The origin of life: Oligomerization of RNA nucleotides on prebiotic Earth

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Abstract

We propose a plausible oligomerization process of RNA nucleotides on prebiotic Earth. The process takes place at tideland and estuary where wet & dry cycle and pH fluctuation occur due to tide. The process proceeds with help of clay minerals that catalyze not only oligomerization but also cross complementary self-replication of RNA oligomers by lowering the activation energy of covalent bonding. The self-replication realizes transfer of molecular information and allows mutation and natural selection, essential steps of evolution of life.

Introduction

A notion of life being originated from oligomerization of RNA nucleotides seems to be corroborated by circumstantial evidence and some experimental results, however, how it was actually proceeded is not well understood. It has been demonstrated that all necessary subunits required for formation of RNA nucleotides can be synthesized under simulated prebiotic environment in modern labs [1-4]. A nucleotide consists of ribose sugar, phosphate and one of 4 nucleobases. These subunits are produced by chemical reactions from simple molecular components presumably existed on prebiotic Earth. How were these subunits chosen from a wide variety of similar molecules (non-canonical subunits) possibly produced by abiotic chemical reactions? It may be explained by thermodynamic consideration, i.e., the canonical subunits were simply thermodynamically more stable than the non-canonical molecules and thus eventually dominated after repeated formation and degradation of the molecules. The notion is not without weakness. It is found that formation of the nucleotides by bonding the subunits without help of enzymes is difficult in modern labs. A reason is that the responsible covalent bond has a high activation energy to be overcome in order to complete the bonding.

As a plausible process to circumvent this difficulty, we proposed the nucleotide formation by cross complimentary self-replication (hereafter called the self-replication for short) with help of clay minerals in a previous paper [5]. The clay minerals acted as a catalyst [6,7]. The process took place at tideland and estuary on prebiotic Earth, where wet & dry cycle and pH fluctuation occurred due to tidal cycle. The subunits of RNA nucleotides dissolved in the oceans were selectively adsorbed on a clay mineral and gradually increased the concentration. Once the concentration reached a certain level, although it was extremely rare, the first nucleotide (say adenosine (A)) is formed. Then, the self-replication started with help of the cyclic environmental fluctuation. As a result, the first complementary nucleotide (uridine (U)) was formed. The joined pair of (A) and (U) was then split by the cycle or fluctuation since the hydrogen bonding between the two bases was weak. Next, the self-replication took place on the two separated nucleotides, and the second (U) and (A) were formed, respectively. The process continued and increased the concentration of nucleotides on the mineral. The same process took place on the guanine (G) and cytosine (C) pair.

The process is consistent with the homochirality of RNA molecules. In nature, the ribose sugar has two forms (D-ribose and L-ribose) which are expected to be formed equally, but RNA

nucleotides only consist of D-ribose. If the first nucleotide consisted of D-ribose, all subsequent self-replicated nucleotides would consist of D-ribose.

Once the concentration of RNA nucleotides had reached a certain level, oligomerization took place, and a single strand of RNA oligomer was formed on prebiotic Earth. An experiment under a simulated prebiotic condition shows that the oligomer can grow up to 40 nucleotide units [8]. However, the length is well short comparing the length of known short functional extant RNAs (70~100 units). Here we measure the length of the oligomer by the number of nucleotides constituted. The max length is determined by stability of the oligomer that is constantly subjected to dissociation (bond breaking). The dissociation rate linearly increases as the oligomer grows in length. In order to grow further, a mechanism that produces longer oligomers had to be operated in prebiotic Earth. RNA oligomers mainly exist in a single strand form, but they can also form double strands like DNA which is much more stable. In this paper, we extend the self-replication process to account for the formation of the longer RNA oligomers.

Oligomerization Process

The process starts with formation of a dimer when first and second nucleotides join. The dimer is adsorbed and properly aligned on a clay mineral which acts as a catalyst and lowers the activation energy for oligomerization. Although oligomerization normally proceeds by joining third nucleotide at an end of the dimer resulting in a trimer, due to a unique structure of the nucleotides, the process differently proceeds by bonding the base of third nucleotide with a complementary base of the dimer first because this bonding does not need to overcome an activation energy and occurs instantaneously when the two bases come to close each other. Next, fourth nucleotide with base which is complementary to the remaining unbonded base of the dimer is bonded and then third and fourth nucleotides join. As a result, a double strand dimer is formed. Subsequently, the wet & dry cycle of environment causes breaking up of hydrogen bond between the bases and the dimer and its complimentary dimer are separated. The self-replication of the dimer is completed. The process independently continues further on each of the two separated dimers.

The process repeats and the number of the replicated dimer that is more stable increases. Although the self-replication reaction dominates, as the number of replicated dimers increases, there is a chance of oligomerization process by which a nucleotide joins at an end of one of the dimers resulting in formation of a trimer (there is a small chance of formation of a tetramer by joining two dimers together). If the trimer (or tetramer) is more stable than the dimers, the self-replication of the trimer starts. Bonding of free complementary nucleotides starts from one end of the trimer and finishes at the other end, forming a double strand trimer. Subsequently, the trimer and its complementary trimer are separated by the wet & dry cycle. The self-replication of the trimer is completed. The process continues and the length of the longest oligomer steadily increases as long as the free nucleotides are available. Growth of the length reaches a limit when the dissociation rate of the oligomer exceeds the self-replication rate. The max length is longer than that of oligomer grown as a single strand because the oligomer in the double strand form is more stable and thus dissociates slower.

The process was certainly initiated at countless places along shorelines of oceans on prebiotic Earth for millions of years until the first RNA oligomer which was long enough to be a functional RNA was finally formed. The first functional oligomer might not be sufficiently functional, but it

underwent mutation and natural selection for formation of efficient functional RNA that helped to form DNA and proteins in later stages of evolution of life.

Discussion

The RNA world hypothesis of the origin of life suggests that life started with simple RNA molecules that could multiply without help from other biotic molecules. How the RNA molecules were formed is the subject of the present paper. We propose formation of RNA oligomers from the nucleotides by the self-replication process with help of abiotic catalysts such as clay minerals, although they are not as efficient as enzymes. Rationality of the process is discussed in the following.

Tideland and estuary on prebiotic Earth are prerequisite for formation of life. Intensity of UV light is known to rapidly vary with change of water depth caused by the wet & dry condition at tideland and is likely responsible for bonding and debonding of covalent bonds [9, 10]. The pH change occurs at estuary due to variation of salt concentration and is known to affect the activation energy. Hydrogen bonding is weak and can be broken simply by temperature fluctuation or water molecule movement around RNA oligomers due to tidal current.

Catalysts are widely used to increase yields in modern chemical syntheses. We speculate that abiotic catalysts played an essential role in oligomerization on prebiotic Earth. Clay minerals are known to be good catalysts and certainly existed on prebiotic Earth. It has been demonstrated that RNA oligomers can be formed with help of a clay mineral under a simulated prebiotic Earth. Roles of the clay mineral in the process are twofold. Firstly, it provides surfaces on which the nucleotides are selectively adsorbed. This reaction consequently increases concentration of the nucleotides on the surface and allows the nucleotides to react each other more frequently. Secondly, it strains and aligns the nucleotides in proper orientations so that particular reactions become easier due to reduction of the activation energy.

RNA oligomers with about 40 nucleotides are experimentally formed [8], but the length is well short of the length of shortest functional extant RNA. A reason is dissociation of the oligomers, which sets a limit on oligomer length. When RNA oligomer takes a form of double strand, it is inherently more stable than single strand and can grow much longer. So far, no minerals are identified for the formation of double strands of RNA by the self-replication. Studying montmorillonite and similar minerals may be the first step to identify possible clay minerals [11].

Growth rate of RNA oligomer is linearly proportional to the concentration of the nucleotides, so if the concentration is high and a suitable abiotic catalyst is available, it may grow to a functional RNA. However, it is statistically unlikely to have the second oligomer with the same sequence nearby. On the other hand, if a functional RNA undergoes the self-replication, multiple copies of the oligomer are available for assisting chemical reactions. For the functional RNA to take hold, many copies of the oligomer are needed.

The first functional RNAs were likely to be biotic catalysts (ribozymes) that engaged in accelerating the formation of themselves through formation of nucleotides from the subunits and self-replication of the nucleotides and the oligomers. These catalysts replaced the abiotic catalysts such as minerals, were much more efficient and allowed the reactions to take place at various

places besides tideland and estuary and were different from enzymes that were proteins and formed with help of RNA in a later stage of evolution. Over many years, some RNAs self-replicated and evolved to a variety of functional RNAs. At some later stages of evolution, DNA and proteins were formed with help of RNA and took over the jobs of storing genetic information and driving chemical reactions, respectively.

Biological evolution is possible due to two essential processes, mutation and selection. Mutation does not always produce a positive result. If a mutant adopts the surroundings better, it thrives and eventually dominates (natural selection). These processes lead to diversity and complexity of biological molecules.

There are competitive hypotheses of the origin of life in literature [12]. Hydro vent in deep ocean bed where life started as a simple metabolic process and hot spring where fresh water contributed for the formation of original life form of proto cells. These hypotheses are plausible in some respects but not in others [10]. We think that these places are occupied later stage of evolution of life by adaptation.

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