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When, Where, and in What Environment Could the RNA World Appear and Evolve?

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Abstract—The environment necessary for the existence, amplification, and evolution of the RNA world, the difficulties of the abiogenous synthesis of RNA, and paradoxical situations with the stability of RNA, its functions, and the place of RNA in the geological history of the Earth are discussed. The chemical instability of the covalent structure of RNA in the aqueous medium is incompatible with the necessity of water for formation of its functionally active conformations ("water paradox"). The stable double-helical structure of RNA required for replication is incompatible with the stable compact conformations of single-stranded RNA molecules that are necessary for catalytic functions (conformational paradox). There was a very short time gap (or no gap at all) between the end of the massive meteorite bombardment of the Earth (3.9 Ga ago) and the appearance of the first evidence of cellular life (bacteria) in the Earth's rocks (3.8–3.85 Ga ago or even earlier) (geological paradox). It is concluded that the RNA world could not appear, exist, or evolve into cellular forms of life on the Earth. This paper briefly discusses the possibility of an extraterrestrial origin of the RNA world and its extraterrestrial evolution with a subsequent distribution in space (mainly by comets) of the cellular form of life as more resistant to the environment as compared with free RNA.

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ANCIENT RNA WORLD

Ribonucleic acid (RNA) is a unique polymer capable of performing the function of both DNA, as the main genetic material, and protein as the substance determining the metabolism of living organisms. On the one hand, RNA can be both a template for replicating its own structure and a carrier of genetic information. On the other, it is capable of forming specific compact structures that provide selective recognition and binding of metabolites and other ligands and the catalysis of chemical transformations of these ligands (see Spirin, 2002). Thus, the ensemble of RNA molecules may be a self-sufficient entity providing its own existence, growth, and reproduction, i.e., an equivalent of living systems, but consisting of only one type of polymer (the so-called single-polymer form of life).[1] This gave rise to a very attractive hypothesis suggesting that this form of life could precede the modern one, which is based on three polymers (DNA, RNA, and proteins) (Woese, 1967; Crick, 1968; Orgel, 1968; Gilbert, 1986). This is a hypothesis of the ancient RNA world as the primitive form of life, the evolution of which led to the appearance of the mechanism of protein biosynthesis, a specialized DNA-based genetic apparatus, and finally the cellular organization of living matter (see Joyce and Orgel, 1999, 2006; Joyce, 2002; Spirin, 2001, 2003; Orgel, 2004).

The existence of ancient forms of life is demonstrated either by finding fossils or by discovering extant relicts. As the ancient RNA world was most probably not preserved in the fossil record, the only evidence of its existence can be relict systems, molecules, reactions, or processes. For instance, RNA genomes and RNA-dependent replication of RNA of viruses can be considered as relict ("pre-RNA") genetic systems, whereas catalytic RNA (ribozymes) can be considered as relict ("pre-protein") catalysts of biochemical processes. However, the RNA viruses per se cannot be considered as extant relicts because they, like many parasites, are apparently a product of reductionary evolution, and their relict systems of storage and replication of genomic RNA are protected and supplemented by proteins. Primer RNAs that initiate the complementary reduplication of DNA and are strictly required for the beginning of the template synthesis in living cells, as well as the telomerase RNA necessary for the elongation of the chromosomal ends, can be considered as relicts. In addition, it is worthy to mention that monomeric ribonucleotides (but not deoxyribonucleotides!) are participants of the most universal and ancient systems of catabolism and energy supply of extant organisms. The hypothesis of the RNA world as a primary form of life is the most strongly supported by the fact that the protein synthesis of all modern organisms is

[1] Viruses cannot be defined as a "single polymer" form of life as, firstly, almost all of them, except viroids of plants, contain proteins, and secondly, and most importantly, they are not capable of maintaining the independent life, including metabolism, growth, and reproduction, based solely on the functioning of the nucleic acid.

catalyzed by RNA (Nissen et al., 2000; Steitz and Moore, 2003).

ABIOGENOUS SYNTHESIS OF RIBONUCLEOTIDES

The appearance of RNA on the Earth is considered to have occurred in the early period of the Solar System and our planet, i.e., the period between the formation of the Solar System (4.6 Ga) and the earliest evidence of the unicellular organisms (chemosynthetic bacteria 3.6–3.85 Ga) (Schidlowski, 1988, 2002; Schopf, 1993; Mojzsis et al., 1996, 1999; Joyce, 2002; Dobretsov et al., 2006; Rozanov, 2006). That time is thought to be the time of abiogenous syntheses of the components of the nucleic acids: ribose, nitrogenous bases (adenine, guanine, cytosine, and uracil), ribonucleosides, phosphorylated ribonucleosides (ribonucleotides) and polyribonucleotides. Numerous attempts to simulate these syntheses in laboratories during the last 40 years have, in many cases, been relatively successful, but, unfortunately only in respect of primary components, such as ribose, phosphorylated ribose, and nitrogenous bases. The synthesis of nucleosides from ribose and bases was less successful, and no direct synthesis of pyrimidine nucleosides has yet been achieved (see the review by Orgel, 2004). The abiogenous phosphorylation of nucleosides to get monoribonucleotides, as monomeric subunits of polyribonucleotides, also proved problematic, especially in an aqueous medium, because of the low yield of reactions and the random phosphorylation of various groups of nucleosides producing a complex mixture of phosphorylated products instead of required nucleosides-5'-phosphates. Chirality remains a completely unresolved problem: the products of abiogenous syntheses of nucleosides in laboratory experiments always represent racemic mixtures, whereas the formation of real RNAs requires only D-stereoisomers. The conclusion that can be reached based on all available data is not encouraging; despite many attempts to simulate various conditions of the primeval Earth, the complete abiogenous synthesis of nucleotides, which are the components (monomers) of RNA, have not been successful (Orgel, 2004; Joyce and Orgel, 2006).

NON-ENZYMATIC POLYMERIZATION OF NUCLEOTIDES

The polymerization of nucleotides in an aqueous medium is a reaction absorbing free energy and therefore requiring either external activating agents, or preliminary activation of nucleotides, for instance, by their polyphosphorylation. All attempts to use an external activating agent, such as cyanamide or water-soluble carbodiimides, have not given positive results, whereas the spontaneous reaction of polymerization of nucleoside-5'-polyphosphates at reasonable temperatures and pH turned out to be too slow to be useful for solving the problem. Nucleotides can be activated by phosphoramidates (phosphorimidasolides), but their existence in sufficient amounts on the primeval Earth is quite doubtful. In addition, the polymerization of nucleoside phosphoramidates gives a complex mixture of short linear and cyclic products, and even in the presence of the best-performing catalysts, such as cations of lead or uranyl, monomers in the newly formed oligoribonucleotides are bound mostly by 2'-5' bonds, instead of 3'-5' bonds required for the production of RNA.

The best success in non-enzymatic polymerization of nucleotides was achieved using the surface of mineral catalysts such as clays, e.g., montmorillonite (Ferris and Ertem, 1993; Ferris et al., 1996, 2004; Huang and Ferris, 2003). In these experiments relatively long oligoribonucleotides (up to 40 nucleotide residues) were synthesized in an aqueous medium from nucleoside phosphoramidates, with normal 3'-5' internucleotide bonds. Nevertheless, it has to be admitted that this success does not solve the problem of non-enzymatic (pre-biotic) polymerization of nucleotides into RNA because the existence of phosphoramidate substrates on the primeval Earth is unlikely.

NON-NUCLEIC PREDECESSOR OF THE RNA WORLD?

The above problems and other unsolvable complications in attempts to overcome the difficulties of abiogenous synthesis of RNA led many workers, including one of the pioneers of the experimental attempts to solve the problem of the origin of RNA, L. Orgel, to conclude that RNA did not appear abiogenously, but was "invented" by another, simpler genetic system which preceded the RNA world, and that this earlier world could exist and evolve in more extreme conditions of temperature, pH, and pressure than would be acceptable for RNA (Orgel, 2004; Joyce and Orgel, 2006). Various models and hypotheses have been proposed, ranging from the concept of self-replicating minerals on the primeval Earth (Cairns-Smith, 1982) to self-replicating organic polymers, different from nucleic acids but similar to them in structure, i.e., polymers with a sugar-phosphate backbone of non-ribose nature possessing purine and pyrimidine side groups (Eschenmoser, 1999). Among possible polymer predecessors of RNA there were also proposed the popular artificial analogs named "peptide nucleic acids" (PNK), which contain the usual nitrogenous bases of nucleic acids, but with the polypeptide backbone instead of the sugar-phosphate backbone of the natural nucleic acids (Egholm et al., 1992, 1993). The above polymers are interesting in that they, like natural nucleic acids, are capable of forming double-helix structures by complementary Watson-Crick pairing of bases and, hence, are potentially capable of self-replicating. However, none of them seems simpler in their structure as compared with RNA, so that no obvious primitive predecessor of RNA has been proposed. In addition, the replacement

of one genetic system by another in the course of evolution seems unlikely. According to evolutionary biologists, biological evolution progresses predominantly by additions rather than by substitutions (Zavarzin, 2001); in the course of evolution "the new does not reject the old, but matches it, in some cases just replacing the functions of some groups" (Zavarzin, 2006a, p. 167). The RNA world did not disappear after the invention of DNA, but progressed by the additions of DNA and proteins, and was preserved as part of the cellular organization of living organisms, not only for the replication of genetic material inside the cell, but also as ligand-binding macromolecules, catalysts, regulators, and other functional structures, without which modern life is impossible (Spirin, 2002, 2003).

"WATER PARADOX"

Whichever way RNA appears on the Earth, water is necessary for the formation of its spatial structures, including both the double helices formed through Watson-Crick base pairing (A : U and G : C) that are required for reproduction, and the compactly folded specific structures that are necessary for all non-genetic functions. Water stabilizes the double helical RNAs, the double-helical hairpins of compactly folded single-stranded RNAs and the compact packing of the whole RNA macromolecules due to hydrophobic interactions between the planes of their nitrogenous base rings. Also liquid water serves as a solvent for RNA allowing the free diffusion of RNA macromolecules, which is required for their functional activity. On the other hand, the covalent polyribonucleotide chain of RNA in water is thermodynamically unstable and spontaneously hydrolyzed, especially at elevated temperatures, pH shifts, and in the presence of cations of di- and polyvalent metals. Unlike DNA, it displays also kinetic instability, mainly due to the nature of the sugar component of its backbone: the ribose residue possesses a free 2'-hydroxyl group in the *cis* position in relation to the phosphorylated 3'-hydroxyl group and thus can attack on the phosphate group linking two ribose residues. This results in the formation of an unstable triester group and its subsequent spontaneous hydrolytic cleavage, thus leading to the breakdown of the ribose-phosphate backbone. In addition, in water, especially under acidic conditions, the bond between the purine base and the ribose residue is unstable (hydrolytic depurinization of RNA), whereas in alkaline conditions adenine and cytosine easily undergo oxidative deamination and are transformed into hypoxanthine and uracil, respectively. All the above-said is called "water paradox" (see Benner et al., 2006).

It is possible to suggest several ways in which RNA on the young Earth could escape from the destructive effects of water as a solvent, especially at high temperatures and pH shifts. One way would be a stabilization of RNA on the surfaces of some minerals (clays). However, in this way, the mobility of the RNA molecules, which is necessary for them to function in the RNA world, would be strongly reduced. Therefore, only periodical temporary stabilization in the cycles of alternating fixation on the surface and release into the liquid aqueous phase can be assumed (see Spirin, 2005b). The desert regime (cycles of drying and moistening) could also facilitate stabilization in a similar way. Perhaps, it could be also possible to consider periodic freezing and thawing as an alternative type of cycling, or even the existence and functioning of RNA at the ice–water interface.

A fundamentally different way of stabilization of RNA on the primeval Earth has also been proposed; namely, the change of solvent; more precisely, formamide that could be sufficiently abundant at the early stages of the evolution of the planet was suggested instead of water to be the solvent for RNA (see Benner et al., 2006). Indeed, RNA is well soluble and at the same time thermodynamically stable in formamide. However, the authors of this hypothesis did not take into account that the existence of functionally active RNA requires not only the integrity of its covalent chain but also the maintenance of its spatial structures, including double helices and compact globules, whereas formamide is a strong denaturing agent in whose milieu these three-dimensional structures cannot exist.

CONFORMATIONAL PARADOX

The sustenance and evolution of the RNA world in any of its compartments on the primeval Earth, it being an RNA-containing water puddle saturated with organic substrates or an individual colony of RNA molecules on the solid moist surface of clay with adsorbed organic substances, requires the simultaneous presence of RNA molecules with various functional activities, including (1) ligand-binding RNA for selective adsorption and accumulation of necessary substances from the environment; (2) a set of ribozymes catalyzing metabolic reactions for synthesis of nucleotides and their activated (phosphorylated) derivatives; and (3) ribozymes catalyzing complementary replication of all RNAs of the puddle or the colony. According to present knowledge, these functions can be performed by the molecules of single-stranded RNAs that form short double-helical regions due to the complementary pairing of adjacent sections of a polynucleotide chain (are so-called hairpins) and are compactly folded into specific three-dimensional structures. However, the complementary replication of the RNA molecules catalyzed by the RNA-replicating ribozyme must result in the formation of an entirely double-stranded helix in the A-form, where one strand is original and the other is a complementary daughter strand, and this double helix conformation is very stable. For further replication and reproduction of initial (functional) RNA chains, this double helix should somehow unwind, and only then each of its chains can again work as a template for replication, including the synthesis of new molecules with the orig-

inal sequence of nucleotides on the complementary chain, i.e., for reproduction. Ribozymes capable of catalyzing the synthesis of complementary chains of RNA on single-stranded RNA templates have been obtained in laboratory experiments (Johnston et al., 2001; see also Joyce and Orgel, 2006), but the problem of the separation of the double-stranded product into single strands is still unresolved (Orgel, 2004). True, the appearance of ribozymes with RNA helicase activity cannot be excluded, but in that case another problem emerges—how to protect from unwinding the local double-helical regions (hairpins) of functionally active single-stranded RNAs.

Apparently, the solution of the above problem is impossible without high-temperature (up to 90°C) melting of the double helix of RNA. As the covalent RNA chain is quite unstable at these temperatures, it has to be assumed that the replication of molecules in the RNA world required cyclic variations of temperature with short-term periods of heating enabling the unwinding of double-helical replicative intermediates, and further fixation of the unfolded single-stranded state upon cooling. It remains unclear how such fixation could be achieved in solution. Again, it may be assumed that the adsorbing surfaces of some minerals (clays) or polycationic polymers could be such fixatives. It is worth mentioning that the possible presence of urea in the primeval puddles or other water pools could lower the melting temperature of double helical RNAs, but the denaturing effect of urea on functional conformations of single-stranded RNAs, including the effect on RNA-replicating ribozymes, should be taken into account.

Thus, the paradox is that the functional activities of RNA molecules in the RNA world requires stable structures of compactly folded single-stranded polyribonucleotides, whereas the reproduction of RNA molecules needs an even more stable structure of the double helix and its subsequent melting, which is not compatible with the functioning of RNA molecules as specific ligand-binding and catalytic agents, including RNA-replicating ribozymes.

GEOLOGICAL PARADOX

The above-said shows that both the covalent and conformational stability of RNA in an aqueous medium, and hence their functional activity, can only be provided under relatively mild living conditions and in a relatively narrow range of these conditions. The presence of liquid water, the presence of dissociating salts in concentrations providing a sufficient ionic strength (about 0.1), and the presence of cations that are capable of well binding to phosphate groups (Mg^{+2}) are the strict requirements for conformational stability and functionality of RNA molecules, whereas neutral pH and maintaining a constant temperature below 40°C with a possibility of just short-term episodes of warming (not exceeding 90°C) are necessary to retain the integrity of covalent bonds, and hence, the entire covalent structure of RNA. However, this concerns only the isolated RNA, and the formation of RNA–protein complexes (as it is the case in extant organisms and viruses) can significantly stabilize RNA. Thus, the conditions of today's Earth seem to be the best for free RNA world.[2] However, the free RNA world does not exist on Earth anymore, having been completely assimilated and included within cellular organisms and viruses, where it is less affected by fluctuations of external conditions due to the stabilizing effect of the protein surroundings and the internal medium.

Apparently, the free RNA world cannot and could not in principle coexist with the world of microorganisms. Firstly, the advantages of the present-day DNA-RNA-protein world over the ancient RNA world in performing all the metabolic and genetic functions and the advantages in resistance against the environment and environmental fluctuations leave no chance to the RNA world in competition for nutrients and habitats. In addition, the habitat of the RNA world with its readily available metabolites and RNA molecules themselves should be an ideal nutritious substrate for microbes.

Thus, as previously noted, the existence of the free RNA world on Earth has to be dated to the very distant past, in the time preceding the appearance of the first cellular organisms (bacteria), i.e., between 4.6 and 3.6–3.8 Ga ago. However, according to the present-day conceptions of the geological evolution of Earth, the existence of such a comfortable environment for the survival of RNA molecules at that time is difficult to assume, not to mention the reproduction and evolution of the RNA world. Even if the possibility of high temperatures that are not compatible with the existence of RNA in an aqueous medium, and the intensive ultraviolet and general cosmic irradiation on the Earth's surface during the primeval phase in the planet's history (supposed by many, although by not all, geologists and astrophysicists) are not taken into account, the problem of the heavy meteorite bombardment of the planets in the Solar System 3.8–3.9 Ga ago still remains (Mojzsis et al., 1999). This was a period of massive falls on the Earth, which had already been formed, mainly of bod-

[2] It is quite remarkable that the evolutionary adaptation of modern microorganisms and viruses to extreme conditions, including high temperature, has not seriously affected the properties of RNA, being almost completely restricted to adaptive changes of proteins and cells in general. For instance, the ratio between the pairs of nitrogenous bases (G + C) / (A + U), which determines the conformational stability of RNA, including its thermal stability, remains more or less constant in mesophiles, thermophiles, and psychrophiles, and major adaptive changes have occurred in proteins of corresponding microorganisms and other components of their intracellular media. This allows the conclusion that thermodynamic and kinetic instability of the polyribonucleotide covalent chain inherent to RNA in aqueous media and even its conformational stability displaying certain (although limited) variations due to possible differences in nucleotide composition were not objects of natural selection throughout the entire history of the RNA world. Hence, when the ancient RNA world is discussed, we can justifiably use the properties of modern RNA.

ies from the asteroid belt initiated by passing the Sun through stellar associations of the Galaxy and continuing with high intensity for several hundred million years (Barenbaum, 2002). It is thought that these falls led to the appearance of liquid water necessary for the existence of life on the Earth's surface. This period was followed by times of much less intensive bombardments of our planet by meteorites and comets, which brought water, carbon, and other elements essential for life. Interestingly, the time of the cessation of the intensive meteorite bombardment is surprisingly close to the time when the first evidence of cellular life on Earth is recorded—3.8 Ga ago (Isua in Greenland; Schidlowski, 1988) and even 3.85 Ga ago (Akilia Island, Greenland; Mojzsis et al., 1996).

The massive meteorite bombardment that stopped only 3.9 Ga ago makes the existence of the RNA world, and even simply RNA molecules, on the Earth before that time unlikely. Thus, there was a very narrow time slit, about 100 million years or less, for the RNA world to appear, reproduce, and evolve up to the level of the first highly organized organisms (bacteria) with their complex molecular mechanisms of heredity, protein synthesis, energy supply, and metabolism. As the temperature and other conditions on the primeval Earth of that time, on the one hand, and the earliest time supposed for the appearance of the cellular forms of life, on the other hand, are determined more precisely, this time slit is becoming even narrower. As a result, many geologists, paleontologists, and microbiologists have to admit that in the "geologically documented history of Earth there is no time for the RNA world and other precellular forms of life" (Rozanov, 2006; see also Zavarzin, 1974; Schopf, 1993; Mojzsis et al., 1999).

EXTRATERRESTRIAL ORIGIN OF THE CELLULAR FORM OF LIFE

Given all the difficulties and failures of laboratory modeling of the syntheses of the RNA components and RNA themselves in the abiogenous conditions and the paradoxical, contradicting conditions necessary to sustain RNA and its ability to self-replicate in the terrestrial environment, as well as the narrow time slit of the geological history of the Earth when the evolution of the RNA world into cellular forms of life could be possible, one has to subscribe to the hypothesis of panspermia advocating the extraterrestrial origin of life on Earth. The above discussion leads to an obvious question: Could the preformed cellular life be brought to the Earth by the meteorites that were bombarding the Earth until 3.9 Ga, or by comets immediately after the bombardment? or Were living organisms, at least single-cellular, brought to the Earth by meteorites and comets repeatedly, each time when the Sun passed the stellar associations in the Galaxy? (i.e., 2.6, 1.65, and 1.05 Ga ago) (see Barenbaum et al., 2007). In any event, it is possible that the appearance of the cellular form of life on the Earth was connected not with the cessation of the meteorite (asteroid) bombardment 3.9 Ga ago, but with the bombardment itself. The further evolution of life on the Earth could also be connected with subsequent, less intense meteorite bombardments. At least the idea that the periods of bombardment were followed by explosive development of the biota, both numerically and taxonomically, has been recently discussed (see Barenbaum et al., 2007).

The hypothesis of the extraterrestrial origin of the cellular form of life on Earth is supported by the new data that the range of environments and habitats available for microorganisms is much wider than it was earlier thought to be. Viable and living microbes are found in the ancient deep ice of the Arctic and Antarctic and in the depths of the permafrost (Zvyagintsev et al., 1985; Gilichinsky et al., 1992; Vorobyova et al., 1997; *Bacterial Paleontology*, 2002). Life in the form of bacterial communities is recorded at depths of 3 and even 5 km in continental rocks and in oceanic depths at huge pressures and high temperatures (Gold, 1992; Stevens and McKinley, 1995; *Bacterial Paleontology*, 2002). Some workers believe that the deep terrestrial and oceanic biosphere may include more than half of the total biomass of the Earth. In this case, the main living component of the biosphere on the Earth are not multicellular eukaryotic photoautotrophs and organotrophs, i.e., plants and animals (which are usually associated with the word "life"), but prokaryotic chemoautotrophs of the deep (hot and cold) biosphere completely independent of the solar energy and free oxygen (Gold, 1992; Hoover, 2006; Zavarzin, 2006b, 2006c). The data from the deep microbiology of the continents on the Earth suggest the possibility of the existence of the deeply settled biosphere on other planets and their satellites (such as Io and Europa, moons of Jupiter). In addition, many free-living terrestrial bacteria are adapted to survive or preserve their viability in a total vacuum, in the dehydrated state, for a long period of time. The ability of bacteria to preserve the viability in high vacuum and at extremely low temperatures allows one to speculate that the nuclei of comets, the polar caps on Mars, and the ice satellites of Jupiter and Saturn can also have potentially viable microbes (Hoover, 2006).

It has to be emphasized that if panspermia is assumed, the possibility of the distribution of life in the cellular form, rather than in the form of the RNA world has unquestionable priority. As previously noted, the existence of the RNA world and the preservation of RNA molecules are strictly limited by the environmental conditions due to purely chemical and physical properties of polyribonucleotides and their conformations (pH = 7 ± 0.5, temperature of conformational stability ranging from 0 to 40°C and that of the relative covalent stability not exceeding 90°C, ionic strength from 0.1 to 0.3, the obligatory presence of magnesium ions, the absence of the heavy metal ions that strongly destabilize RNA, etc.). At the same time, proteins can retain their native (functional) conformation and integrity in a much wider range of conditions and, in the case

of forming complexes with RNA, can stabilize those. Microbes have even wider opportunities to adapt to extreme conditions, not only because of the stability of proteins, but also because of the intracellular medium that can resist unfavorable environmental conditions, and also because of the presence of strong reparation mechanisms that correct the damages in nucleic acids and proteins. Therefore, the dissemination of life in the cellular form over the Universe seems more realistic than in the form of free RNA molecules.

Space observations show that water is the main volatile substance of comets, both of the Solar System comets (see Mumma et al., 2005) and possibly of galactic comets, which may appear with certain periodicity (Barenbaum et al., 2007). It is presently known that the nuclei of comets of the Solar system have a black crust (with a very low albedo of about 0.03), which can reach temperatures up to 400 K in the perihelion. Images of craters, depressions, peaks, eruptions, and flows on the nuclei of some comets suggest that the crust may be thick and can hold a sufficient interior pressure that allows the local zones of liquid water and salt solutions to be formed when the comet is in perihelion (Hoover, 2006). Even the occasional presence of liquid water in comets supports the hypothesis that active microbial life on some of those is possible. In that case comets may be considered to be carriers of life within the Solar System and even outside it, and hence, can be responsible for the semination of the Earth.

Indeed, the similarity of the ratio of deuterium to hydrogen (D/H), the albedo value, and chemical composition of the comets and some meteorites of the carbonaceous chondrites group supports the old hypothesis that the meteorites of that type are remains of the comets that had disappeared and lost their volatile substances. At the same time, modern analytical approaches show the presence in them not only of organic substances, but also distinct microfossils, predominantly bacterial cells (see Zhmur et al., 1993; Gerasimenko et al., 1999; Rozanov, 2000; Hoover and Rozanov, 2002; Hoover, 2006). Carbonaceous granules and their properties studied on the famous Martian meteorite ALH84001 (i.e., a meteorite thought to be a piece of the planet Mars, which fell on the Earth 13000 years ago in the Antarctic, can also be considered as remains of primitive living organisms similar to nanobacteria and as the evidence of the existence of life outside the Earth (McKay et al., 1996). The time of formation of these, supposedly biogenous, granules on Mars is estimated as 3.6 Ga, which is close to the time when the meteorite bombardment of the planets of the Solar System ended.

At the same time, if we accept that life arrived to the Earth and was distributed in the Universe as organized single-cellular organisms, it does not take away the problem of the origin of the cellular forms of life,—if not on the Earth, but somewhere in the Universe. In any case, by now the evolution of the simplest cells from the RNA world remains to be the most likely scenario based on the present-day knowledge of the molecular basis of life.

WHERE IN THE UNIVERSE COULD THE RNA WORLD ARISE, EXIST, AND EVOLVE?

If it is true that living or viable microorganisms can exist in the nuclei of comets and on some other extraterrestrial bodies (e.g., Mars, or the satellites of large planets, such as Jupiter or Saturn), and if any cellular form of life did evolve from the RNA world, this raises the question: Where is the place which allowed this single-polymer world of self-reproducing molecules to arise, exist, and evolve into cellular forms of life capable of spreading in the Universe? Certain additional conditions for the existence and evolution of the RNA world can be formulated based on the analysis of the above-considered paradoxes. Firstly, along with liquid water, there is an obvious necessity of RNA-adsorbing surfaces. Secondly, the evolution of the RNA world is difficult to explain without the cycles of drying and moistening (or flooding), warming and cooling, freezing and thawing. Thirdly, the existence of some mechanisms of protection of RNA against cosmic irradiation or/and its temporary conservation seems essential.

The possibility that these conditions (at least partially) could be fulfilled in the comets of the Solar System cannot be excluded. As previously mentioned, recent studies of the comets directly indicate the presence of large amounts of water, organic substances (the so-called CHON particles), and numerous adsorbent surfaces in the nuclei of the comets (in particular, the surfaces of microscopic particles, from 1 to 100 μm, together with ice forming a thick—of many meters—loose layer immediately underneath the crust of the nucleus) (A'Hearn et al., 2005). Periodical passing through the perihelion and then moving away from the Sun, as well as possible encounters with other extraterrestrial bodies, can provide the necessary cyclic changes of states and processes. In other words, the comets can be considered as natural space laboratories in which the RNA world could exist, evolve, and be temporarily conserved. For instance, in the comets the principle of the cyclically alternating amplification and selection of RNA, similar to that realized in the artificial method of SELEX ("systematic evolution of ligands by exponential enrichment"; see Tuerk and Gold, 1990) may occur (Spirin, 2005b). Indeed, as a result of the comet moving through the perihelion, the phase states of water in the nucleus of the comet must change according to the following scenario: (1) liquid water is formed in the cavities inside the nucleus due to the heating and provides the environment for massive amplification of all RNA molecules in solution; (2) intensive evaporation of water and drying of the surfaces inside the cavities provide the growth of successful combinations of RNA molecules in the form of colonies on moist solid surfaces (selection stage); (3) condensation of water, dissolving of the RNA colonies and

again massive amplification of the RNA molecules, but this time with development of a population enriched by the "best molecules" of RNA; and (4) conservation of this population as the distance from the perihelion increases, up to the next cycle of approximation to the Sun. Thus, the comets of the Solar System could be the cradle for the RNA world and its evolution.

This elegant hypothesis, however, has a weak point: the time of the existence of the tailed comets orbiting the Sun (i.e., the time after the comet leaves the Oort Cloud and before the stored water and other volatile substances are exhausted in the cycles of movements through the perihelion) is relatively short. Even if it is granted that a tailed comet perform several thousand passages through the perihelion, this time fits within as little as one million years for short-period comets, and it is unlikely that the RNA world could appear and evolve into the world of cellular forms of life within this time interval or within so few cycles of heating. Besides, this hypothesis can hardly help to solve the problem of the primary abiogenous synthesis of ribonucleotides and polyribonucleotides. Another difficulty is the absence or deficiency of phosphorus, at least in the comets of the Solar System so far studied. In such a case all problems of the abiogenous synthesis of nucleotides and nucleic acids, origin of the RNA world, its evolution, and the appearance of the cellular form of life must be solved by placing the cradle into the further Cosmos.

However, if the RNA world, including its origin and evolution, is placed in the outer Cosmos, an agnostic approach becomes justifiable as we do not know and cannot even imagine conditions elsewhere in the Universe. Therefore, we should accept nucleotides, polyribonucleotides, the RNA world, and, perhaps, the first cellular forms of life that evolved from the RNA world, as the creation of some unimaginable conditions and forces, the products that were supplied ready-made to the Earth, and probably to some other planets and bodies in the Solar System.

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