonia, methane, nitrogen, water and hydrogen — was originally postulated by Oparin.[5] This was based on evolutionary requirements rather than geochemical evidence.

So, Maddox has said, "After more than a decade of speculation, it's now clear that when life began the atmosphere of the earth was rich in materials such as methane, ammonia, hydrogen and water vapour."[3a] But this is either ignorance or a "burying of the head in the sand." Abelson[6] has shown that the evidence counters this and proposes an alternative model of carbon monoxide and hydrogen (by volcanic outgassing) with nitrogen and water. Walton[7], in turn, has produced evidence which shows that, rather than carbon monoxide and hydrogen, such sources produce 90% water and carbon dioxide. Furthermore, Brinkman[8] has argued that ultraviolet production of oxygen would have given an atmospheric concentration of 25% early in the earth's history, that is, long before life began, so preventing it by oxidation of the vital materials. Fyfe[9] believes that the primordial temperatures would have been too high for successful abiotic synthesis.

A detailed analysis of Precambrian rocks indicates that the atmosphere was of a similar nature to that known today, in that these rocks are also in a partly oxidised state.[10] Even the very earliest known sedimentary rocks of $4.0 - 4.1 \times 10^9$ years old show some oxidation.[9b] As Hoyle and Wickramasinghe have written.[11] "There is a disconcerting lack of evidence for any large scale nitrogenous carbonaceous deposits in the oldest sedimentary rocks ...; their absence in the geological record may be construed as evidence against the soup." A. Henderson-Sellers[12] has come to a similar conclusion by studying surface temperatures. She believes that the popular view stems "as much from ignorance of recent advances as from active opposition to them."

Furthermore, Shimizu[13] has shown that methane would last for only 1% of the time required by evolutionists. Abelson[14] found that "a quantity of ammonia equivalent to the present atmospheric nitrogen would be destroyed in about 30,000 years." An additional complication arises from the great solubility of ammonia in water, so removing a large proportion of the gaseous atmosphere. On the basis of energy sources available, "life times in the primitive environment would have ranged from seconds to many years, but few would have survived over geologically long periods."[17] Those models based on water fare no better, because the water vapour would dissociate as a result of ultraviolet radiation and so produce an oxidising atmosphere.[8] Henderson-Sellers and Schwartz[16] have sought to salvage the situation by proposing a TiO_2-catalysed fixation of nitrogen, but acknowledge the problem of photochemical destruction. So, the long times required by the evolutionary theory are disastrous to the chemicals.

Synthesis of the Biochemical Building Blocks

Let us assume though, that these problems are trivial and ultimately resolvable, in spite of the contrary evidence. We must now expose the supposed reducing gases of the early atmosphere to a high energy source to make them react.

In 1951, Calvin[17] irradiated a mixture of carbon dioxide and water in a cyclotron and produced a number of organic compounds. More famous is the work of Miller and Urey[18] who subjected a mixture of methane, ammonia and water to an electric discharge and obtained a number of amino acids. Other significant biochemical species have also been detected. (Table I). Palm and Calvin[19], using their electron bombardment technique, also obtained hydrogen cyanide, to the significance of which we shall return. Groth[20], using Miller's mixture and ultraviolet radiation, obtained traces of only two amino acids: glycine and alanine. Even in the most successful work, that of Miller, using idealised conditions, only small amounts of amino acids etc. were obtained. On this basis, the edifice of chemical evolution has been built.

AMMONIA — METHANE — WATER

Formaldehyde	Amino acids	HCN
Sugars	Peptides	Nitrogen bases
Polysaccharides	Proteins	ATP/RNA/DNA

Table I. Products in Miller's electric discharge experiment.

SUBSTANCE*	YIELD/MICROMOLES PER MOLE METHANE
Formic acid	40,000
Glycine	10,700
Glycollic acid	9,500
Alanine	5,800
Lactic acid	5,250
β-alanine	2,500
Acetic acid	2,500
Propionic acid	2,200
Iminodiacetic acid	930
Sarcosine	850
α-aminobutanoic acid	850
α-hydroxybutanoic acid	850
Succinic acid	680
Urea	340
N-methylurea	250
Iminoaceticpropionic acid	250
N-methylalanine	170
Glutamic acid	100
Aspartic acid	70
α-aminoisobutyric acid	20

(*Yields of compounds associated with the origins of life in the experiments of Miller and Urey In addition there was a larger amount of tar; only four of the commonly occurring amino acids were identified.)

Miller's experiments represent an unrealistic situation, one not available on the primitive earth, namely the use of a cold trap. The compounds can be isolated only because of its presence; without it, no detectable quantity of the product would ever have been produced. Furthermore, to have removed the chemicals from this high energy source would hinder subsequent reactions and so facilitate degradation.

Let us look more closely at this primeval soup that has been postulated. Firstly, if *all* the atmospheric nitrogen were converted to a single nitrogenous compound (e.g. glycine), its concentration would be only 0.2 molar. In fact, this must be divided, not only between the twenty amino acids, but also between such species as the nucleotides and porphyrins.

But, this is unrealistic. Hull[21] examined the most favourable reaction: that for the equilibrium production of glycine —

$$2CH_4 + NH_3 + 2H_2O \rightleftharpoons H_2N{\cdot}CH_2COOH + 5H_2$$

The proportions of products and reactants present at equilibrium is given by the relationship,

$$K = \frac{p(gly) \cdot p(H_2)^5}{p(CH_4)^2 \cdot p(NH_3) \cdot p(H_2O)^2}$$

where p(A) represents the partial pressure of A. For this reaction, K has the value 2×10^{-40}. Substitution of the appropriate values for the pressures of the reactants in the primeval atmosphere shows that glycine would have a maximum concentration of 10^{-27} mol.dm^{-3} (i.e. one molecule in ten thousand litres). Even then, the glycine is so unstable to ultraviolet radiation (photodecomposition being 10^4 - 10^5 times more efficient than the photosynthesis), that 97% of this glycine would decompose before it reached the earth's surface.

In an alternative, kinetic calculation, Hull deduces that the amount of glycine might reach a maximum of 10^{-12}mol.dm^{-3}. (This is equivalent to 0.2 mg in a swimming pool). The amount is far too small to achieve any significant amount of subsequent reaction, since this concentration would adversely affect both the equilibrium yield and the rate of formation of subsequent compounds.

And this is the situation for the most favoured compound! And we have seen that the fact that a compound has been obtained in the laboratory is no real indication that it was present in significant quantities in the prebiotic soup.[15] Unbelievably, Eigen speaks of this as "a rich soup!"[22] Hull, reasonably, says that "the

conclusion from these arguments presents the most serious obstacle, if indeed it is not fatal, to the theory of spontaneous generation."[21] Sillen claims[23] that the concentrations are so low "that the concept of a prebiotic soup (is) an entire myth."

Bernal[28] has suggested mechanisms that might have concentrated the organic molecules in the sea. (A basic problem is that there must be sufficient molecules of the right type in the first place!) Again, considering the amino acids, we note that, including their stereo-isomers, there would be thirty-nine α-amino acids corresponding to the twenty naturally-occurring ones, and there would also be β- and γ- isomers formed in the prebiotic soup. And, once the amino acids and carbohydrates reach the required concentration, at the pH of the ocean they would react.[10] Abelson has shown[6] that even at 0° C amino acids and carbohydrates are incompatible. He and Hare[29] found that for all the amino acids they tested, substantial yields of humic acids or kerogens were formed by reaction with carbohydrates. In fact, since the amino acid concentration would have greatly exceeded carbohydrate concentrations (as shown below), there would be no sugars at all in the soup!

Kinetically, the problems are just as great. Under the conditions of the proposed synthesis, the rate of decomposition exceeds the rate of production by a factor of 10^4.[21] Reaction rates are affected by concentration, temperature and catalysis. They are low, very low, at low concentrations even for thermodynamically favoured processes. At the concentrations described, even geological times are too short. Increases in temperature accelerate reactions; but this means all reactions, including the degradation of the essential prebiological intermediates.[15] Some surfaces (e.g. rocks and clays) might absorb the reactants and so catalyse the process. But, as Hulett emphasises,[15] to argue for the importance of catalytic surfaces only increases the rate at which these poor yields are reached.

Hulett summarises the problem[15] when he writes, "It is, in fact, hard to reconcile the thermodynamic and kinetic characteristics of these compounds with the postulated pathways for chemical evolution in the primitive environment."

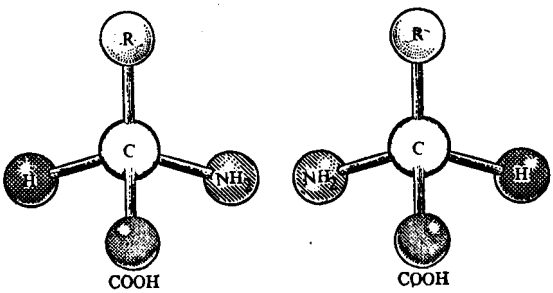
Matthews and Moser[26] have suggested that polyamino acids, and other nitrogenous materials, might be obtained by the polymerisation of hydrogen cyanide. This compound also is produced when suitable gaseous mixtures are subjected to electrical discharge.[27] This compound polymerises to a black solid, which undergoes hydrolysis in an acidic medium to generate fourteen amino acids. It is proposed that iminoacetonitrile was the intermediate.

$$HCN \longrightarrow {}^{\cdot}HN{=}CH{\cdot}CN \leftrightarrow H_2N{\cdot}\overset{+}{C}{=}\overset{-}{C}{=}N \longrightarrow \left(-\underset{NH_2}{C}{=}C{=}N-\right)_n \longrightarrow \text{polypeptides}$$

Experimental work has been based on *high* concentrations of hydrogen cyanide. It has been suggested by Sanchez[28] that these might be achieved by freezing. Intermediates are apparently formed more readily under these conditions. However, polypeptides have yet to be isolated from this reaction medium. In addition, as R.E.D.Clark has pointed out, if hydrogen cyanide had been present on the earth in early times, the iron-cyanide complex, Prussian Blue, should be present as a mineral; yet it does not appear to occur at all.[29]

Stereoselectivity

Even if these massive problems could be overcome, there is still a problem to which no successful explanation has been given — why do we get only one stereochemical isomer of each of the amino acids?



In experiments such as those of Miller, both enantiomers are formed. Yet, in nature, almost exclusively, the L-form occurs. Even in the very rare situations in which the D-isomer is found,[30] the occurrence is highly specific and our arguments would still apply. Indeed, Bodansky and Perlman[31] were able to show that the D-amino acids in antibiotics arose from the L-forms; the D-forms are not incorporated directly!

The main differences between these two isomers occur in two areas. One is their effect on optical activity; the other distinction is a biological one. If a chain is constructed from the L-acids, and then one of the units is replaced by a D-acid, it breaks the symmetry of the helix, since the functional groups are in the wrong positions (figure 1c). This distortion of the helix destroys the tertiary structure and activity of the protein.

A number of attempts have been made to explain this selectivity, either by stereospecific synthesis or by selective destruction of

one isomer, without experimental success. Yet, the importance of this topic cannot be over estimated. J.D. Bernal stated that this is "the key unsolved problem of detailed biogenesis."[32] W.E. Elias, in a well-balanced review on this subject, has said that "acceptable theories must provide answers to at least five important question."[33] These he gives as follows:

"(1) Were single isomers created by asymmetric synthesis, or did they appear as racemic pairs, one isomer of which was preferentially eliminated?

(2) If asymmetric synthesis or decomposition is postulated, what was the asymmetric agent?

(3) Was the production of an optically-active compound... an oft-repeated event or one of single occurrence?

(4) Are the rotation of compounds the result of chance...?

(5) Was the asymmetry introduced at an early or late stage of chemical evolution, or was it delayed until the appearance of inchoate life...?"

The chemical synthesis of an optically active compound always generates an equal mixture of the D- and L- forms, unless another chiral compound is used in the process. Several recent reviews[34,84] indicate the difficulty the chemist has in preparing "optically pure" products. One can summarize these efforts by saying that, in order to achieve a stereospecific synthesis, one must use an optically pure reagent, catalyst or solvent. Fortunately, for the chemist, methods are also available for the resolution (separation) of D and L forms. But, what about the natural synthesis of the L-amino acids? Currently, biological cells achieve this by the use of enzymes. But, how did the optically pure enzymes originate? Here is the crux of the problem. A number of models have been suggested and abandoned as unacceptable (table II).

1. *Polarised electrons.* When beta radiation is slowed down, it becomes polarised. In an experiment, Garay[35] showed that a mixture of D- and L- tyrosine, in alkaline medium, exposed to this bremsstrahlung for eighteen months experienced a significantly greater destruction of the D- isomer than of the L- isomer. The implication is, of course, that from a synthetic mixture of the two forms in the "primeval soup," the D- isomers would be selectively destroyed. Hodge *et al*[36] have tested this method and have concluded, "we observed no single case of preferential decomposition of the enantiomers... on irradiation with polarised electrons."

Table II. Proposed models for the origin of asymmetry.

1. Polarised electrons
2. Circularly polarised light
3. Adsorption on quartz and clay
4. Spontaneous crystallization
5. Statistical variation
6. Autocatalysis
7. Contamination from space

A similar principle is implied in the use of *circularly polarised light*. A number of workers have attempted to induce stereo-selective disintegrations and synthesis by irradiating mixtures with polarised light. It is suggested that the polarised light might originate through the influence of the earth's magnetic field.[37] The best result obtained using reasonable concentrations is 20% optical activity.

Harada[37] has suggested that optical activity may be related to the non-conservation of parity. That is, the existence of the L-amino acids is pre-determined because of the inherent dissymmetric nature of matter. We must ask the source and reason for this dissymmetry. But, as we have seen, the experimental evidence does not lend support to the hypothesis anyway.

2. The most popular idea is that this selective synthesis might be achieved by the *selective adsorption* of the L-amino acids and D-glucose on clays or quartz.[38] This has recently been challenged by Youatt and Brown.[39] Quartz occurs in nature in its two optical enantiomorphs. Reactions occurring through adsorption on one of these forms are often selective, resulting in asymmetric synthesis of disintegrations. Akabori[40] proposed that adsorption of an initial unit on clay would result in an alignment of molecules to produce a specific conformation. Ponnamperuma has found that these claims cannot be substantiated.[41] Terentev and Klabunovskii[42] claim to have brought "about a number of asymmetric syntheses with different catalysts on quartz crystals under many variable conditions." Even though quartz has two crystalline forms, these seem to be unable to distinguish between the amino acids according to other research.[43]

3. Other workers have tried to explain the selective synthesis by proposing a mechanism of *spontaneous crystallisation*. Eliel[41] says, "If, in a solution of a racemic modification supersaturated

with respect to the enantiomers, a nucleus of one of the enantiomeric crystals begins to form spontaneously and fortuitously, this nucleus is apt to grow by the addition of molecules of its own configuration, and it is quite possible that a macroscopic crystal of this particular enantiomer results before any other enantiomer crystallises. If, through some accident, the mother liquor is at this point separated from the crystal, a partial resolution of the material... will have been affected." Note the importance of chance here. In fact, it requires an impossible situation — a highly concentrated solution ("supersaturated"); we have seen that the concentration is infinitesimal anyway!

Fox[45] predicted that preferential crystallisation might be induced by "seeding" the solution with an L-crystal, which might have originated from a meteorite. Prof. Burke referred to the concept of contamination from space and said,[46] "Since the production of L-amino acids is associated with living cells... it is clear that these amino acids are formed by chemical processes, possibly catalytically on the surface of a meteorite." However, as he also reported, so far only mixtures of D + L have been found from these sources.

To attempt to account for the selectivity by seeding or contamination is to push the problem back one step.

The suggestion that one form might crystallise selectively from a mixture of the two is challenged by Fox *et al*,[45] who stated that "any one DL- amino acid is thermodynamically more stable as the racemate than as either the L- or D- enantiomorph." The spontaneous process is not resolution but racemization.

Statistical variation[47] is a simple model that has been invented to account for selective crystallisation. While, on the average, a racemate will contain equal quantities of the two isomers, it is statistically possible for a racemate to crystallize out with a predominance of one form. Such a possibility has been shown to be experimentally viable. However, it only happens in a minority of cases and then still gives both isomers. There is no statistical bias for one isomer over the other.

Terentev and Klabunorskii[42] dismiss this mechanism, (of preferential crystallisation), by saying that it "need hardly be taken into account in connection with the complicated substances of colloidal structure which undoubtedly played the essential part in the building up of the primeval protoplasm."

4. *Autocatalysis.* According to this hypothesis, once one isomer has been produced selectively, the rest of the process is self-catalysed in that the L- isomer will show preference for reaction with other L- isomers over that with the D- form. As we have seen,

the preliminary selectivity is an unsubstantiated hypothesis. There is, however, no basis for confidence here either. While it is true that a protein formed from a solution containing only the L forms grows longer and faster than a protein produced from a mixed medium, there is no evidence that it would be formed exclusive to the formation of the mixed form or to the protein based on the D- isomers. The formation of an optically homogeneous protein can only be described as being faster than that for the heterogeneous form. In fact, Steinman found that the experimental evidence failed to substantiate this hypothesis at all: "These results suggest that the synthesis of stereohomogeneous polypeptides would have to depend on chance associations at the simple peptide level and then on stabilisation of homopolymers by the α-helix at higher degrees of polymerisation."[48] It has been shown that the large helical polymers required for information storage do not form spontaneously unless optically pure monomers are used; racemates yield shorter polymers and these don't form helices.[49]

The hypothesis also proposes that, since the two forms exist in equilibrium, the removal of the L- isomer would cause a shift in the equilibrium to replenish, so re-establishing equilibrium and causing an overall shift in favour of the L- isomer. For such a mechanism to occur, the initial selection would be necessary and the maintenance of the optical purity (over against racemization) must be preserved.

Eigen, recognising that this optical selectivity is a characteristic of a self-replicating system, concludes that it was only a matter of time before natural selection isolated the one form. But this position is tautological[50] because the natural selection would have to operate on the initial racemic system and this contradicts the first part of his hypothesis, that is, that a natural system is dependent on optical purity.

Resolution is a teleonomic process: it requires knowledge as well as the enantiomer and energy. Most of the proposed techniques, in so far as they can be demonstrated to have any validity at all, generate an enantiomeric excess (rather than optical purity),[51] and fail to explain why the same isomer should be selected on each occasion that the amino acid is synthesised. For example, *if* the surface characteristics of the levorotatory quartz favoured the formation of the L- amino acid, this does not account for the failure of dextrorotatory quartz generating a parallel system based on the D- isomer.

The only successful synthetic route is one that involves enzymes. But these need our L- amino acids for their own synthesis and so assume the answer to the problem!

Harada[37] has come to the conclusion that "the origin of optical activity might not be a single process. Several individual or cooperative processes could constitute the origin of optical activity."

We posed a set of questions postulated by Elias. We quote him again, "This... does not obviate the fact that not one of the five questions posed... can be answered!... It also appears unlikely that experiments can be designed to provide the desired definitive evidence, for chemical evolution cannot be duplicated." We must concur with Wald, that the selection of one enantiomer may be the *result* of life rather than its *prerequisite*.[52] Brown[53] has said, "Questions such as... how optical activity arose are points of current controversy where persuasive evidence is hard to find." No wonder Elias concludes, "Only speculations on this subject are possible at the present time." It is our belief that the concept under investigation lacks substance, not only experimentally, but in terms of the underlying scientific laws.

All these methods fail in that they do not, in the final analysis produce exclusively the L- isomer. So, what happened to the D- forms? There is another related problem. The enantiomers undergo a process of racemisation. We must ask why we do not find extensive deposits involving complete racemisation. A period of approximately six half-lifes (of the order of ten million years) should be sufficient for this condition. So, if the synthesis of life along these hypothetical lines had been successful so many million years ago, we would be faced with another problem: the amino acids should be thoroughly mixed in D- and L- forms now; but they are not. Kvenvolden[54] has found that Fig Chert contains only the L- amino acids, yet it is supposedly 3,000 million years old.

Polymerization

We have identified a series of problems (table III). Let us be generous and assume that these barriers can be overcome. What happens next? The amino acids must join together to form proteins; we call this polymerization.

Let us first see this process as the evolutionist views it. Horne writes[55] "Once in hand the building blocks (amino acids, etc) must be put together. The putting together was a long and delicate sequence and each step was highly improbable. Fortunately the time span allotted to the beginnings of life was exceedingly long, perhaps billions of years, so that the improbable was not necessarily the impossible. Biogenesis is pushed further into the realm of possibility if there were mechanisms operative for the

Table III. Problems in the prebiotic synthesis of amino acids

A.	*The atmosphere*
1.	Requirement: absence of oxygen — evidence opposes this.
2.	Instability of a reducing atmosphere — would last only tens of thousands of years.
B.	*The reaction*
3.	Conditions are unrealistic — the use of a cold trap.
4.	Yields negligible even for the most favoured compounds.
5.	Reactions between the products at higher concentrations.
C.	*Their stereochemistry*
6.	There is only one kind: L-amino acids — chemical synthesis gives a racemate and selective degradation cannot be substantiated.
7.	Geological ages would result in racemization.

concentration of the pieces. Let us imagine then the proto-biological substances being absorbed on bubble surfaces, transported upwards to the sea's surface and joined with other materials absorbed there, then tossed up by the waves and carried by the seaspray up to the beaches and estuarine mud, where in the richer warmer waters the pieces began to react and aggregates to grow." Is Horne being unnecessarily pessimistic when he says that each step was highly improbable? Not at all. First of all, monomers do not polymerise spontaneously. Energy must be supplied. This is very definitely true of protein formation. The reverse reaction, hydrolysis, occurs much more readily. A study of body processes will show this. Proteins in our food are rapidly broken down to amino acids in the duodenum; their synthesis in the body's cells are complex processes by comparison.

Consider a polypeptide of one hundred amino acids, and so 99 peptide bonds. The free energy change for the formation of a peptide bond is +2.09 $kJ.mol^{-1}$.[56] So, 99 bonds require 206.9 $kJ.mol^{-1}$. Therefore, at 300K, $\log_{10}K = 36$. So, the equilibrium constant for the polymerization reaction is 10^{-36}. So,

$$K = \frac{[peptide]}{[aa]^{100}} = 10^{-36}$$

We have shown that if all the atmospheric nitrogen were converted to one amino acid, the concentration would be less than 0.2 $mol.dm^{-3}$.

So, $[protein] = 10^{-36}.(0.2)^{100}$

$$\approx 10^{-106} mol.dm^{-3}$$

In the cell, the condensation requires activation by ATP and a specific enzyme and specific t-RNA for each amino acid. These were not produced in Miller's synthesis. It is only by a mechanism such as this that polymerization can be achieved. Furthermore, a mixture of the amino acids with other carboxylic acids, amines and carboxaldehydes (which must be present in the proposed prebiotic soup) would prevent polymerization.

The thermodynamic barrier to spontaneous polymerisation is not easily overcome. Matthews and Moser say[57] "Since the thermodynamic barrier to spontaneous α-amino acid polymerisation is not easily overcome, and indeed seems impossible by any reasonable condensation mechanism, a completely different sequence of events leading to polypeptide formation has been postulated..." So, where can we find such a generous energy source? Sidney Fox[58] felt that he had found the answer and confidently entitled a paper "In the beginning..... life assembled itself." He heated a mixture of amino acids at 175° C for six hours. Leaching of the mixture with water showed that some substances related to proteins had been produced. These were called "proteinoids." He suggested that a natural equivalent of this laboratory reaction would have been the rims of volcanoes, and that rain would have leached out the proteins. How realistic is this claim?

Firstly, these "proteinoids" are not proteins. His product is no more than a peptide chain. Proteins, as shown earlier, are much more complex. Also, in contrast to the large variety found in nature, only a few polypeptides are synthesised by Fox. The sequence of the acids in Fox's peptides have no apparent significance either. Miller and Orgel[59] commented that "the degree of non-randomness in thermal polypeptides so far demonstrated is minute

compared with the non-randomness in proteins. It is deceptive, then, to suggest that thermal polypeptides are similar to proteins in their non-randomness." For a protein of a hundred units, made up from twenty amino acids (assuming only the L-forms are available) the chances are 10^{70}: 1 against a meaningful combination. Mathematicians would write it off; only evolutionists would try to make something out of it.

Furthermore, the reaction mixture consists of the pure, anhydrous acids — water or other chemicals interfere. Volcano gases consist of 70% water and this would result in depolymerisation. Then, the reaction conditions are specific — heating for more than six hours would lead to destruction. The rain had to fall right on time! This would result in the hydrolysis of the proteins as well, though, of course, the rate of this reaction could be low. Also, the volcano temperature is much greater than 175° and this would lead to racemization. Hulett agrees that volcanism might have provided an environment conducive to dehydration, but acknowledges that it also favours the degradation of most prebiological molecules. Miller and Orgel[59] put it like this: "Another way of examining this problem is by asking whether there are places on the earth today where we could drop, say, 10 grams of a mixture of amino acids, and obtain a significant yield of polypeptides.....We cannot think of a single such place."

Fox found that either aspartic acid or glutamic acid must be present in excess with lysine.[60] But this is very different from the proportions found in nature. (Nor is it compatible with Miller's experiment). In addition, threonine and serine are destroyed in this reaction; yet they are very prominent in proteins, making up 10-20% of the total amino acid content.

Miller and Orgel state that "we doubt that.....biological polymerisation could have taken place except in an aqueous environment."[59a] Oro and Guidry[61] produced a peptide of up to eighteen units of glycine by heating the monomer in aqueous ammonia solution at 160°C. But, the aqueous medium is unsuitable for extensive polymerisation as the reaction is reversible and the water would aid hydrolysis of the peptide. So, the ocean is practically the last place for the spontaneous formation of life. It has been suggested that warm lava would cause evaporation and so aid the condensation reaction; but this would lead to denaturation. Ponnamperuma and Peterson,[62] Calvin *et al*[63] and Schramm *et al*[64] have suggested alternative dehydration routes, but these are irrelevant in that the reagents proposed have no apparent natural significance.[65]

Recognising the difficulty, Eigen proposed that some peptides have the capacity to condense some amino acides into a chain;

other peptides would join these peptides. A contribution from chance is then needed to set up a cycle in which the newly made protein is, for practical purposes, the same as one of the proteins contributing to its manufacture, thus creating a reproductive cycle. Eigen thinks it would occur often enough in aggregations amongst the vast numbers of molecules in the soup.[22a] But, where are these vast numbers of molecules; we have seen how dilute the solution is!

Wald[4] has said that "one of the most difficult problems is to attempt to understand how such unit structures combined with one another and polymerised against thermodynamic gradients that tended rather towards hydrolysis...apart from the precise activating mechanisms that guide and provide the energy for such syntheses in cells." In other words, we need the result (modern proteins) before we can get the result!

Carbohydrates

It has been shown that, in the presence of calcium carbonate, methanal (formaldehyde) polymerises to give ribose, but only as a minor product.[66] A 0.5 molar solution at pH 8.5 gave a 40% conversion to sugars after an induction period. A 0.01 molar solution gives sugars, but they are not produced from 0.001 molar solutions. Crabel and Ponnamperuma[67] got similar results using alumina rather than calcium carbonate. However, these latter writers conclude that "We do not believe that the formose reaction .....is a plausible model for prebiotic accumulation of sugars." Reid and Orgel[68] consider that the conditions are too extreme for primitive earth because the formaldehyde concentrations were too high. Also, the sugars undergo rapid decomposition in an aqueous environment. Hullett[15] examined the likely maximum yield of formaldehyde by photo-chemical irradiation of the proposed reducing atmosphere. Hull[21] showed that the equilibrium yield of glucose would be 10^{-134} moles per litre. This is a non-sensical amount — it means a concentration of one molecule in 10^{111} litres. Since the volume of the observable universe is of the order of 10^{80} litres, this one molecule would be in a volume 10^{30} times that of the universe!

Nucleotides

The abiotic synthesis of these presents a major problem. The most likely route seems to be via hydrogen cyanide. Hullett[15] examined its rate of synthesis (10^{-6}mol.cm^{-2}.y^{-1}) and stability. It is photochemically reasonably stable, but is hydrolysed by water

(3% p.a. at 25°C at pH of the oceans). This gives it a half-life of thirty years at this temperature, but of hundreds of years at 0°C. So Hullett estimated a maximum concentration of 10^{-6}mol.dm^{-3}.

The most promising route to adenine required the concentration of cyanide by eutectic freezing at about -10°C.[69] Besides its polymerisation to amino acids, hydrogen cyanide can be conceived as the precursor of these nitrogen bases. Calvin[70] describes a 3% yield of a nucleoside (base and sugar) by condensation of the components with phenyl polyphosphates (but no experimental evidence is presented), which is analogous to a supposed primitive environment, for their condensation or polymerisation.

But, if the nucleic acids had been formed by some yet-to-be-discovered method, they would have been very susceptible to ultra-violet radiation damage. Also they would be unstable to water — the only medium that could offer them any protection (ten metres or more down) from UV. Similarly ATP has a half-life of only a few years at 25°C.

An important component of the nucleotides is the phosphate group. Surely there is no difficulty in obtaining this? But there is. In the presence of calcium ions, the phosphate ion is precipitated out leaving a solution 10^{-6} molar.

Primitive cells

Oparin suggested that the first "cells" would have consisted of coacervates.[5] These are colloidal particles formed by the association of macro-molecules of different types. This association results from physical or chemical properties of the macromolecules and is non-selective, is not self-organising and is unstable.

Fox[71] claimed that his peptides formed microspherical proteins and that these would be a step towards a living cell. We have seen that his peptides are not proteins. But then, cells are significantly more than proteins anyway. His claims[72] to have found that they have enzyme-like properties display either a desperate hope or an ignorance of both enzyme action and that of the catalytic properties of histidine[73] which was a key amino acid unit in his peptide. More recently,[74] he has produced lysine-rich peptides which, *with ATP*, catalyse the formation of other polypeptides. Even so, one enzyme would have been meaningless without the others still needed. For example, besides the one needed to produce the substrate, another will be required to utilise the product. Without these complementary enzymes, the single enzyme activity would not only be useless, but destructive.

Fox admits that his microspheres are rather unstable — they are dissolved when the microscope slides, on which they are examined, are warmed. Also, they dissolve on dilution — and we know how much water there is on the earth! His claim that the polymers are not completely random and contain identical structures are unsubstantiated. Fox has also described the multiplication of these primitive cells by a process related to cell division. In fact, the two mechanisms are unrelated. In the case observed, the division is due to physicochemical effects as in the division of soap bubbles; there is no reproduction or replication.

The cell is a (the?) most complex machine. Whenever in history did a machine arise spontaneously from matter? Potter has said that the simplest form of life requires not less than a thousand molecules, "but whether it is 3,000 or 10,000 or greater is anyone's guess."[75] Morowitz estimates that the simplest conceivable cell requires 124 different protein molecules plus the sugars, lipids, nucleic acids, etc.. The free energy of formation for the average microorganism from a solution of its monomer units is 326 $J.g^{-1}$. From this it can be shown that the probability of its spontaneous formation is 10^{-10^8}.[76]

Information coding

Even if we are able to form our polypeptides by random processes, there is still a big jump from these to the specific properties required for biological activity. These properties are coded into the molecule by the sequence of amino acids. In living systems, this is generated from the nucleic acids with their specific sequence of nucleotides which is a code in itself. How big a problem is this? This question is crucial. If the problem is trivial, the solution is relatively easy.

Let us consider the production of an abiogenetic enzyme and of the corresponding DNA molecule required to code it. We consider a relatively simple system of one hundred units. Since these 100 units are made up from twenty amino acids, the enzyme has $20^{100}(=10^{130})$ different combinations. The probability of obtaining a specific structure is therefore 10^{-130}. But experience shows that some variation is possible without loss of activity. For example, of the 101 residues in cytochrome c, 27 are invariant and a few positions can have up to ten different acid units.[77] If we allow an average of five variations per position (which is considerably more than yet observed), then the number of acceptable structures will be $5^{100}(=10^{70})$. The probability of getting an active enzyme is, then, $10^{70}/10^{130} = 10^{-60}$. This probability only becomes significant if the time factor is very large so as to allow sufficient trials.

But are we really being realistic with this option? If 1% of the atmospheric nitrogen was fixed into one hundred residue proteins, it would give 10^{40} such molecules (450 $kg.m^{-2}$ of the earth's surface!). If such a yield was obtained every year of the earth's history, it would give us the chance of finding a viable protein as 10^{-11}.

Now we also want to get the right DNA — protein interaction for our scenario. If the polynucleotides formed as readily as the proteins so that we had 10^{40} molecules of each, and they collided 10^{10} times a second, no collision repeated, we would have 10^{66} collisions in the period under consideration. From this, we can show that the chance of a successful pairing would be 10^{-55}.[77] The significance of this should become apparent shortly.

Eigen realised that there was a large jump from the chemical flask to a living cell, and so has set himself the task of determining the minimum assemblage of molecules needed for this leap.[22] His approach was to apply "the Darwinian logic"[2b] to the inanimate material. Since the primordial soup contained a mixture of chemicals, there had to be a selection process acting on the molecules now known to be essential to life, and yet the system had to tolerate the biologically unacceptable compounds too.[78] Maddox described these as "evolving molecules."[2] Eigen refers to the "fittest molecular assemblies."[78] But this is not a meaningful description — we are talking about chemical fitness, not life; there is no chemical distinction between one protein assembly and another. As Eigen sees it, in order to achieve some selection, "certain forms of cooperation were essential." An expansion of the information system in a molecule required double feedback loops known as hypercycles.

The hypercycles are cyclic pathways in which polynucleotides first arose by chance and then coded for the first protein. But, we can immediately make two comments. The abiogenesis of these polymers is more problematic than for proteins; it also avoids the question of the origin of the code translation system required to produce the proteins.

However, in spite of the failure to produce the required starting materials, Eigen supposes that there was an endless supply of activated RNA monomers and that the lifetimes of the RNA's were infinite.[78a] Of course, initially the RNA sequences were random. But, since the continued existence of RNA is against the rules of thermodynamics, then some kinds of molecules should be preferred over others. Which? Those strands with stable structures (for example, resistance to hydrolysis) survive and are the only ones capable of stable self-replication. Some mutants would be copied more rapidly than others or would be less susceptible to errors in copying and so their concentration would increase more

rapidly. Sooner or later these faster-growing mutants would take over.[78a] The maximum gene lengths in a prebiotic system for stable self-replication is found to be less than a hundred nucleotides (in the absence of enzymes). This is confirmed by experimental tests on copying fidelity. Such a polynucleotide would give a peptide of about thirty units. To extend beyond this, we need the production of enzymes: non-self-reproducing proteins. So, neither can be optimized without the other; interaction is needed. A second, linked hypercycle was needed to produce these proteins.[22]

Ultimately, Eigen sees these cycles as possessing the ability to wrap themselves "up in small packets...escaped poisoning...and scattering its key products."[22a]

Smith has pointed out that there is no experimental justification for the concept.[79] The arguments "...raise more problems than they solve." As Calder admits, "The hypercycle is, of course, nothing but a theory..... The only test is plausibility."[22a] The neodarwinian concept of the chance origin of the code is without experimental basis and contrary to the second law.

On this latter point, Eigen postulates a mechanism which is inherent in his hypercycles but not in matter. It requires a mechanism to receive and store reduced entropy locally. A mechanism or machine is essential for storage; without it, the second law of thermodynamics forbids autoorganisation. Neither existed in the prebiotic world because both constitute expressions of teleonomy which is not a property of inorganic matter but of life.

But, does a decrease in entropy correspond to information generation?[80] Systems of decreased entropy, for example the Morse Code, are available for the transmission of information because the accidental production of such systems is improbable and they will not appear everywhere instantaneously and simultaneously. So, information can be inserted into them. Information and concepts are *inserted* by human conventions onto reduced entropy systems, but the system is not the same as the information it carries.[81] All experimental work in the realm of biogenesis involves matter + energy + teleonomy; evolutionary theory substitutes chance for intelligence.

Chance, however, is not adequate. It does not develop new information nor does it form an information storage system; it can only modify a pre-existent system. It is contrary to the tenets of information theory to attribute the origins of coded programmes to chance and autoorganisation of inorganic material. Increased order, decreased entropy, does not necessarily carry meaningful information. The meaning of a sequence is not inherent in that sequence. The random selection of the letters A-N-D in "Scrabble"

is chance, but its meaning is not the result of chance; its meaning is the result of human convention not chance. So, A-N-D has no significance to the Frenchman, German, Dutchman, etc.. Similarly, identical sequences can have different meanings to different people; for example, T-E-E has different significances to the English golfer and to the German housewife. To Eigen, that meaning and information appears only in the translation. And how was the translation apparatus obtained? By chance! However, this translation machine must produce both the information and the concepts. Better than any man-made computer!

Molecular movements do not produce increasing genetic information. For an increase in order, "rectified energy" must be supplied, that is, the product of a machine. Living cells are programmed genetically and so can direct non-directional energy. The biological cell has no apparent mechanism to generate *new* information. The energy is utilised for replication, not for new information. If this is not possible in biological systems, what hope is there in the original inorganic ones?

The synthetic protenoids of Fox *et al* exhibit normal molecular architecture, not that required for physiology. The informational code is developed from the chemical order. Wilder-Smith[50a] uses the illustration of ink on paper. The dried ink has a molecular structure. Over and above this, we have the information those marks carry. A mutation would occur if it was splashed with water! The mutation modifies or destroys; it does not create. A living organism is a hybrid between the two types of order. But the first type of order cannot spontaneously provide for the second by chance. So Yockey says, "The (chemical evolutionary) scenario does not generate even one molecule of the biopolymers of reasonable specificity from which the non-linear processes of evolution considered by Eigen *et al* could start."[82]

Other points that have been made against this theory include the fact that Eigen's hypothesis is based on a non-equilibrium system, which is highly improbable in view of the time-scale involved. The concept of the generation of information by these means ignores the fact that the laws of nature provide a basis for function, not genesis. The laws of nature never bring forth a machine spontaneously. Eigen's reference to natural selection and its application to molecules[78] not only involves the unscientific principle of extrapolation into the unknown, but seeks to apply at the molecular level a concept which is even questioned at the organic. The concepts behind all organisms and their inter-relationships require (a) a knowledge of the laws of nature providing the functioning basis, and (b) the know-how in order to transform such knowledge into practice and apply it. Eigen has not succeeded at these points.

Conclusion

We have cast our net wide over this subject in order to see if there is any plausible mechanism of chemical evolution. To Calder, the "astounding coincidence" becomes possible "given enough time."[22a] However, we have sought to show that chance is an inadequate tool for the production of life.

We have also to conclude that there is no satisfactory synthesis for half of the amino acids even in the laboratory. Similarly, the fatty acids, sugars and nucleotides are lacking in the proposed primeval soup. What is more, under the proposed prebiotic conditions, they are incompatible. Even when they have been synthesised, these biochemicals have to face up to conditions which guarantee their destruction within short life-times. As Miller and Orgel have pointed out,[69a] the ocean will lead to the depurination of nucleic acids, the hydrolysis of the polymers and decomposition of sugars — unless, of course, we can drop the temperature to -10/-20 degrees Celsius. Aside from the difficulty of deriving such conditions, they would have adverse effects on the reaction rates. Once formed, we have still to select out a limited number of amino acids etc. from the soup.

A study of the early atmospheric conditions has shown that biochemists are looking at artificial conditions that have no reality in practice. Future work must at least be based on the proven oxidising conditions known to have existed. Furthermore, Vallentyne[83] has pointed out that "the results obtained from experiments run over a few hours may bear no relation whatever to the actual state of affairs resulting after a period of thousands or millions of years." Additionally, we would hardly describe the laboratory experiments as primitive conditions. Another problem is that the work done generally assumes different — if not, inconsistent — conditions for the various classes of compound required. According to Bernal, "....the principles of experimental science do not apply to discussions on the origins of life, and indeed cannot apply to any problem of origin."[69b] They cannot, because they are devastating. We would be surprised if intelligent chemists did not find ways of solving many individual steps; but would that not prove the importance of intelligence?

Clearly, the results obtained in simulation studies can only be as accurate as the model they seek to represent. The evidence for what did happen is not available. Asked by Maddox, "Do you think it will ever be possible to reconstruct with fidelity..... the course of this evolutionary process — in detail?", Eigen replied: "No..... I don't think in detail.... but we want only to see that it's a possible process."[2b]

So, we have seen that the evolutionary theory must stand on chemical principles. We have followed the path of the proposed evolutionary synthesis and polymerisation of one chemical family: the amino acids. There is not one step in the sequence that can be justified in terms of a prebiotic synthesis. We have seen that the theory is both unable to explain consistently and coherently the origin of life, and is, in fact, flatly contradicted by basic chemical laws, both thermodynamic and kinetic. Hull has wisely concluded[23] that "the physical chemist, guided by the proved principles of chemical thermodynamics and kinetics, cannot offer any encouragement to the biochemist, who needs an ocean full of organic compounds to form even lifeless coacervates." Wilder-Smith has concluded[50b] that the theory of evolution (spontaneous biogenesis and spontaneous automatic transformism) is dead at its roots. Certainly in the area covered in this paper, it still has to prove its case.

Of course, we cannot prove a negative position completely. Each new piece of research must be assessed on its own terms. But, equally, success in synthesising any of the chemicals of life in the laboratory does not confirm what happened originally. Merely its feasibility as a mechanism. However, we can assess the improbability of such a position. That we have sought to do.

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