UNIVERSAL PROTEIN ANCESTORS FROM HYDROGEN CYANIDE AND WATER

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Abstract. Current research in cosmochemistry shows that crude organic solids of high molecular weight are readily formed in planetary, interplanetary and interstellar environments. What are the components of these intractable materials and how are they connected, if at all, with the beginnings of life? It is proposed here that underlying much of this ubiquitous chemistry is a low energy route leading directly to the synthesis of heteropolypeptides from hydrogen cyanide and water. Evidence from laboratory and extraterrestrial investigations suggests that this hydrogen cyanide polymerization is a truly universal process that accounts not only for the past synthesis of protein ancestors on Earth but also for reactions proceeding elsewhere today within our solar system, on planetary bodies around other stars and in the dusty molecular clouds of spiral galaxies. The existence of this preferred pathway adds greatly to the probability of life being widespread in the universe.

The Miller-Urey Paradigm

Thinking about the origin of life has become one of the most fruitful exercises in science since the Miller-Urey experiment in 1953 sparked renewed interest in this age-old problem. On the grounds that hydrogen is by far the most abundant element distributed within our galaxy, Urey[1] had reasoned that new-born planets must possess reducing atmospheres consisting mainly of molecular hydrogen, methane, ammonia and water. By subjecting mixtures of these gases to continuous electric discharges, Miller[2] obtained several kinds of organic compounds including, most dramatically, some of the α-amino acids known to be among the building blocks of proteins today. At one stroke this imaginative investigation established a link between two of the most far-reaching generalizations of our time: the unity of cosmochemistry determined the nature of the starting materials, and the unity of biochemistry pointed to the significance of the results. It now seemed possible that on the primitive Earth "simple organic compounds reacted to form polymers, which in turn reacted to form structures of greater and greater complexity until one was formed which could be called living."[3]

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Studies of the presumed polymerization process followed, centered on the question of the origin of proteins.[4,5] Successful syntheses of peptides in various kinds of laboratory environments appeared to be consistent with the generally accepted belief that the prebiotic formation of primitive proteins occurred in two stages: α-amino acid synthesis initiated by the action of natural high energy sources on the components of a reducing atmosphere, followed somehow by polycondensation of the accumulated monomers in the oceans or on land. A more critical examination of the experimental evidence, however, shows that the specific conditions selected -- anhydrous, high temperature, acidic, for example -- are not necessarily characteristic of a young, developing planet. How plausible are these attempted simulations as models of prebiotic chemistry? On the primitive Earth the inherent thermodynamic barrier to spontaneous polymerization of α-amino acids might not have been so easily overcome.

The Cyanide Hypothesis

An alternative hypothesis for the origin of proteins proposed by Matthews and coworkers[6-9] bypasses this problem by postulating the direct synthesis of protein ancestors from hydrogen cyanide and water without the intervening formation of α-amino acids. Following the initial production of hydrogen cyanide in the upper atmosphere by photolysis of methane and ammonia, a key step was the rapid vapor phase polymerization of clouds of HCN to polyaminomalononitrile (IV), perhaps *via* azacyclopropenylidenimine (II) and its polymer (III) (Figure 1). Subsequent reactions of hydrogen cyanide with the activated nitrile groups of IV then yielded heteropolyamidines (V) which settled in the oceans and became converted to heteropolypeptides (VI) after a series of hydrolysis and decarboxylation steps.

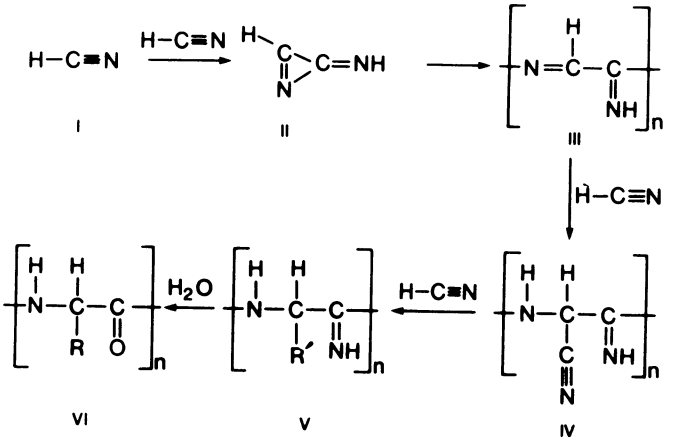

Figure 1. Proposed route for heteropolypeptide synthesis from hydrogen cyanide and water (I → VI). R' represents the precursors of protein side chains R.

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Several kinds of experiments have provided results consistent with this route. In general, we find that water-soluble, yellow-brown solids can be extracted from the products of each of the following types of reactions:

1. base-catalyzed polymerization of liquid HCN, alone or in solvents other than water;[7]
2. electric discharge experiments yielding HCN from methane-ammonia mixtures;[6]
3. alkaline hydrolysis of aminoacetonitrile, aminomalononitrile (HCN trimer), and diaminomaleonitrile (HCN tetramer), all of which are ready sources of HCN at high pH;[10]
4. HCN modification of the reactive nitrile side chains of poly-α-cyanoglycine, a synthetic polyamide analog of polyaminomalononitrile (IV).[11]

As predicted, acid hydrolysis of these yellow-brown polymers yields not just glycine but other α-amino acids as well, such as alanine, aspartic acid, glutamic acid, serine, threonine and leucine. Also as predicted, the glycine is perdeuterated when D_2O/DCl is used for hydrolysis instead of H_2O/HCl.[12] Further, recent ^{15}N NMR studies of labelled cyanide polymers synthesized from $H^{13}CN$ and $HC^{15}N$ show unambiguously the presence of peptide bonds.[13] Taken together, these results invite the reexamination and possible reinterpretation of almost all studies concerned with the origin of proteins. Which came first, we ask, amino acids or their polymers? (Figure 2).

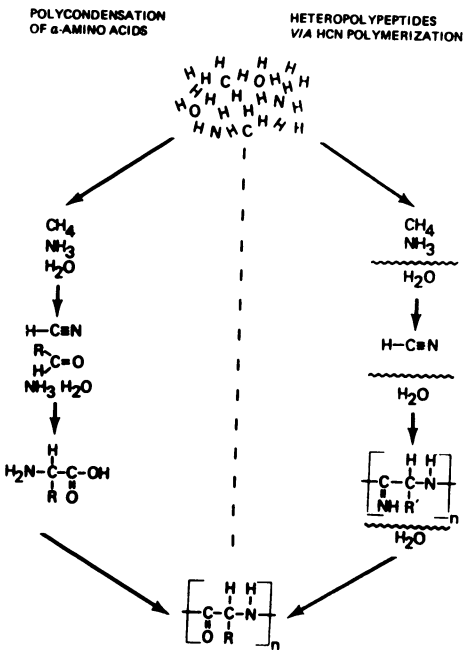

Figure 2. Two opposing models for the origin of proteins. Which came first, amino acids or their polymers?

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In the Miller-Urey experiment, for example, it seems clear from our reinvestigations that the primary products were not α-amino acids, as claimed, but rather HCN polymers, the HCN being formed from methane and ammonia by electric discharge reactions and by elimination from intermediates such as aminoacetonitriles and HCN oligomers. The polymers then became hydrolyzed to amino acids either during reflux in the reaction flask, or later during the working up procedure. The same conclusion, we believe, applies to virtually all reported experiments simulating primitive atmospheric chemistry, as well as to studies of aqueous cyanide reactions by Ferris[14] and others. In our view, these investigations ostensibly yielding α-amino acids actually supply evidence for the abundant prebiotic existence of protein ancestors -- heteropolypeptides synthesized directly from hydrogen cyanide and water.

This appears even more probable in the light of extraterrestrial research suggesting that HCN polymers are to be found throughout the solar system. Analysis of the Murchison meteorite that landed in Australia in 1969 provided the first unambiguous evidence for the presence of indigenous amino acids, or their precursors, in C2 carbonaceous chondrites.[15,16] Water-soluble yellow-brown solids can be extracted that give rise to α-amino acids only after acid hydrolysis. For example, the amount of glycine in an extract was doubled following acid treatment.[17] Also, when D_2O was used for extraction, carbon-bound deuterium became incorporated in many of the amino acids.[18,19] In particular, perdeuterated glycine was detected, indicating that the extracts contain peptide segments derived from hydrogen cyanide polymers.[19]

Hydrogen cyanide polymerization could account, too, for much of the yellow-brown-orange coloration of Jupiter and Saturn. Indeed, HCN has been found in Jupiter's reducing atmosphere and in the atmosphere of Titan, the largest moon of Saturn. Of great interest is an orange haze high in Titan's stratosphere that may consist of organic polymers.[20] These could be polycyanides formed directly from HCN. After settling on the frozen surface of Titan the heteropolyamidines (V) would be converted by water to heteropolypeptides.[21] While life is hardly to be expected in such an environment or in the cold reducing atmospheres of the giant planets, the visible cyanide chemistry on these bodies is a continuing reminder that hydrides of the elements O, C, N are a ready source of prebiotic molecules, as Miller and Urey and subsequent workers have amply demonstrated.[3-5,16]

Most important then and now was the spontaneous synthesis of heteropolypeptides from hydrogen cyanide and water. This truly universal chemistry must be proceeding today within our solar system -- on giant planets and their satellites, in asteroids and meteorites and in comets. Presumably also on planetary and interplanetary bodies around other stars, and in the dusty molecular clouds of the Milky Way, known to be rich in hydrogen cyanide.[3] Optimum conditions[9] might well have existed on the primitive Earth with its methane-ammonia atmosphere, a ready source of HCN. As polycyanides formed, settling onto land and sea together with other products of

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atmospheric photochemistry, a proteinaceous matrix developed able to take part in and promote the interactions leading to the emergence of life.[9] If Earthlike planets are natural companions of stars throughout our galaxy and beyond, then the existence of this preferred pathway -- HCN polymerization -- surely increases greatly the probability of life being widespread in the universe.

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