Origin of Life: Molecular Model of a Protobiont

Comments on *View on Lipids of Microorganisms from the Standpoint of Prebiotic and Biological Evolution*

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Origin of life on Earth has yet to find its own paradigm, and this fact overshadows the capabilities of contemporary science, although in reality it is well equipped for solving this problem. It is generally believed that the main cause of this predicament is the lack of material evidence that could provide a clue about the events that some four billion years ago had the life get started amidst the inorganic matter. Proceeding from that premise is a methodological deadlock: how to define the borderline between the non-life and the start of life – i.e. at what point in retrospect does the trail of evidence stop? If we take the most remarkable biological property inherent in all contemporary forms of life – reproduction – and try to trace it back so as to pinpoint its inception in the earliest forms of the living matter, we have to start with the emergence of the replication mechanism. But first there had to emerge something that was worth of replication.

Due to the lack of agreement on what can be qualified as a primordial sign of life, researchers in the origin of life have undertaken investigations on all probable and improbable leads, including anything of at least remote relevance to biosynthesis of molecules involved in contemporary organisms: synthesis of amino acids from simple inorganic molecules, catalytic properties of clay minerals, spontaneous formation of membrane-like structures, etc., up to ideas about spontaneously emerging DNA and RNA, which, in the opinion of the idea's authors, should have resulted in miraculous appearance of biologically purposeful structures. All of such theories are based on presumption of spontaneity of transformation of nonliving matter into living matter. Essentially, all things considered, the difference between evolutionism and creationism is nothing but the extent of passion about the object of faith; and, on the scale of integrity and logic consistency, the science-wealthy evolutionism married to mysticism stands lower than creationism.

Twenty years ago, I published a paper explaining my hypothesis of the origin of life on Earth and presenting a molecular model of a protobiont, a hypothetical earliest ancestor of the biological cell. The paper was published in a collection of articles on evolution of bacteria, by the Center for Biological Research in Pushchino of the then USSR Academy of Sciences. Recently, having stumbled upon a few research papers dealing with the problem of the origin of life on Earth, I went on to see what has changed in general in this field within the past twenty years and have found out that there was nothing new. This has been a good stimulus for me to finally get to translate my 1984 paper into English and post it on this web site.

Back then, I had every reason to muse on the role of lipids in the functioning of live organisms. Due to my years-long work in express identification of bacteria, I had had an opportunity to investigate the fatty acid (and occasionally phospholipid) composition of over 25,000 strains of bacteria. By the time when I had both the theoretical grounds and methodology developed to the level that provided an efficient and reliable system for identification of bacteria, I was able, in less than 10 minutes upon getting a single colony of the bacterium to be identified, to tell a lot about a given strain: its Gram-staining type, ecological preferences, maximal growth and development rate, morphology, potential pathogenicity, and many other details. A more comprehensive analysis of the fatty acid composition of certain taxonomic groups bacteria – which I was undertaking when I knew that a colleague who needed my help was well familiar with the biology of that particular group and would be able to confirm or disprove my results – provided 100% accurate information that would take weeks or months to obtain by legacy methods. One of such groups is methanotrophic bacteria: a few minute-long analysis of their fatty acids would determine the biochemical mechanism of methane oxidation, provide almost error-free identification at the species level, etc.[1]

The wealth of information that I gained through that work was at odds with the state of the art in lipidology and, in particular, studies of the fatty acid composition of bacterial lipids, where the generally accepted approach was complete dissociation between the biological (physiological, ecological, morphological, etc.), biochemical, analytical, and biophysical aspects of the problem. As a result, research papers on bacterial lipids, in the part of interpreting concrete facts, contained nothing but useless clichés. For example, biophysics that makes conclusions based on the melting temperatures of membrane lipids, cannot explain the fact that in fast-growing aerobic Gram-negative bacteria, the cells' physiological activity is strictly proportional to the share of cis-Δ^9- hexadecenoic acid in the total fatty acid content. Solving this problem requires the answers to such questions as, for instance: Why does methylenation of cis-Δ^9 – 16:1 double bond, with the production of the cyclopropanic ring, correlate with the reverse effect? What is the role of cis-Δ^9 double bonds in fatty acids and why does a shift to cis-Δ^{11} correlate with a very slow growth and substrate consumption, as well as developed morphology of Gram-negative bacteria? Why does production of phosphatidyl choline (PC), a methylated derivative of phosphatidyl ethanolamine (PE), in eukaryotes correlate with the presence of endoplasmic reticulum, and why PC is mostly characteristic of membranes which have no oxidative phosphorylation? There are many other puzzling things about bacterial lipids. So, my effort on the problem of the origin of life had been fueled by my own research needs. Unfortunately, soon

[1] The study was done in collaboration with Dr. V. F. Galchenko and described in the book: V. F. Galchenko, L. V. Andreev, Yu. A. Trotsenko, *Taxonomiya i identifikatsiya obligatnykh metanotrofnykh bakteriy* (Taxonomy and Identification of Obligately Methanotrophic Bacteria). *ONTI NCBI, Pushchino, 1986* (in Russian).

thereafter I had to discontinue that effort but wanted to have at least a part of the work summarized in print. As reputable peer-reviewed journals have never been terribly fond of anything unconventional, I submitted the article (quite hastily written, I must admit) to a locally published collection of papers on evolution of bacteria so as to explain my hypothesis about the first possible way for accumulation of energy in the form of MgO, hoping to get back to that work in the future, which, unfortunately, has appeared impossible.

Now that I have posted the English translation of my *View on Lipids of Microorganisms from the Standpoint of Prebiotic and Biological Evolution* on this web site, I would like to add a few comments to it. The purpose of the following commentary is to augment some of the positions of the hypothesis which are too concisely framed in the original paper and to point out how organically the proposed formula of a protobiont corroborates with the modern knowledge in biology and medicine.

1. To get the energy and growth substrates, any live organism needs a metabolism system. The assumption that metabolic cycles were by default given to the earliest forms of life would be as groundless as a belief in spontaneous emergence of nucleic acids ready to function in the absence of a system for energy synthesis and metabolism. The answer to the question of what was the first event in the hypothetical process of emergence of life on Earth is closely connected with a purely philosophical issue: which of the numerous properties of the living matter is superior in relation to all others? Obviously, the answer is: a strive for autonomy, i.e. lesser dependence on the environment. Proceeding from this premise is a simple inference: if some micelles of protobionts, which contained certain organic substances that could be spontaneously formed in the prebiotic Earth environment (including, in particular, lipids, porphyrins, etc.), could accumulate energy from external sources, in the form of a certain macroergic component, then not only had they a stimulus to further strengthen that mechanism for energy accumulation but it also made them, of all micelles, capable to develop a certain semblance of metabolic processes.

2. Keto-enol tautomerism is a widely distributed state of substances that possess a carbonyl group. Usually, tautomeric equilibrium is strongly shifted toward the keto-tautomer. Enolization of the lipid ester carbonyl and substitution of two protons in lipid molecules by a magnesium ion is a highly unlikely, yet not prohibited by the laws of chemistry, event. (If that event was a trivial one and could be easily simulated in a laboratory, I would not be now writing this paper, as the problem of the origin of life would have been solved long ago.)

3. The claim that it was Mg^{2+}, and not Ca^{2+} or any other bivalent cation, which was involved in energy accumulation by a protobiont, is primarily based on analysis of the role of magnesium in contemporary organisms. It could be due to various factors: e.g. the ionic radius of Mg^{2+}, which is 1.5 times less than that of Ca^{2+}; the water exchange lifetime, which is 1000 times higher for Mg^{2+} as compared to Ca^{2+}, etc. From the point when first Mg-lipid derivatives were formed, calcium and magnesium – two very close relatives – became antagonists in most of the biochemical processes occurring in live cells, and their antagonism is expressly exhibited in contemporary forms of life.

4. Dissociation of Mg-lipid derivatives, accompanied with the release of MgO, could occur due to conformational changes in proto-micelles, caused by fluctuations in the amount of energy available from the environment. This mechanism, further improved in those protocells that had the energy leverage due to ability to accumulate MgO, has survived till today and is utilized, in the evolutionarily more developed and elegant form, in oxidative phosphorylation and other metabolic processes. In oxidative phosphorylation, the trans-membrane transfer of protons, occurring as a result of MgO hydrolysis, is believed to be the main part of the process – because it can be measured, whereas the conformational changes in ATP-synthetase proteins are much more difficult to register, hence their role is difficult for evaluation. Thus, MgO is the evolutionary predecessor of ATP.

5. Conformational changes in the Mg-lipid complex, causing the MgO split-off, required the lipid structure to undergo certain changes: in particular, preventing the rotation of fatty acid chains. Therefore is the important role of the amino group of phosphatidyl ethanolamine (PE) and cis-Δ^9 unsaturated bonds in fatty acid residues. If the amino group in PE would be substituted for by the tetramethylammonium group, resulting in formation of phosphatidyl choline, or in case of the shift of the double bond in fatty acid residues, external energy fluctuations would not cause the synthesis of a macroergic compound, MgO, because of a too high degree of freedom in the MgO-synthesizing complex.

6. Photosynthesis emerged in the anaerobic atmosphere of the early Earth, as an improved process of MgO formation. In that embodiment of the method for production of a macroergic compound, Mg, immobilized and activated by four atoms of nitrogen, was interacting, according to the mechanism described in *View on Lipids of Microorganisms from the Standpoint of Prebiotic and Biological Evolution*, with the enol hydroxyls of two other molecules of protochlorophyll. Under the energy of light, the Mg-protochlorophyll complex was breaking down, releasing chelated MgO. Thus improved mechanism for utilization of the inexhaustible source of energy had provided for the emergence of metabolism. Once the photosynthesis process was in place, protobionts began releasing oxygen into the primitive atmosphere.

7. Polyphosphates, and later – nucleosil polyphosphates, were the primary acceptors of the macroergic MgO, which allowed the translocation of energy into the water phase of primitive micelles and thus facilitated the emergence of metabolic reactions. In contemporary forms of life, as well, 90% of the intracellular Mg^{2+} is bound by nucleic acids: for instance, magnesium serves as a cofactor in ATPases, ATP-synthases, kinases, and other enzymes.

In conclusion, I should add that it is a mistake to think that contemporary forms of life bear no pieces of evidence that can help to reconstruct the events that had resulted in the emergence of life on Earth. In fact, there is a lot of evidence everywhere, but finding it takes a desire and the knowledge of where to look for it – which is a whole different topic, though. The initial mechanism that underlain the emergence of life can be traced, for instance, in the toxic effect of beryllium ions substituting for Mg in Mg-lipid complexes, which results in formation of indecomposable compounds, thus blocking the activity centers. Carcinogenesis might be a consequence of development of alternative mechanisms for energy synthesis which do not require strong consolidation of energy-synthesizing biological membranes.

Magnesium is a metal of life – not only in the context of life's emergence on Earth but also in its contemporary forms. As to lipids – one of the most important classes of bioorganic molecules – they deserve a much higher, than currently achieved, level of scientific study of their role in the functioning of the living matter. A major problem of modern lipidology is the gap between the biological level of knowledge and the myriads of bits and pieces of details provided by biochemical and physico-chemical analytical methods. Unlike proteins, nucleic acids and polysaccharides, lipids isolated from cells do not retain their natural structural and functional state. Even the examining of whether or not there are any traceable amounts of MgO in mitochondria and cytoplasmic membranes of bacteria is an incredibly difficult task. In these areas of study, neither attempts of experimental proof nor clichéd and convenient explanations of concrete facts, but only logical consolidation of the totality of those facts can produce scientific knowledge and reveal the truth.