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FROM ORGANIC MOLECULES IN SPACE TO THE ORIGINS OF LIFE AND BACK

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ABSTRACT

Delivery of organic molecules much simpler than building blocks of biological structures may have been sufficient to initiate the process of chemical evolution leading to the first forms of life. By defining the simplest protocellular systems, it is possible to deduce what organic molecules were likely to be necessary for this process. Some of these molecules were building blocks of protocellular structures which self-assembed from amphiphilic compounds into vesicles and other structures, such as micelles and multilayers. There must also have been relatively simple mechanisms by which amino acids or their precursors were incorporated into simple peptides. At some point this process became compartmented in vesicles, which would require the emergence of cellular transport and metabolism. Energy required for these processes may have been provided by the coupling of the transmembrane proton gradient to the synthesis of high energy compounds, such as thioesters, or by carbon disproportionation reactions, starting with sugars. If these conjectures are correct, it follows that the first forms of life emerged as self-contained molecular systems, rather than as macromolecules that somehow incorporated the basic properties associated with the living state.

INTRODUCTION

The emergence of cellular life on the early earth, approximately 3.9 Ga ago, was the key step in the long evolutionary pathway that transformed inanimate organic matter into contemporary living organisms. There is no direct record of this phase of evolution, so attempts to reconstruct the process must be based on our understanding of contemporary cells and knowledge about the organic molecules that were likely to exist on the early earth. One source of these molecules is the rich reservoir of organic matter present in the meteorites, comets, micro-meteorites and interplanetary dust particles that would have contributed to the late accretion of the Earth. Since this process continues today it can be a subject of rigorous investigations. Alternatively, part of the inventory of organic matter may have been of terrestrial origin, synthesized in the earth's atmosphere or in hydrothermal regions of the Earth's oceans and crust.

To develop the connection between organic molecules available on the prebiotic earth and the simplest living structures we can adopt two different points of view. We can start by identifying organic compounds, and then reconstruct protocellular systems from the knowledge of physical and chemical properties of these compounds. Alternatively, we can first define a minimal living system on the early Earth and deduce what molecules would be required to form such a system. The first approach is a traditional one and has been attempted many times before [Chang, 1993]. This brief overview is focused on the second point of view, which is related to recent studies on the main attributes of life, such as self-organization into functional units, emergent properties, control, reproduction and evolution. In this sense,

the processes leading to life are considered "backwards". Consistent with this view, detailed discussion of the literature on organic matter in space is not included. Instead, readers are referred to several recent reviews on this subject [Cronin and Chang, 1993, Irvine, 1999, Ehrenfreund and Charnley, 2000].

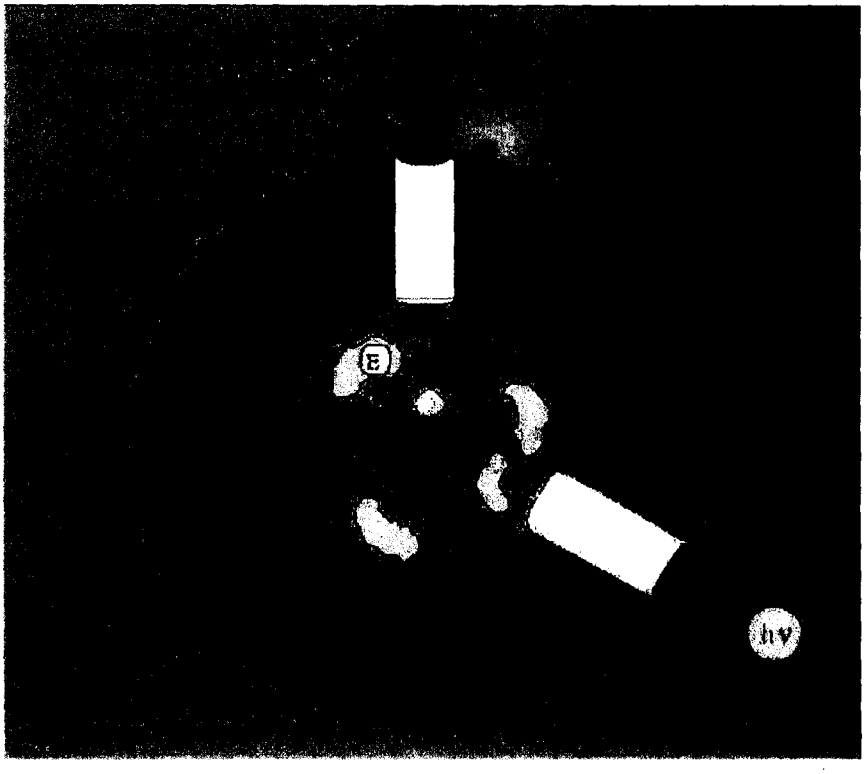

Fig. 1. Schematic of a protocell. Embedded in the membrane bilayer are structures responsible for capture and transduction of energy from the environment (lower right corner) and transport of ions and nutrients across cell walls (lower left corner and top, respectively). Enzymes (E) catalyzing ubiquitous metabolic reaction, and informational molecules (shown symbolically as a helix) are depicted inside the cell.

The simplest cellular structures that could be considered as living or, at least, would be recognized as precursors of contemporary cells will be called "minimal protocells" [Morowitz *et al.*, 1988]. These protocells, no matter how simple, had to perform several essential cellular functions known today, such as separating cell content from the environment, capturing energy and chemical substrates from the environment and using them to support the chemical reactions (metabolism) needed for self-maintenance and growth. Further, communities of such protocells must have been capable of self-reproduction and evolution towards higher complexity [Pohorille *et al.*, 1996, Deamer, 1999]. The ubiquitous cellular functions are shown schematically in Figure 1. Even though minimal protocells were extremely simple by cellular standards, they were still quite complicated, compared to the suite of organic molecules that might have been delivered extraterrestrially.

It would be highly desirable to have an experimentally testable scenario for the transformation of organic matter into protocells. Unfortunately, such a scenario is not available and this paper is not aimed at presenting one. Instead, several basic physical and chemical processes that may have led to life and involved simple organics are discussed. One of the objectives of this discussion is to identify "useful" molecules, which in turn can be used to search for them, or their precursors, in space. First, however, it should be specified what is considered as useful molecules. Clearly, all molecules capable of performing

protocellular functions or participating in pathways leading to the formation of such molecules will belong to this category. There is also another class of useful molecules, which consists of compounds that do not perform protocellular functions themselves, but provide environments that facilitate the formation of functional molecules.

INTERFACIAL STRUCTURES AND ENVIRONMENTS IN THE ORIGIN OF LIFE

One way to classify organic molecules is based on their polarity. This classification has several advantages. In particular, it stresses the relationship between the polarity of organic molecules and their role in the emergence of life, and implies preferred locations of these molecules in inhomogeneous, multi-phase environments that might have existed on the early earth. Finally, it helps to highlight self-organizing properties of organic matter, which were essential for the formation of living systems.

Polar molecules are relatively soluble in water and are often called "hydrophilic". They are characterized by a high, relative content of atoms, such as oxygen, nitrogen, sulfur or phosphorus. Formic acid, formaldehyde, and most ketones, ethers and sugars are typical examples of hydrophilic molecules. Many polar molecules are chemically reactive. Some of them are building blocks of biological molecules, whereas others have been implicated as reactants in chemical pathways towards these building blocks. Because most prebiotic aqueous environments are thought to have low concentrations of these molecules it is essential to identify mechanisms that would increase concentration of polar compounds.

One such mechanism is provided by interfaces between water and non-polar phases. These phases are formed by non-polar, or "hydrophobic", molecules, such as alkanes or polycyclic aromatic hydrocarbons (PAHs), which are common in space. These molecules are poorly soluble in water and, at sufficient concentrations, spontaneously separate from aqueous solution. Oil slicks on water are typical examples of such separation. Any hydrophobic molecules delivered to environment consisting of two co-existing phases will dissolve in the non-polar, rather than aqueous, phase.

Low solubility of non-polar molecules in water and the resulting phase separation are consequences of the hydrophobic effect [Allamandola *et al.*, 1987, Ehrenfreund and Charnley, 2000]. This effect has its origin in the small size of water molecules and highly networked, hydrogen bonded structure between them. As a result, the creation of space that is sufficiently large to allow for the insertion of a solute molecule, and the accompanying disruption in water structure are associated with considerable free energy costs [Pratt and Pohorille, 1992]. For non-polar molecules, these costs are not compensated by gains due to favorable solute-solvent interactions. Thus, non-polar molecules or molecular fragments tend to minimize their contacts with water and, eventually, may separate from aqueous solution. In general, the tendency to minimize contacts between water and non-polar molecules or molecular fragments is probably the most important, self-organizing force in nature [Tanford, 1978, 1982].

Interfaces between water and non-polar liquids form unique environments, in which macroscopic properties of the medium, such as density, dielectric response and viscosity, change, sometimes quite dramatically, over a microscopic length scale, usually not exceeding a few nanometers. As a consequence, concentrations, orientations and conformations of solute molecules at the interface can be significantly different than in the adjacent bulk phases. In particular, it was found that a broad range of organic molecules tends to accumulate at the interface [Pohorille *et al.* 1997, Pohorille *et al.*, 1998]. In Figure 2 concentration profiles of several small solutes at the water-hexane interface are shown. These profiles were determined from molecular dynamics computer simulations [Pohorille *et al.* 1997]. Although the molecules considered have no particular protobiological significance, the figure clearly conveys the point that solutes, which differ markedly in chemical structure, all exhibit increased concentrations in the interfacial region.

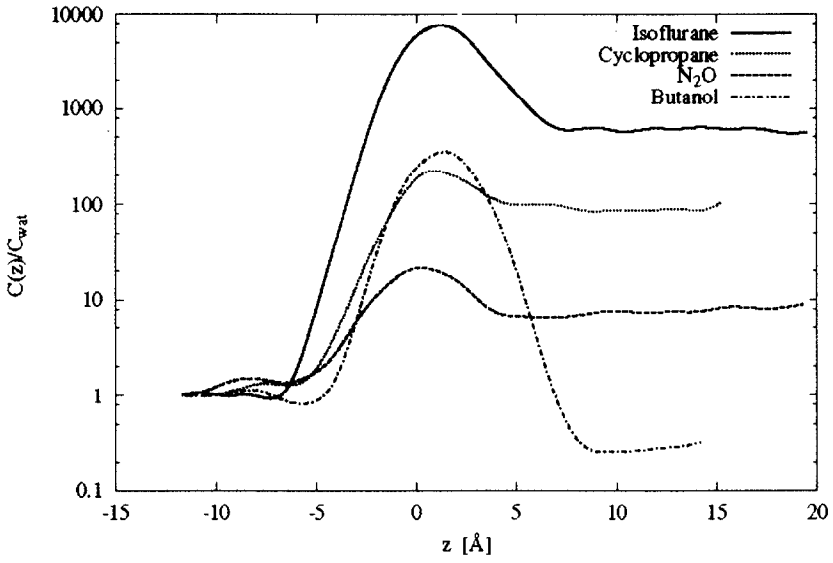

Fig. 2. Concentration profiles, C(z), of butanol, N_2O, cyclopropane and isoflurane across the water-hexane interface relative to the concentrations in bulk water, C_{wat}. The interface is set at z=0, water is to the left and hexane is to the right.

Molecules concentrated at the interface tend to exhibit increased chemical reactivity, sometimes by several orders of magnitude. There are two main reasons for this increase [Pohorille and Wilson, 1995]. First, at the interface molecules move in two-dimensional space, in contrast to bulk aqueous solution, where they move in three dimensions. As a consequence, their encounters, which are a necessary condition for chemical reactions, are much more frequent. Second, one product of many reactions of protobiological interest, especially polymerization, is water molecule. Such reactions are often highly unfavorable in bulk aqueous solution because the large excess of water drives the reactions towards the reactants. However, they become much more likely at the interface, where the concentration of water decreases rapidly.

The third, distinct group of molecules shares structural properties with both polar and non-polar compounds. These molecules are called amphiphilic because they contain spatially segregated polar and non-polar portions. Examples of such molecules are long-chain alcohols, carboxylic acids, fatty acids and lipids. Their polar groups show high affinity toward water whereas their non-polar groups are only sparingly soluble in aqueous solution. Amphiphilic molecules tend to accumulate at interfaces forming monolayers, such that the polar portions are immersed in water while the non-polar portions are buried in the non-polar phase.

At sufficient concentrations, amphiphilic molecules can spontaneously form a variety of ordered structures, such as vesicles, micelles, reversed micelles and multilayer phases [Degiorgio and Corti, 1995]. They are shown in Figure 3. The structures being formed depend both on the chemical structure of the participating amphiphilic molecules and on external conditions, such as pH, degree of hydration or ionic strength. In each case, the hydrophobic effect is at play in promoting the self-organizing behavior of the system [Tanford, 1982].

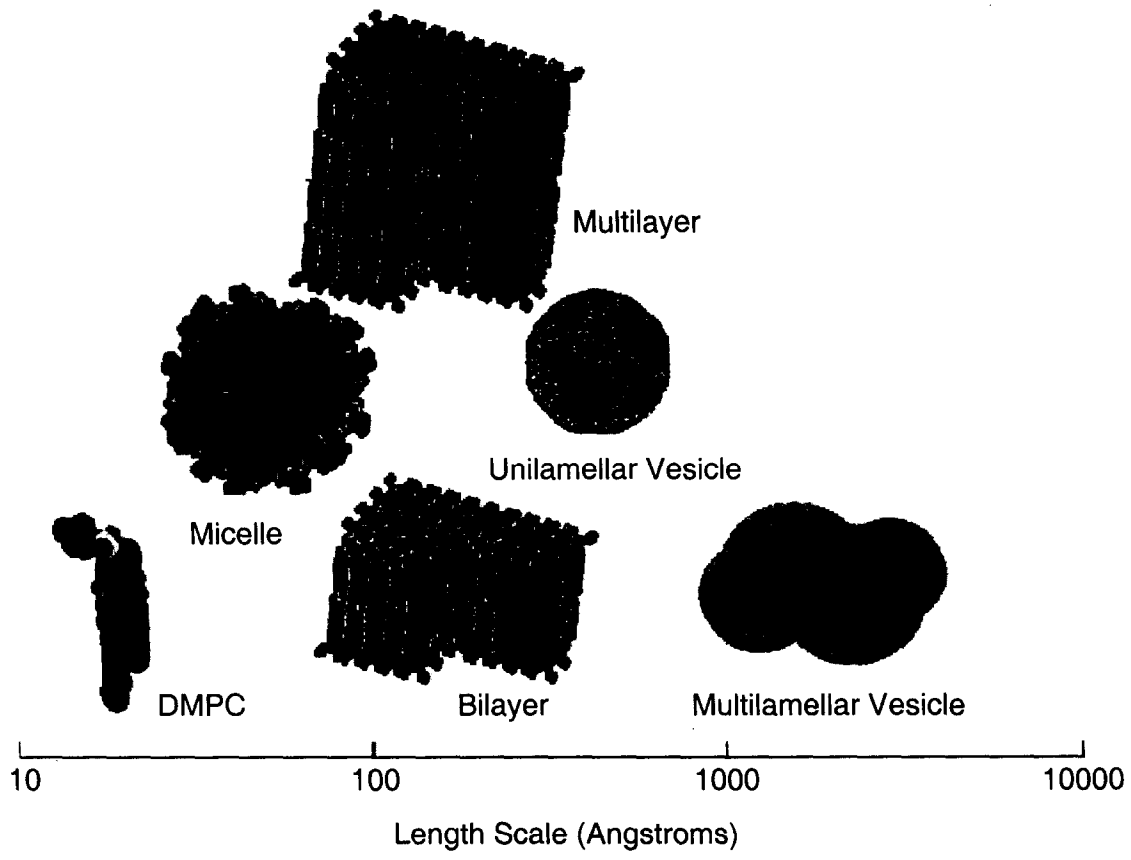

Fig. 3. Protobiologically relevant, organized structures formed by amphiphilic molecules. An example of a bilayer-forming molecule (DMPC) is shown in the lower left corner.

The structures most significant for the formation of life were vesicles — closed, spheroidal assemblies enclosing an aqueous medium. The walls of vesicles are built of amphiphilic molecules, which are arranged in bilayers such that the hydrophilic head groups point toward water and the hydrophobic tails are removed from water and form the interior of the bilayer. In this respect, the vesicle walls closely resemble modern cell membranes, which represent the permeability barrier defining all cellular life. Cell membranes are typically composed of phospholipids. However, in the absence of primitive biosynthetic pathways yielding phospholipids, it is unlikely that these molecules were present on the early earth. Instead, the most likely candidates for protocell-forming material were monocarboxylic acids and alcohols with chain lengths sufficient to stabilize self-assembled structures. Recent studies have shown that under narrowly defined conditions of pH (close to 7), temperature and concentration, a monocarboxylic acid as short as nine carbons in length (nonanoic acid) is able to assemble into vesicular membranes. However, the addition of small amounts of an alcohol —nonanol — markedly stabilized the bilayers, so that vesicles were present at any pH above 7 and at lower concentrations of carboxylic acid (Deamer, D. W., unpublished results). It has even been shown that vesicles can self-replicate [Walde, *et al.*, 1994]. Significantly, monocarboxylic acids and alcohols are also the main components of the amphiphilic material extracted from the Murchison meteorite and shown to form vesicles [Deamer and Pashley, 1989, Mautner, *et al.*, 1995]. Simple amphiphiles obtained in laboratory simulations of interstellar or cometary material can also yield vesicles [Dworkin et al., 2001]. This points to extraterrestrial infall as a possible source of the membrane-forming material.

Although other structures formed by amphiphilic molecules did not participate directly in the creation of cellular life, they could have assisted in this process. Micelles dissolved in water provided a very large, total interfacial area for concentrating organic material. Reversed micelles, which exist in non-polar phases, could have provided the means of capturing polar molecules in non-aqueous environment, such as oil slicks, and, by doing so, facilitating chemical reactions involving water as one of the products. Multilayer structures can be formed by drying vesicles. Their formation during wetting and drying cycles in tidal pools may have provided a mechanism to exchange content of vesicles. Furthermore, they created highly confined environments for organic molecules captured between the layers, which was favorable for polymerization reactions.

Considering that interfaces between water and non-polar media have properties conducive to concentrating organic material and increasing rates of chemical reactions, it is only natural to postulate that they played an important role in the origin of life. The existence of these interfaces required a supply of non-polar or amphiphilic molecules. Many of these molecules are rather unreactive or, more generally, are not utilized by simple cells. This, however, does not make them useless for the origin of life. They could have participated in the emergence of ancestral cells not as their building blocks but by providing an environment, in which these building blocks could have been synthesized. In this context, amphiphilic molecules capable of forming vesicles had a special, and different, role to play, because they yielded boundary structures of protocells. Considering protobiological significance of vesicles, searching for amphiphiles in space and determining the rates of their delivery to the early earth is becoming one of the key research areas of astrochemistry.

PROTOCELLULAR FUNCTIONS

Vesicles became the precursors to cells (protocells) only after acquiring the functions needed to survive and reproduce. The essential protocellular functions were the transport of ions and organic matter from the environment across cell membranes, synthesis of the molecules necessary for self-maintenance and growth, and transduction of environmental energy to support these processes. The identity of the earliest functional molecules in protocells is open to debate. Since in modern organisms all of these functions are carried out by proteins the most parsimonious assumption is that their precursors were peptides (short, single-domain protein fragments).

Unfortunately, most peptides have disordered structures in aqueous solution and, therefore, do not appear to be suitable for performing cellular functions. However, many of them can acquire a well-defined secondary structure at water-membrane, water-oil or water-air interfaces, providing that they have a proper sequence of polar and non-polar amino acids [Degrado and Lear, 1985, Chipot and Pohorille, 1999, Maget-Dana *et al.*, 1999]. The specific identity of amino acids appears to be less important. This is a desirable protobiological property because neither a precise protein synthesis mechanism nor the full suite of amino acids are required. The dominant factor determining the interfacial structure of peptides is, again, the hydrophobic effect, which is manifested at aqueous interfaces as a tendency for polar and non-polar amino acids to segregate into the aqueous and non-polar phases, respectively.

The folded peptides can readily change their orientation with respect to the interface from parallel to perpendicular and incorporate into the membrane, especially in response to local electric fields. Their protocellular potential is illuminated by the fact that a wide range of simple, naturally occurring [Cafiso, 1994] or synthetic [Lear *et al.* 1997] peptides can self-assemble into channels capable of transporting material across cell walls. For example, some exceedingly simple peptides, built only of leucine and serine residues, were shown to form voltage-gated ion channels [Oliver and Deamer, 1994, Lear *et al.* 1997]. In another example, a transmembrane tetramer of a 25-amino acids long fragment of the M2 protein from the Influenza virus has been shown to exhibit highly efficient, gated transport of protons, but not other ions [Pinto *et al.*, 1997, Schweighofer and Pohorille, 2000]. Structural and functional similarities between simple, synthetic channels and cellular channels and receptors suggest that assemblies of transmembrane peptides lie at the origin of charge-transporting systems.

One of the main functions of a protocell was to catalyze the various chemical reactions needed for its metabolism. The essential features of enzymatic catalysis are the formation of substrate-enzyme associations accompanied by the entropic effects of substrate immobilization, the exclusion of solvent from the active site, the presence of specific chemical groups at fixed locations in the enzyme and the preferential stabilization of the transition state complex. All of these features are difficult to achieve with small, flexible, water-soluble peptides. In this context it is not surprising that efforts to design peptide catalysts have been, until recently, mostly unsuccessful [Corey and Corey, 1996].

There are also some positive examples [Johnsson *et al.*, 1993, Brack and Barbier, 1990, Perez-Paya *et al.*, 1994, Severin *et al.*, 1997]. Their common feature is a well-defined geometry of the catalyst interacting with the substrate. In some cases, properties of surfaces were exploited [Brack and Barbier, 1990, Perez-Paya *et al.*, 1994], indicating that interfaces could have promoted simple peptide catalysts.

Recent breakthroughs in experimental protein chemistry opened the gates for systematic tests of catalytic and evolutionary potential of peptides. In a series of elegant experiments, the Ghadiri group [Severin *et al.*, 1997] demonstrated that a 33-residue synthetic peptide, based on the α-helical structural motif, efficiently catalyzes the condensation of two shorter peptide fragments with sequence- and diastereo-selectivity. Depending on the substrates used, the rate enhancement of 10-fold to 4000-fold over the background was observed. These experiments have demonstrated not only how to overcome the limitations of short peptides by employing a protobiologically relevant ligation mechanism but also how a population of peptides can evolve with an inherent error-correction mechanism. Building on these results, the Chmielewski group [Yao *et al.*, 1998] constructed another peptide system capable of auto- and cross-catalysis and generating self-replicating peptides that were not present in the original mixture.

Equally promising are the recent techniques for *in vitro* evolution of functional peptides, which allow screening very large peptide libraries [Cho *et al.*, 2000]. These techniques have already yielded the first functional molecules selected from a pool of peptides with random sequences, and should eventually bring the wealth of information about the catalytic potential of peptides.

The discussion presented above has focused on the capabilities of simple peptides to support basic protocellular functions. Protocells, however, must have been able not only to maintain themselves but also to self-reproduce and evolve. Although these properties have been demonstrated for some peptides [Severin *et al.*, 1997, Yao *et al.*, 1998] it is not clear whether they can be generalized to whole protocells. Only recently, a model has been developed, which demonstrates that self-replication of functional molecules is not a pre-requisite for evolution [New and Pohorille, 2000]. According to this model, the replication of functions and their inter-relationships, rather than the precise identities of the functional molecules, was sufficient for survival and evolution of protocells. The capabilities of protocells could have increased further if, occasionally, peptides capable of performing novel functions were produced in the system and integrated into the protocellular metabolism. Eventually, this process could have led to the emergence (or utilization) of nucleic acids and their coupling with peptides into a genomic system.

An alternative view holds that RNA molecules rather than proteins were the first functional biopolymers (the "RNA World" hypothesis) [Gilbert, 1986]. Short polymers of RNA are attractive candidates for this role because they could act as both catalysts and information storage systems. Since even small RNA molecules can maintain a rigid three-dimensional structure, they are well suited to carry out proto-enzymatic functions [Joyce, 1996]. In fact, several simple RNA enzymes have already been created in the laboratory [Hager *et al.*, 1996]. However, the concept of RNA molecules as the sole functional species in protocells encounters difficulties. RNA is fragile, easily hydrolyzed in water, and no efficient prebiotic syntheses of its building blocks (nucleotides) have been found. Furthermore, it has not been shown that RNA can be incorporated into membranes to perform functions that, in modern cells, include energy transduction and regulated transport. Nevertheless, the search is on to make nucleotides from simple substrates that include, for example, HCN and formaldehyde. Another avenue that is being pursued is to explore potential protobiological role of polymers not found in modern cells. These may be analogs of nucleic acids or may combine properties of nucleic acids and proteins [Nielsen, 1999, Schöning et al., 2000].

FROM SIMPLE ORGANIC MOLECULES TO PEPTIDES

If peptides are assigned a key role in the origin of life it raises a question about the sources of their building blocks - amino acids - on the early earth. Fortunately, amino acids appear to be relatively abundant in extraterrestrial sources. In particular, they constitute an important fraction of organic material in the Murchison carboneceous chondrite, where over 70 amino acids, including biologically occurring glycine, alanine and valine, have been identified [Cronin and Chang, 1993]. Amino acids have been also identified in simulated cometary material [Bernstein, personal communication], and most likely form through reactions on icy grains. However, it should be kept in mind that, so far, only a small subset of the biologically relevant amino acids has been found in extraterrestrial sources, and only some of them could have survived their delivery to earth [Pierazzo and Chyba, 1999].

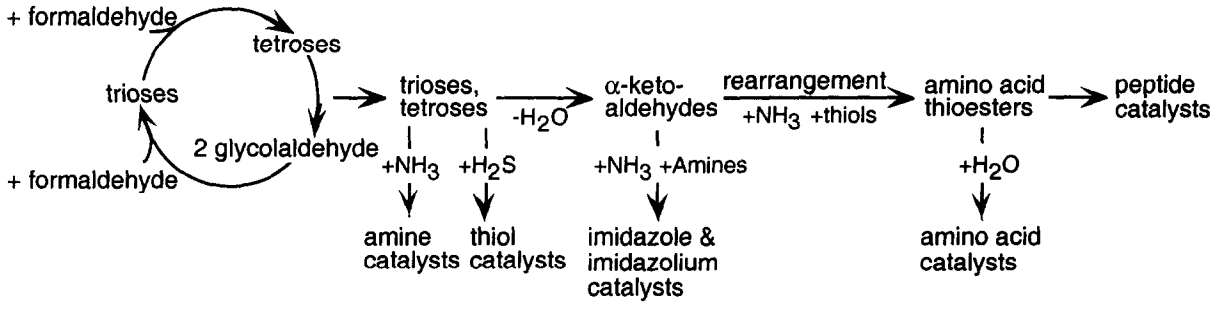

Fig. 4. The pathway from formaldehyde to peptides in the Sugar Model (Weber, 2000). The first cycle represents the Formose reaction.

Alternatively, amino acids could have been synthesized from simpler material present on the prebiotic earth. This idea has received considerable attention since the original Miller-Urey experiment, which yielded glycine, alanine, aspartic acid and glutamic acid from electric discharge in the presence of CH_4, NH_3, H_2O and H_2 [Miller, 1953]. However, a comprehensive model for the synthesis of amino acids and peptides from simple organic material that incorporates other elements highly relevant to the origin of life has been proposed only recently [Weber, 1998, Weber, 2000]. This model has been called the Sugar Model because it describes a process driven by the sugar redox reactions, which also drive modern biosynthesis. Its essential features are that it provides a mechanism for autocatalytic feedback , all reactions occur under the same environmental conditions (a "one-pot" process) and the underlying chemistry resembles modern metabolism. According to the model, shown in Figure 4, formaldehyde and glycoladehyde are converted to sugar intermediates, which subsequently react with ammonia in the presence of thiols to give amino acids. A possibility of forming peptides along the same pathway is being studied. Formaldehyde and glycolaldehyde, the primary substrates for the Sugar Model, could have been synthesized under a variety of conditions in strongly, weakly or non-reducing atmospheres (for discussion see Weber, 1998). This required the presence of only very simple molecules, such as CH_4, CO or CO_2, H_2O or H_2, and NH_3 or N_2. The Sugar Model indicates that extraterrestrial delivery of compounds much simpler than amino acids may have been sufficient for the emergence of peptides.

PROTOCELLULAR BIOENERGETICS

One of the essential functions of protocells was to capture energy from the environment and utilize it to synthesize the high-energy compounds that served as the source of energy to drive other protocellular reactions. The initial source of environmental energy may have been light or chemical energy [Deamer, 1997]. All known modern organisms transduce environmental energy by creating a transmembrane proton

gradient which is coupled to the production of adenosine triphosphate (ATP) from adenosine diphosphate (ADP) and inorganic phosphate. The synthesis of ATP is performed by membrane proteins called ATP synthases (ATPases). Although phylogenetic studies indicate that ATPases must have emerged before the last common ancestor, these molecules are too complex to be a part of an early protocell and the nature of the earliest energy transduction system is unknown.

Probably the simplest system capable of converting light into transmembrane proton gradients consists of PAHs incorporated into vesicle membranes [Deamer, 1992]. Upon photo-excitation, the PAHs release protons either to the exterior or the interior of the liposome. Protons in the environment dissipate while those inside the liposome accumulate, thereby creating a proton gradient. Since protons in the interior of the liposome are also used to regenerate the initial state of the system, this proton gradient is only transient. What is needed is a "gate-keeper" mechanism to ensure that reprotonatation of the proton source does not dissipate the already formed proton gradient. The structural and energetic requirements for a simple, transmembrane, protein-based proton pump have been formulated [Pohorille *et al.*, 1996], but no model pump based on these principles has been synthesized so far. Its closest natural analog is bacteriorphdopsin, a membrane protein in the microorganism *Halobacterium salinarium*. However, this protein is too complex to serve as the earliest proton pump.

Another established, simple way to drive ATP synthesis is with a synthetic system which uses a redox chain consisting of linked carotene-porphyrin-naphtoquinone that spans the liposome membrane [Steinberg-Yfrach, 1998]. Light causes the migration of an electron, oxidizing the carotene moiety and reducing the naphtoquinone, on the interior and exterior surfaces, respectively. A mobile quinone returns the dislocated electron, and a proton with it, to the interior surface, thereby generating an inward-directed electrochemical proton gradient, in a reaction cycle that resembles those of proton pumps. In relation to this system, it is interesting to observe that quinones have been found in laboratory simulations of organic material in comets [Bernstein et al., 1999b, 2001]. It has been hypothesized that their initial role was to absorb light and, by doing so, prevent photo-dissociation of organic molecules captured in vesicles. Only later quinones were recruited into the photosynthetic system.

In contrast to the formation of proton gradient, finding a simple mechanism to couple this gradient with synthesis of ATP remains an elusive goal. This is one of the reasons why thioester bonds, rather than ATP, have been suggested as an earlier energy storage system [deDuve, 1991]. However, no continuous source of thioesters on the early earth has been identified and no general mechanism of their utilization has been demonstrated [Deamer, 1997].

It is possible that the initial mechanism of energy utilization in protocells was not based on proton gradients across membranes. Instead, only fermentative and biosynthetic pathways driven by electron transfer reactions resulting in carbon redox disproportionation may have been operational. These pathways start with sugars and continue energetically downhill to yield amino acids, lipids and nucleotides [Weber, 1999].

CONCLUSIONS

In this paper, the simplest cellular structures, and their minimal functions, have been analyzed. From this perspective, an attempt has been made to identify organic molecules that must have existed on the prebiotic earth through, for example, extraterrestrial delivery to facilitate the emergence of protocells. In this sense, it represents a "backwards" approach - from the origin of life to molecules in space.

One focus of this paper has been on the fact that molecules necessary for the emergence of life were not only the building blocks of cellular components but also molecules that formed environments conducive to the concentration, processing and self-organization of these building blocks. In this context, interfaces between water and non-polar or amphiphilic, organic phases may have played a special role.

It was also emphasized here that peptides were likely to be important ingredients of the first protocells. They can self-organize into functional structures, exhibit excellent catalytic properties, and even have potential to self-replicate and evolve. Furthermore, protobiologically plausible pathways for synthesis of both amino acids and peptides are available.

The emerging picture suggests that a relatively broad range of organic molecules could have participated, directly or indirectly, in the formation of protocells. There is, however, no clear indication that delivery of complex, biological building blocks from space was necessary to start life. Such a delivery is a required component of the "magic bullet" hypothesis, which states that a small set of molecules that were delivered to the early earth seeded life [Bernstein *et al.*, 1999a]. In this sense, the hypothesis can be considered as a modest version of panspermia. However, it appears more likely that prebiotic evolution followed a long and torturous path from simplicity to complexity, and physical and chemical processes on earth may have been sufficient to process simple organic material into protocellular structures. But perhaps the clearest lesson from this attempt to link molecules in space with the origin of life is that there is an enormous unknown territory lying in-between.

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