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Chapter 6

Oligomerization of Nucleic Acids and Peptides under the Primitive Earth Conditions

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Additional information is available at the end of the chapter

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1. Introduction

1.1. Why are nucleic acids and peptides so important for the emergence of life-like systems?

Question how life originated on the primitive earth is still a frontier of science. Nowadays, primitive life-like system is mostly considered to have emerged by chemical evolution on the Earth although some scientists are evaluating the possibility of panspermia hypothesis [1-3]. External and internal energies from the earth, such as cosmic rays, ultra violet radiation, meteorite impacts, volcanic eruption, submarine hydrothermal vent system, etc. resulted in organic molecules from inorganic materials, such as primitive atmospheric gas, minerals, materials solved in the ocean. Organic molecules were polymerized and finally resulted in several biological functions. Complex mixtures of the organic molecules should have evolved to primitive life-like systems. By the Miller-Urey experiment at 1953, a scenario from simple molecules to organic molecules in a simulated primitive atmosphere – ocean system was evaluated for the first time [4]. After the Miller-Urey experiment, the origin of life problem became as a scientific subject and a number of simulation experiments were carried out to elucidate how life-like system was originated on this planet [5-7].

The knowledge regarding the primitive environments of the Earth and surrounding universe in relation to chemical evolution has been accumulated as well as the simulation experiments. For instance, an environment, which was assumed at the time of the Miller-Urey experiment, is not already acceptable nowadays although it does not mean that the Miller-Urey experiment was devalued; the knowledge on the primitive earth has continuously accumulated to improve the reliability of simulation experiments. The primitive earth environments are difficult to estimate since the evidences regarding oldest rocks and fossil organisms are merely capable to trace back to near 3.9 billion years ago, where almost oldest evidence of life-like system has been obtained [8, 9], although the best current evidences are closer to 3.5 billion years ago [10].

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DNA, RNA, and proteins are realized as most important biological materials, which play central roles in the present life-like systems. These molecules possess a number of functions, such as genetic information storage, transcription and translation of genetic information, enzymatic activities, which are based on their unique three-dimensional structures of oligo- and polynucleotides and proteins. A certain length of polymerized nucleic acid and peptide chains is the essential to display systemized biological functions although small molecules also play important roles in living organisms. Thus, the formation and accumulation of a certain length of polymers of nucleic acids and peptides are essential process toward the emergence of life-like system.

Metabolism, amplification (replication), and evolution are generally considered as essential requisites, for which a life-like system is regarded as alive [11]. The requisites are strongly related to a train of machinery, which maintains the genetic coding and translation system in cell consisting of DNA, RNA, and proteins as shown in Figure. 1. It was generally considered that the phenotype molecules of cell-type of organism are proteins while the genotype molecules are DNA molecules until the discovery of ribozymes. The function of DNA is storage of genetic information. A DNA sequence is copied to mRNA and translated to amino acid sequence of polypeptide on ribosome using tRNA (Figure 1 left). The peptide becomes a protein by final processing and folding of three-dimensional structure. In the modern organisms, DNA is regarded as blueprint and protein is regarded as building block created on the basis of the blueprint. The information flow from DNA and protein is universal in all the present organisms [12]. On the other hand, one of the important functions of proteins is enzymatic function. It is considered that protein enzymes control the formation of other biologically important molecules, such as sugar, lipid, vitamin, coenzyme; these functional molecules are constructed indirectly by the catalytic actions of protein enzymes. In addition, protein enzymes maintain the several reactions regarding the DNA replication, the RNA formation, and the protein metabolism itself.

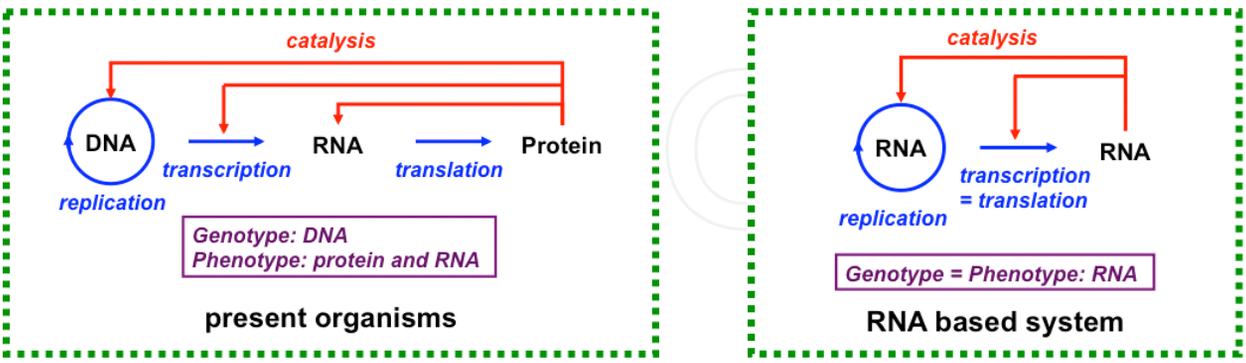


Figure 1. Information flow in the present organisms (left) and in an RNA-based life-like system (right)

A schematic pathway for chemical evolution of RNA and protein-like molecules is illustrated in Figure 2. According to the modern functions of RNA and proteins, it is assumed that proteins could not have possessed capability for storage of information during the chemical evolution in contrast to RNA molecules. However, the interactions between RNA and protein-like

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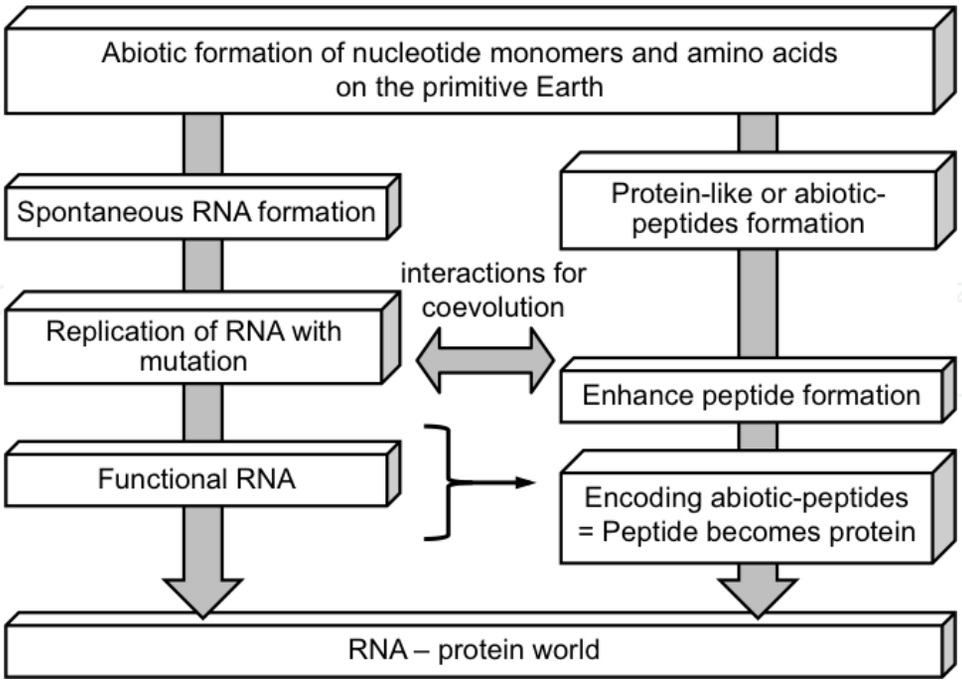


Figure 2. Chemical evolution of RNA and protein-like molecules towards RNA-protein world

molecules would have facilitated chemical evolution each other. Such cooperative chemical evolution would have resulted in an RNA – protein world after the RNA world system.

Here, the term "protein" and "peptide" should be reconsidered in the present chapter. Normally, a protein is ambiguously defined just as a very long peptide, which has a biochemical function. On the other hand, peptides are frequently regarded as just smaller molecules than proteins. However, an important characteristic from the viewpoint of the origin of life, that is, the fact that proteins are synthesized on the basis of genetic translation system in cell should be pointed out. So, if a primitive long peptide were synthesized on the basis of genetic information, which might be constructed from RNA molecules, the long peptide is regarded as a protein. Thus, the assignment method must be elucidated simultaneously during the evaluation of the origin of protein. Thus, in the present chapter the term "a protein" is defined as a certain length of peptide molecule, which is created using an assignment method in a life-like system. Thus, the term "abiotic-peptide" or "protein-like" will be used as describing oligomerized molecules made from amino acids including peptide bonding. On the other hand, the length of abiotic-peptides, which could have gained biological functions would be also important to consider the oligomerization of amino acids. Biological functions of proteins and peptides are based on the three-dimensional structures. Thus, a minimum length of oligopeptides would be regarded as a candidate functional molecule. The minimum length of a peptide possessing a biological function might be down to 10-mer oligopeptides since a 10-mer peptide could form a rigid three-dimensional structure [13].

Conclusively, DNA, RNA, and proteins are regarded as most important molecules, which play important roles regarding the genetic information flow. Then, the origin of the genetic information is important issue in relation to the origin of life. The relationship between DNA

and protein has been an issue for many years, which is so-called as "egg and chicken problem". DNA replication, the transformation of DNA to RNA, the translation to proteins are maintained by protein enzymes and the genetic information of such proteins is coded in DNA sequences. Thus, the relationship between DNA and protein resembles the relationship between egg and chicken. However, discovery of RNA enzyme [14], that is ribozyme, suggested that RNA molecules should have played a central role in ancient life-like systems, where RNA preserves genetic information, but also enzymatic functions. This is so-called the RNA world hypothesis [15-17] and extensively investigated for the last 2 decays. The genetic information flow in an RNA-based life-like system is shown in Figure 1 (right). RNA molecules play both the functions, that are, storage of genetic information and expression of enzymatic activities. Evidences, such as, important functions of mRNA, tRNA, rRNA during the translation of DNA to protein, the enzymatic functions of ribozymes, the role of ATP as high energy phosphate, the roles of coenzyme possessing nucleotide moieties, support the RNA world hypothesis. Nowadays, it is understood that the DNA sequences as genotype molecules are assigned to the amino acid sequences and RNA sequences as phenotype molecules in cell. The presence of an assignment method between genotype and phenotype is added as an important requisite for life-like system [18, 19]. In an RNA based life-like system, RNA molecules should have played both the roles of genotype and phenotype.

2. Difficulties of dehydration in aqueous solution

Both the formations of nucleic acids and proteins *in vivo* are the dehydration process in aqueous medium. In other words, the hydrolytic degradation of both nucleic acids and proteins spontaneously proceeds in aqueous medium from the thermodynamic viewpoint. Thus, the formation of these biopolymers is not advantageous from the viewpoint of thermodynamics unless using a condensation reagent and/or an activation technique of monomer. In the present organisms, triphosphate nucleotide monomers are primarily used to form nucleic acids as monomer unit, and the activated amino acids by forming aminoacyl-tRNA (Figure 3) are adopted to form peptide bonding on ribosome. Similarly, the dehydration using condensation agent and/or activation of the monomers in organic solvent are a standard strategy for the organic chemical synthesis of nucleic acids and proteins.

On the other hand, RNA oligomerization proceeds by RNA polymerases on a DNA template from nucleotide 5'-triphosphates (Figure 4), which are the activated nucleotide monomers *in vivo*. A polypeptide forms on a ribosome in the presence of mRNA molecules and aminoacyl-tRNA molecules, which are formed from amino acids and tRNA molecules by aminoacyl tRNA synthetase molecules. On the other hand, modern DNA templates, ribosomes, and enzymes were not present on the primitive earth. Thus, the processes of RNA formation without these organic materials should be identified to clarify the origin of primitive life-like system.

Furthermore, an important factor should be pointed out for the investigation of prebiotic oligomerization; life-like system is a thermodynamically open system, of which energy and materials inflow and outflow from and to the environment. Thus, the formation of dissipative

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structures could be formed in an open system, which could not be formed under the equilibrium state. Thus, it should be considered that oligonucleotides and abiotic-peptides could have accumulated under conditions, which are far from equilibrium conditions.

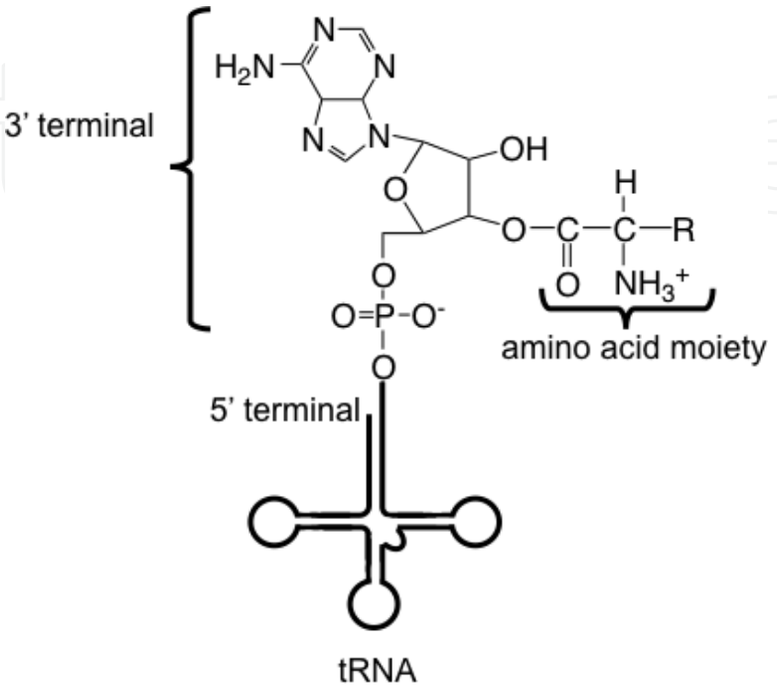


Figure 3. Activation of amino acid in aminoacyl-tRNA

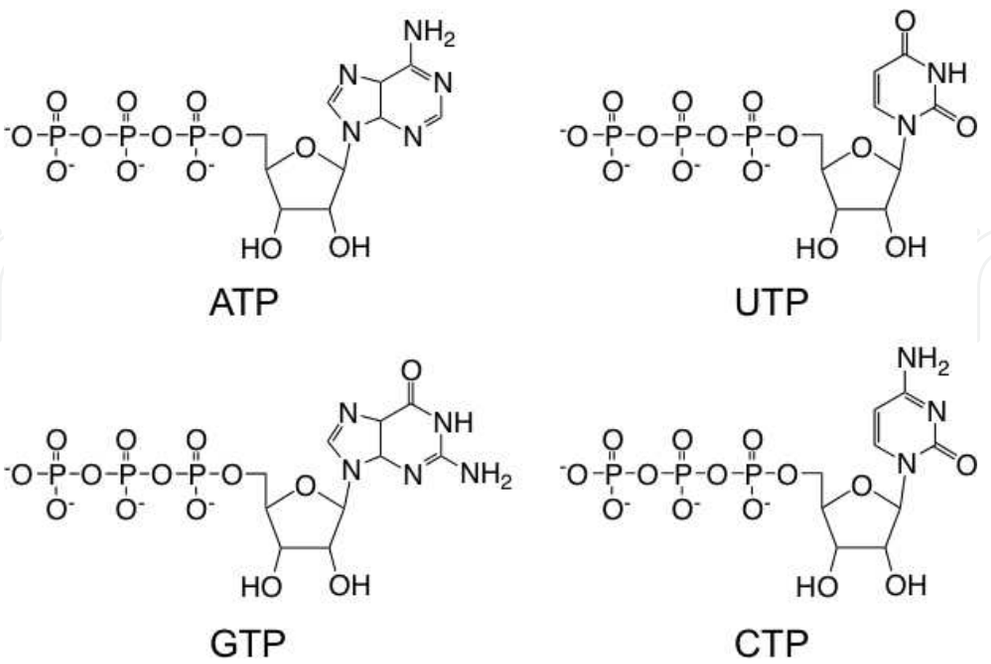


Figure 4. Structures of nucleoside 5'-triphosphate

3. Primitive earth environments: So extreme as comparing to the present earth environments

The time that a most primitive life emerged on the primitive earth is considered between from 4.6 to 3.9 billion years ago; the earth formed 4.6 billion years ago and the oldest evidence in 3.8 billion year old rock has been pointed out [8]. Thus, since physical evidences between 4.6 – 3.9 billion years ago are hardly obtained the theoretical estimation on the basis of astrophysics and earth science regarding the environments of the earth between 4.6 – 3.9 billion years ago has been carried out. At the early stage of the earth, the surface of the earth is covered with magma-ocean. Presumably, a large number of giant meteorite impacts, celestial bodies, and planetesimals attacked the primitive earth until 3.8 billion years ago [20]. Thus, the giant meteorite impact could have evaporated totally the water of the ocean while the ocean would have formed until 4.2 billion years ago [21, 22]; life-like system, which might have emerged before 3.8 years ago, could have been destroyed under such extreme conditions. Furthermore, the moon was much closer than today which caused strong tidal actions. These factors should have strongly affected the surface temperature of the earth. On the other hand, some scientists assumed that the primitive earth was frozen since the solar luminosity was relatively less than at present [23, 24]. Thus, the temperature of the primitive ocean, in which life originated, remains speculative [25-27] although the temperature would have been higher than the present.

At the same time, it should be also considered that the ancient environments of the earth should be heterogeneous as the present environments are. It would be more difficult to elucidate the local heterogeneity of the ancient environments because of the limitation by theoretical estimation. The presence of the ocean would suggest the presence of mantle convection on the ancient earth before 4.2 billion years ago [28] so that hydrothermal vent systems would have been present in the primitive ocean. In addition, it should be considered that large continents were not formed on the primitive earth. On the other hand, the primitive atmospheric conditions should be taken into account since the primitive atmosphere is nowadays considered including CO_2, CO, N_2, H_2O mainly as such strong reductive one [4] dispite the relatively strong reductive atmosphere at the time of Miller-Urey experiment was assumed to include CH_4, NH_3, H_2O [27].

Conclusively, the primitive earth environments should have been extreme and heterogeneous. Nevertheless, the simulation experiments of chemical evolution of nucleic acids and abiotic-peptides have been normally carried out under mild conditions. One reason is that the ancient environments of the earth should have been so extreme that these simulation experiments could not be easily carried out. Thus, these extreme conditions must be considered as possible earth environments for the simulation experiments of chemical evolution.

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4. Successful examples of the formation of nucleic acids

4.1. RNA formation using the present high-energy nucleotide monomers

Discovery of ribozyme suggested that RNA molecules played important roles in the emergence of life. If the RNA world hypothesis is correct then RNA or RNA-like molecules should have accumulated on the primitive earth. It is now getting known that diversity of RNA molecules in the present organisms is very large including mRNA, tRNA, rRNA, ribozymes, small non-coding RNA [29]. The biological functions of tRNA, rRNA, and ribozymes are caused by the formation of three-dimensional structures. Presumably, a certain length of RNA oligomers would be necessary to display such functions.

The importance of RNA molecules to the origin of life had been speculated many years ago [30, 31] before the time when the RNA world hypothesis was proposed [15]. Thus, the simulation experiments of chemical evolution of RNA molecules were extensively carried out before the proposal of the RNA world hypothesis. RNA molecules should have evolved without enzymes and template DNA molecules. On the other hand, there are some enzymes in modern organisms and viruses (Table 1) that catalyze the formation of RNA molecules with and without using a template nucleic acid. RNA polymerase catalyzes the RNA formation from nucleotide 5′-triphosphate (NTP) in the presence of DNA template [32], and Qβ replicase from a virus catalyzes the RNA formation in the presence of an RNA template [33]. Besides, polynucleotide phosphorylase (PNPase) catalyzes the formation of RNA from nucleotide 5′-diphosphate (NDP) without a template nucleic acid [34]; it is considered that the role of PNPase is primarily to form NDP from polynucleotides, but the enzyme also catalyzes the formation of polynucleotide from NTP. Thus, the enzyme is used for the preparation of polynucleotide in the laboratory. The presence of different enzymes in the formation of RNA indicates that oligonucleotides would have formed under the primitive earth conditions through multiple pathways.

The pathways for the formation of oligonucleotides without enzymes were extensively investigated. The potential of the present high-energy nucleotide phosphate as monomer unit, that is, NDP and NTP, was examined in the absence of the enzyme and a template nucleic acid. However, the efficient formation of oligonucleotides from neither NDP nor NTP has been observed [35]. The high-energy nucleotide phosphates possess the sufficient Gibbs free energy to form oligonucleotides so that the reason of the difficulty of oligomerization of NDP and NTP is probably due to the relatively small rate constants of formation of oligonucleotide without enzyme as comparing to the degradation of these monomers or the hydrolysis of monomers. Thus, condensation agents were used for the oligomeriation of nucleotide monomers on a template nucleotide polymer although these reactions are normally not so efficient [36-40]. These condensation agents are not considered as prebiotic so cyclic 2′, 3′-phosphate were also verified [41, 42]. Recently, the acceptable prebiotic pathway of 2′, 3′-cyclic pyrimidine nucleotide monomers was proposed, which might have been an activated nucleotide monomer for oligoucleotides [43]. Very recently, nucleoside 3′, 5′-cyclicmonophosphate was used to

produce oligonucleotides at medium temperatures, where oligonucleotides were detected using gel electrophoresis [44].

Enzyme	Monomer	Template
Ribonuclease	Nucleoside 5′-triphosphate	DNA
Qβ replicase	Nucleoside 5′-triphosphate	RNA
Polynucleotide phosphorylase	Nucleoside 5′-diphosphate	No template

Table 1. Formation of RNA in the presence of different types of enzymes.

It was not successful for an efficient template-directed formation of oligonucleotides from nucleoside 5′-monophosphate monomers [36-40, 45] or using an activated nucleotide intermediate [46] in the presence of the condensation agent. Finally, it was discovered an acceptable primitive activated nucleotide monomer, that is, nucleotide 5′-monophosphorimidazolide (ImpN) (Figure 5), which is activated with N-P bound on the phosphate group of the nucleotide monomer [47-49]. For instance, adenosine 5′-monophophorimidazolide (ImpA) forms oligoadenylate (oligoA) in the presence of Zn^{2+}without a template [50] and guanosine 5′-monophosphorimidazolide (ImpG) forms efficiently oligoguanylate (oligoG) up to 40 nucleotide units in the presence of a polycytidylic acid template (polyC) without using enzyme in the presence of Pb^{2+}or Zn^{2+}[51, 52]. The prebiotic RNA formation reactions in detail will be summarized in the following sections.

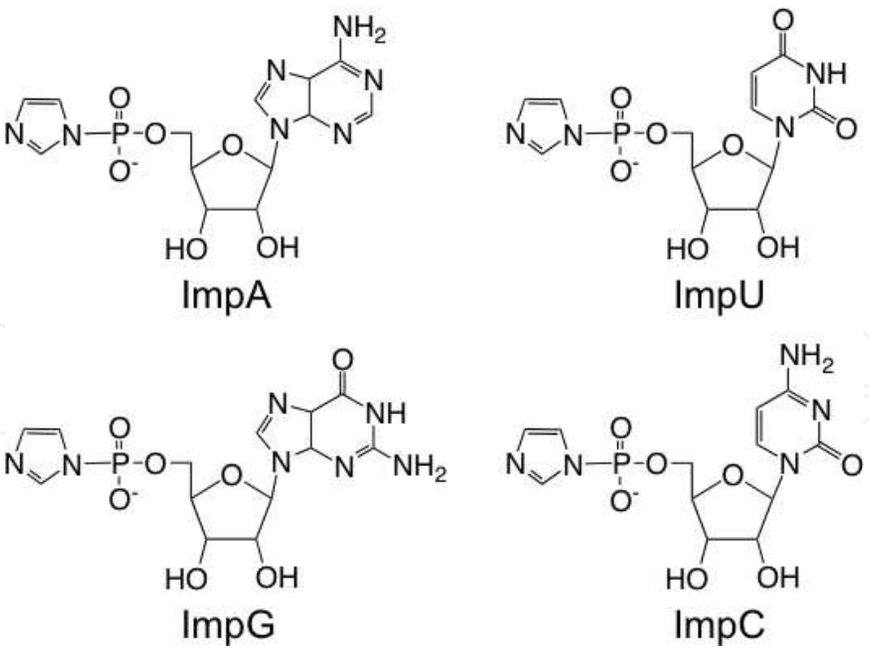


Figure 5. Activated nucleotide monomers

The details and variation of the reaction using activated nucleotide monomers have been extensively investigated in the absence and presence of template, in the presence of metal ion

catalysts, clay mineral catalysts, using different types of activated nucleotide monomers, using non-ribose based nucleotide analogues. As a variation of ImpN, nucleoside 5′-monophospho-2-methylimidazolde (2MeImpN) has been frequently used [53].

4.2. Prebiotic formation and organic synthesis of the activated nucleotide monomer

It was successfully demonstrated that oligonucleotides form from the activated nucleotide monomers without enzyme. However, the formation of the activated nucleotide under the primitive earth conditions is also an important issue. Possible pathways for the spontaneous formation of the activated nucleotide had been barely elucidated [48, 54, 55]. However, the accumulation of the activated nucleotide monomers would not be so likely since the moisture controlled N-P bond formation and the formation of nucleotide phosphate under dry conditions are included [54]. Furthermore, the activated nucleotide monomers are substantially hydrolyzed to nucleoside 5′-monophosphate [56]. The yield of the activated nucleotide monomers formed under these simulation conditions is not so high that the simulation experiments of oligonucleotide formation from the activated nucleotide monomers under the primitive earth are normally carried out using a sufficient amount of the activated nucleotide monomers, such as ImpN, which are prepared using an organic synthetic technique. Organic synthesis of ImpN was established and the yields of ImpN and the analogues are normally over 95 % by coupling method using a sulfide compound [57].

4.3. Spontaneous formation of oligonucleotide using metal catalyst (Metal-catalyzed reaction)

Spontaneous oligomerization of the activated nucleotide monomers should be a next step for the chemical evolution of oligonucleotide once these formed under the primitive earth conditions. A spontaneous formation pathway in the presence of metal ion catalysts was found for the first time (Figure 6) [50, 58]. The maximum length of the oligonucleotide formed by the Metal-catalyzed reaction of RNA reaches to ca. 10-mer nucleotide units [59-61]. The efficiency of Metal-catalyzed reaction is less dependent on the type of nucleotide bases. Catalytic metal ions, such as Zn^{2+}, Pb^{2+}, and UO_2^{2+}, are normally active at fairly high concentrations in the simulation experiments as comparing to the concentration in the present ocean. Regioselective formation of 3′, 5′-or 2′, 5′-linked oligonucleotides has been observed that the formation of 2′, 5′-linked oligonucleotide is preferable using Pb^{2+}or $UO_2^{2+}$and that of 3′, 5′-linked oligonucleotide is preferable using Zn^{2+}[50, 59-61]. Although the reason 3′, 5′-linked RNA oligonucelotide was selected by the chemical evolution of RNA is not yet established, these experimental data would be related to the reason 3′, 5′-linked olignucelotide was selected. In addition, it is pointed out that the 2′, 5′-linked oligonucelotide formation was applied to a practical synthetic method of 2′, 5′-linked oligonucleotide [59]. Mechanistic analysis of Metal-catalyzed reactions suggested that the acceleration by metal ions is due to the formation of the metal ions with phosphate group and/or bases, which enhance the association between two monomers or that between a monomer and an elongating oligomer prior to the phosphodiester bond formation [62].

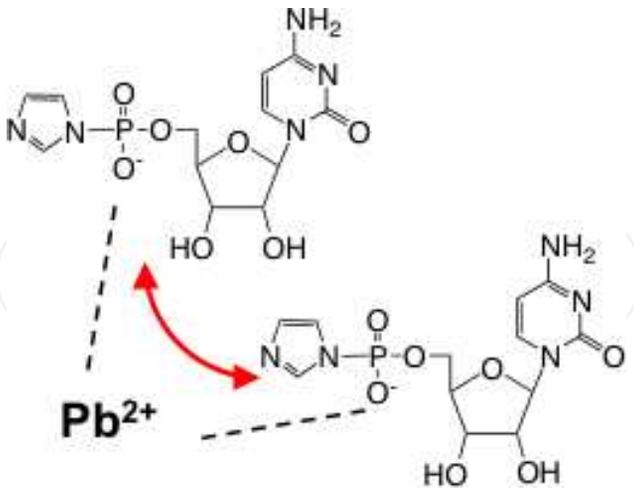


Figure 6. Metal-catalyzed reaction

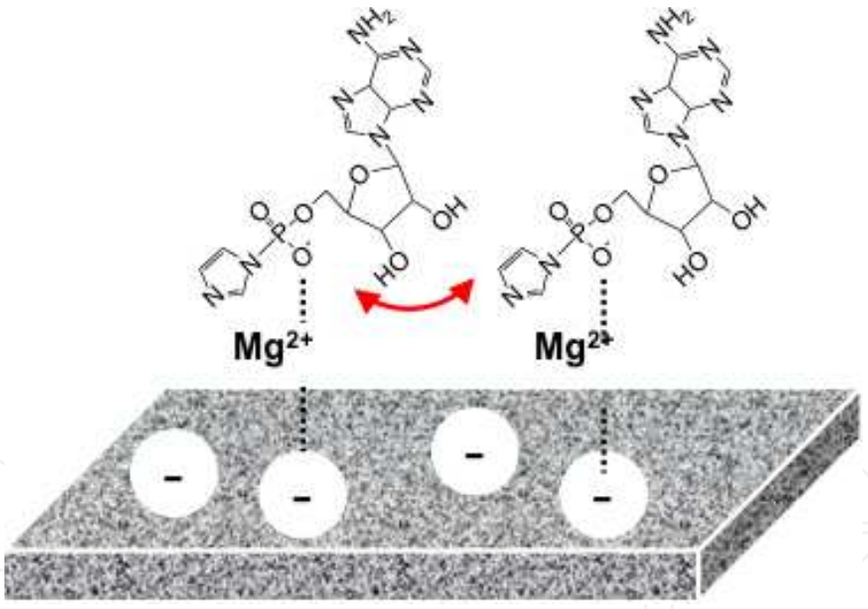


Figure 7. RNA formation of montmorillonite clay

4.4. Spontaneous formation of oligonucleotide using clay catalyst (Clay-catalyzed reaction)

The importance of minerals for the chemical evolution of biomolecules and biopolymers was frequently assumed from old days [63]. Thus, the simulation experiments of oligonucleotide formation have been extensively carried out [64-66]. An efficient formation of oligonucleotide

on a clay mineral, naturally-occurring montmorillonite, was discovered for the first time at 1992 and the reaction was extensively investigated [67]. The oligonucleotides up to ca. 10-mer nucleotide monomer units are formed spontaneously in one pot reaction in the presence of montmorillonite catalyst. The efficiency of Clay-catalyzed reaction is somewhat dependent on the type of nucleotide bases; the formation of oligoguanylate (oligoA) is somewhat less effective as comparing to the others [68-71]. By these reactions, both the 2′, 5′-linked and 3′, 5′-linked oligonucleotides form and pyrophosphate-linked isomers were observed. There is a trend that the oligonucleotides formed from ImpN consisting of purine base involve mainly 3′, 5′-linked isomers and those formed from ImpN consisting of pyrimidine base involve mainly 2′, 5′-linked isomers. The percentage of pyrophosphate-linked isomers is normally small.

Furthermore, it is noted that a fairly large amount of cyclic oligonucleotides, such as cyclic-2-mer, cyclic-3-mer, and cyclic-4-mer, are generally observed. The ratio of the cyclic isomers is also dependent on the type of nucleotide bases [70]. For instance, the 2-mer fraction on an anion-exchange HPLC column of the products using ImpU and ImpI involves 60 – 96% of cyclic-3-mers. Longer cyclic oligomers are also observed in higher length fractions. The cyclization of nucleotide 6-mer and higher oligomers, which possess phosphate group at 5′-terminal and 2′-OH at 3′-terminal, was observed in the presence of condensation agent [72, 73]; this reaction was designed for the competition reaction between elongation and cyclization. The cyclization of oligonucleotides is considered as termination reaction for the chemical evolution of RNA.

The oligonucleotide formation proceeds using different sources of montmorillonite, but the oligonucleotide formation does not proceed at all using a clay from Otay [69]. The binding of ImpN on different clay mineral is observed in these reaction systems, and there is a strong correlation between the yield of oligonucleotide and the binding constant of the activated nucleotide monomer on the clay. Thus, binding is necessary step for the acceleration of oligonucleotide formation on the clay. The activated nucleotide monomer is bound to the surface of montmorillonite ca. 80%, where negative charges are present, and bound to the edge of the montmorillonite 20% [74]. The activated nucleotide monomer is bound through Mg^{2+}ion bridge, which forms complex with phosphorimidazolide group (Figure 7) [69]. Low efficiency of oligonucleotide formation in the absence of Mg^{2+}supports the Mg^{2+}bridge binding model, and Ca^{2+}ion can also form the bridge [69].

On the other hand, the binding of the activated nucleotide monomers is fairly dependent on the types of nucleotide bases [69, 70]. The strength of binding of ImpN consisting of purine base is larger than that consisting of pyrimidine base. Although the apparent binding ratio of ImpC and ImpU on the clay is very low, the yields of oligonucleotide are not much different from those of ImpA and ImpG. This fact suggests that the apparent binding of ImpN includes an effective and non-effective binding on the clay mineral for the oligonucleotide formation. Non-effective binding reflects that the binding is dependent on the hydrophobicity and staking by nucleotide bases.

By using Clay-catalyzed reaction, it was elucidated that oligonucleotides up to ca. 50-mer nucleotide units form by a continuous feeding of ImpN to the montmorillonite-aqueous

solution system [75]. Furthermore, a ImpN analogue replaced the imidazole moiety with purine derivative forms oligonucleotides with ca. 50-mer nucleotide units in one-step reaction [76, 77]. The modifications of Clay-catalyzed reaction indicate that oligonucleotides could have accumulated under the primitive earth conditions if the conditions were mild as present.

The reaction mechanism of Clay-catalyzed reaction was extensively investigated on the basis of reaction kinetics and binding thermodynamics. The binding of ImpN or analogues is the first step for the formation of oligonucleotides. Mg^{2+}ions are necessary for the binding of ImpN through the bridge with Mg^{2+}, which attaches to phosphate group of ImpN on the negatively charged clay surface [69, 74]. Kinetic analysis showed that the formation rate constant of 2-mer is much smaller than that of 3-mer and longer oligonucleotides. This fact would suggest that the association of two ImpN molecules to form 2-mer is much weaker than that of ImpN with elongating olignucleotide. A similar trend was observed in the cases of Metal-catalyzed reaction [62]. The regioselectivity of 2′, 5′-or 3′, 5′-linked isomers using pyrimidine or purine ImpN is probably due to the different binding conformation of the activated nucleotide monomer on clay surface. During the oligomerization, the hydrolysis of ImpN simultaneously proceeds, but the formation of oligonucleotide is much faster than that of ImpN hydrolysis.

4.5. Template-directed formation of oligonucleotide (Template-directed reaction)

According to the scenario of chemical evolution of RNA, the replication of oligonucleotides should be a next step after the spontaneous formation of oligonucelotides by Metal-catalyzed and Clay-catalyzed reactions since the replication of RNA would have resulted in the replication of genetic information. Orgel and coworkers showed that template-directed formation of oligoG from ImpG or 2MeImpG on a polyC without using any enzyme (Figure 8) [51-53]. These reactions produce oligonucleotides up to ca. 40-mer. The efficiency of Template-directed reaction using ImpG is dependent on metal ions, where Pb^{2+}ion catalyzes the 2′, 5′-linked oligoG and Zn^{2+}ion catalyzes the 3′, 5′-linked oligoG. It is interesting that $Zn^{2+}$is present in the active center of modern RNA polymerase (Figure 9) [78]. Besides, 2MeImpG forms 3′, 5′-linked oligoG without using any metal ions. Formation of cyclic isomers is less in Template-directed reaction while the cyclic 2-mer, 3-mer, and higher oligomers are frequently observed for Clay-catalyzed reactions. The Template-directed reaction is dependent on pH and temperature. Normally, the efficiency of the reaction is highest at around pH 8 [53]. This is due to the activity of the activity of the activated nucleotide monomers.

It is noted that Template-directed reactions using different ImpN or 2MeImpN with different nucleotide bases, that is, adenine, uracil, and cytosine do efficiently not proceed to form oligonucleotides; oligoA forms with very low efficient from ImpA on polyU template [49] and oligoU and oligoC are not formed at all from ImpU and ImpC on a complementary template. The low efficiency using activated nucleotide monomers is probably due to that the association between two ImpN molecules or that between ImpN and an elongating oligonucleotide on a complementary template is very weak for ImpN consisting of adenine, uridine, or cytidine base.

A possible pathway was demonstrated that Template-directed reaction from a mixture of 4 types of ImpN with different bases on a template including complementary bases enable to

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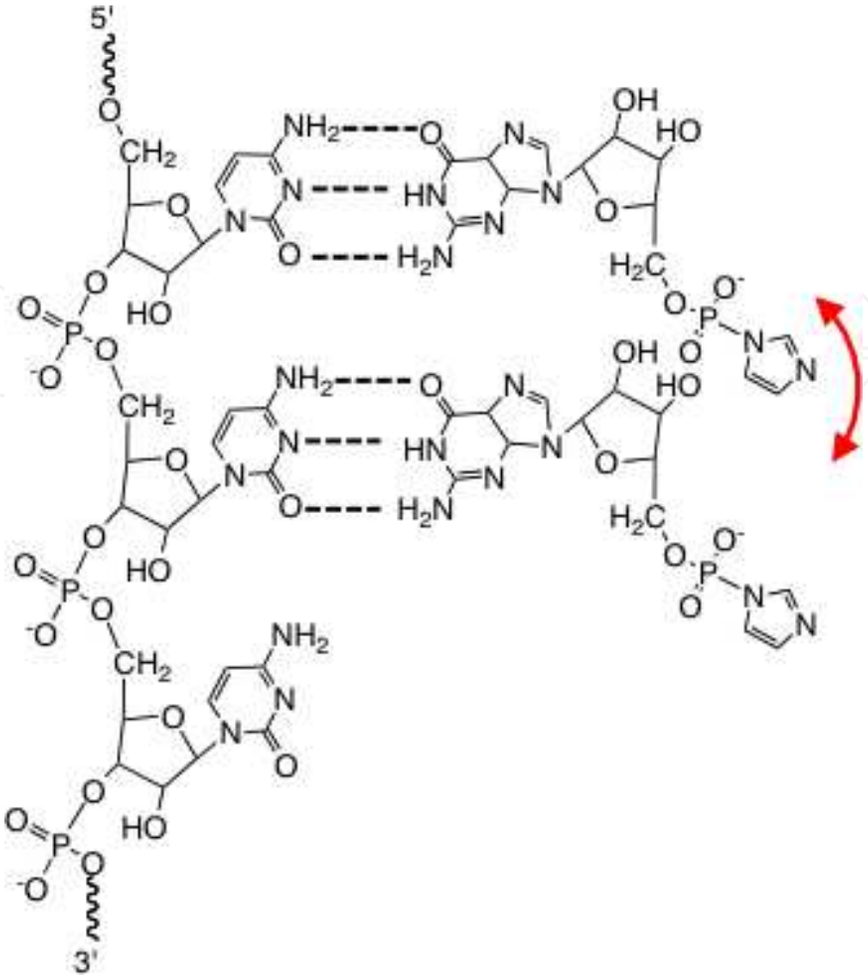


Figure 8. Template-directed formation of RNA

partially incorporate different bases in the oligonucleotides other than oligoG [57, 79]. The efficiency of the Template-directed reaction increases with increasing of the ratio of cytidine of the template. In addition, it was confirmed that Template-directed reaction using ImpA, ImpU, and ImpC would partially proceeds using hairpin oligonucleotides [80]. Furthermore, Template-directed reaction proceeds if the activated oligoU is used as starting material on a polyA template, of which the association of oligoU would be stronger than that of ImpU monomers [81]. Although these results suggest that Template-directed reaction partially proceeds in mixed oligonucleotides, thus the fidelity of Template-directed reaction is not high. The limitaition of Template-directed reaction as prebiotic formation of RNA has been pointed out [82]. In other words, these facts would suggest that there is still a drawback how the replication of oligonucleotide could have proceeded in the absence of enzyme. In addition, protocell and vesicles could have enhanced the chemical evolution of RNA molecules [83, 84]. Conclusively, a universal pathway for the replication using activated nucleotide monomers is not yet identified.

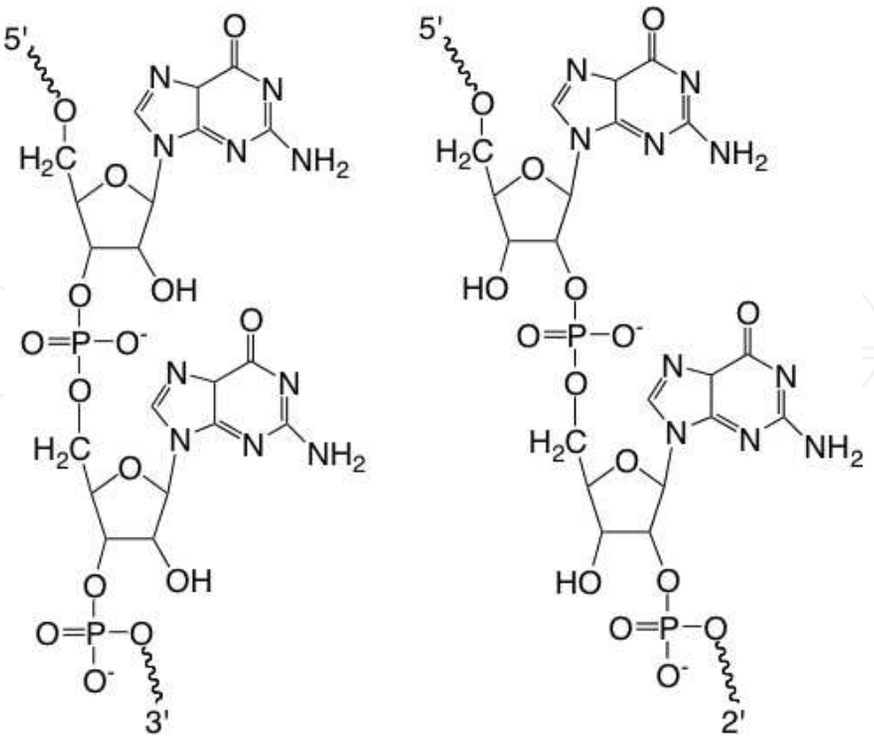


Figure 9. 3′, 5′-linked (left) and 2′, 5′-linked (right) RNA

4.6. Kinetic analysis of prebiotic oligonucleotide formation

First, the reaction mechanism of Template-directed reaction has been extensively investigated on the basis of kinetic analysis [85]. The rate constants for the formation of 2-mer, 3-mer and longer increase in the order 2-mer << 3-mer < 4-mer and higher. The hydrolysis of the activated nucleotide proceeds simultaneously to the oligomerization (Figure 10) [56, 85]. The rate constants of oligomerization are greater than that of hydrolysis in the presence of template. The association between two activated monomers and that between activated monomer and the elongating oligoG is important for the oligonucleotide formation. A similar trend was observed for Clay-catalyzed reaction [69, 70]. This was evaluated in detail and kinetic analysis in details showed a trend that two or three activated nucleotide monomers align on the polyC template prior to the phosphodiester bond formation [85]. For instance, the association between two ImpG molecules would be stronger than that between two ImpC molecules, which is determined by the strength of stacking of nucleotide bases. This is compatible to the fact that the efficiency of Template-directed reaction with ImpA, ImpU, and/or ImpC is much lower than Template-directed reaction with ImpG.

On the other hand, kinetic analysis of the reaction mechanism of Clay-catalyzed reaction showed that the rate constants for the formation of 2-mer, 3-mer, and 4-mer and higher oligonucleotide increase in the order of 2-mer < 3-mer < 4-mer and higher; this trend is consistent with Template-directed reaction [69, 70]. Thus, the hydrolysis of the activated nucleotide monomer is somewhat competitive reaction to the oligomerization in the presence of clay. The kinetics suggested that the association between two activation monomers and that

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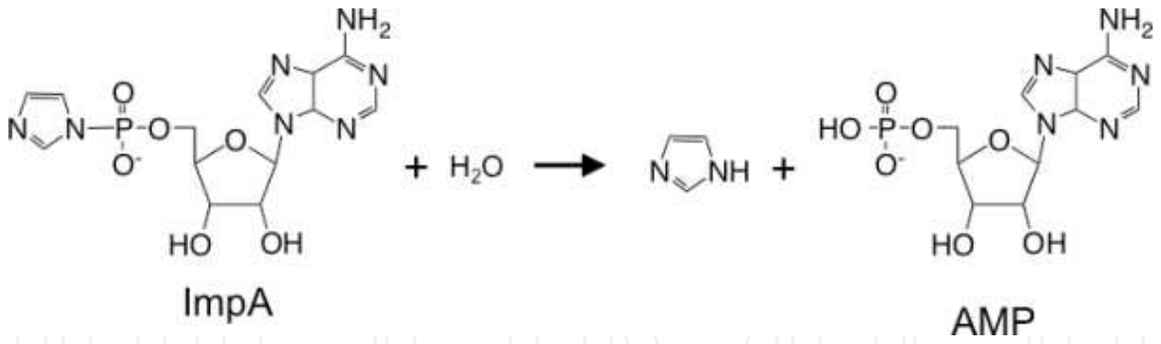


Figure 10. Hydrolytic degradation of the activated nucleotide

between activated monomer and elongating oligomer are important to determine the rate constants of 2-mer, 3-mer, and 4-mer formations, which is similar to Template-directed reaction. The association is mainly due to the stacking through nucleotide bases, which increases with length of oligonucleotide up to 4-mer and remains constant. Kinetic analysis of Metal-catalyzed reaction also implies a similar mechanism to that for Template-directed and Clay-catalyzed reactions (Figure 11). Conclusively, the kinetic investigations summarize that the association of an activated nucleotide monomer with another one activated nucleotide monomer or an elongating oligomer is important to determine the efficiency of oligomerization in the presence of any additives, such as a polynucleotide template, clay surface, and metal ions.

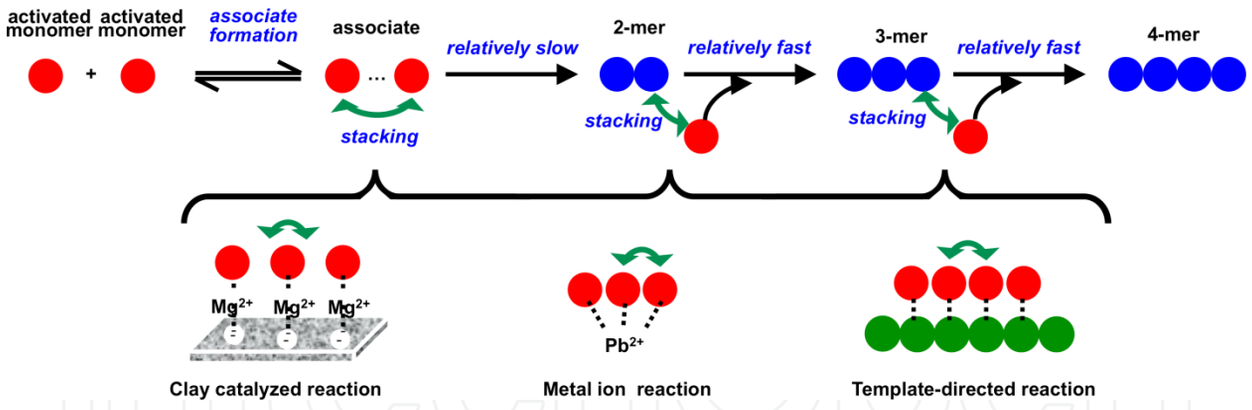


Figure 11. Importance of associate formation for oligonucleotide elongation

4.7. Variations of the activated nucleotide monomers

The activated nucleotide monomers with N-P bond were normally tested using ImpN or 2MeImpN, where imidazole and 2-methylimidazole moieties are the leaving group from N-P bound with phosphate group. Although the methyl group does not seem to be so effective, this causes fairly large influence for the formation of long oligonucleotides [86]. For instance, the efficiency of Template-directed reaction using 2MImpG in the absence of metal catalyst is higher than that using ImpG. This is probably due to the enhancement of association between

monomers or that between monomer and elongating oligomer by stacking of 2-methyl-imidazole. The solubility of 2MeImpN is lower than that of ImpN in aqueous solutions. Both imidazole and 2-methy-limidazole are potentially prebiotic compounds. Analogues of ImpN with different leaving group were examined. It was found that the efficiency of the oligonucleotide formation using different leaving group with N-P bond is correlated to the acidity of the leading group. Oligonucleotide formation indeed proceeds efficiently using such ImpN analogues for Clay-catalyzed reactions, where higher oligonucleotides were observed in some cases (Figure 12) [87, 88]. These studies suggest that a variation of pathways should have been possible for the formation of RNA under the primitive earth conditions.

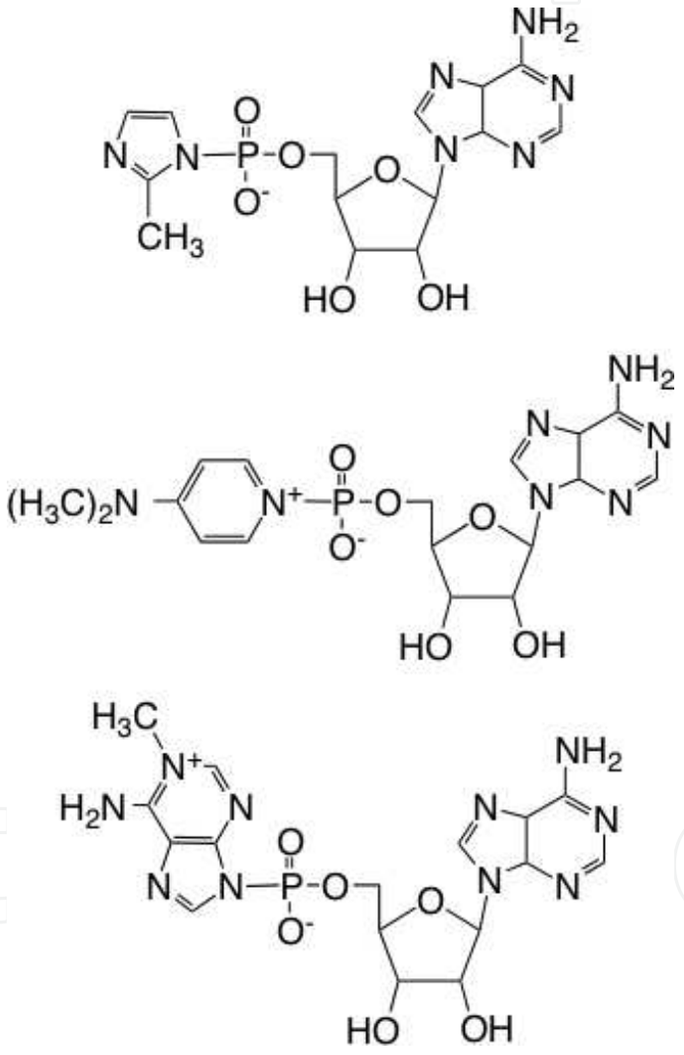


Figure 12. Variations of the activated nucleotide

On the other hand, it is claimed that RNA would not be suitable as an initial material to preserve genetic information since ribose as an RNA moiety is considered normally difficult to form under the primitive earth conditions. Ribose does not form efficiently under prebiotic conditions although many types of sugars are readily formed by formose reaction [89, 90]; it is

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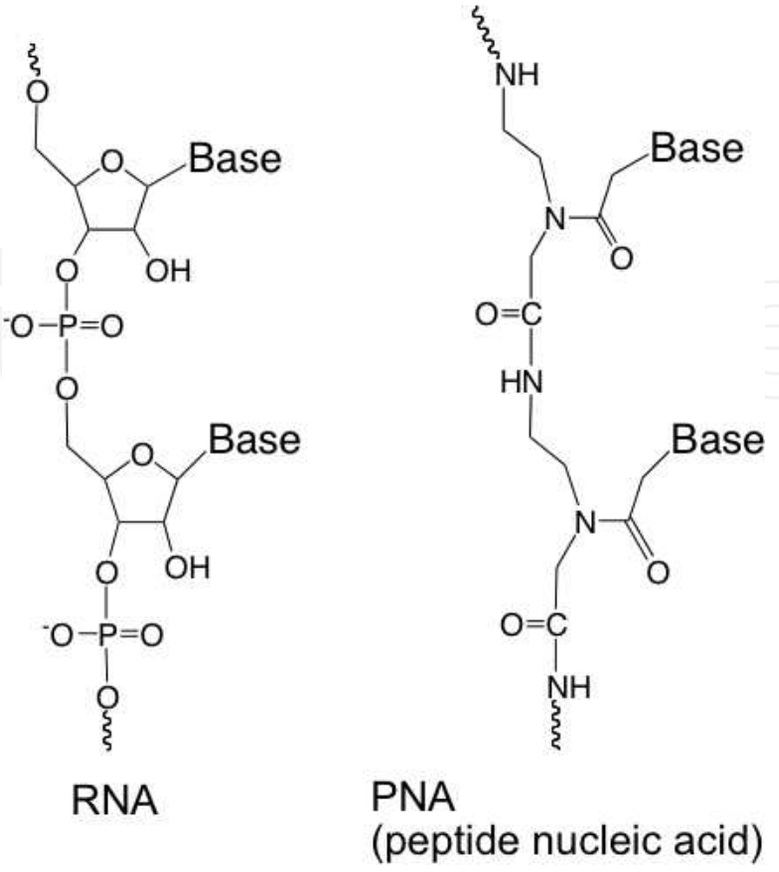


Figure 13. RBA and peptide nucleic acid

considered as a major pathway for the formation of sugars. In addition, RNA is considered unstable as comparing to hexose. Naturally, the nucleotide analogues of RNA instead of ribose could be formed under prebiotic conditions. Furthermore, the backbone of phosphodiester bond could be replaced with peptide bonding backbone [91-93] (Figure 13). These possibilities were also experimentally verified. Conclusively, the reactions of the activated nucleotide analogues using hexose backbone also proceed to form oligonucleotide analogues using Template-directed reaction [94, 95]. These examples suggest that template direction could have played important roles in a variety of analogical materials under the prebiotic conditions.

Finally, as mentioned above, it is known that ImpN monomers consisting of deoxyribose do not form oligonucleotides since the reactivity of ImpN with deoxyribose is very low. This is due to the less reactivity of 2'-H group of ribose. The formation of DNA from such activated nucleotide monomers is not yet deeply investigated since DNA molecules are not considered as initial genetic material on the primitive earth.

4.8. Chiral selection of oligonucleotide using the prebiotic RNA formation models

The RNA polymerization model reactions were extensively studied. Normally, these studies were normally carried out using homochiral materials because of the difficulty of preparation of starting materials. The selection of a single chirality, which is L-ribose for the present nucleic

acid, is a great issue in the field of the origin of life study. Although this question is not yet solved, some attempts were carried out for the evaluation of the efficiency of Template-directed, Clay-catalyzed, and Metal-catalyzed reactions by using heterochiral materials [96-99]. The preparation of the activated nucleotide monomers with L-ribose was succeeded although it involves very complicated organic synthetic procedures. These reactions showed that the homochiral oligomerization is preferable instead of the heterochiral oligomerization for both the Clay-catalyzed and Template-directed reactions. The results would imply the reason how homochiral biochemistry was selected during the chemical evolution of nucleotide and abiotic-peptide (Figure 14).

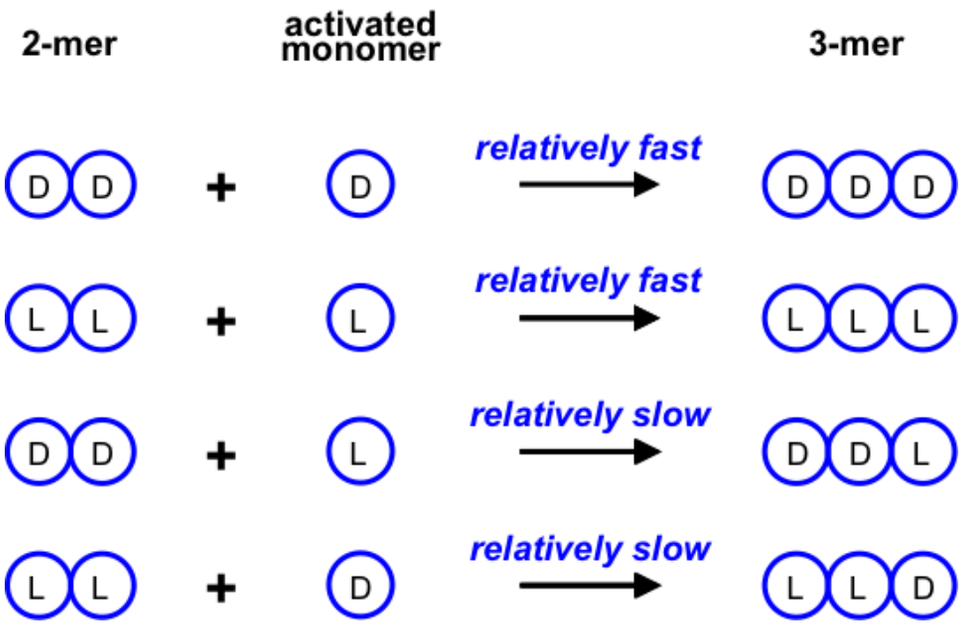


Figure 14. Homochiral selectivity for prebiotic RNA formation

4.9. Temperature dependence of the pebiotic oligomerization at medium to high temperature

According to the evidences of geoscience, the temperature of the primitive earth would be much higher than that of present. In addition, submarine hydrothermal vent system would have been present and played important roles for the emergence of life and the last universal common ancestor, which is deduced from phylogenetic tree analysis, could be close to hyperthermophiles [100, 101]. Naturally, the heterogeneity of the primitive earth environment should be considered so the previous studies on the formation of RNA are regarded to bias very mild conditions. As mentioned above, the oligomeriation of the activated nucleotide monomers does not proceed in acidic and alkaline solutions because of the hydrolysis of the activated nucleotide. Besides, the temperature dependence of these reactions was extensively investigated in relation to the hydrothermal origin of life hypothesis.

In general, the efficiency of oligonucleotide formation by Metal-catalyzed, Clay-catalyzed, and Template-directed reactions decreases with increasing temperature. Kinetic analyses clarified successfully the reason of the low efficiency at high temperatures [102-104]. The investigations provided the rate constants regarding these reaction systems, that is, the formation of oligomers 2-mer (k_2), 3-mer (k_3), 4-mer (k_4), the hydrolysis of the activated nucleotide (k_{hy}), the formation of pyrophosphate-linkage (k_{py}), and the hydrolysis of oligonucleotide formed by these prebiotic oligomerizations. Comparison of the temperature dependence of k_2, k_3, k_4 shows that k_2 has a smaller activation energy than that for k_3 and k_4. In addition, the relative magnitude of k_2 becomes small as comparing to k_{hy} with increasing temperature although that of k_3 and k_4 does not; the activation energy for k_2 is smaller thant that for k_{hy}, but that for k_3 and k_4 is comparable to that for k_{hy}. The main reason of low efficiency of oligonucleotide formation at high temperature is that the formation of 2-mer becomes relatively slow as comparing to the hydrolysis of the activated nucleotide at high temperature.

The similar trend was observed for Metal-catalyzed and Clay-catalyzed reactions on the basis of kinetic analysis [103, 104]. In addition, the association does not only affect the efficiency of these reactions but also the regioselectivity, and effective to the formation of cyclic-isomers. The fact that the formation of DNA double-helix is primarily stabilized by the base-stacking rather than hydrogen bonding is minor factor [105] is consistent with the trend in the primitive RNA formation reactions. These analyses suggest that the accumulation of the activated nucleotide monomer would be difficult at high temperatures since the hydrolysis of the activation nucleotide becomes fast unless the activated nucleotide monomers are continuously supplied by a plausible pathway. Nevertheless, such conformation of DNA and RNA must be held at high temperatures since a thermophilic organism could survive at least 100-120 °C [106, 107].

5. Successful examples of the formation of abiotic-peptides

5.1. Introduction

Proteins are regarded the practical entity for maintaining life-like system while DNA in the present organisms or the primitive RNA in RNA worlds is regarded as blueprint of life-like systems. The question, which was the first material between nucleic acids and proteins for the emergence of life-like system on the primitive earth, has been controversy for many years although this might be solved by the proposal of the RNA world hypothesis. However, there are a number of drawbacks regarding the RNA world hypothesis so the question is continuously discussed. As mentioned above, the term ”protein” in the present chapter involves the meaning that protein must be a functional material, which is synthesized on the basis of genetic information. If a protein-like molecule is merely consisting of peptide, but the sequence is not encoded in a genetic coding system, the material is called as just abiotic-peptide. As mentioned, such peptides are called as abiotic-peptides to distinguish from the peptides possessing biological functions *in vivo*. Naturally, for instance, this is not inconsistent with a hypothesis that both the RNA and protein-like molecules formed independently and became interrelated only after the accumulations of these molecules.

In the first place, abiotic-peptide formation from amino acids is also the dehydration so this is not preferable in aqueous medium unless using the activation of amino acid or a condensation agent. Peptides are normally regarded more stable against the hydrolysis as comparing to nucleic acids although peptides in aqueous medium are normally exposed under the pressure to hydrolytic degradation. In the present organisms, peptides form on ribosomes from aminoacyl-tRNA, which is regarded as activation of amino acid activation. Furthermore, condensation agent and activation techniques are used for modern organic synthesis of peptides. Thus, it should be noted that abiotic-peptides do not form spontaneously from the viewpoint of thermodynamics even if amino acids are mixed in aqueous medium. This is the same situation as the oligomerization of DNA and RNA.

5.2. Thermal condensation of amino acid mixture

Spontaneous condensation of amino acid mixtures does not or less proceeds in aqueous solutions. This is due to that dehydration is disadvantageous in aqueous medium. It was found that thermal condensation products form from amino acid mixtures, such as glutamic acid and aspartic acid, under dry conditions at temperatures 180-200 °C [108-110] (Figure. 15). Microspheres can be formed by treatment of the condensation products in boiling water; the microspheres were named as proteinoid. It is surprising that these condensation products readily form with normally molecular weight over 10000 Da involving peptide bonding, but the peptide bonds are not controlled; probably branched sequences and non-peptide bonding would be involved. Lacton formed by heating glutamic acid etc. is melted at high temperatures, where other amino acids are dissolved and then result in polymerization. The biochemical functions of proteinoids have been extensively investigated [111-113].

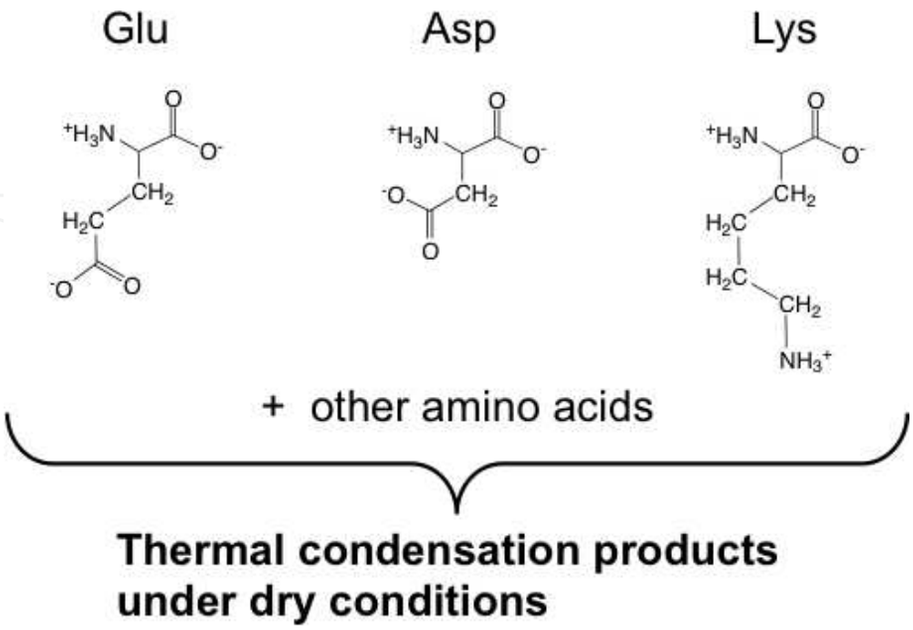


Figure 15. Thermal condensation of amino acids

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Although the proteinoids involve partially peptide bonding, proteinoids might not reflect a plausible ancient accumulation pathway of protein-like molecules since large continents were not present on the primitive earth. The question how the proteinoids containing peptide bonding incompletely had evolved to the modern proteins is a great drawback. In addition, as mentioned above these condensation products are not categorized as proteins since these are not synthesized by the direction of genetic information. Normally, it is realized that protein does not replicate alone. Furthermore, these condensation products do not seem to be useful in an organic synthetic method. Thus, the research regarding the thermal condensation of amino acids does not progress so far.

5.3. Formation of protein-like and abiotic-peptide molecules in aqueous medium

The condensation from amino acids to form peptide bonding is disadvantageous in aqueous medium [114]. Activation of amino acids or usage of a condensation agent is necessary for peptide bond formation [115-120]. Thus, the pathways for oligopeptides have been investigated as simulation experiments under the primitive earth environments. Several types of minerals and metal ions were evaluated to see whether these materials enhance the formation of long oligopeptides. Nevertheless, the plausible oligomerization has met with limited success [119].

5.4. Hydrothermal synthesis of oligpeptides

Presumably, the temperature of the primitive earth surface should have been much higher than present. Furthermore, the phylogenetic analysis of present organisms suggested that last universal common ancestor (LUCA), which is located to the branches between Bacteria and Archaea, would have been a hyperthermophilic organism [100, 101] although this assumption is still strongly disputed [121, 122]. The importance of such hydrothermal systems has been extensively investigated [123]. The hypothesis is named as “hydrothermal origin of life hypothesis”. Although LUCA is not the origin of life, it would reflect old organisms and the environments, where life had emerged. Recent discoveries of ecosystem present near submarine hydrothermal vent systems in deep-ocean support the hydrothermal origin of life hypothesis [124]. Thus, simulation experiments have been carried out for the formation of oligopeptides under the hydrothermal conditions using batch reactors at the beginning of such simulation experiments. Condensation products, which involve peptide bonding and bonding between silicate and organic materials, were observed in the products [125].

Recently, flow reactors were developed and behaviors of biomolecules in hydrothermal systems have been extensively investigated to simulate the submarine vent system in deep-ocean [126]. The simulation experiment showed that oligopeptides are formed from glycine monomers at temperature over 250 °C, where oligoglycine up to 6 amino acid units was detected. The efficiency of the direct oligopeptide formation from amino acid is normally low; the maximum yield is normally 0.1 – 1 % at most [126, 127]. The reason is due to primarily the fact that dehydration in aqueous solution is not advantageous so that the oligopeptides once produced are always exposed under the degradation pressure. In addition, the formation of diketopierazine (DKP) inhibits the further elongation of oligopeptides (Figure 16); DKP is

cyclic dipeptide and considered as very stable. Rapid accumulation of DKP from glycine is also observed in the simulation reaction of submarine vent system.

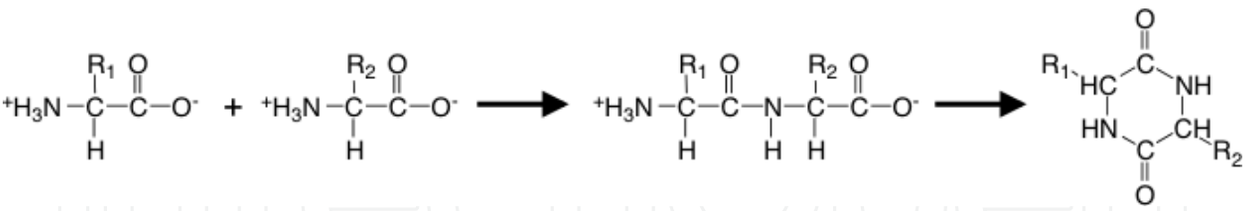


Figure 16. DKP formation from amino acids

On the other hand, in our group, a hydrothermal micro flow reactor using fused-silica capillary has been developed (Figure 17) [128-130]. This enables to monitor hydrothermal reactions at temperature up to 400 °C at time scale between 2 ms – 200 s. By using the flow reactor, a more efficient elongation of 4-mer and 5-mer of alanine to 5-mer and 6-mer was discovered at 250 – 310 °C within 5 – 20 s [131]. Furthermore, it was found that oligopeptides including 20 amino acid units form within 180 s at temperatures 270 – 310 °C [132]. These reactions were designed to avoid the formation of DKP during the direct oligomerization of monomeric amino acids; the formation of DKP is regarded as a problem for the organic synthesis of peptide. DKP readily forms from dipeptide at high temperatures, for instance DKP forms from alanine dipeptide within 10 s at 275 °C (Figure 18). On the contrary, DKP formation is relatively slow if the elongation starts from 4-mer and 5-mer of alanine. In these reactions, 4-mer and 5-mer are converted to DKP finally, but the DKP formation is relatively slow. Thus the elongation of these peptides is observed during the conversion of the 4-mer and 5-me to DKP. The reaction scheme is shown in Figure 18. The elongation yield reaches to 10 %, which is ca. 100-fold greater than that of direct formation from monomeric amino acids. This is surprising since neither condensation reagent nor catalyst is necessary. The kinetic analysis implies that peptide bond within 4-mer would compensate the elongation of peptide bonding to form 5-mer at very high temperatures.

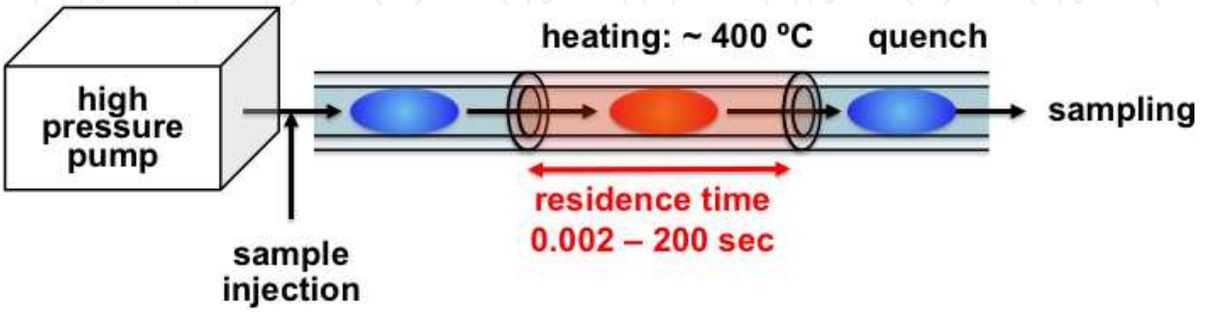


Figure 17. Principle of hydrothermal flow reactor

To investigate the role of minerals under hydrothermal conditions, a new type of flow reactor technique was established in our group [133]. The system consisting a mineral-packed column

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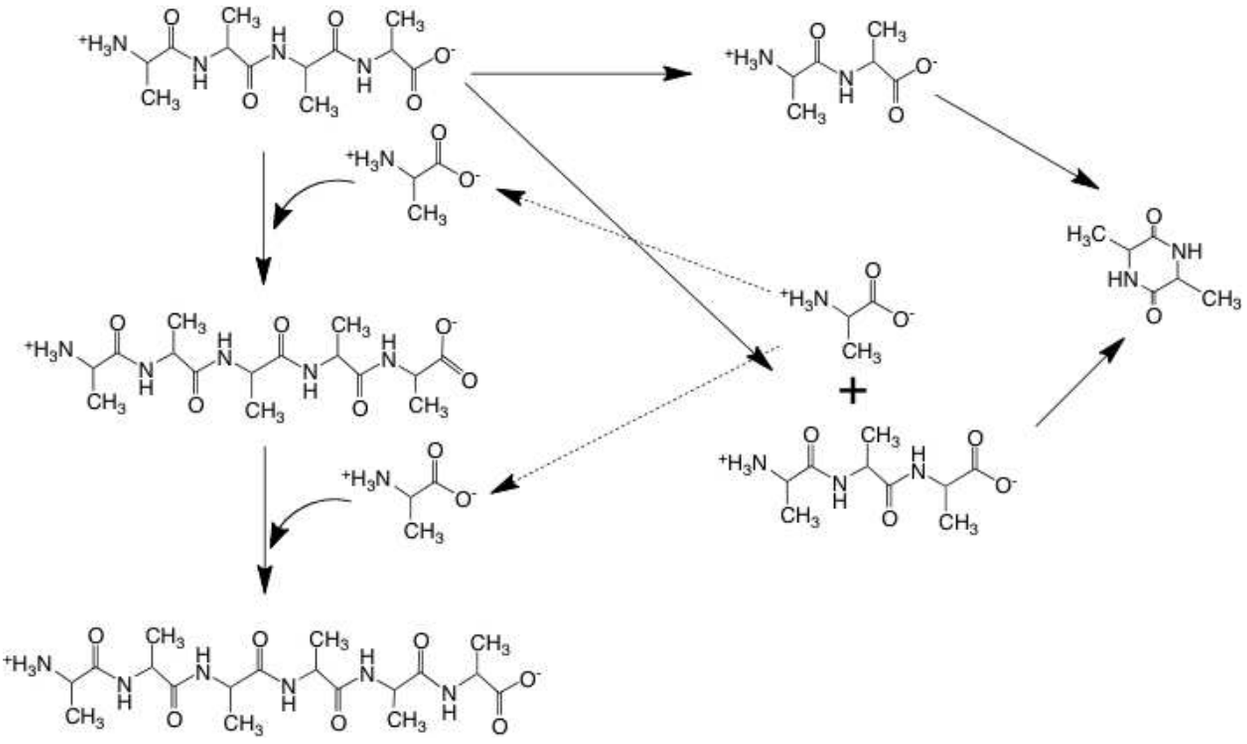


Figure 18. Pathways of elongation and degradation of oligopeptides

reactor is settled in a high temperature heating system. This system enables to monitor hydrothermal reactions at temperatures up to 300 °C at the time scale 2 – 200 s in the presence of mineral particles. By using the method, it was discovered that the oligopeptide elongation reaction from alanine 4-mer to 5-mer within 5 – 20 s is notably enhanced by naturally-occurring carbonate minerals, such as calcite and dolomite.

6. Unsolved drawbacks regarding the origin of building blocks for a primitive life-like system

6.1. General difficulties of oligomerization of nucleic acids and abiotic-peptides

First, the dehydration in aqueous solution is disadvantageous from the viewpoint of thermodynamics. As we evaluated the difficulties of oligonucleotides and oligopeptides in a former section, activation method is a key technique to form long oligomers. For the case of nucleotide, the activated nucleotide monomer, that is, imidazolide of nucleoside 5′-monophosphate is useful material. However, the prebiotic activation method, which is regarded as compatible to the primitive earth environments, is not identified for the peptide formation. Aminoacyl-tRNA is universally used in the present organisms and some minerals would have played roles for activation or condensation agents for the oligopeptide formation. However, these possibilities are not yet extensively evaluated.

Second, it is generally true that the formation of short cyclic-oligonucleotides [70, 72, 73, 134] and DKP [131] inhibits the further elongation of oligomers (Figure 19). The cyclization of oligonucleotides is completely controlled by RNA polymerase and peptide synthetic method on ribosomes *in vivo*. Nucleic acid templates, mineral catalysts, and metal ion catalysts tend to inhibit the cyclization reaction. The additives probably enhance suitable steric alignment of monomers to inhibit cyclization although the general rules for inhibition of cyclization are not elucidated. Actually as a primitive oligomerization, there is less cyclic-dinucleotide for the formation of oligoG in Template-directed reaction. This is probably due to Watson-Crick type hydrogen bonding and base stacking. On the contrary, cyclic-2-mer, 3-mer, and 4-mer somewhat readily form in Clay-catalyzed reactions. On the other hand, the elongation from 4mer or higher is effective for inhibition of DKP formation. In the present organisms, the alignment of amino acid monomers is supported by the machinery of ribosome as well as mRNA and tRNA. However, if the hydrothermal hypothesis is correct, then the oligopeptide formation would have occurred even under such extreme conditions involving the submarine hydrothermal vent system. In such a system, it is assumed that the alignment of amino acids would be so difficult since weak interactions among biomolecules would not act at high temperatures.

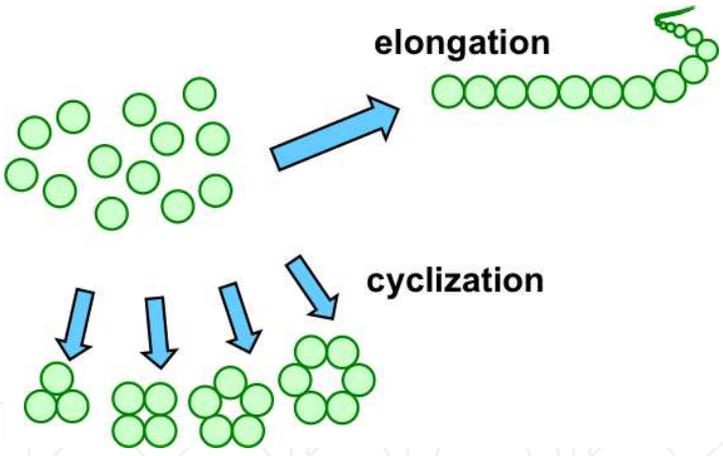


Figure 19. Cyclization and elongation of prebiotic oligomers

Third, the estimation of the primitive earth environments is not yet succeeded. Furthermore, the heterogeneity of earth conditions should be considered. Improvement of knowledge about the primitive environment is essential and a variety of conditions of simulation experiments would be helpful. Most of simulation reactions for the oligonucleotide formation have been carried out under the fairly mild temperatures and pressures. Beside, abiotic-peptide formations were carried out under a variety conditions from mild conditions to hydrothermal conditions. Wider range of simulation experiments should be carried out unless the exact earth environments are readily identified. General rules would be found on the basis of such a variety of simulation experiments in future.

6.2. Formation of simple oligomers to functional entities

The genetic information flow in present organisms consists of DNA replication, transformation of DNA sequence to mRNA, translation of mRNA sequence to protein. According to the RNA world hypothesis, the roles of DNA and protein should have been covered by RNA molecules so the replication of RNA molecules is the first step in an RNA based life-like systems [135, 136]. Here, the possibility of the prebiotic RNA replication is briefly discussed.

In a former section, the difficulty if Template-directed reaction for the cases of A, U, C as nucleotide bases on the complementary template was described. This would be due to the weak stacking between the activated monomers and elongating oligomer. Thus, the enhancement of the association has been attempted. It has been shown that intercalator somewhat enhances the efficiency of oligonucleotide by enhancement of the association [137]. However, the practical replication conditions using primitive activate nucleotide monomers are not identified [82, 135].

The biological functions of oligonucleotide and oliopeptide would be displayed with a certain length of oligomers, such as 30-mer, 50-mer, and 100-mer. Transfer-RNA (tRNA) would be one of smallest functional RNA consisting of ca. 80-mer. On the other hand, recently it has been extensively found that small non-coding RNA and so-called microRNA possess important roles *in vivo*. In addition, it is also known that short peptides possess several important roles while the average length of proteins is ca. 100-mer. Oligonucleotides with 40 – 50-mer can form from Template-directed and Clay-catalyzed reactions. This fact suggests that different types of functional RNA molecules should have been included in a randomly formed large RNA pool on the primitive earth. Several functional RNA sequences would have amplified by replication machinery, that is ribosome, of which some main parts are made of RNA molecules. As mentioned, Template-directed reaction is only efficient for the case of the formation of oligoG on a polyC template. However, the Template-directed reaction could proceed using the activated oligonucleotide as a monomer for the case of oligoU formation of a polyA template. If this type of Template-directed reaction is universal for the different types of combination of monomer and template, a replication of RNA molecules could have evolved under the primitive earth conditions. Nevertheless, it was confirmed that a heterogeneous oligoC template spontaneously formed by Clay-catalyzed reaction containing 2′, 5′-and 3′-5′-linked isomers could have preserved as template for the Template-directed reaction of oligoG formation [138]. On the other hand, the oligopeptide formation from amino acid mixtures is not yet elucidated although some thermal condensation products of amino acids, such as proteinoids, were observed. Actually, it is considered that the formation of amino acids seems to be easier than that of nucleotide monomers since amino acids are readily found in gas reaction products with different types of energy sources. However, it could not straightforwardly mean that the oligopeptide formation using prebiotic materials is easier than the oligonucleotide formation.

In vitro selection technique has been extensively investigated to create several types of artificial functional RNA molecules [139, 140]. This technique elucidated that a RNA replication system catalyzed by RNA molecule could have evolved if amplification and selection processes were present. Naturally, the molecular biological tools and materials are necessary for the *in vitro*

selection technique. However, if the amplification on the basis of Template-directed reaction under the primitive earth conditions, amplified RNA molecules are exposed under different types of selection pressure. This would cause the accumulation of functional RNA molecules, such as RNA replicase function, under the primitive earth conditions.

6.3. Relationship between RNA and protein-like molecules

Cooperation of RNA and proteins is definitely important in modern organisms. Thus, it should be evaluated that the formation of RNA and that of peptides could be enhanced by each other. According to previous studies, Template-directed reaction is not enhanced in the presence of proteinoids [141]. On the other hand, possible roles of nucleotides and oligonucleotides for the formation of oligopeptides are not yet well evaluated. Presumably, nucleotides and oligonucleotides would not be helpful for the abiotic-peptide synthesis under hydrothermal conditions since nucleotides and oligonucleotides are much more unstable than amino acids and peptides [129, 135, 136, 142]. This fact implies that chemical evolution of RNA would have started after the accumulation of oligopeptides.

6.4. Accumulation of RNA molecules and abiotic-peptide under the primitive earth conditions

According to the former sections, RNA could have formed from the activated nucleotide in the absence of enzyme. Abiotic-peptides also form without using the *in vitro* translation system on ribosome. However, the accumulation of oligonucleotides and oligopeptides would not have been easy under the primitive earth conditions since these are spontaneously hydrolyzed in aqueous medium although the rates of hydrolysis of these oligomers are normally slower than those of formation at low temperatures. The hydrolysis rate increases with increasing temperature.

The accumulation of oligomers should be considered from the viewpoint that the life-like system is considered as thermodynamically open system. That is, the accumulation of oligomers is determined by both the rates of formation and degradation of oligomers. Thus, although the rate of degradation of oligomers at high temperatures is large, the accumulation would be possible if the formation rate is much lager than that of degradation. The formation rate would be possibly enhanced by several prebiotic catalysts. Experimental simulations of these conditions are not yet well succeeded while most of simulation experiments were carried out under static conditions. Some experiments, of which activated monomers were fed to batch reaction, successfully showed the possible formation of long oligonucleotides and oligopeptides [75]. Flow reactor would be useful to design where the activated monomers are fed to a chemical evolutionary system.

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7. Conclusive remarks: Possible future applications by learning the primitive oligomerization processes

These studies support the fact that oligomer formation in aqueous solution in the absence of enzyme is possible. The reaction processes are different from normal organic synthetic techniques. Therefore, the improvement of the formation reactions of oligomers, which possess biological functions, should be achieved by learning chemistry of living organisms. Recently, organic chemistry is expected to be a technology compatible with the global environmental protection. Obviously, organic synthesis requires a large amount of organic solvent, which is not suitable to the environmental protection. On the contrary, nowadays, creation of a environmental harmless system for organic synthetic methods is expected by learning the living organisms. However, the organic synthesis is generally difficult in aqueous medium. According to the examples shown here, oligonucleotides and oligopeptides could be synthesized in aqueous medium. The fundamental researches will facilitate such demand of environment harmless organic synthesis.

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References

[1] Arrhenius S. Die Verbreitung des Lebens im Weltenraum. Die Umschau 1903; 7: 481–485.

[2] Crick FHC., Orgel LE. Directed Panspermia. Icarus 1973; 19(3): 341-346.

[3] Horneck G., Rettberg P., Reitz G., Wehner J., Eschweiler U., Strauch K., Panitz C., Starke V., Baumstark-Khan C. Protection of Bacterial Spores in Space, A Contribution to the Discussion on Panspermia. Origins Life Evol Biospheres 2001; 31: 527-547.

[4] Miller SL. A Production of Amino Acids under Possible Primitive Earth Conditions. Science 1953; 528-529.

[5] Ferris JP., Joshi PC., Edelson EH., Lawless JG. HCN-Plausible Source Of Purines, Pyrimidines And Amino-Acids on Primitive Earth. J Mol Evol 1978; 11: 293-311.

[6] Schlesinger G., Miller, SL. Prebiotic Synthesis in Atmospheres Containing CH_4, CO, and CO_2. J Mol Evol 1983; 19: 376-382.

[7] Cleaves HJ. Chalmers JH, Lazcano A. Miller SL, Bada JL. A Reassessment of Prebiotic Organic Synthesis in Neutral Planetary Atmospheres. Origins Life Evol Biospheres 2008; 38(2): 105-115.

[8] Mojzsis SJ., Arrhenius G. McKeegan KD., Harrison TM., Nutman AP., Friend CRL. chopfbefore 3, 800 Million Years Ago. Nature 1996; 384(7): 55-59.

[9] Van Kranendonk, MJ. Volcanic Degassing, Hydrothermal Circulation and the Flourishing of Early Life on Earth: A Review of the Evidence from c. 3490-3240 Ma Rocks of the Pilbara Supergroup, Pilbara Craton, Western Australia. Earth Sci Rev 2006; 74(3-4): 197-240.

[10] Kuppers, BO. Molecular Theory of Evolution. Outline of a Physico-chemical Theory of the Origin of Life. Berlin: Springer-Verlag; 1985.

[11] Schopf, JW. Microfossils of the Early Archean Apex Chert: New Evidence of the Antiquity of Life. Science 1993; 260: 640-646.

[12] Crick F. Central Dogma of Moecular Biology. Nature 1970; 227: 561-563.

[13] Honda S., Yamasaki K., Sawada Y., Morii H. 10 Residue Folded Peptide Designed by Segment Statistics. Structure 2004; 12: 1507-1518.

[14] Cech TR., Zaung AJ., Grabowski PJ. In Vitro Splicing of the Ribosomal RNA Precousor of Tetrahymena: Involvment of a Guanosine Nucleotide in the Excision of the Intervening Sequence. Cell 1981; 27: 487-496.

[15] Gilbert W. Origin of life: the RNA world. Nature 1986; 319: 618–618.

[16] Cech TR. A model for the RNA-catalyzed replication of RNA. Proc Natl Acad Sci USA 1986; 83: 4360–4363.

[17] Lazcano A. The Biochemical Roots of the RNA World: from Zymonucleic Acid to Ribozymes. Hist. Phil. Life Sci. 2012; 34(3): 407-423.

[18] Nemoto N., Husimi Y. A Model of the Virus-type Strategy in the Early Stage of Encoded Molecular Evolution. J. Theor Biol 1995; 176: 67-77.

[19] Kawamura K. Civilization as a Biosystem Examined by the Comparative Analysis of Biosystems. BioSystems 2007; 90: 139-150.

[20] Gomes R., Levison HF., Tsiganis K., Morbidelli A. Origin of the cataclysmic Late Heavy Bombardment period of the terrestrial planets. Nature 2005; 435(7041): 466-469.

[21] Maher KA., Stevenson, DJ. Impact Frustration of the Origin of Life. Nature 1988; 331(6157): 612-614.

[22] Sleep NH., Zahnle KJ., Kasting IF., Morowitz HJ., Annihilation of Ecosystems by Large Asteroid Impacts on the Early Earth. Nature 1989; 342(6246): 139-142.

[23] Sagan C., Mullen G. Earth and Mars: Evolution of Atmospheres and Surface Temperatures. 1972; 177(4043): 52-56.

[24] Newman MJ., Rood RT. Implications of Solar Evolution for the Earth's Early Atmosphere. Science 1977; 198(4321): 1035-1037.

[25] Walker JCG. Carbon-dioxide on the Early Earth. Origins Life Evol Biosphere 1985; 16(2): 117-127.

[26] Kasting JF., Ackerman TP. Climatic Consequences of Very High-carbon Dioxide Levels in the Earths Early Atmosphere. Science 1986; 234(4782): 1383-1385.

[27] Kasting JF. Earth's early atmosphere. Science 1993; 259(5097): 920-926.

[28] Mojzsis SJ., Harrison TM., Pidgeon, RT. Oxygen-isotope Evidence from Ancient Zircons for Liquid Water at Earth's Surface 4, 300 Myr Ago. Nature 2001; 409: 178-181.

[29] Olivas WM., Muhlrad D., Parker R. Analysis of the Yeast genome: Identification of New Non-coding and Small ORF-containing RNAs. Nucl Acid Res 1997; 25(22): 4619-4625.

[30] Eigen M. Selforganization of Matter and the Evolution of Biological Nacromolecules. Naturwissenschaften 1971; 58: 465-523.

[31] Orgel LE., Crick FHC. Anticipating an RNA World Some Past Speculations on the Origin of Life: Where are They Today? FASEB J 1993;7: 238-239.

[32] Chamberlin N., berg P. Deoxyrinonucleic Acid-directed Synthesis of Ribonucleic Acid by an Enzyme from Escherichia Coli. Proc Natl Acad Sci USA 1962; 48(2): 81-94.

[33] Haruna I., Spiegelman S. An RNA "Replicase" Induced by and Selective for a Viral RNA: Isolation and Properties. Proc Natl Acad Sci USA 1963; 50(2): 905-911.

[34] Grunberg-Manago M. Enzymatic Synthesis of Nucleic Acids. Ann Rev Biochem 1962; 31: 301-332.

[35] Kawamura K., Kuranoue K., Umehara M. Chemical Evolution of RNA and RNA Polymerases: Implications from Search for the Prebiotic Pathway of formation of RNA

from Adenosine 5′-Triphosphate in the Presence of Thermal Condensation Products of Amino Acids as Primitive Enzymes. Viva Origino 2002; 30(3): 123-134.

[36] Sulston J., Lohrmann R., Orgel LE., Todd Miles H. Nonenzymatic Synthesis of Oligoadenylates on a Polyuridylic Acid Template. Proc Natl Acad Sci USA 1968; 59: 726-733.

[37] Sulston J., Lohrmann R., Orgel LE., Todd Miles H. Specificity of Oligonucleotide Synthesis Directed by Polynucleic Acid. Proc Natl Acad Sci USA 1968; 60: 409-415.

[38] Lohrmann R., Orgel LE. Prebiotic Synthesis: Phosphorylation in Aqueous Solution. Science 1968; 161(3836): 64-66.

[39] Sulston J., Lohrmann R., Orgel LE., Schneider-Bernloehr H., Todd Miles H. Non-enzymatic Synthesis of Deoxyadenylate Oligonucleotides on a Polyuridylate Template. J Mol Biol 1969; 37: 151-155.

[40] Sulston J., Lohrmann R., Orgel LE., Schneider-Bernloehr H., Todd Miles H. Non-enzymatic Oligonucleotide Synthesis on a Polycytidylate Template. J Mol Biol 1969; 40: 227-234.

[41] Renz M., Lorhmann R., Orge LE. Catalyst for the Polymerization of Adenosine Cyclic 2′, 3′-Phosphate on a Poly(U) Template. Biochim Biophys Acta 1971; 240: 463-471.

[42] Verlander MS., Lorhmann R., Orge LE. Catalysts for the Self-Polymerization of Adenosine Cyclic 2′, 3′-Phosphate. J Mol Evol 1973; 2: 303-316.

[43] Powner MW., Gerland B., Sutherland JD. Synthesis of Activated Pyrimidine Ribonucleotides in Prebiotically Plausible Conditions. Nature 2009; 459: 239-242.

[44] Costanzo G., Pino S., Ciciriello F., Di Mauro E. Generation of Long RNA Chains in Water. J Biol Chem 2012; 284(48): 33206-33216.

[45] Ibanez JD., Kimball AP., Oró J. Possible Prebiotic Condensation of Mononucleotide by Cyanamide. Science 1971; 173: 444-445.

[46] Schneider-Bernloehr H., Lorhmann R., Sulston JE., Orge LE., Todd Miles H. Specific of Template-directed Synthesis with Adenine Nucleotides. J Mol Biol 1970; 47: 257-260.

[47] Weimann BJ., Lorhmann R., Orge LE., Schneider-Bernloehr H., Sulston JE. Template-Directed Synthesis with Adenosine-5'-phosphorimidazolide. Science 1968; 161(3839): 387-387.

[48] Orgel LE., Lohrmann R. Prebiotic Chemistry and Nucleic Aicd Replication. Acc Chem Res 1974; 7: 368-377.

[49] Lohrmann R., Orgel LE. Studies of Oligoadenylate Formation on a Poly(U) template. J Mol Evol 1979; 12: 237-257.

[50] Sawai H., Orgel LE. Oligonucleotide Synthesis Catalyzed by the Zn^{2+}ion. J Am Chem Soc 1975; 97(12): 3532-3533.

[51] Lohrmann R., Orgel LE. Efficient catalysis of polycytidylic acid-directed oligoguanylate formation by Pb^{2+}. J Mol Biol 1980; 142(4, 5): 555-567.

[52] Bridson P.K., Orgel LE. Catalysis of accurate poly(C)-directed synthesis of 3′-5′-linked oligoguanylates by Zn^{2+}. J Mol Biol 1980; 144(4): 567-577.

[53] Inoue T., Orgel LE. Oligomerization of (Guanosine 5′-Phosphor)-2-methylimidazolide on Poly(C): An RNA Polymerase Model. J Mol Biol 1982(1); 201-207.

[54] Lohrmann R. Formation of Ncleoside 5′-Phosphamidates under Potentially Prebiological Conditions. J Mol Evol 1977; 10: 137-154.

[55] Lohrmann R., Orgel LE. Prebiotic Activation Processes. Nature 1973; 244: 418-420.

[56] Kanavarioti A., Bernasconi CF., Doodokyan DL., Alberas DJ. Magnesium-ion Catalyzed P-N Bond Hydrolysis in Imidazolide-Activated Nucleotides-Relevance to Template-directed Synthesis of Polynucleotides. J Am Chem Soc 1989; 111(18): 7247-7257.

[57] Joyce GF., Inoue T., Orgel LE. Non-enzymatic template-directed synthesis on RNA random copolymers: Poly(C, U) templates. J Mol Biol 1984; 176(2): 279-306.

[58] Sawai H. Oligonucleotide Formation Catalyzed by Divalent Metal Ions. The Uniqueness of the Ribosyl System. J Mol Evol 1988; 27(3): 181-186.

[59] Sawai H., Shibata T., Ohno M. Preparation of Oligoadenylates with 2'-5' Linkage Using Pb^{2+}Ion Catalyst. Tetrahedron 1981; 37(3): 481-485.

[60] Sawai H., Kuroda K., Hojo T. Uranyl Ion as a Highly Effective Catalyst for Internucleotide Bond Formation. Bull Chem Soc Jpn 1989; 62(2): 2018-2023.

[61] Sawai H., Higa K., Kuroda K. Synthesis of Cyclic and Acyclic Oligocytidylates by Uranyl Ion Catalyst in Aqueous Solution. J Chem Soc Perkin Trans 1 1992; (4): 505-508.

[62] Kawamura K., Maeda J. Kinetic Analysis of Oligo(C) Formation from the 5′-Monophosphorimidazolide of Cytidine with Pb(II) Ion Catalyst at 10-75 °C. Origins Life Evol Biospheres 2007; 37: 153-165.

[63] Bernal JD. The Physical Basis of Life. Proc R Soc Lond A 1949; 62: 537-558.

[64] Ponnamperuma C., Shimoyama A., Friebele E. Clay and the Origin of Life. Origins Life 1982; 12: 9-40.

[65] Ferris JP., Huang CH., Hagan WJ. Montmorillonite: A Multifunctional Mineral Catalyst for the Prebiological Formation of Phosphate Esters. Origins Life Evol Biosphere 1988; 18(1-2): 121-133.

[66] Ferris JP., Ertem G., Agarwak VK. The Adsorption of Nucleotides and Polynucleotides on Montmorillonite Clay. Origins Life Evol Biosphere 1989; 19: 153-164.

[67] Ferris JP., Ertem G. Oligomerization of Ribonucleotides on Montmorillonite: Reaction of the 5'-Phosphorimidazolide of Adenosine. Science 1992; 257(5075): 1387-1389.

[68] Ferris JP., Ertem G. Montmorillonite Catalysis of RNA Oligomer Formation in Aqueous Solution. A model for the Prebiotic Formation of RNA. J Am Chem Soc 1993; 115(26): 12270-12275.

[69] Kawamura K., Ferris JP. Kinetics and Mechanistic Analysis of Dinucleotide and Oligonucleotide Formation from the 5'-Phosphorimidazolide of Adenosine on Na^+-Montmorillonite. J Am Chem Soc 1994; 116(17): 7564-7572.

[70] Kawamura K., Ferris JP. Clay Catalysis of Oligonucleotide Formation: Kinetics of the Reaction of the 5'-Phosphorimidazolides of Nucleotides with the Non-basic Heterocycles Uracil and Hypoxanthine. Origins Life Evol Biosphere 1999; 29(6): 563-591.

[71] Ertem G., Ferris JP. Template-directed Synthesis Using the Heterogeneous Templates Produced by Montmorillonite Catalysis. A Possible Bridge between the Prebiotic and RNA Worlds. J Am Chem Soc 1997; 119(31): 7197-7201.

[72] Kawamura K., Nakahara N., Okamoto F., Okuda N. Temperature Dependence of the Cyclization of Guanine and Cytosine Mix Hexanucleotides with Water-soluble Carbodiimide at 0-75 °C. Viva Origino 2003; 31(4): 221-232.

[73] Kawamura K., Okamoto F., Okuda N. Influence of Template Oligonucleotides on the Condensation of Oligonucleotides in the Presence of Water-soluble Carbodiimide: Search for Model Reactions of the Formation of RNA Which Could Be Effective at High Temperatures. Viva Origino 2004; 32: 68-80.

[74] Ertem G., Ferris JP. Formation of RNA Oligomers on Montmorillonite: Site of Catalysis. Origins Life Evol Biosphere 1998; 28: 485-499.

[75] Ferris JP., Hill AR., Liu RH., Orgel LE. Synthesis of Long Prebiotic Oligomers on Mineral Surfaces. Nature 1996; 381: 59-61.

[76] Huang WH., Ferris JP. Synthesis of 35-40 Mers of RNA Oligomers from Unblocked Monomers. A Simple Approach to the RNA World. Chem Comm 2003; 12: 1458-1459.

[77] Huang WH., Ferris JP. One-step, Regioselective Synthesis of up to 50-mers of RNA Oligomers by Montmorillonite Catalysis. J Am Chem Soc 2006; 128(27): 8914-8919.

[78] Lorhman R., Bridson PK., Orgel LE. Efficient Metal-ion Catalyzed Template-Directed Oligonucleotide Synthesis. Science 1980; 208(4451): 1464-1465.

[79] Inoue T., Orgel LE. A nonenzymatic RNA polymerase model. Science 1983; 219(4586): 859-862.

[80] Wu TF., Orgel LE. Nonenzymatic Template-Directed Synthesis on Oligodeoxycytidylate Sequences in Hairpin Oligonucleotides. J Am Chem Soc 1992; 114(1): 317-322.

[81] Sawai H., Wada K. Nonenzymatic Template-Directed Condensation of Short-chained Oligouridylates on a Poly(A) Template. Origins Life Evol Biosphere 2000; 30: 503-511.

[82] Hill Jr AR, Orgel LE., Wu T. The Limits of Template-directed Synthesis with Nucleoside-5′-Phosphoro(2-Methyl)Imidazolides. Origins Life Evol Biosphere 1993; 23(5-6): 285-290.

[83] Szostak JW., Bartel DP., Luisi PL. Synthesizing Life. Nature 2001; 409: 387-390.

[84] Mansy SS., Schrum JP., Krishnamurthy M., Tobe S., Treco DA., Szostak JW. Template-directed Synthesis of a Genetic Polymer in a Model Protocell. Nature 2008; 454: 122-126.

[85] Kanavarioti A., Bernasconi CF., Alberas DJ., Baird, EE. Kinetic Dissection of Individual Steps on the Poly(C)-Directed Oligoguanylate Synthesis from Guanosine 5'-Monophosphate 2-Methylimidazolide. J Am Chem Soc 1993; 115(19): 8537-8546.

[86] Inoue T., Orgel LE. Substituent Control of the Poly(C)-Directed Oligomerization of Guanosine 5′-Phosphorimidazolide. J Am Chem Soc 1981; 103: 7666-7667.

[87] Prabahar KJ., Cole TD., Ferris JP. Effect of Phosphate Activating Group on Oligonucleotide Formation on Montmorillonite-the Regioselective Formation of 3', 5'-Linked Oligoadenylates. J Am Chem Soc 1994; 116(24): 10914-10920.

[88] Prabahar KJ., Ferris JP. Adenine Derivatives as Phosphate-activating Groups for the Regioselective Formation of 3', 5'-Linked Oligoadenylates on Montmorillonite: Possible Phosphate-activating Groups for the Prebiotic Synthesis of RNA. J Am Chem Soc 1997; 119(19): 4330-4337.

[89] Oscar L. Ueber Formaldehyd und Dessen Condensation. J Prak Chem 1886; 321: 321-351.

[90] Breslow R. On the Mechanism of the Formose Reaction. Tetrahedron Lett 1959; 21: 22-26.

[91] Eschenmoser A., Loewenthal E. Chemistry of Potentially Prebiological Natural-products. Chem Soc Rev 1992; 21(1): 1-16.

[92] Dueholm KL., Egholm M., Behrens C., Christensen L., Hansen HF., Vulpius T., Petersen KH., Berg RH., Nielsen PE., Buchardt O. Synthesis of Peptide Nucleic-acid Monomers Containing the 4 Natural Nucleobases-Thymine, Cytosine, Adenine, and Guanine and their Oligomerization. J Org Chem 1994; 59(19): 5767-5773.

[93] Joyce GF. The Antiquity of RNA-based Evolution. Nature 2002; 418: 214-221.

[94] Pitsch S., Krishnamurthy R., Bolli M., Wendeborn S., Holzner A., Minton M., Lesueur C., Schlonvogt I., Jaun B., Eschenmoser A. Pyranosyl-RNA (P-RNA)-Base-Pairing Selectivity and Potential to Replicate-Preliminary Communication. Helv Chim Acta 1995; 78(7): 1621-1635.

[95] Bolli M., Micura R., Eschenmoser, A. Pyranosyl-RNA: Chiroselective self-assembly of base sequences by ligative oligomerization of tetranucleotide-2', 3'-cyclophosphates (with a commentary concerning the origin of biomolecular homochirality). Chem & Biol 1997; 4(4): 309-320.

[96] Joyce GF., Schwartz AW., Miller SL., Orgel LE. The Case for an Ancestral Genetic System Involving Simple Analogs of the Nucleotides. Proc Natl Acad Sci USA 1987; 84: 4398-4402.

[97] Joshi PC., Pitsch S., Ferris JP. Homochiral Selection in the Montmorillonite-Catalyzed and Uncatalyzed Prebiotic Synthesis of RNA. Chem Commun 2000; 2497–2498.

[98] Urata H., Ando C., Ohmoto N., Shimamoto Y., Kobayashi Y., Akagi M. Efficient and Homochiral Selective Oligomerization of Racemic Ribonucleotides on Mineral Surface. Chem Lett 2001; 324–325.

[99] Osawa K., Urata H., Sawai H. Chiral Selection in Oligoadenylate Formation in the Presence of a Metal Ion Catalyst or Poly(U) Template. Origins Life Evol Biosphere 2005; 35: 213-223.

[100] Nisbet EG. Origin of life: RNA and Hot-water Springs. Nature 1986; 322: 206–206.

[101] Pace NR. Origin of Life—Facing up to the Physical Setting. Cell 1991; 65: 531–533.

[102] Kawamura K., Umehara M. Kinetic Analysis of the Temperature Dependence of the Template-directed Formation of Oligoguanylate from the 5'-Phosphorimidazolide of Guanosine on a Poly(C) Template with Zn^{2+}. Bull Chem Soc Jpn 2001; 74(5): 927-935.

[103] Kawamura K., Maeda J. Kinetic Analysis of Oligo(C) Formation from the 5′-Monophosphorimidazolide of Cytidine with Pb(II) Ion Catalyst at 10–75°C. Origin Life Evol Biospheres 2007; 37: 153–165.

[104] Kawamura K., Maeda J. Kinetics and Activation Parameter Analysis for the Prebiotic Oligocytidylate Formation on Na^{+}-Montmorillonite at 0–100°C. J Phys Chem A 2008; 112: 8015–8023.

[105] Yakovchuk P., Protozanova E., Frank-Kamenetskii MD. Base-stacking and Base-pairing Contributions into Thermal Stability of the DNA Double Helix. Nucl Acid Res 2006; 34(2): 564-574.

[106] Blochl E., Rachel R., Burggraf S., Hafenbradl D., Jannasch HW., Stetter KO., Pyrolobus Fumarii, Gen. and Sp. Nov., Represents a Novel Group of Archaea, Extending the Upper Temperature Limit for life to 113 °C. Extremophiles 1997; 1: 14-21.

[107] Cowan DA. The Upper Temperature for Life-Where Do We Draw the Line? Trends Micobiol 2004; 12: 58-60.

[108] Fox SW., Harada K. Thermal Copolymerization of Amino Acids to a Product Resembling Protein. Science 1958; 128(3333): 1214-1215.

[109] Fox SW., Harada K. The Thermal Copolymerization of Amino Acids Common to Protein. J Am Chem Soc 1960; 82: 3745–3751.

[110] Harada K., Fox SW. The Thermal Copolymerization of Aspartic Acid and Glutamic Acid. Arch Biochem Biophys 1960; 86(2): 274-280.

[111] Fox SW., Krampitz G. Catalytic Decomposition of Glucose in Aqueous Solution by Thermal Proteinoids. Nature 1964; 203: 1362-1364.

[112] Nakashima T., Fox SW. Selective Condensation of Aminoacyl Adenylates by Necleoproteinoid Microparticles. Proc Natl Acad Sci USA 1972; 69(1):106-108.

[113] Fox SW. Metabolic Microspheres Origins and Evolution. Naturwissenschaften 1980; 67: 378-383.

[114] Shock EL. Stability of Peptides in High-temperature Aqueous-solutions. Geochim Cosmochim Acta 1992; 56(9): 3481-3491.

[115] Rode BM., Schwendinger MG. Copper-catalyzed Amino Acid Condensation in Water — A Simple Possible Way of Prebiotic Peptide Formation. Origins Life Evol Biosphere 1990; 20(5): 401-410.

[116] Bujdak J., Rode BM. Silica, Alumina, and Clay-Catalyzed Alanine Peptide Bond Formation. J Mol Evol 1997; 45: 457-466.

[117] Rode BM. Peptides and the Origin of Life. Peptides 1999; 20(6): 773-786.

[118] Meng M., Stievano L., Lambert JF. Adsorption and Thermal Condensation Mechanisms of Amino Acids on Oxide Supports. 1. Glycine on Silica. Langmuir 2004; 20(3): 914-923.

[119] Leman L., Orgel LE., Ghadiri MR. Carbonyl Sulfide-mediated Prebiotic Formation of Peptides. Science 2004; 306(5694): 283-286.

[120] Lambert J-F., Adsorption and Polymerization of Amino Acids on Mineral Surfaces: A Review. Origins Life Evol Biospheres 2008; 38: 211-242.

[121] Forterre P., A Hot Topic: the Origin of Hyperthermophiles. Cell 1996; 85: 789–792.

[122] Galtier N., Tourasse N., Gouy M. A Nonhyperthermophilic Common Ancestor to Extant Life Forms. Science 1999; 283: 220–221.

[123] Holm NG., Marine Hydrothermal Systems and the Origin of Life. Origin Life Evol Biosphere 1992; 22: 1–242.

[124] Baross JA., Hoffman SE. Submarine Hydrothermal Vents and Associated Gradient Environments as Sites for the Origin and Evolution of Life. Origin Life Evol Biosphere 1985; 15(4): 327-345.

[125] Yanagawa H., Kojima K. Thermophilic Microspheres of Peptide-Like Polymers and Silicates Formed at 250°C. J Biochem 1985; 97: 1521-1524.

[126] Imai E., Honda H., Hatori K., Brack A., Matsuno K. Elongation of Oligopeptides in a Simulated Submarine Hydrothermal System. Science 1999; 283: 831-833.

[127] Imai E., Honda H., Hatori K., Matsuno K. Autocatalytic Synthesis of Oligoglycine in a Simulated Submarine Hydrothermal System. Origin Life Evol Biosphere 2000; 29: 249-259.

[128] Kawamura K. Monitoring of Hydrothermal Reactions In 3 ms Using Fused-silica Capillary Tubing. Chem Lett 1999; 125-126.

[129] Kawamura K. Monitoring Hydrothermal Reactions on the Millisecond Time Scale Using a Micro-tube Flow Reactor and Kinetics of ATP Hydrolysis for the RNA World Hypothesis. Bull Chem Soc Jpn 2000; 73: 1805-1811.

[130] Kawamura K. Development of Micro-flow Hydrothermal Monitoring Systems and their Applications to the Origin of Life Study on Earth. Anal Sci 2011; 27(7): 675-683.

[131] Kawamura K., Nishi T., Sakiyama T. Consecutive Elongation of Alanine Oligopeptides at the Second Time Range Under Hydrothermal Condition Using a Micro Flow Reactor System. J Am Chem Soc 2005; 127: 522-523.

[132] Kawamura K., Shimahashi M. One-step Formation of Oligopeptide-like Molecules from Glu and Asp in Hydrothermal Environments. Naturwissenschaften 2008; 95: 449-454.

[133] Kawamura K., Takeya H., Kushibe T., Koizumi Y. Mineral-enhanced Hydrothermal Oligopeptide Formation at the Second Time Scale. Astrobiology 2011; 11: 461-469.

[134] Horowitza ED., Engelharta AE., Chena MC., Quarlesa KA., Smitha MW., Lynna DG., Hud NV. Intercalation as a Means to Suppress Cyclizationand Promote Polymerization of Base-pairing Oligonucleotides in a Prebiotic World. Proc Natl Acad Sci USA 2010; 107(12): 5288-5293.

[135] Kawamura K. Drawbacks of the Ancient RNA-based Life-like System Under Primitive Earth Conditions. Biochimie 2012; 94(7): 1441-1450.

[136] Kawamura K. Reality of the Emergence of Life-like Systems from Simple Prebiotic Polymers on Primitive Earth. In: Seckbach J., Gordon R. (ed.) Genesis-in the Beginning: Precursors of Life, Chemical Models and Early Biological Evolution. Springer; 2012. p123-144.

[137] Hud NV., Jaina SS., Lia X., Lynn DG. Addressing the Problems of Base Pairing and Strand Cyclization in Template-Directed Synthesis A Case for the Utility and Necessity of 'Molecular Midwives' and Reversible Backbone Linkages for the Origin of proto-RNA. Chem & Biodiversity 2007; 4: 768-783.

[138] Ertem G., Ferris JP. Synthesis of RNA Oligomers on Heterogeneous Templates. Nature 1996; 379: 238-240.

[139] Tuerk C., Gold L. Systematic Evolution of Ligands by Exponential Enrichment: RNA Ligands to Bacteriophage T4 DNA Polymerase. Science 1990; 249: 505-510.

[140] Ellington AD., Szostak JW. In Vitro Selection of RNA Molecules That Bind Specific Ligands. Nature 1990; 346: 818-822.

[141] Kawamura K., Kuranoue K., Nagahama M. Prebiotic Inhibitory Activity of Protein-like Molecules to the Template-directed Formation of Oligoguanylate from Guanosine 5′-Monophosphate 2-Methylimidazolide on a Polycytidylic Acid Template. Bull Chem Soc Jpn 2004; 77(7): 1367-1375.

[142] Kawamura K., Yukioka M. Kinetics of the Racemization of Amino Acids at 225-275 °C Using a Real-time Monitoring Method of Hydrothermal Reactions. Thermochimica Acta 2001; 375(1-2): 9-16.

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