

Synthesis of Magnesium Oxide as ATP Precursor and a Matrix for Abiogenic Origin of Life

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A life-origin hypothesis is proposed based on a concept of spontaneous emergence, in the abiogenic Earth conditions, of a structure that was capable to accumulate energy in the form of MgO from Mg ions. Having emerged in protobiont membranes, the energy-accumulation system has served as the starting point, matrix and vector of the origin of life. Protomicelles that acquired the capability to produce MgO as a source of energy had thus acquired the status of living matter, whose most important and determining characteristic is a combination of two features: autonomy in energy accumulation, and cooperative organization of the membrane system. It is postulated that magnesium oxide was the evolutionary precursor of ATP and is involved in F_0F_1 ATPase functioning in all the extant forms of life.

Introduction

The problem of the origin of life is the subject of many thousands of research journal volumes, books, and World Wide Web sites, and the interest in this problem is constantly growing. It is obvious that finding the answer to the question of how life has emerged on Earth is the biggest challenge the science has ever had to face. The fact that there are so many different hypotheses contradicting to each other and to the totality of scientific knowledge, along with the absence of commonly accepted life-origin theories with predictive potentials, is hard to be explained by any large gaps in contemporary science or any serious obstacles in obtaining new knowledge. Biology (especially, systematics, physiology, biochemistry, and ecology), chemistry, physics, geology, astrobiology – all of these fields of science offer all the special knowledge to anyone who is concerned with solving the problem of the origin of life on Earth; and, in all fairness, it should be admitted that scientists use a great deal of creativity in sorting out and putting together lots of various available facts, as if hoping that changing the order of knowledge addends may change the sum of knowledge.

The below described hypothesis of energy accumulation in protobionts as the groundbreaking event of the origin and evolution of life on Earth is consistent with the “matrix reasoning” paradigm which is based on the concept that observable similarities and differences between objects and phenomena, as well as comparative primeness or secondariness of facts, are only relative and, as a rule, provide little information about the underlying relationships, whereas the absolute value of any given relationship between the system’s components can be revealed only in dynamics of the system as a whole. Therefore, the below discussed concept does not address many a detail the explanation of which is generally deemed to be of crucial importance – from the mechanism of abiogenic synthesis of lipid membranes in protobiont, to the emergence and evolution of the genetic apparatus. Metaphorically speaking, we are not concerned with fine details of operating the ship of life; instead, we are concerned with the question of what keeps this gigantic machine afloat. To a certain extent, the proposed hypothesis can serve as substantiation of vitalism, as it demonstrates that there is a certain borderline, beyond which the reductionism in a study of a biological phenomenon results in losing sight of the subject of study.

Spontaneous emergence of life could not occur without a matrix

Since the 1920's when the principles of abiogenic origin of life had been formulated in clear and simple terms by Oparin [1] and Haldane [2], the number of proponents of abiogenesis has been continuously growing, and every bit of newly emerging scientific knowledge about the principles of functioning of bioorganic molecules is readily used as an opportunity to create a new hypothesis of the abiogenic origin of life. It is generally implied that such hypotheses should portray successive development of the process of the emergence of life, and therefore they are collectively referred to as evolutionism. Evolutionism is oftentimes regarded as a theory that is concerned only with development of life forms after the appearance of the first replicator. We understand evolutionism as a theory that covers a gradual and continuous chain of events that started in abiogenic environment and resulted in the emergence of substances that can be qualified as living matter and evolutionary development of the first living organisms. In reality, however, more often than not, hypothesizing in evolutionism involves events that have zero probability of spontaneous occurrence in randomness conditions [3], making such hypotheses completely contrary to common sense and, therefore, not pertaining to the field of evolutionism, despite their being intended as such.

Among all of the properties of contemporary forms of life, the most remarkable and impressive is the mechanism of genetic inheritance through nucleic acids, which involves synthesis of proteins in a strictly determined sequence, which regulate biologically rational metabolism in cells. That is why the notion of 'living matter' is traditionally and primarily used in the meaning of 'self-replicating living units', implying that it automatically includes growth, metabolism and other functions. However, the mechanism of spontaneous formation of the universal genetic code is practically inconceivable. The problem of understanding of how the genetic code mechanism has emerged is well formulated by F. J. Dyson [4]: "Either life began only once, with the functions of replication and metabolism already present in rudimentary form and linked together from the beginning, or life began twice, with two separate kinds of creatures, one kind capable of metabolism without exact replication, the other kind capable of replication without metabolism". In fact, here we deal with two processes whose spontaneous emergence is simply improbable: 1) the spontaneous emergence of metabolism, regulated by proteins as catalyzers; and 2) the emergence of the genetic code wherein each amino acid involved in protein biosynthesis is represented by a respective universal codon.

Many scenarios of spontaneous emergence of life would probably have been stricken out by their own authors if, prior to writing those scenarios, they would have taken time to calculate the probability of the occurrence of proposed events, at least those whose probability can be fairly easily computed. Usually omitted in evolutionists' works, the courtesy of probability computations has been provided, for instance, by Arthur V. Chadwick in an excellent treatise "Abiogenic Origin of Life: A Theory in Crisis" [5] published in 2005, who convincingly demonstrates, in particular, that spontaneous synthesis of biopolymers (polypeptides and polynucleotides) on the prebiotic Earth – even assuming that they would consist of only a few dozens of monomers – was absolutely impossible. There is a number of other scientifically strong works by authors who oppose evolutionism ideas, e.g. [6], which provide facts to the same effect.

The overwhelming majority of scientists worldwide maintain the evolutionism approach to the problem of the origin of life. In the United States, only 0.15% of the earth and life scientists stand on positions of creationism [7]. However, among evolutionists there is a great deal of those who believe that evolution's arrow must have been shot from the bow of spontaneity. In essence, they differ from creationists only in respect of the symbol of faith. It is understandable, therefore, that the ideas of spontaneous synthesis of biologically active polymers are most harshly criticized by creationists. Creationism, which is based solely on faith but uses only one unverifiable assumption – that "the Lord made the heavens and the earth, the sea and all that is in them" in six day – rightly expects its antipode, evolutionism, to be a science based on clear and complete proofs. The most valuable lesson that evolutionism can learn from creationism is: to be successfully completed, a process with low probability of occurrence needs a matrix, i.e. a template, as the evolution alternative to creation "in the image and likeness".

Quest for the right matrix

In fact, the role of a suitable matrix for evolutionarily logical spontaneous synthesis of biologically active polymers could be played by any reasonably simple system or process, occurring in protomicelles, which provided them with certain advantages over those protomicelles in which such a process did not occur or was significantly less efficient. Such a matrix could become a real driving force for and a vector of evolution, as each step toward the improvement of the matrix-dependent process would be instantly rewarded, thus organizing the unlikely, for the lack of a matrix, process of spontaneous synthesis of active biopolymers into a multitude of successive stages of building up the monomers, whereas the efficiency of each stage was directly controlled by the matrix. To a certain extent, the concept of the evolutionary matrix provides new insight into the problem of probability of spontaneously emerging processes.

The acceptance of the idea that spontaneous synthesis of biologically active polymers is impossible without an adequate matrix opens lots of opportunities in the quest for the right matrix. Another, no less important, question is: should any evolutionarily positive step in biopolymer synthesis have been followed with protomicelle division in biology's traditional understanding of the re-enforcement of "positive" mutations? Could it be that the precursor of living matter was a single protocell that, due to certain exceptionally favorable conditions, had been developing without undergoing the division? In other words, could it be that it took just one single micelle to turn into the first cell from which everything else started? It would be extremely difficult to provide definitive answers to these questions; however, in case of a matrix scenario of life origin, the possibility of the protocell development toward self-improvement prior to division does not look as improbable as it would in case of non-matrix spontaneous evolution of biopolymers.

Choice of a matrix, i.e. a system or process which can qualify for the role of the evolution starting point and vector is a highly responsible task not only because the chosen matrix must run through the whole process of development of living matter – from the first cell to contemporary life forms – and serve as an important consolidating factor in cell growth and development. The idea that once the active biosynthesis of proteins and nucleic acids had been established, everything else would have been automatically set up for organization and development, without the guiding matrix, is not just naïve – it is plainly unsound. The nature of the matrix must be of such a kind that, based on it, it should be possible to answer the questions of why the life processes are unique in general, why they are different from chemical processes in test tubes, and, on the whole, why the science of life origin is so challenging and the problem itself is so far from being solved.

Any organism, be it a bacterial cell or a human-being, is, first of all, a closed system. The closeness of biological systems is by far more complex a notion than the closeness in thermodynamics, both classical and non-classical. Moreover, the degree of closeness of a given biological system may vary within a wide range, dependent on both endogenous and exogenous factors. Fungal and bacterial spores and nematode cysts, for instance, represent significantly more closed systems than vegetative cells, and the degree of their closeness is a result of complex interrelations of internal and external factors. The notion of 'living matter' cannot be complete if it does not include a system's capability to autonomously self-regulate the degree of its closeness. Even a purely abiogenic system may be capable to autonomously carry out certain processes. For the said reasons, the first and foremost requirement to a matrix that can underlie the commencement of life is its capability to lessen the early protomicelles' total dependence on the environment. Thus, spontaneous emergence of such a matrix system should be regarded as revolution in the life-origin process, whereas the development of the first protobiont with living matter characters towards the functionality level of extant forms of life should be considered as evolution of life. It would be fair to say that the life-origin matrix is the central dogma of molecular biology with "bottom end up on top", as the DNA control over the cell autonomy is decreasing along the replication-transcription-translation (etc.) row.

Previously [8-10], I have proposed that the matrix of evolution from nonliving to living matter could be embodied in the process of accumulation of energy from environment through formation of an energy-rich intermediary MgO as the ATP precursor. The chemical process according to the proposed model has a few unique features that make it especially plausible a candidate for the role of the prebiotic matrix. First of all, this reaction cannot occur in a solution; instead, it could be realized only in membrane structures under the influence of mechanical shifts at the molecular level. Secondly, formation of MgO from Mg^{2+} ions, which could spontaneously occur in protomicelles due to environmental energy fluctuations, would have extremely high and

versatile potentials in the increase of efficiency (i.e. evolution stimuli), and the respective opportunities that were available to the early primitive system for MgO synthesis striving to increase its efficiency very well coincide with those that would be necessary for protobionts to evolve into full-fledged biological cells. Thirdly, it is easy to demonstrate that all what MgO synthesis as a matrix for biogenesis start and evolution would provide to the first cell is equally important for all of the contemporary life forms (we will come back to this issue further in this article). And, finally, synthesis of such a chemically active compound as MgO could stimulate the emergence of primitive metabolism in protobionts. In this paper, we will discuss some of the aspects of the previously proposed scenario [8-10] from the standpoint of the possible paths of the evolution of MgO synthesis in protobionts as a matrix for the emergence and evolution of living matter.

On the issue of the origin of living matter

Even the most credible and scientifically grounded scenarios of the emergence of life cannot pass the elementary logic test if they do not specify when and how the transition from the non-living state to the state of living – i.e. the event to which such scenarios are dedicated – had occurred. If they do specify, they have to deal with a number of straightforward questions:

- a) Based on what criteria an organism that emerged at a certain point of evolution should have been qualified as ‘living’?
- b) Was the ability to self-reproduce mandatory in order to be a ‘living organism’?
- c) Did the properties of the alive emerge in that organism at once or were they developed step-by-step?
- d) If the development of the first living organism was gradual, i.e. through successive development of its various parts, then which of them came first?
- e) If all of the parts emerged concurrently, irrespective of their evolutionary sufficiency, then how was polyphyly (in other words, total chaos) avoided at the starting point level?

These concrete questions pertain solely to the science of biology and not to physics or chemistry or computer science. Ideas about spontaneous self-emergence of RNA, proteins and even DNA have very little relevance to these issues. That is why, as long as there is no clear definition of an object (substance) that can be considered as the first manifestation of life on Earth, the whole multitude of life-origin scenarios will stay in the state of a “primordial ocean of hypotheses” which, unlike the one that had emerged on Earth in the period of its infancy as a result of chemical evolution and is believed by many to have given impetus to biological evolution, cannot be a source of understanding of the origin of life.

To be discussible, a scenario of the emergence and evolution of terrestrial life must include a definitive starting point (such as, for example, the primordial soup) and concrete physico-chemical matrix processes as the vector of events described in a given scenario. Assume that the vector is hypothetical spontaneous synthesis of RNA, which, at a certain sequence of monomers, should have acquired its characteristic 3D conformation and become able to bind amino acids, according to a popular concept, also known as the “RNA World”, or, for instance, polypeptides specifically catalyzing their own formation. In both cases, it would be only a vector of creating conditions for prebiotic evolution but not of the start of biological evolution, as both the initial and end products are chemical substances and not biological formations.

As we all understand, a biological object is not just a membrane sack filled with “smart” macromolecules, but something else. To answer to and prove one’s position on the question of what was the very initial form of that “something else” is extremely difficult – mainly because the distinctive autonomy of biology as a science [11] creates a high barrier between hypothesizing on the issues of prebiotic chemical evolution and the ideas on the emergence of the earliest organisms. Laws of biology are compatible with the laws of physics and chemistry, but they are neither determined by the latter two nor directly follow from them. Biology as a science could be defined as such an approach to the study of living organisms, whose basic principles are inapplicable to the non-living matter and – conversely – to which the principles that are effective in the study of the non-living matter cannot be applied.

Among the well-known forms of living, there is anabiosis, a deathlike state in which organisms can stay during practically unlimited time before revival or death. Anabiosis occurs not only in bacterial and fungal spores, but even some of the foliar plant nematodes have been shown to have survived in anabiosis for at least 39 years [12]. Moreover, epidemiologists have been finding more and more evidence that many of Gram-negative bacteria that cause anthroponoses (e.g. plague, cholera, pseudotuberculosis, etc.) and are not supposed to survive outside the human body, appear to perfectly survive in soil and water communities. Apparently, the discovered colonies were in a special state of anabiosis and were impossible to be re-cultivated by regular methods in artificial nutrient media – therefore, they can hardly be considered as alive. However, they have all characteristics of living matter. Although this paper is concerned with a different issue, I have chosen to digress to this example and remark that in the above-mentioned organisms in the state of anabiosis, the genetic apparatus remains fully conserved, whereas the organization and functioning of the membrane apparatus gets radically restructured. The restructuring consists in joining the energy-producing enzymatic complexes into particular loci of the membrane system. The addition of substrates in higher than extremely low concentrations to nutrient media results in dedifferentiation and destruction of entire membranes, which happens primarily because in response to nutrition supply the system of energy synthesis becomes automatically deployed whereas all other loci of the membrane system remain at the level of the state of anabiosis. DNA is only indirectly engaged in this process.

Biologically, organisms in the state of anabiosis are certainly very much different from those in the state of active growth, development and reproduction; however, in both states they represent living matter. Other, very close to anabiosis but qualitatively different from it form of life is extremely slow growth and development, occurring, for example, in some of Gram-negative oligotrophic bacteria which can grow on media containing micrograms of carbon per liter. Clearly, in all of these cases, we are dealing with living matter. In biology, there is no cross between living matter and nonliving matter. Therefore, anyone who would like to undertake proving that a protocell (protobiont) had emerged from nonliving matter must be able to clearly explain what exactly that protobiont was like. In the event that a proposed transition must have involved a certain intermediary which was neither a nonliving nor living substance, then – taking into account the exceptionality of such an idea – a clear explanation must be offered on what that intermediary substance was.

Synthesis of ATP or its evolutionary precursor as a life-origin matrix

The energy-producing and energy-utilizing processes in live cells and supracellular formations are collectively referred to as metabolic processes. Their flowcharts have much in common and are strictly and specifically determined by Nature, but they have enough plasticity to adequately respond to environmental changes. The key factor of the cell metabolism commonality in different organisms is the monopoly of adenosine triphosphate (ATP) in energy transfer. ATP is the “fuel” used for all energy-dependent processes in a cell, and the history of this monopoly is unknown. Why ATP? Why has not, for instance, GTP become a universal carrier of energy? Why is ATP the universal currency for all organisms, including even the most distant – metabolically and biologically – phyla? Nature could use a combination of a few other intermediators that would fit this role both chemically and physically.

At first sight, it may seem as if the answer to this question is obvious. As was noted by Kornberg [13], ATP is "used to build complex molecules, contract muscles, generate electricity in nerves, and light fireflies. All fuel sources of Nature, all foodstuffs of living things, produce ATP, which in turn powers virtually every activity of the cell and organism. Imagine the metabolic confusion if this were not so: Each of the diverse foodstuffs would generate different energy currencies and each of the great variety of cellular functions would have to trade in its unique currency." However, a more thorough analysis of this issue shows that the above explanation is at least disputable. Energetic autonomy is inherent in any organism, be it a human organism with its almost hundred trillion cells or a single bacterial cell. The amount of energy currency kept by an organism is meager as compared to its turnover in the same organism: for instance, in humans, the amount of ATP is about 0.05% of the body weight, whereas a daily ATP turnover amount equals or exceeds the body weight. Parasites, for example, use hosts' proteins as a source of amino acids and glucose as the ATP source, but not ATP itself. Eucaryotic parasites, such as, for instance, *Leishmania* spp., fulfill minimal energetic requirements through

oxidative phosphorylation [14], as living on the hosts' ATP would not be realistic for them. At any rate, the amount of ATP supplied by exogenous sources is negligibly low in any given organism. Even if each taxonomically individual group would synthesize a different energy intermediary, it would not result in any metabolic confusion at all. On the contrary, diversification of energy carriers would be in conformity with the highest ecological purposefulness.

It is commonly pointed out that the structural basis for ATP as an energy carrier is provided by its phosphor-anhydride bond; but it is also known that there are many other natural compounds with the same quality bonds. It is easy to explain the choice of ATP as a universal currency once the fact is known. In a same way, the advantage of ATP over ADP or adenosine tetraphosphate can be conveniently explained by resonance stability (distribution of electrons). Nevertheless, it would be useless to try to define some mystical peculiarities of the ATP chemical structure, which could certainly explain the reason for this particular substance having been chosen by evolution for the role of a universal energy carrier. This fact in itself is very strong evidence of evolution monophyletism starting from the very first living cell – much stronger than, for instance, the DNA universal code, as the ATP molecule is a simple structure and there are many other compounds that could be used in the same role. Thus, the process of ATP synthesis seems to be the most qualifying candidate for the role of the evolution matrix, as ATP is practically the only supplier of energy which supports the whole system of metabolic activities of living organisms. All active biopolymers need ATP for their synthesis, but the majority of them are not relevant to the ATP synthesis. Without molecules capable of energy supply and regulation, there cannot be any kind of metabolism at all. Spontaneity *per se* cannot be used as fuel for evolution.

However, there are certain circumstances that make it hard for origin-of-life researchers to accept the synthesis of ATP or its evolutionary predecessor as the groundbreaking event of the emergence of life. First of all, the ATP molecule is quite simple and bears no historical information, hence does not present as much interest to evolutionists as proteins and nucleic acids do. Unlike nucleic acids and proteins, it has no records of its synthesis history. Secondly, and most importantly, the system of ATP synthesis through oxidative phosphorylation is exceptionally complex and is not yet fully clear. While biopolymer sequences of any degree of complexity can be easily determined nowadays by routine methods, the process of oxidative phosphorylation by F_1F_0 ATPase in bacterial membranes, chloroplasts and mitochondria has not yet been fully investigated. There have been known a few hypotheses to explain the mechanism of oxidative phosphorylation [15-20], including two that were awarded the Nobel Prize; however, none of them can be definitively proven to describe the actual processes.

F_1F_0 ATPase appears to be an extremely complex and perfectly finished product of evolution: mammalian F_1F_0 is only slightly more complex than that of bacteria. F_1 consists of five polypeptides, and F_0 has three polypeptides in different stoichiometric proportions. The largest F_1 subunits in *E. coli* have 513 and 460 amino acid residues, i.e. are quite complex proteins. Thus, it seems to be impossible to have the mechanism of F_1F_0 ATPase action transformed to the level of simplicity which is required in the life-origin science.

Nevertheless, it is probable that the reason for extraordinary complexity of F_1F_0 ATPase, representing a molecular rotary motor [21], is in the fact that it had undergone drastic and efficient improvement in the course of evolution. In other words, it is quite possible that the chemical core of the process is both unique and exceptionally plain, and that the complexity of its actual organization is a result of the tremendous efforts made by evolution in pursuit of maximally possible improvement of this process of biologically universal importance. If the underlying principle of ATP synthesis in membrane were not uniquely simple, the structural details of ATPases isolated from different organisms would not be so strikingly similar. Also, there is a simple, but not so easy to find a definitive answer, question: Why is the most part of ATP synthesized on cell membranes, even though there is an alternative of ATP synthesis in the cytosol?

At this point, it will be appropriate to go back to discussion of the earlier-referenced model of spontaneous synthesis of the energy-rich proto-intermediator MgO [8-10]; but before that, we should mention about the following important detail, hardly ever discussed in the context of prebiotic evolution: having appointed ATP to perform that important and universal duty, Nature provided it with a permanent companion, the Mg ion. The binding of the magnesium ion with ATP plays an essential role in the metabolic pathways (cf., for example, [22]). It is believed that ATP requires Mg^{2+} in order to offset and balance off the -ve charges. Without Mg^{2+} , repulsion would cause rapid breakdown to $ADP + P_i$. In a cell, the essential amount of Mg is

associated namely with ATP. However, the problem of formation of Mg (ATP) complexes is much more complex. For instance, X-ray analysis of crystal structures shows that they contain ATP salts, but no direct Mg (ATP) complexes have ever been found to occur as a result of spontaneous non-enzymatic hydrolysis during crystallization [23]. The problem of determining the exact mechanism of ATP hydrolysis in water with Mg²⁺ is extremely complex (see, e.g. an effort by Akola and Jones [24]). However, an even more difficult question for traditional biochemistry is: why does ATP occur in cells mostly in a complex with Mg and not Ca or any other metal? The answer to this question is simple if we accept that Mg (ATP) complex is not formed by interaction of Mg²⁺ with ATP, but the interaction of ADP, P_i and MgO is one of the stages of ATP synthesis by F₁F₀ATPase.

Magnesium oxide as the evolutionary precursor of ATP and its role in the emergence of metabolism

According to my previously proposed hypothesis [8-10], the first chemical process that served as a matrix for subsequent events that eventually resulted in origination of life on Earth was energy accumulation with the help of MgO as intermediary. The idea itself that life started due to the emerging opportunity for energy accumulation is sufficiently logical and does not need special defense. For any contemporary life form, the loss of capability to synthesize energy (ATP) is the beginning of death. As to MgO as a concrete candidate for the role of the first accumulator of energy, as well as the proposed mechanism of its synthesis based on magnesium-derived lipids and their following breaking up under the impact of a mechanical shift at the molecular level, this issue raises some very difficult questions, which, however, is only natural, taking into account a status extraordinaire of the system that gave impetus to the commencement of life on Earth.

As was postulated in [8-9], production of magnesium-lipid molecules is a result of enolization of ester carbonyl of lipids. This reaction is impossible to occur in a solution. For its realization, it requires that two lipid molecules are specifically and precisely positioned in respect of the Mg ion and each other. Thus, the said process is obligately structural.

The next stage – the break-up of the magnesium-lipid complex – also strictly requires a specific structural arrangement. It could occur under the exogenous influence of, for instance, ultrasound wave energy – at least at the initial stages of evolution – but only if the magnesium-lipid complex was located in the protomembrane's rigid loci where the energy impact could not be smoothly absorbed or dissipated by the oscillatory and rotatory motion of the membrane's molecules. However, any biological membrane, as well as the primitive protobiont membrane is supposed to perform certain other functions along with production of the energy intermediate. It would be logical to assume that performance of those functions should require different physico-chemical statuses of different loci of the membrane. Another, no less important requirement would be the presence of a certain factor interfering with rotation of fatty acid hydrocarbon chains around the carbon-carbon bonds.

With that being said, let us note also that the detection of isolated MgO molecules in cells is practically impossible even with the most powerful physico-chemical analytical methods available nowadays – and even more improbable to happen accidentally – which makes it clear that the hypothesis on MgO synthesis in membrane cells of contemporary life forms, let alone protobiont membranes, can be proven mostly based on circumstantial evidence and proofs. Fortunately, there is a great deal of strong circumstantial evidence, starting from the evidence at the general biological level and up to the fact of a strange mechanical behavior of the γ -subunit of F₁ATPase [20, 25]. First, we will discuss the biological factors.

The scenario proposed in my previous articles on a molecular model of a protobiont [8-10] involves two key factors as protobiological functions, i.e. characteristic of the transition from nonliving to living matter:

a) spontaneous emergence, in protomicelles, and further evolution of a molecular-membrane mechanism that provided protobionts with energy independence from the environment (energetic autonomy) as a prerequisite for active development based on internal stimuli rather than, or to a greater extent than, external; and

b) the impossibility of having the above function performed along with and in the same loci as all other processes of the emerging metabolism (i.e. incompatibility of different membrane functions), which facilitated

the protomicelle progress through the dialectic conflict of opposites and made the protobiont membrane an integral and cooperative system.

The proposed scenario concerns only the initial stage of the emergence of life, but it can be extrapolated, although with significant modifications, onto contemporary forms of life.

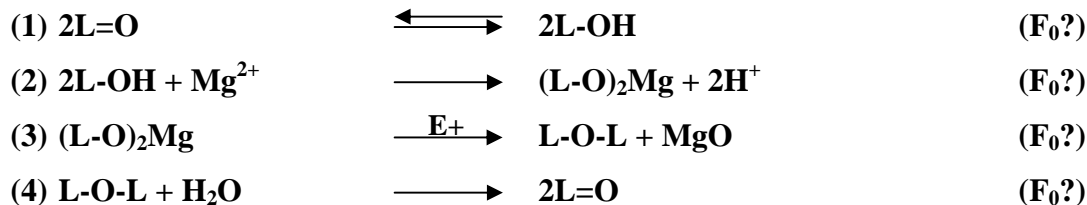
Thus, the first criterion for qualification of a protobiont as being similar to a biological structure is the capability for membrane-dependent synthesis of energy accumulator and carrier – MgO – to provide for catabolism and anabolism, contrary to belief that the primary characteristic of living matter is the ability to inherit. At the prebiotic stage of evolution, there was yet nothing to be inherited.

The second criterion – the principle of incompatibility of different membrane functions – played and still plays an important role at all of the stages of biological evolution, from the early formations with rudimentary features of biological organisms to contemporary forms of life. A convincing experimental proof of this principle would require a large amount of additional investigation with a new approach to the study of the membrane structure and functions in prokaryotes (mainly, in nonsporulating Gram-negative bacteria), and, as long as no such study is done, this principle will have to be axiomatic. The most well-known manifestation of the principle of membrane incompatibility is the evolutionary separation of the eukaryotes' energy-producing apparatus in the form of mitochondrial organelles.

Based on the foregoing, it should be concluded that the protomicelle which appeared to be capable of MgO synthesis had thereby acquired the status of biological organism (this was the first and last revolution in the course of the emergence of life), in a state similar to what is observed in contemporary organisms in the state of anabiosis or extremely slow growth and development. All other evolutionary acquisitions, including metabolism and capability for division, which made the protobiont a fully functional organism, were implemented in the afore-said organism, already in the status of "living matter".

Thus, I believe that the emergence of living matter happened at the moment of and due to the emergence of MgO synthesis in protobiont membranes, as that moment was the manifestation of the joint occurrence of the two afore-specified properties that characterize living matter.

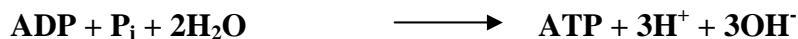
The process of MgO formation in protobiont membranes according to my model can be described by a set of equations:



The interaction of MgO with ADP and inorganic phosphate P_i results in formation of the Mg(ATP) complex:



Thus, the total reaction can be presented as follows:



Symbols used in the above notation denote: $\text{L}=\text{O}$, a molecule of lipid; L-OH , a molecule of lipid with enolized ester carbonyl; $(\text{L-O})_2\text{Mg}$, a molecule of Mg-lipid derivative formed by substitution of Mg^{2+} protons in two

molecules of enolic tautomers of lipids; and E, energy that causes the break-up of the (L-O)₂Mg molecule with formation of MgO.

As is seen, the above system of equations for ATP synthesis through magnesium oxide very well agrees with the hypotheses by P. Mitchell [15] and P. D. Boyer [17]: according to the stoichiometry of the above equations, this process occurs with the release of three protons and the charge separation. However, there is one but significant difference: according to Boyer and Mitchell, the transmembrane charge transfer is the cause and the driving force of phosphorylation, whereas in ATP synthesis according to my hypothesis, it is a result of phosphorylation.

The key role of Mg²⁺ in membrane phosphorylation has been beyond any doubt since long ago (cf., for example, [26]). Vinogradov et. al. [27], in a study of Mg²⁺ requirement for Mg·ATP hydrolysis in F₀F₁ mitochondrial ATPase, put a question: Where is the single M²⁺-specific site located? The authors find that it is possible that “the binding of M²⁺ to the F₁ part of F₀F₁-ATPase/synthase must be Δμ_{H+}-dependent, which perfectly agrees with the proposed mechanism of MgO involvement in ATP synthesis.

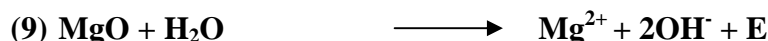
As of lately, the interest in the problem of F₀F₁-ATPase, which represents one of Nature’s most elegant mechanisms, has been increasingly high. There is a special area of study – mechanochemistry – which is concerned with the mechanism of the interaction between numerous parts of that intricate motor of the size of fractions of a nanometer [25]. For nanotechnology, F₀F₁-ATPase biomolecular motor is a model of perfection, as its technical specifications are, indeed, ultimately perfect: e.g. rotation speed of the F₁ portion gamma subunit is up to 17 revolutions per second [28], and the F₁ portion of ATPase can act independently, i.e. it can be separated from the F₀ portion which will continue working.

We should point out, however, that in case the assumption that magnesium oxide, produced on the ATPase F₀ portion, is an intermediary of ATP synthesis is valid, the examining of the nuts and bolts of this nanomolecular motor is not the best way to find out how it works and to get the perspective of the evolution of its construction and improvement. Needless to say that the currently accepted model of proton binding to the sections formed by ATPase subunits upon their rotation, which is as good as industrial robot diagrams, cannot be accepted simply based on being illustrative.

Coming back to the MgO synthesis equations, the summing up of equations (1) through (4) results in:



If MgO appears to be in water medium, it breaks up as follows:



As shown above, the spontaneous process of MgO synthesis and dissociation in a protobiont caused two molecules of water dissociate into two protons and two hydroxyls, as a result of which the inner and outer surfaces of the protomicelle membrane were capable of acquiring opposite charges. Thus, even in a situation when H₂O was the only available acceptor of energy accumulated in MgO, synthesis of the latter was crucially important from the standpoint of the origin of life. Based on that, it appears that the membrane-bound F₀ATPase, where MgO synthesis supposedly was occurring, plays a special role in the cell metabolism, whereas the soluble F₁ATPase provides for ATP synthesis with the help of the energy intermediary MgO produced in the F₀ATPase.

Based on the foregoing, the mechanism of action of F₀F₁ATPase can be presented as follows. Upon the interaction of Mg²⁺ with enolic lipid hydroxyls, the F₀ part of ATPase releases two protons which, upon migration to F₁ATPase, cause rotation of the F₁ γ-subunit, which, in turn, results in breakup of the MgO-lipid derivative, producing MgO. The latter migrates to F₁ATPase and participates in the bonding of P_i to ADP. Thus, only one of the three protons is directly involved in ADP phosphorylation, whereas two others are released as a result of formation magnesium oxide, an intermediary product of phosphorylation.

Being a highly active substance, magnesium oxide could participate in organization of the initial stages of protocell metabolism – for instance, as a catalyzer of aldol condensation and other reactions. Its interaction with orthophosphate could produce Mg-pyrophosphate and, eventually, polyphosphates. There must have been some

powerful biochemical stimulus for MgO, which could not be stable outside the hydrophobic area of the protomicelle, to transform into pyrophosphate and ATP – derivatives capable of delivery of MgO energy for the processes occurring in the aqueous space of the protomicelle.

This scenario can also provide insight into the issue of the possible stimuli and mechanisms for the emergence of nucleic acids. It would not be a far stretch to imagine that as a result of spontaneously occurring MgO synthesis on the protomicelle membrane, there could have developed the areas of the most efficient synthesis of MgO, which could further become the centers of production of long-chain polyphosphates if they could be used as a channel for receiving exogenous orthophosphate. Views on the possible connections between synthesis of polyphosphates, ATP and nucleic acids are presented in historical perspective in the work by Kulaev et al. [30].

The concept that synthesis of magnesium oxide not only provided a matrix for the emergence of life on Earth but also constitutes the most important, however yet undiscovered, element of metabolism in all of the contemporary forms of life, can be proven by the overwhelming amount of facts that provide convincing circumstantial evidence. Conversely, the understanding that many metabolic processes, including first and foremost ATP synthesis, largely depend on magnesium oxide synthesis occurring in hydrophobic parts of biological membranes could have a revolutionizing effect on many aspects of medical biochemistry. To mention just one example, extremely high toxicity of beryllium (II) may be explained by the fact that it completely disables the centers for MgO synthesis by forming highly stable and non-degradable derivatives L-O-Be-O-L, wherein the Be atom has the inert helium electron orbit. The fact that the primary element of skeletons of all organisms is Ca can be explained by and directly follows from the discussed hypothesis according to which Mg, and not Ca, is involved in energy synthesis. There are many other similar examples to the same effect.

In this paper, focused on probability of the emergence, in abiogenic environment, of spontaneous MgO synthesis, providing a matrix for the emergence of life, we would also like to draw attention to the fact that based on that “proto-substance” one can trace the evolution paths for emergence and development of the mechanisms that underlie the biology of contemporary life forms. For instance, analysis of the chemical structure of chlorophylls points to the presence of the same mechanism as above described, with the only difference that in this case MgO synthesis involves three molecules of chlorophyll: one as a source of Mg, and two other as a source of enoyl hydroxyl protons. The produced MgO can further be involved in the process of photosynthesis. However, each of the two cases involves a different and specific evolutionary mechanism which is difficult to trace and evaluate without a thorough and extensive investigation. For instance, the involvement of MgO in ATP synthesis from ADP and P_i seems to be a self-explanatory reaction; however, from the standpoint of its realization in membranes of contemporary life forms, it clearly represents an enormously complex system.

As was noted above, the presumable process of MgO synthesis in protobiont membranes must have been dependent on a variety of factors. Each of them, causing specific influence on the efficiency of the process, could serve as a specific stimulus for improvement of MgO synthesis at the very early stages. Below, we will consider two of the directions in which spontaneous MgO synthesis in protobiont membranes might have been improving in the course of its evolution. In reality, there is obviously much more of such directions; however, in the context of this paper, we will consider only those directly connected with MgO synthesis.

1A. Mitigation of the UV radiation effect that was causing chaotic fluctuations of the motion of lipid and other molecules of the protobiont membrane. It would be logical to suggest that the mitigating effect could be provided by spontaneous synthesis of melanin – naturally occurring pigments that perfectly absorb the energy of UV-radiation. In Nature, melanins are synthesized from tyrosine, which, in turn, is formed from **phenylalanine** (RNA codon UUU).

1B. Elimination of rotation of fatty acid residues at the time of mechanical shifts causing the dissociation of the magnesium-lipid derivative. One of the ways to prevent rotation of fatty acid residues (employed mostly by Gram-positive bacteria) was making them have a branched structure (iso- and anteiso). In Gram-positive bacteria, the precursors of branched fatty acids are **leucine (CUU)**, **isoleucine (AUU)**, and **valine (GUU)**.

2. Synthesis of simplest peptides whose contractility properties were exhibited in response to certain stimuli – for instance, upon interaction with H⁺. The emergence of contractile peptides as a primitive precursor of ATPase could be the beginning of autonomous generation of energy by protobionts. As to amino acids from which the first contractile peptides could be synthesized, the most probable candidates for that role, based on

general considerations, could be amino acids with more than two functional groups – e.g. **lysine** (diamino carboxylic acid, **AAA**), **glutamic acid** (amino dicarboxylic acid, **GAA**), and **glutamine** (**CAA**). If contractile motion of peptides was further substituted by rotary motion, that could, in principle, stimulate the emergence of laevorotary enantiomers of amino acids.

It would be possible to identify various other connections between MgO synthesis in protobiont membranes and particular metabolic blocks of living cells. As it follows from the above reasoning, all four amino acids supposedly involved in improvements 1A and 1B have the RNA codons with U in the second and third positions (along with other synonymous codons). As to **glutamine**, **lysine**, and **glutamic acid**, their codons have A in the second and third positions. This certainly does not look as a mere coincidence and requires a more in-depth consideration, as well as, for instance, a possible connection between MgO synthesis and the emergence of the genetic code mechanism. Another intriguing issue is a possible relation of MgO synthesis to the lipid composition of cells, which is definitely seen in rapidly growing Gram-negative bacteria [30]. These and many other aspects of cell biochemistry and physiology are extremely interesting issues that deserve special discussion.

Conclusions

1. The concept of life origin through spontaneous synthesis of biopolymers and subsequent spontaneous development of metabolism and inheritance mechanism cannot be valid as it has no realistic ground.
2. The emergence and evolution of life on Earth required a matrix that would determine the starting point and the vector, providing the life commencement and evolution toward contemporary forms of life.
3. The life-origin matrix had appeared in the form of the spontaneously emerged capability of protomicelles to accumulate energy from environment through formation, in their lipid membranes, of magnesium oxide which carries a supply of energy in the same amount as the energy released upon ATP hydrolysis.
4. The process of MgO formation in the protobiont membrane structure was structurally obligate and could not occur in solutions.
5. A combination of autonomy in energy generation and incompatibility of different functions in same loci of the membrane provides the membrane integrity and cooperativeness and is the minimum requirement for transition from nonliving to living matter. Thus, a protobiont that is capable of spontaneous synthesis of the energy intermediate MgO must be qualified as a biological organism even if, at its earliest stages of evolution, it was incapable of reproduction.
6. Magnesium oxide was the evolutionary precursor of ATP and is an intermediary product of F_0F_1 ATPase activity in contemporary organisms.
7. Synthesis of MgO, hence ATP, is the cornerstone process in biology; it pervades the history of living matter from the moment of appearance of the first cell and proves the monophyletic development of evolution of terrestrial living matter.
8. Synthesis of magnesium oxide is an extremely important, yet undetected, part of biological activity of any contemporary forms of life.
9. The proposed hypothesis creates new opportunities in search for primitive extraterrestrial life forms.

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