

*Walking over 4 Gya: Chemical Evolution  
from Photochemistry to Mineral and  
Organic Chemistries Leading to an RNA  
World*

**Kunio Kawamura & Marie-Christine  
Maurel**

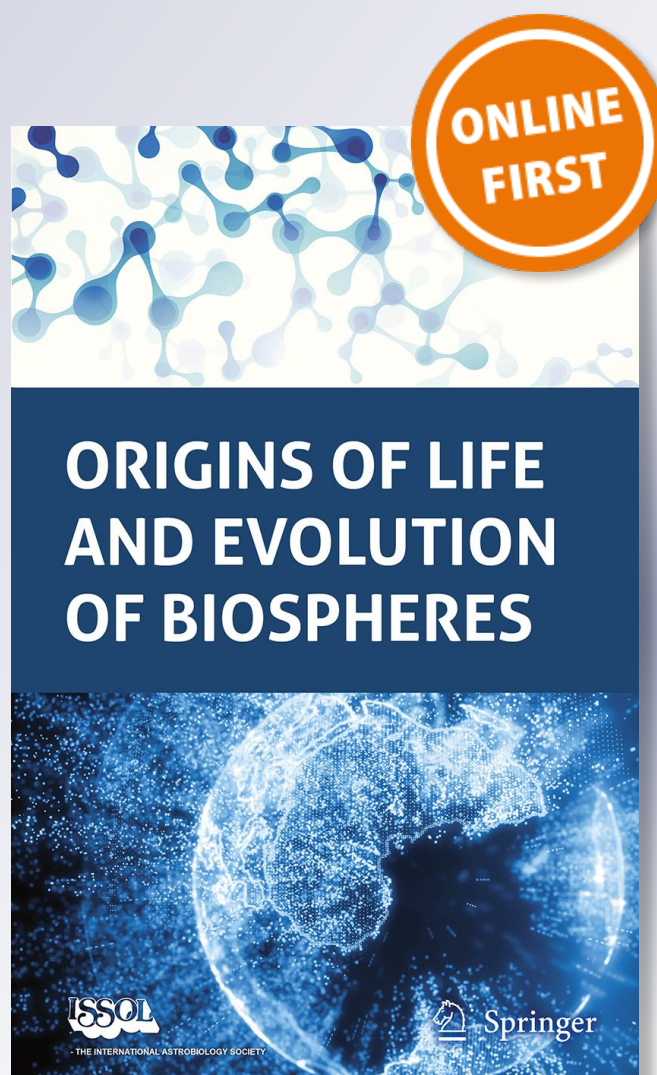
**Origins of Life and Evolution of  
Biospheres**

The Journal of the International  
Astrobiology Society

ISSN 0169-6149

Orig Life Evol Biosph

DOI 10.1007/s11084-017-9537-2



 Springer

**Your article is protected by copyright and all rights are held exclusively by Springer Science +Business Media Dordrecht. This e-offprint is for personal use only and shall not be self-archived in electronic repositories. If you wish to self-archive your article, please use the accepted manuscript version for posting on your own website. You may further deposit the accepted manuscript version in any repository, provided it is only made publicly available 12 months after official publication or later and provided acknowledgement is given to the original source of publication and a link is inserted to the published article on Springer's website. The link must be accompanied by the following text: "The final publication is available at [link.springer.com](http://link.springer.com)".**



# Walking over 4 Gya: Chemical Evolution from Photochemistry to Mineral and Organic Chemistries Leading to an RNA World

Kunio Kawamura<sup>1</sup> · Marie-Christine Maurel<sup>2</sup>

Received: 10 September 2016 / Accepted: 20 January 2017

© Springer Science+Business Media Dordrecht 2017

**Abstract** Here we overview the chemical evolution of RNA molecules from inorganic material through mineral-mediated RNA formation compatible with the plausible early Earth environments. Pathways from the gas-phase reaction to the formation of nucleotides, activation and oligomerization of nucleotides, seem to be compatible with specific environments. However, how these steps interacted is not clear since the chemical conditions are frequently different and can be incompatible between them; thus the products would have migrated from one place to another, suitable for further chemical evolution. In this review, we summarize certain points to scrutinize the RNA World hypothesis.

**Keywords** Photochemistry · Mineral catalysis · RNA world · RNA bricks · Hadean environment · Hydrothermal sites · Prebiotic chemistry

## A Brief Survey of the RNA World Hypothesis

The discovery of ribozymes at the beginning of the 1980s radically changed research on the origins of life by revealing the existence of modern RNAs that could have been preceded by a

---

Dedicated to the memory of Jim Ferris.

---

✉ Kunio Kawamura  
kawamura@shudo-u.ac.jp

Marie-Christine Maurel  
marie-christine.maurel@upmc.fr

<sup>1</sup> Department of Human Environmental Studies, Hiroshima Shudo University, 1-1-1 Ozuka-higashi, Asaminami-ku, Hiroshima 731-3195, Japan

<sup>2</sup> Institut de Systématique, Evolution, Biodiversité (ISYEB), UMR 7205 CNRS MNHN UPMC EPHE, Sorbonne Universités, 50, 57 rue Cuvier, 75005 Paris, CP, France

more ancient RNA World (Gilbert 1986). It is well-known today that RNA is used for the storage and transfer of genetic information and for the catalysis and regulation of biochemical reactions.

The RNA World hypothesis rests on the idea that at certain stages of evolution, the metabolism depended essentially on the activity of RNA molecules. Genetic continuity was then secured by the replication of RNA molecules, by the interplay of weak interactions and without intervention of protein enzymes. Catalysis that is the combined reactions of synthesis, activation, cleavage etc. was achieved by ribozymes, accompanied by the activity of small peptides. This scenario is based on a certain number of observations of contemporary metabolism interpreted as vestiges of the past activity of the RNA World. Moreover, it suffices to examine the phylogenetic distribution of nucleic acids in the three domains of life to fully appreciate their large number, their ubiquity and their functional diversity. In addition to the coding RNA, one also finds other RNAs that can fragment themselves to perform new functions (Tuck and Tollervey 2011). Other RNAs are multi-specific and are both transfer RNAs and messenger RNAs (tmRNAs) (Valle et al. 2003).

A major discovery of the last 15 years was the demonstration that « *The ribosome is a ribozyme* », (Cech 2000) meaning that the structural bases of ribosomal RNA trigger the formation of a peptide bond between two amino acids without the intervention of protein enzymes. Obviously, this constitutes a solid argument in favor of an ancestral RNA World (Agmon 2009, 2016). Furthermore it has been suggested that the modern ribosome evolved from a simpler entity, the proto-ribosome (Krupkin et al. 2011; Zaccai et al. 2016). The ancient peptide bond-forming machinery consisted exclusively of short RNA chains and the entire ribosome could have evolved progressively around a semi-symmetrical region, until it acquired its final shape.

Transfer RNA (tRNA) also plays a crucial role during proteins synthesis. Certain researchers even consider them as molecular fossils of an ancient RNA World (Maizels and Weiner 1994).

Indeed, within a molecule of tRNA formed by 4 stems surmounted by 3 loops, numerous non-standard nucleotides are found that could have a distant pre-biotic origin (Cermakian and Cedergren 1998). Such an unexpected feature is not without consequences, since these modified nucleotides are common to the three domains of life and play a decisive role in interactions with proteins and in the fidelity of translation.

Finally, RNA viruses and viroids (the smallest pathogens of plants) have a cruciform motif. This motif resembles that of tRNAs (Maizels and Weiner 1993) and could correspond to molecular fossils of an RNA World. In their structure, certain RNA viruses and certain satellite RNAs, which are molecular parasites, possess motifs of catalytic RNAs that are active during viral replication. These viral motifs, known as “hammerhead” (HHR) or “hairpin” because of their shape, can reversibly self-cleave and thus shape the viral genome. It is tempting to view these RNA particles as initiators of the living world. This is specifically proposed for viroids (Diener 1989) that bear an HHR motif presenting the efficient flexibility and plasticity required for catalytic activity (Leclerc et al. 2016).

We still have to understand how the first nucleotides, formed of a nitrogenous base (purine - A,G - or pyrimidine - U,C -), a sugar (ribose) and phosphoric acid, were assembled. Some scientists propose that alternative genetic systems (AGS) or xeno-nucleic acids (XNAs), composed of unusual nucleotide-like compounds, were formed at the very beginning of life, leaving space for a kind of heterogenetic system (Joyce et al. 1987; Pinheiro et al. 2012).

Did that which can be performed in vitro in laboratories, also occur 3.8–4 billion years ago? No one will be able to confirm this, but clearly, from all these investigations one can draw the contour of a hypothetical scenario of the key steps of primordial life.

Free RNA is a sturdy molecule capable of adapting to various physico-chemical and cellular environments. This is the case of viroids and of the ribozymes that are resistant to extreme temperatures and pressures and adapt to non-specific hosts (Kaddour et al. 2011; El-Murr et al. 2012; Delan-Forino et al. 2011; Latifi et al. 2016).

One can speculate that viroids or their ancestors that resemble free catalytic RNAs and carry information were encapsulated in a special environment, be it lipidic, membranous or crystalline, and this is how a new compartmentalized world emerged from such structures. This archaic ensemble may have brought together many forms of proto-viruses, and later of proto-cells capable of organizing the initial steps of a metabolism and of facing Darwinian evolution. New populations evolved towards cells with complex RNAs, capable of deploying a large array of activities preparing the transition to the modern DNA world.

The message deduced from decades of scientific research is now quite clear. The stature of RNA has changed from a simple molecule with a transient role allowing it to build more complex objects with new discoveries to a molecule with multiple metabolic functions.

Despite the massive body of work devoted to research on RNA, the mechanisms of synthesis of the RNA nucleotides and their subsequent polymerization under realistic prebiotic conditions are far from being understood.

Furthermore, experiments are poorly evaluated as to whether they are compatible with the environments of the primitive Earth, since our knowledge of Hadean environments is extending rapidly. In the following sections we summarize plausible chemical evolution of RNA starting from inorganic materials, with special focus on photochemistry and mineral chemistry based on the presumed duration of early chemical evolution on the Earth.

## Early Earth Environments with Gas Phase Photochemistry

A large diversity of the early Earth environments should be taken into account in considering how life began since a large variety of environments are observed in the present-day Earth. Such environmental diversity with long periods of chemical evolution (between 4.55–3.8 Gya) was assumed to have been a period of chemical accumulation from the birth of the Earth (Allègre et al. 1995) to the oldest evidences of life on Earth (Barghoorn and Schopf 1966; Schopf 1993; Mojzsis et al. 1996). This has been recently improved by the discovery of Nutman et al. (2016) who assume that life arose during the Hadean time (> 4 Gya) within a relatively short time range according to the evidence of life at 3.7 Gya, and constitutes a new challenge to understand the advent of the RNA World.

The presence of 4.3–4.4 Gya-old zircons (Peck et al. 2001; Mojzsis et al. 2001) suggests that oceans were present by that time. The dry ancient Earth should have acquired a tiny amount of water by accretion from asteroid and/or comets in the solar system beyond the snowline until around 4.4 Gya (Maruyama et al. 2013).

Carbon dioxide, methane and nitrogen are sources of compounds leading to nitrogenous bases from HCN (Tian et al. 2011). Pyrimidines are known to be formed from cyanoacetylene that were formed with electric discharges (Sanchez et al. 1966; Ferris et al. 1968). These reactions may be consistent with the environments of the early Earth, which have been assumed by simulation experiments. The occurrence of these processes would depend on the temperature, partial pressures of CO<sub>2</sub>, CH<sub>4</sub> and N<sub>2</sub>, altitude, and presumably latitude. The products of the gas phase would have mixed with the atmosphere of the primordial Earth if the gas phase reaction proceeded in the troposphere. Otherwise, the reaction products would have

migrated to other environments on the early Earth much more slowly. The migration processes of the gas phase products within the ancient troposphere, stratosphere, and higher atmosphere have as yet not been sufficiently inspected as chemical evolutionary processes. Sources of ribose and other sugars, that is, the formation of formaldehyde in the gas phase are also important. Glycolaldehyde is also an important reagent for ribose formation (Kopetzki and Antonietti 2011). The products of the gas phase should have been dissolved into the primitive ocean or ponds followed by the chemical evolution of ribose. Furthermore, moieties dissolved in water should have traveled for interaction to form nucleosides and nucleotides in the ancient Earth (Maruyama et al. 2013).

The surface of the early Earth initially covered by magma-ocean should not be suitable for the formation of higher organic molecules. At the same time such Hadean earth environment would be suitable for chemical evolution of simple organic molecules at high temperatures for gas phase photo-reactions. The early Earth may have been covered with a few MPa CO<sub>2</sub> and with ca. 0.1 MPa N<sub>2</sub> (Kasting and Pollack 1984; Kasting 1993; Maruyama et al. 2013). It is known from early studies that photochemical processes can lead to nitrogenous bases and related molecules from HCN (Oró 1961; Ferris and Orgel 1965; Ferris et al. 1969; Ferris et al. 1978). Furthermore, the role of minerals for the polymerization of HCN has already been investigated (Ferris et al. 1979; Rao et al. 1980). Although in the early times the luminosity of the Sun was about 70% that of the present-day (Sagan and Mullen 1972; Gough 1981), the partial pressure of CO<sub>2</sub> is an important factor in determining the first steps of photosynthetic processes since the light from the Sun should be partially absorbed in the atmosphere.

Recent studies have shown that purine nitrogenous bases, adenine (A), guanine (G) and pyrimidine nitrogenous bases, cytosine (C) and uracil (U), can be produced by heating formamide in the presence of mineral catalysts and UV photons and/or alternative pathways (Saladino et al. 2007; Hud et al. 2013; Sutherland 2016). The four RNA bases could thus have been formed on a primitive Earth devoid of an ozone layer and under the direct influence of UV rays. Furthermore, the discovery of a wide range of nitrogenous bases in meteorites as products of ammonium cyanide chemistry, provides yet another mechanism for their availability on the primitive Earth (Callahan et al. 2011).

One can assume that photo-processes may have proceeded at higher atmospheric altitudes since the light path is gradually absorbed in the atmospheric layer from top to bottom. The low luminosity of the primitive Sun suggests that chemical evolution might have occurred at much lower temperatures (Schwartz and Goverde 1982; Schwartz et al. 1982). Investigations of prebiotic photochemical reactions leading to biological materials were carried out extensively in the 1970s (Ferris and Chen 1975; Ferris 1979; Ferris and Joshi 1979; Ferris and Morimoto 1981). Gas phase reactions are also important to form formaldehyde that is a source of ribose (Ferris and Chen 1975).

Since these experiments do not sufficiently simulate the extreme temperatures during which the Earth surfaces were covered by the magma ocean, the high partial pressure of CO<sub>2</sub>, and the altitude within the primitive atmosphere simulating such environments, should be envisaged as future experiments. Thus, gas-phase experiments using very high partial pressure of CO<sub>2</sub> should be attempted.

On the other hand, given the poor yield of ribose from formaldehyde during the formose reaction, we should reconsider how to stabilize ribose and catalyze ribose formation in prebiotic conditions (Shapiro 1988). One pathway proceeds with phosphate esters of glycoaldehyde (that decrease the nucleophilicity of hydroxylcarbonyl groups (Kim et al. 2011)). Considering this possibility, we now propose to go further to a crucial biomolecule,

phosphoribosyl pyrophosphate (PRPP) that is at the cross-road of purine nucleotide and pyrimidine and histidine biosynthesis in present-day metabolism. This important metabolic intermediate might be a clue to understand the passage from prebiotic to biochemical worlds.

As stated by Benner, the second pathway that can stabilize ribose involves ulexite and colemanite that are borate minerals (Prieur 2009; Ricardo et al. 2004). Moreover, Kim et al. (2011) complete the pathway of synthesizing carbohydrates thanks to molybdate and calcium acting as mineral guides.

Ribose on amorphous silica provides a realistic chert model. The interactions protect the sugar from degradation processes and significantly increase the proportion of ribofuranose compared to ribopyranose (Georgelin et al. 2015). Adsorption of ribose on silica stabilizes the cyclic molecules up to about 150 °C, thus extending the useful “temperature window” for prebiotic reactions. At 150 °C, the ring begins to open up, and this can lead to pentose isomerization and loss of chemical specificity. Complexation with alkaline earth and transition metal salts (such as ZnCl<sub>2</sub>) influences the anomeric ratios, favoring the furanose forms and the β isomer. Zinc is interesting since it preserves cyclic ribose at least up to 180 °C. It will be interesting to study the reactivity of ribose-Zn/SiO<sub>2</sub> complexes in further reactions that might lead to RNA (Akouche et al. 2016).

Indeed the formose reaction can be enhanced by several minerals (Weber 1992; Schwartz and De Graaf 1993; Lambert et al. 2010). These kinds of environments may have contributed to the formation of ribose in a weakly acidic ocean that formed by neutralization of a strongly acidic ocean (Maruyama et al. 2013).

## **From Prebiotic Chemistry to Life: The Special Case of Ribonucleotides and RNA**

Most present-day protein enzymes are frequently assisted by co-factors of which ribonucleotide co-factors are involved. This is the case of nicotinamide adenine dinucleotide (NAD) that can be phosphorylated (NADP), riboflavins and flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN). Prebiotic synthesis of nicotinamide was first obtained from ethylene and ammonia by Friedmann et al. in Friedmann et al. 1971. Flavin is a heterocycle based on a pteridine nucleus. Purines derived from nicotinamide and pteridines are obtained from photochemical rearrangement of hydrogen cyanide (HCN) abundant in the universe. Co-factors are considered molecular fossils of an ancient RNA World (White 1976) and a common origin starting from HCN can be retained. The structural similarity of purines and pteridines is also very interesting. The abiogenic formation of pteridines and isoalloxazines has been reported (Kolesnikov and Kritsky 2001). Pteridine is currently found in pigments, in flavins and folates, co-factors sensitive to light. Folates (precursors of the tetrahydrofolate co-factor, THF) are also involved in the biosynthesis of purine nucleotides. Without going into the details of the biochemical pathways, one must stress that all of these components sensitive to light participate today in biological redox reactions producing energy.

## **Remaining Questions for Prebiotic Evolution in the Primitive Ocean**

As mentioned above, the local and global ocean environments are important to estimate a scenario for the prebiotic formation of nucleosides. It has been pointed out that late heavy

bombardment (LHB) may have frequently evaporated the primitive ocean (Wells et al. 2003; Jørgensen et al. 2009). The age of the LHB is now being estimated as going back to a previous period, around 4.1–4.3 Gya (Morbidelli et al. 2012; Abramov and Mojzsis 2016), than previously estimated, around 3.8–3.9 Gya (Wetherill 1975; Ryder 2002). If this new estimation is correct, there should have been sufficient time for chemical evolution from the LHB up to the appearance of the oldest evidence of organisms (ca. 3.8 Gya) (Mojzsis et al. 1996; Nutman et al. 2016). In addition, temperature and pressure, where liquid water exists, are fundamental factors to determine the chemical evolutionary processes. The partial pressure of CO<sub>2</sub> is important to determine the surface pressure of the atmosphere so that the incorporation of CO<sub>2</sub> into the ocean and into the crust must be taken into account. On the other hand, since N<sub>2</sub> gas is not readily absorbed into the crust, almost 0.1 MPa N<sub>2</sub> remains in the atmosphere. Detailed knowledge of the profile of the temperature and pressure of the Earth's surface, especially the partial pressure of CO<sub>2</sub>, still remains limited (Kasting 1993). It has been pointed out that the formose reaction is not considered a plausible process for the formation of ribose and other sugars (Shapiro 1988) since the yield of ribose is not high and the reaction may require alkaline conditions; this was disputed earlier (Reid and Orgel 1967) and revived in highly specific conditions according to the stabilisation of ribose adsorbed on silicate (Georgelin et al. 2015). The synthesis of ribose should be evaluated over a wider range of conditions as a function of temperature, pressure, pH (Reid and Orgel 1967), and in the presence of minerals (Gabel and Ponnampereuma 1967; Schwartz and de Graaf 1993). Some alkaline vents are proposed to have been present on the primitive Earth (Sojo et al. 2016).

This is compatible with the formation of ribose by the formose reaction (Mizuno and Weiss 1974; Shigemasa et al. 1977; Holm et al. 2006; Kopetzki and Antonietti 2011) if reasonable concentrations of HCHO were present in these environments. At the same time, the environments suitable for the ribose formation should not always have been suitable for the formation and oligomerization of ribonucleic acids.

The freshly formed ocean may have been acidic, as in current black smokers or in hydrothermal fields (Kamchatka) due to the influence of volcanic gases, while the presence of carbonate minerals suggests that the pH was around 5–6 (Walker 1985; Grotzinger and Kasting 1993; Morse and Mackenzie 1998). In addition, the primitive ocean might have been frequently evaporated by LHB. The time required to neutralize ancient strong acidic oceans is not yet known. If the formose reaction is not compatible with an acidic ocean (Larralde et al. 1995), fresh water environments apart from atmosphere with thick CO<sub>2</sub> was important for the formation of ribose and the following nucleosides.

## Formation of Nucleosides and Nucleotides Associated with Minerals

The formation of nucleosides, nucleotides, and RNA involves dehydration processes. Thus, these dehydration processes are disadvantageous in aqueous media from a thermodynamic viewpoint. Several activation processes, such as dry-wet cycles and the use of activated phosphate materials, were successfully applied in laboratory conditions for the formation of nucleosides and nucleotides (Sanchez and Orgel 1970; Fuller et al. 1972; Yamagata et al. 1982; Joyce 1986; Yamagata et al. 1995; Saladino et al. 2003; Schwartz 2006). Some potential prebiotic phosphorylating agents have been investigated (Ferris et al. 1984). The formation of nucleosides and nucleotides was successfully demonstrated in the presence of phosphate minerals (Reimann and Zubay 1999; Costanzo et al. 2007). Since phosphate is not abundant



in the present ocean, where the presence of calcium ion reduces the solubility of phosphate, the possible source of phosphorylation must be investigated if the ancient ocean would have involved low concentration of phosphate (Pasek and Lauretta 2005; Schwartz 2006; Paytan and Maclaughlin 2007). The origin of reactive prebiotic phosphorus in phosphite form is of crucial interest to understand the training of phosphorylated biomolecules (Yamagata et al. 1992; Gull et al. 2015; Britvin et al. 2015).

It is important to explain how ribose, ribonucleosides and phosphate merged in a particular environment suitable for dry conditions or mineral surfaces. For the formation of ribonucleotides, such dehydration processes should have occurred in the presence of phosphate minerals.

## Oligomerization of RNA Associated with Minerals

Oligomerization of RNA involves the same difficulty as the formation of nucleosides and nucleotides since oligomerization involves dehydration. In general, dehydration can be enhanced by two types of approaches. First, the dry-wet cycle is a suitable process for the formation of oligonucleotides. Recently, the importance of dehydration by dry-wet cycles was pointed out for the formation of long RNA molecules (Costanzo et al. 2009) even from standard nucleotides (5'-NMPs) (Da Silva et al. 2015). Second, the formation of activated nucleotide monomers, such as nucleoside triphosphate, nucleoside cyclic-phosphate, nucleoside phosphorimidazolid, are alternative pathways. Historically, activated nucleotide monomers were investigated to simulate experiments of RNA formation (Sawai 1976; Lohrmann and Orgel 1980; Ferris and Ertem 1992).

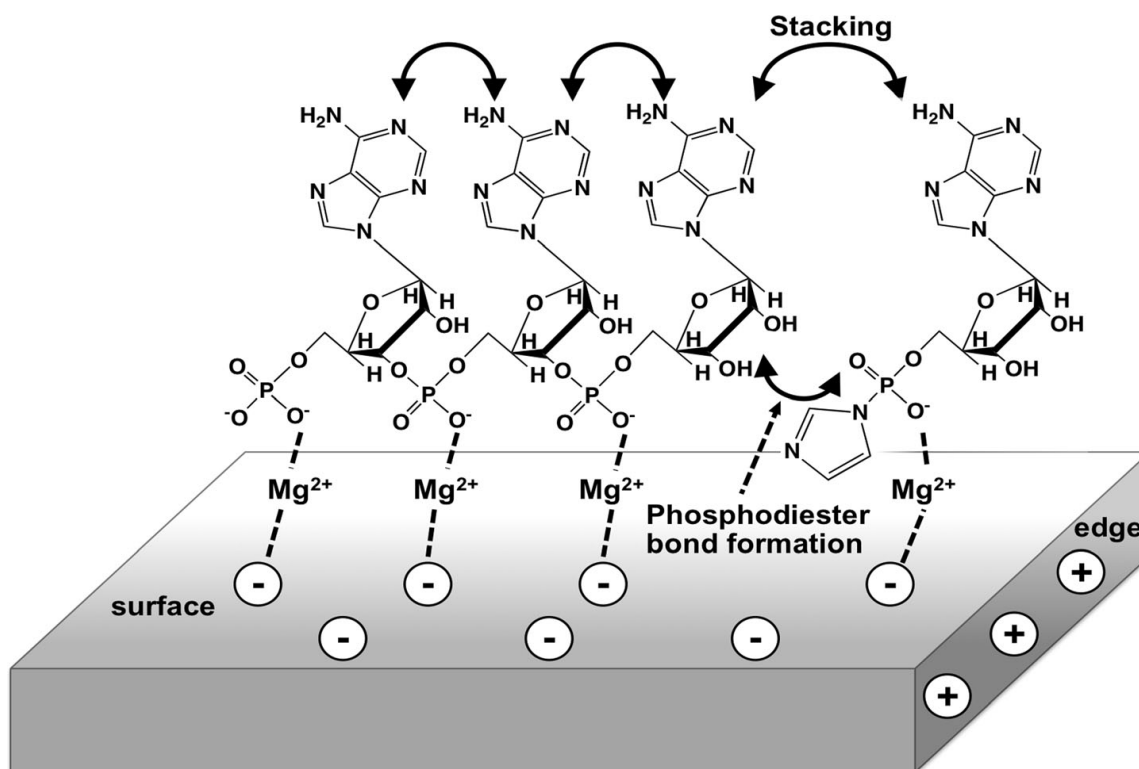
To investigate RNA synthesis, nucleoside 5'-phosphorimidazolides have mainly been used as prebiotic monomers (Lohrmann and Orgel 1973; Orgel and Lohrmann 1974; Lohrmann 1977). Metal ion catalysts (Sawai 1976), clay catalysts (Ferris and Ertem 1992), or template-directed synthesis (Lohrmann and Orgel 1980; Inoue and Orgel 1983) have been extensively studied. Investigations on the association of nucleotides with clay and other minerals were efficiently demonstrated for RNA synthesis (Ferris et al. 1988). Efficient oligomerization of RNA-like products by clay minerals using activated nucleotides according to the pioneering studies by Ferris and his coworkers, is now well established (Ferris and Ertem 1992). The extensive investigations of the roles of natural minerals for the adsorption and possible activation for the formation of oligonucleotides (Ferris and Hagan 1986; Ferris et al. 1988; Ferris and Kamaluddin 1989; Ferris et al. 1989a, b; Ferris and Ertem 1992; Ertem and Ferris 1996) is also well documented. Scope of clay-catalyzed formation of RNA was investigated in detail by analyzing the reaction kinetics and mechanisms on clay (Kawamura and Ferris 1994, 1999; Ertem and Ferris 1998; Ding et al. 1996), the effect of nucleotide bases (Prabaha et al. 1994; Prabaha and Ferris 1997), regio-selectivity (Ferris and Ertem 1992; Miyakawa and Ferris 2003), chiral evolution (Joshi et al. 2000, 2007), and the formation of long oligonucleotides (Huang and Ferris 2002; Ferris 2002).

The kinetic analysis of the clay-catalyzed formation of oligonucleotides showed that the elongation rates of oligonucleotides increase with increase in the length of the oligonucleotides. This fact led to the deduction that the association between two monomers or a monomer with an elongating oligomer is important during this process, and can be enhanced by montmorillonite clays (Kawamura and Ferris 1994; Kawamura and Maeda 2008). In addition, adsorption or approaching of elongating oligomers and monomers on the clay surface, which is negatively charged, is an essential step. The reaction mechanism estimated is illustrated in

Fig. 1, where the clay minerals possess negative charges on clay surface and positive charges on clay edge. The catalytic effect of montmorillonite is due to the negatively charged surface, rather than to the positively charged edge (Ertem and Ferris 1998). This is also supported by earlier studies, in which the activated nucleotide monomers adsorb onto the negative charges of the clay surface by bridging with  $Mg^{2+}$  the negative charge of the phosphorimidazole group. This can also be enhanced with  $Ca^{2+}$ , supporting the adsorption model of bridging by  $Mg^{2+}$  cation (Kawamura and Ferris 1994). The enhancement by the montmorillonite depends on the capability of adsorption of the activated nucleotides on the different types of clay, which seems to be correlated with the structural defect by the low content of iron in montmorillonite (Kawamura and Ferris 1994). The adsorption of the activated nucleotide monomers is also affected by the hydrophobicity of the nucleotide bases; thus the adsorption decreases in the order  $G > A > C \sim U$  (Kawamura and Ferris 1999). Although the activated nucleotide monomers with C or U nucleobases showed very low adsorption ability on montmorillonite clay, the overall yields of oligonucleotides is not or less reduced as compared to those with G or A nucleobases. This fact indicates that the contribution of hydrophobicity of nucleotide bases should be a partial effect for the enhancement of phosphodiester (Kawamura and Ferris 1994, 1999). Based on kinetic analyses one can deduce that the interaction between two monomers or between a monomer and an elongating oligomer is the first step in the formation of the phosphodiester bond (Kawamura and Ferris 1994, 1999; Kawamura and Maeda 2008). This coincides with the role of the hydrophobicity of the leaving group of the activated nucleotide monomers (Prabahar and Ferris 1997) and the fact that the oligomerisation proceeds more effectively at very low temperatures in eutectic phases in ice (Kanavarioti et al. 2001; Monnard et al. 2003).

By the clay-catalyzed oligomerization of the activated nucleotide monomers, both 2',5'- and 3',5'-linked oligonucleotides, pyrophosphate-linked isomers, and cyclic oligonucleotides are formed. Naturally, isomer formation is also observed in the metal ion-catalyzed oligonucleotide formation and the template-directed oligonucleotide formation. By the template-directed oligonucleotide formation, oligonucleotides with 3',5'-linked isomers are mainly formed in the presence of  $Zn^{2+}$  (Bridson and Orgel 1980) and 2',5'-linked oligomers are formed in the presence of  $Pb^{2+}$  (Lohrmann and Orgel 1980). The role of  $Pb^{2+}$  was also observed for the metal ion-catalyzed formation of oligonucleotides (Sawai et al. 1981). On the contrary, there is a tendency for the yield of 3',5'-linked isomers to shift to 2',5'-linked isomers by the clay-catalyzed oligonucleotide formation that varies with the difference of nucleotide bases. The activated pyrimidine nucleotides produces largely 2',5' oligonucleotides, and those with purine nucleotides produce largely 3',5'-linked oligonucleotides. Furthermore, it is surprising that fairly large amounts of cyclic oligonucleotides were observed by the clay-catalyzed oligonucleotide formation, sometimes reaching over 50% among the same length of oligonucleotides (Ding et al. 1996; Kawamura and Ferris 1999). These trends can also be understood by the reaction model, in which the activated nucleotide monomer and elongating oligonucleotides bound on the clay surface associating with these reactants. Presumably, the local conformation during association formation between the elongating oligonucleotide and the activated nucleotide monomer on the clay surface would vary with different nucleotides resulting in different yields of oligonucleotide isomers.

The elongation of long oligomers up to 50 mers is possible by the addition of an activated nucleotide if it starts with long oligonucleotides that selectively react with activated monomers for efficient elongation (Ferris et al. 1996; Huang and Ferris 2002; Ferris 2002). The high efficiency of long oligonucleotide formation is consistent with the estimation that the



**Fig. 1** Model for the elongation of oligonucleotide on a clay surface

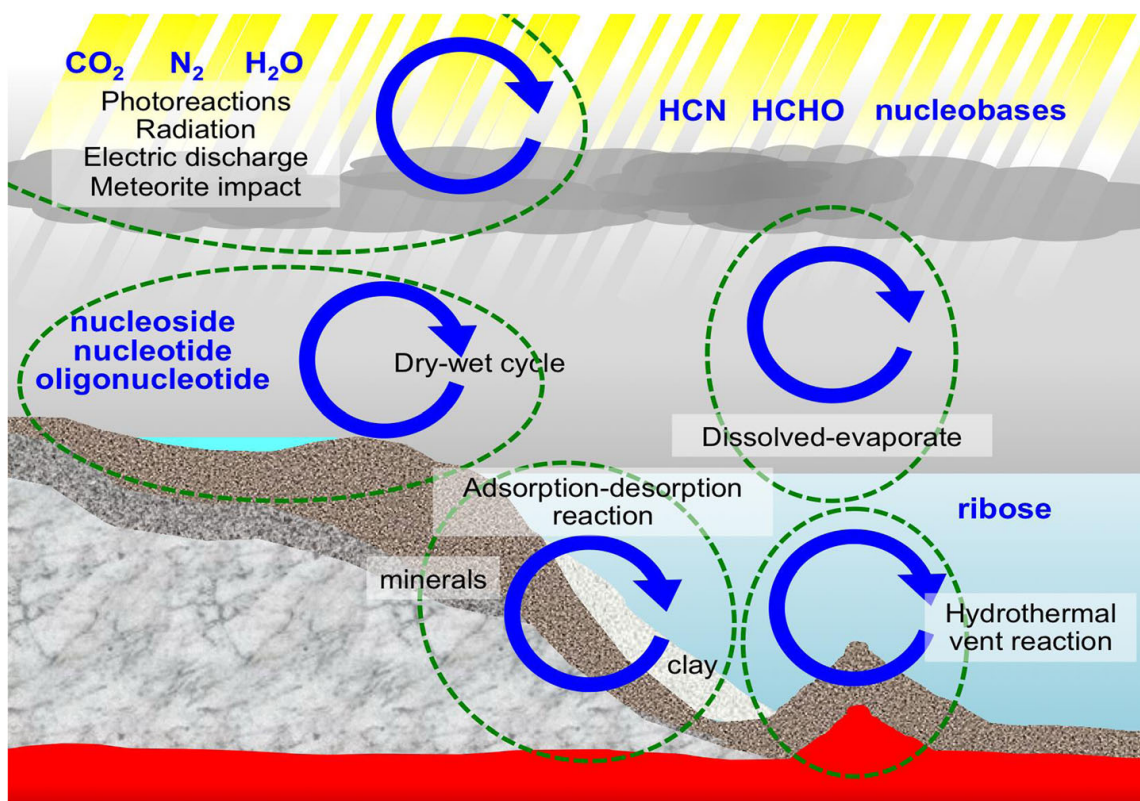
elongating oligonucleotides effectively associate with an activated nucleotide monomer rather than with two activated nucleotide monomers. In addition, the upper limit of temperature where clay mineral enhancement would be effective was kinetically investigated (Kawamura and Maeda 2008). These mechanistic analyses suggest that clay mineral catalysis is possible even at high temperatures (Kawamura and Maeda 2008; Kawamura 2012). These results also support the reaction mechanism mentioned above.

It is estimated that clay minerals were present ever since the formation of the primitive ocean (Ponnamperuma et al. 1982). As mentioned above, the initial ocean may have been strongly acidic so that clay catalysis did not work efficiently. Clay catalysis would have become efficient after the pH of the ocean was neutralized and after CO<sub>2</sub> dissolved in the ocean was removed by precipitation with calcium ions (Paytan and Maclaughlin 2007). In addition, the concentration of the activated nucleotides would need to have been sufficiently high in the primitive ocean.

## Conclusion

In this paper we attempt to summarize numerous studies reporting the step-by-step formation of RNA oligomers from gas phase photo-reactions to mineral-catalyzed reactions in order to combine these steps.

The environments from chemical evolution to RNA accumulation are illustrated in Fig. 2. Finally, each step leading ultimately to the RNA goal is separated from the other steps from the point of view of location and time. Since we have strong assumptions regarding the processes required for the formation of RNA, we can attempt to explain how these steps were conjugated with other processes (Fig. 3). In other words, experiments of chemical evolution processes are

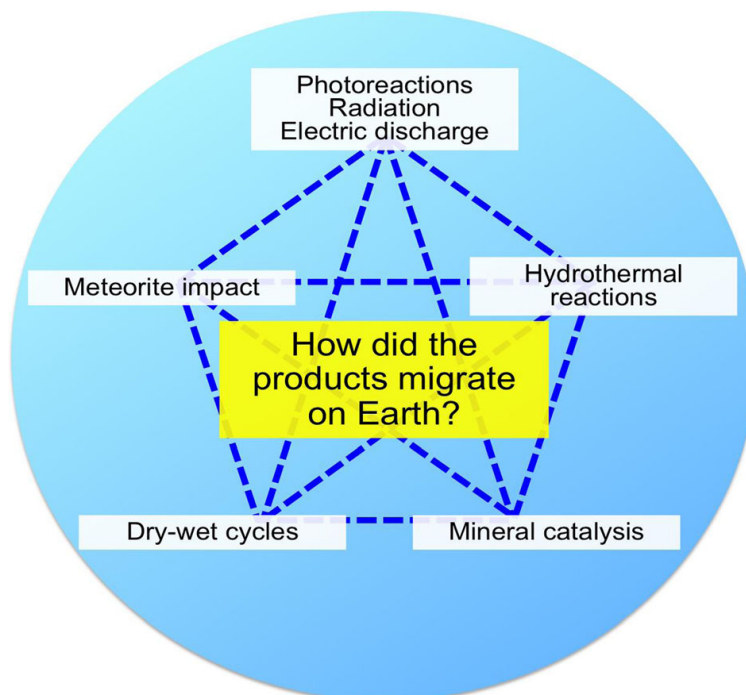


**Fig. 2** Illustration indicating environments of isolated reactions for the processes from gas phase reaction to RNA formation

presently focused on suitable conditions for particular molecules. The question is how such molecules can interact in specific environments with other molecules for further chemical evolution (Fig. 3).

This is more significant for liquid phase reactions rather than for gas phase reactions since diffusion in liquid phase reactions is much slower than in gas phase reactions. If the

**Fig. 3** Symbolic illustration taking into account the connection and interaction between the prebiotic processes for RNA formation

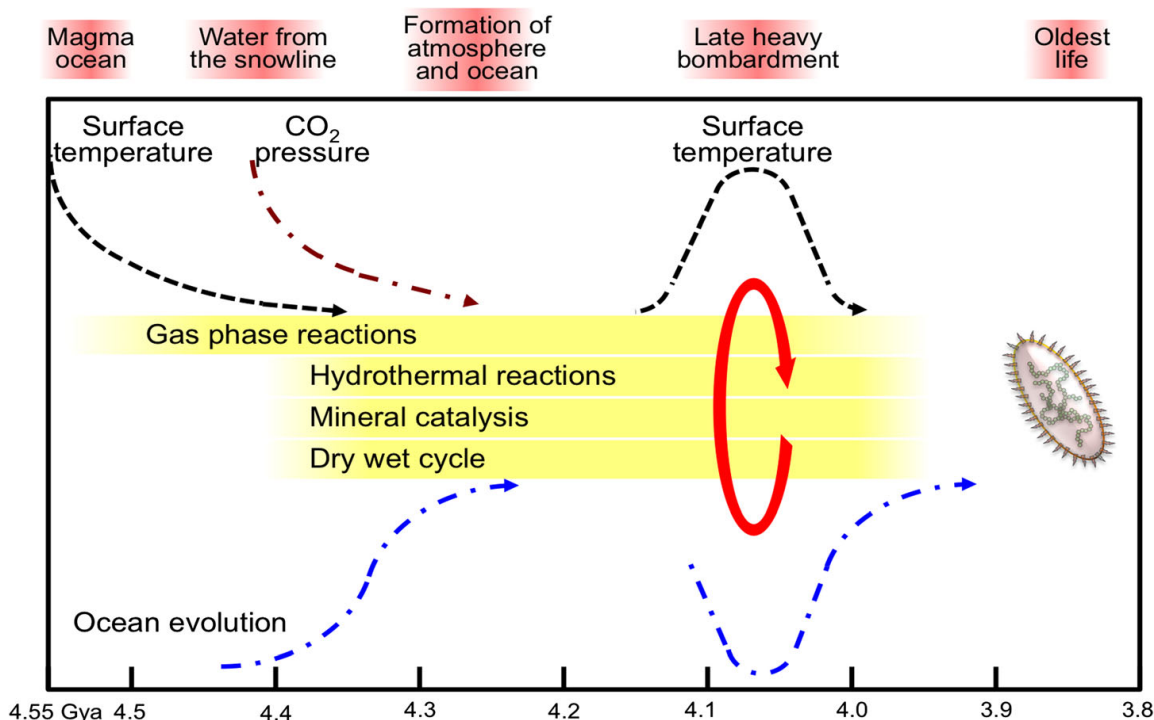


environments suitable for these processes were not close to each other, migration processes of the products should be considered. Thus, migration of reaction products such as ribose, to other suitable areas is necessary. However, a long migration time from one place to another degrade these materials. The migration of reaction products via hydrothermal sites to other places may have been very limited since these might have been geologically isolated. The problem regarding the migration of chemical evolution products is highlighted in this review. Thus, the migration of products formed by chemical evolution processes within the Earth may be an important factor from theoretical and geological viewpoints.

Facing this difficulty, one can assume several possibilities. Two of them are developed in this review.

The first one is that the consecutive chemical evolutionary steps from the formation of ribose, phosphate and nitrogenous bases to oligonucleotides may have occurred in relatively isolated areas. To assume such a situation, we need to propose the existence of such local areas, where all or almost all the steps were handled in a local and relatively small area.

The second possibility is to consider that the products could have been forced to interact due to some events or geological phenomena. Here we have focused on the importance of LHB since this was a major event that occurred after chemical evolution. It is assumed that LHB was an efficient factor (Marchi et al. 2014) in mixing organic molecules with meteorites since a large number of mixing phenomena may have been necessary to connect different chemical evolution processes. A scenario is illustrated in Fig. 4. This indicates that temperature decreases, the drop in the CO<sub>2</sub> pressure and the formation of the ocean coincides with the chemical evolution of gas phase reactions, and the subsequent formation of nucleosides, nucleotides, and oligonucleotides. Naturally, it is unknown how much time was necessary to accumulate these materials and whether the LHB was a suitable event for their mixing that resulted in further chemical evolution. This postulate can be evaluated by experimental simulations in future projects.



**Fig. 4** Synchronized evolution towards life-like systems by chemical evolution, which proceeded separately in isolated Earth environments, and possibly met during the late heavy bombardment

**Acknowledgements** This study was supported by the Bilateral Joint Research Projects/Seminars between the Japan Society for the Promotion of Science (JSPS) and the Centre National de la Recherche Scientifique (CNRS) in 2015-2017, and the JSPS KAKENHI Grant Numbers JP15H01069 in 2015-2017 and JP15K12144 in 2015-2017. We are grateful to Anne-Lise Haenni for English improvement of the manuscript.

## References

- Abramov O, Mojzsis SJ (2016) Thermal effects of impact bombardments on Noachian Mars. *Earth Planet Sci Lett* 442:108–120
- Agmon I (2009) The dimeric proto-ribosome: structural details and possible implications on the origin of life. *Int J Mol Sci* 10:2921–2934
- Agmon I (2016) Could a proto-ribosome emerge spontaneously in the prebiotic world? *Molecules* 21:1701. doi:10.3390/molecules21121701
- Akouche M, Jaber M, Zins E-L, Maurel M-C, Lambert J-F, Georgelin T (2016) Thermal behavior of d-ribose adsorbed on silica: effect of inorganic salt coadsorption and significance for prebiotic chemistry. *Chem Eur J* 22:15834–15846
- Allègre CJ, Manhès G, Göpel C (1995) The age of the earth. *Geochim Cosmochim Acta* 59:1445–1456
- Barghoorn ES, Schopf JW (1966) Microorganisms three billion years old from the precambrian of south africa. *Science* 152:758–763
- Bridson PK, Orgel LE (1980) Catalysis of accurate poly(C)-directed synthesis of 3'-5'-linked oligoguanylates by  $Zn^{2+}$ . *J Mol Biol* 144:567–577
- Britvin SN, Murasko MN, Vapnik Y, Polekhovskiy YS, Krivovichev SV (2015) Earth's phosphides in Levant and insights into the source of archean prebiotic phosphorus. *Sci Rep* 5:8355
- Callahan MP, Smith KE, Cleaves HJ, Ruzickad J, Sterna JC, Glavina DP, Houseb CH, Dworkin JP (2011) Carbonaceous meteorites contain a wide range of extraterrestrial nucleobases. *Proc Natl Acad Sci U S A* 108:13995–13998
- Cech TR (2000) The ribosome is a ribozyme. *Science* 289:878–879
- Cermakian N, Cedergren R (1998) Modified nucleosides always were: an evolutionary model. In: Grosjean H, Benne R (eds) *Modification and editing of RNA*. ASM Press, Washington DC, pp 535–541
- Costanzo G, Saladino R, Crestini C, Ciciriello F, Di Mauro E (2007) Nucleoside phosphorylation by phosphate minerals. *J Biol Chem* 282:16729–16735
- Costanzo G, Pino S, Ciciriello F, Mauro D (2009) Generation of long RNA chains in water. *J Biol Chem* 284:33206–33216
- Da Silva L, Maurel M-C, Deamer D (2015) Salt-promoted synthesis of RNA-like molecules in simulated hydrothermal conditions. *J Mol Evol* 80:86–97
- Delan-Forino C, Maurel M-C, Torchet C (2011) Replication of avocado sunblotch viroid in the yeast *Saccharomyces cerevisiae*. *J Virol* 85:3229–3238
- Diener TO (1989) Circular RNAs: relics of precellular evolution? *Proc Natl Acad Sci U S A* 86:9370–9374
- Ding PZ, Kawamura K, Ferris JP (1996) Oligomerization of uridine phosphorimidazolides on montmorillonite: a model for the prebiotic synthesis of RNA on minerals. *Origins Life Evol Biosph* 27:107–118
- El-Murr N, Maurel M-C, Rihova M, Vergne J, Hervé G, Kato M, Kawamura K (2012) Behavior of a hammerhead ribozyme in aqueous solution at medium to high temperatures. *Naturwissenschaften* 99(9):731–738
- Ertem G, Ferris JP (1996) Synthesis of RNA oligomers on heterogeneous templates. *Nature* 379:238–240
- Ertem G, Ferris JP (1998) Formation of RNA oligomers on montmorillonite: site of catalysis. *Orig Life Evol Biosph* 28:485–499
- Ferris JP (1979) Organic chemistry on titan. *Rev Geophys* 17:1923–1933
- Ferris JP (2002) Montmorillonite catalysis of 30-50 mer oligonucleotides: laboratory demonstration of potential steps in the origin of the RNA world. *Orig Life Evol Biosph* 32:311–332
- Ferris JP, Chen CT (1975) Chemical evolution. XXVI. Photochemistry of methane, nitrogen, and water mixtures as a model for the atmosphere of the primitive earth. *J Am Chem Soc* 97:2962–29676
- Ferris JP, Ertem G (1992) Oligomerization of ribonucleotides on montmorillonite: reaction of the 5'-phosphorimidazolide of adenosine. *Science* 257:1387–1389
- Ferris JP, Hagan WJ Jr (1986) The adsorption and reaction of adenine-nucleotides on montmorillonite. *Orig Life Evol Biosph* 17:69–84
- Ferris JP, Joshi PC (1979) Chemical evolution. 33. Photochemical decarboxylation of orotic acid, orotidine, and orotidine 5'-phosphate. *J Org Chem* 44:2133–2137

- Ferris JP, Kamaluddin (1989) Oligomerization reactions of deoxyribonucleotides on montmorillonite clay - the effect of mononucleotide structure on phosphodiester bond formation. *Orig Life Evol Biosph* 19:609–619
- Ferris JP, Morimoto JY (1981) Irradiation of NH<sub>3</sub> CH<sub>4</sub> mixtures as a model of photochemical processes in the Jovian planets and titan. *Icarus* 48:118–126
- Ferris JP, Orgel LE (1965) Aminomalononitrile and 4-amino-5-cyanoimidazole in hydrogen cyanide polymerization and adenine synthesis. *J Am Chem Soc* 87:4976–4977
- Ferris JP, Sanchez RA, Orgel LE (1968) Studies in prebiotic synthesis: III. Synthesis of pyrimidines from cyanoacetylene and cyanate. *J Mol Biol* 33:693–704
- Ferris JP, Kuder JE, Catalano AW (1969) Photochemical reactions and the chemical evolution of purines and nicotinamide derivative. *Science* 166:765–766
- Ferris JP, Joshi PC, Edelson EH, Lawless JG (1978) HCN: a plausible source of purines, pyrimidines and amino acids on the primitive earth. *J Mol Evol* 11:293–311
- Ferris JP, Edelson EH, Mount NM, Sullican AE (1979) The effect of clays on the oligomerization of HCN. *J Mol Evol* 13:317–330
- Ferris JP, Yanagawa H, Hagan WJ Jr (1984) The prebiotic chemistry of nucleotides. *Orig Life Evol Biosph* 14:99–106
- Ferris JP, Huang C-H, Hagan WJ Jr (1988) Montmorillonite: a multifunctional mineral catalyst for the prebiological formation of phosphate esters. *Orig Life Evol Biosph* 18:121–133
- Ferris JP, Ertem G, Agarwal V (1989a) Mineral catalysis of the formation of dimers of 5'-AMP in aqueous-solution - the possible role of montmorillonite clays in the prebiotic synthesis of RNA. *Orig Life Evol Biosph* 19:165–178
- Ferris JP, Kamaluddin, Ertem G (1989b) Oligomerization reactions of deoxyribonucleotides on montmorillonite clay - the effect of mononucleotide structure, phosphate activation and montmorillonite composition on phosphodiester bond formation. *Orig Life Evol Biosph* 20:279–291
- Ferris JP, Hill AR Jr, Liu R, Orgel LE (1996) Synthesis of long prebiotic oligomers on mineral surfaces. *Nature* 381:59–61
- Friedmann N, Miller SL, Sanchez RA (1971) Primitive earth synthesis of nicotinic acid derivatives. *Science* 171:1026–1027
- Fuller WD, Sanchez RA, Orgel LE (1972) Studies in prebiotic synthesis: VI. Synthesis of purine nucleosides *J Mol Biol* 67:25–33
- Gabel NW, Ponnampertuma C (1967) Model for origin of monosaccharides. *Nature* 216:453–455
- Georgelin T, Jaber M, Fournier F, Laurent G, Costa-Torro F, Maurel M-C, Lambert J-F (2015) Stabilization of ribofuranose by a mineral surface. *Carbohydr Res* 402:241–244
- Gilbert W (1986) Origins of life - the RNA world. *Nature* 319:618
- Gough DO (1981) Solar interior structure and luminosity variations. *Solar Phys* 74:21–34
- Grotzinger JP, Kasting JF (1993) New constraints on precambrian ocean composition. *J Geol* 101:235–243
- Gull M, Mojica MA, Fernandez FM, Gaul DA, Orlando TM, Liotta CL, Pase MA (2015) Nucleoside phosphorylation by the mineral schreibersite. *Sci Rep* 5:17198
- Holm NG, Dumont M, Ivarsson M, Kohn C (2006) Alkaline fluid circulation in ultramafic rocks and formation of nucleotide constituents: a hypothesis. *Geochem Trans* 7:7
- Huang W, Ferris JP (2002) Synthesis of 35–40 mers of RNA oligomers from unblocked monomers. A simple approach to the RNA world. *Chem Comm* 1458–1459
- Hud NV, Cafferty BJ, Krishnamurthy R, Williams LD (2013) The origin of RNA and “my grandfather’s axe”. *Chem Biol* 20:466–474
- Inoue T, Orgel LE (1983) A nonenzymatic RNA polymerase model. *Science* 219:859–862
- Jørgensen UG, Appel PWU, Hatsukawa Y, Frei R, Oshima M, Toh Y, Kimura A (2009) The earth–moon system during the late heavy bombardment period – geochemical support for impacts dominated by comet. *Icarus* 204:368–380
- Joshi PC, Pitsch S, Ferris JP (2000) Homochiral selection in the montmorillonite-catalyzed and uncatalyzed prebiotic synthesis of RNA. *Chem Comm* 2497–2498
- Joshi PC, Pitsch S, Ferris JP (2007) Selectivity of montmorillonite catalyzed prebiotic reactions of D, L-nucleotides. *Orig Life Evol Biosph* 37:3–26
- Joyce GF (1986) RNA evolution and the origins of life. *Nature* 338:217–224
- Joyce GF, Schwartz AW, Miller SL, Orgel LE (1987) The case for an ancestral genetic system involving simple analogues of the nucleotides. *Proc Natl Acad Sci U S A* 84:4398–4402
- Kaddour H, Vergne J, Hervé G, Maurel M-C (2011) High-pressure analysis of a hammerhead ribozyme from chrysanthemum chlorotic mottle viroid reveals two different populations of self-cleaving molecule. *FEBS J* 278:3739–3747

- Kanavarioti A, Monnard PA, Deamer DW (2001) Eutectic phases in ice facilitate nonenzymatic nucleic acid synthesis. *Astrobiology* 1:271–281
- Kasting JF (1993) Earth's early atmosphere. *Science* 259:920–926
- Kasting JF, Pollack JB (1984) Effects of high CO<sub>2</sub> levels on surface temperature and atmospheric oxidation state of the early earth. *J Atom Chem* 1:403–428
- Kawamura K (2012) Drawbacks of the ancient RNA-based life-like system under primitive earth conditions. *Biochimie* 94:1441–1450
- Kawamura K, Ferris JP (1994) Kinetic and mechanistic analysis of dinucleotide and oligonucleotide formation from the 5'-phosphorimidazolide of adenosine on Na<sup>+</sup>-montmorillonite. *J Am Chem Soc* 116:7564–7572
- Kawamura K, Ferris JP (1999) Clay catalysis of oligonucleotide formation: kinetics of the reaction of the 5'-phosphorimidazolides of nucleotides with the non-basic heterocycles uracil and hypoxanthine. *Orig Life Evol Biosph* 29:563–591
- Kawamura K, Maeda J (2008) Kinetics and activation parameter analysis for the prebiotic oligocytidylate formation on Na<sup>+</sup>-montmorillonite at 0–100 °C. *J Phys Chem A* 112:8015–8023
- Kim HJ, Ricardo A, Illangkoon HI, Kim MJ, Carrigan MA, Frye F, Benner SA (2011) Synthesis of carbohydrates in mineral-guided prebiotic cycles. *J Am Chem Soc* 133:9457–9468
- Kolesnikov MP, Kritsky MS (2001) Study of chemical structure and of photochemical activity of abiogenic flavin pigment. *J Evol Biochem Physiol* 37:507–514
- Kopetzki D, Antonietti M (2011) Hydrothermal formose reaction. *New J Chem* 35:1787–1794
- Krupkin M, Matzov D, Tang H, Metz M, Kalaora R, Belousoff MJ, Zimmerman E, Bashan A, Yonath A (2011) A vestige of a prebiotic bonding machine is functioning within the contemporary ribosome. *Phi. Trans R Soc B* 366:2972–2978
- Lambert JB, Gurusamy-Thangavelu SA, Ma K (2010) The silicate-mediated formose reaction: bottom-up synthesis of sugar silicates. *Science* 327:984–986
- Larralde R, Robertson MP, Miller SL (1995) Rates of decomposition of ribose and other sugars: implications for chemical evolution. *Proc Natl Acad Sci U S A* 92:8158–8160
- Latifi A, Bernard C, Da Silva L, Andéol Y, Elleuch A, Risoul V, Vergne J, Maurel M-C (2016) Replication of avocado sunblotch viroid in the cyanobacterium *Nostoc* sp. PCC 7120. *J Plant path Microbiol* 7:341. doi:10.4172/2157-7471.1000341
- Leclerc F, Zaccari G, Vergne J, Řihová M, Martel A, Maurel M-C (2016) Self-assembly controls self-cleavage of HHR from ASBVd (–) : a combined sans and modeling study. *Sci Rep* 6:30287. doi:10.1038/srep30287
- Lohrmann R (1977) Formation of nucleoside 5'-phosphorimidates under potentially prebiological conditions. *J Mol Evol* 10:137–154
- Lohrmann R, Orgel LE (1973) Prebiotic activation processes. *Nature* 244:418–420
- Lohrmann R, Orgel LE (1980) Efficient catalysis of polycytidylic acid-directed oligoguanylate formation by Pb<sup>2+</sup>. *J Mol Biol* 142:555–567
- Maizels N, Weiner AM (1993) In: Gesteland RF, Atkins JF (eds) *The RNA world*. Cold Spring Harbor Lab Press, Plainview, pp 577–602
- Maizels N, Weiner AM (1994) Phylogeny from function: evidence from the molecular fossil record that tRNA originated in replication, not translation. *Proc Natl Acad Sci U S A* 91:6729–6734
- Marchi S, Bottke WF, Elkins-Tanton LT, Bierhaus M, Wuennemann K, Morbidelli A, Kring DA (2014) Widespread mixing and burial of Earth's Hadean crust by asteroid impacts. *Nature* 511:578–582
- Maruyama S, Ikoma M, Genda H, Hirose K, Yokoyama T, Santosh M (2013) The naked planet earth: most essential pre-requisite for the origin and evolution of life. *Geosci Front* 4:141–165
- Miyakawa S, Ferris JP (2003) Sequence and regioselectivity in the montmorillonite-catalyzed synthesis of RNA. *J Am Chem Soc* 125:8202–8208
- Mizuno T, Weiss A (1974) Synthesis and utilization of formose sugars. *Adv Carbohyd Chem Biochem* 29:173–227
- Mojzsis SJ, Arrhenius G, McKeegan KD, Harrison TM, Nutman AP, Friend CRL (1996) Evidence for life on earth before 3,800 million years ago. *Nature* 384:55–59
- Mojzsis SJ, Harrison TM, Pidgeon RT (2001) Oxygen-isotope evidence from ancient zircons for liquid water at the Earth's surface 4,300 Myr ago. *Nature* 409:178–181
- Monnard PA, Kanavarioti A, Deamer DW (2003) Eutectic phase polymerization of activated ribonucleotide mixtures yields quasi-equimolar incorporation of purine and pyrimidine nucleobases. *J Am Chem Soc* 125:13734–13740
- Morbidelli A, Marchi S, Bottke WF, Kring DA (2012) A sawtooth-like timeline for the first billion years of lunar bombardment. *Earth Plant Sci Lett* 355:144–151
- Morse JW, Mackenzie FT (1998) Hadean ocean carbonate geochemistry. *Aquatic Geochem* 4:301–319
- Nutman AP, Bennet VC, Friend CRL, Van Kranendonk M, Chivas AR (2016) Rapid emergence of life shown by discovery of 3,700-million-year-old microbial structures. *Nature* 537:535–538



- Orgel LE, Lohrmann R (1974) Prebiotic chemistry and nucleic acid replication. *Acc Chem Res* 7:368–377
- Oró J (1961) Mechanism of synthesis of adenine from hydrogen cyanide under possible primitive earth conditions. *Nature* 191:1193–1194
- Pasek MA, Lauretta DS (2005) Aqueous corrosion of phosphide minerals from iron meteorites: a highly reactive source of prebiotic phosphorus on the surface of the early earth. *Astrobiology* 5:515–535
- Paytan A, Maclaughlin K (2007) The oceanic phosphorus cycle. *Chem Rev* 107:563–576
- Peck WH, Valley JW, Wilde SA, Graham CM (2001) Oxygen isotope ratios and rare earth elements in 3.3 to 4.4 Ga zircons: ion microprobe evidence for high  $d^{18}\text{O}$  continental crust and oceans in the early Archean. *Geochim Cosmochim Acta* 65:4215–4229
- Pinheiro VB, Taylor AI, Cozens C, Abramov M, Renders M, Zhang S, Chapu JC, Wengel J, Peak-Chew S-Y, McLaughlin SH, Herdewijn P, Holliger P (2012) Synthetic genetic polymers capable of heredity and evolution. *Science* 336:341–344
- Ponnampertuma C, Shimoyama A, Friebele E (1982) Clay and the origin of life. *Origins Life* 12:9–40
- Prabakar KJ, Ferris JP (1997) 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* 119:4330–4337
- Prabakar KJ, Cole TD, Ferris JP (1994) Effect of phosphate activating group on oligonucleotide formation on montmorillonite: the regioselective formation of 3',5'-linked oligoadenylates. *J Am Chem Soc* 116:10914–10920
- Prieur B (2009) Phosphorylation of ribose in the presence of borate salts. *Origins Life Evol Biosph* 39:264–265
- Rao M, Odom DG, Oró J (1980) Clays in prebiological chemistry. *J Mol Evol* 15:317–331
- Reid C, Orgel LE (1967) Model for origin of monosaccharides: synthesis of sugars in potentially prebiotic conditions. *Nature* 216:455
- Reimann E, Zubay G (1999) Nucleoside phosphorylation: a feasible step in the prebiotic pathway to RNA. *Orig Life Evol Biosph* 29:229–247
- Ricardo A, Carrigan MA, Olcott AN, Benner SA (2004) Borate minerals stabilize ribose. *Science* 303:196–196
- Ryder G (2002) Mass flux in the ancient earth-moon system and benign implications for the origin of life on earth. *J Geophys Res-Plan* 107:E4
- Sagan C, Mullen G (1972) Earth and Mars: evolution of atmosphere and surface temperatures. *Science* 177:52–56
- Saladino R, Ciambecchini U, Crestini C, Costanzo G, Negri R, Di Mauro E (2003) One-pot  $\text{TiO}_2$ -catalyzed synthesis of nucleic bases and acyclonucleosides from formamide: implications for the origin of life. *Chembiochem* 4:514–521
- Saladino R, Crestini C, Ciciriello F, Costanzo G, Di Mauro E (2007) Formamide chemistry and the origin of informational polymers. *Chem Biodivers* 4:694–720
- Sanchez RA, Orgel LE (1970) Studies in prebiotic synthesis: V. Synthesis and photoanomerization of pyrimidine nucleosides *J Mol Biol* 47:531–543
- Sanchez RA, Ferris JP, Orgel LE (1966) Cyanoacetylene on prebiotic synthesis. *Science* 154:784–785
- Sawai H (1976) Catalysis of internucleotide bond formation by divalent metal ions. *J Am Chem Soc* 98:7037–7039
- Sawai H, Shibata T, Ohno M (1981) Preparation of oligoadenylates with 2'-5' linkage using  $\text{Pb}^{2+}$  ion catalyst. *Tetrahedron* 37:481–485
- Schopf JW (1993) Microfossils of the early Archean apex Chert: new evidence of the antiquity of life. *Science* 260:640–646
- Schwartz AW (2006) Phosphorus in prebiotic chemistry. *Phil Trans R Soc B* 361:1743–1749
- Schwartz AW, De Graaf RM (1993) The prebiotic synthesis of carbohydrates: a reassessment. *J Mol Evol* 36:101–106
- Schwartz AW, Goverde M (1982) Acceleration of HCN oligomerization by formaldehyde and related compounds: implications for prebiotic syntheses. *J Mol Evol* 18:351–353
- Schwartz AW, Joosten H, Voet AB (1982) Prebiotic adenine synthesis via HCN oligomerization in ice. *Biosystems* 15:191–193
- Shapiro R (1988) Prebiotic ribose synthesis: a critical analysis. *Orig Life Evol Biosph* 18:71–85
- Shigemasa Y, Shimao M, Sakazawa C, Matsuura T (1977) Formose reactions. IV. The formose reaction in homogenous systems and the catalytic functions of calcium ion species. *Bull Chem Soc Jpn* 50:2138–2142
- Sojo V, Herschy B, Whicher A, Camprub E, Lane N (2016) The origin of life in alkaline hydrothermal vents. *Astrobiology* 16:181–197
- Sutherland JD (2016) The origin of life—out of the blue. *Angew Chem Int Ed* 55:104–121
- Tian F, Kasting JF, Zahnle K (2011) Revisiting HCN formation in Earth's early atmosphere. *Earth Planet Sci Lett* 308:417–423
- Tuck AC, Tollervey D (2011) RNA in pieces. *Trends Genet* 27:422–432

- Valle M, Gillet R, Kaur S, Henne A, Ramakrishnan V, Frank J (2003) Visualizing tmRNA entry into a stalled ribosome. *Science* 300:127–130
- Walker JC (1985) Carbon dioxide on the early earth. *Orig Life Evol Biosph* 16:117–127
- Weber AL (1992) Prebiotic sugar synthesis: hexose and hydroxy acid synthesis from glyceraldehyde catalyzed by iron(III) hydroxide oxide. *J Mol Evol* 35(1):1–6
- Wells LE, Armstrong JC, Gonzalez G (2003) Reseeding of early earth by impacts of returning ejecta during the late heavy bombardment. *Icarus* 162:38–46
- Wetherill GW (1975) Late heavy bombardment of the moon and terrestrial planets, lunar Science conference, 6th, Houston, Tex., march 17-21, 1975, proceedings. Volume 2:1539–1561
- White HB III (1976) Coenzymes as fossils of an earlier metabolic state. *J Mol Evol* 7:101–104
- Yamagata Y, Kojima H, Ejiri K, Inomata K (1982) AMP synthesis in aqueous solution of adenosine and phosphorous pentoxide. *Origins Life* 12:333–333
- Yamagata Y, Watanabe H, Namba T (1992) Volcanic production of polyphosphates and its relevance to prebiotic evolution. *Nature* 352:516–519
- Yamagata Y, Inoue H, Inomata K (1995) Specific effect of magnesium ion on 2',3'-cyclic AMP synthesis from adenosine and trimeta phosphate in aqueous solution. *Orig Life Evol Biosph* 25:47–42
- Zaccai G, Natali F, Peters J, Rihova M, Zimmerman E, Ollivier J, Combet J, Maurel M-C, Bashan A, Yonath A (2016) The fluctuating ribosome: thermal molecular dynamics characterized by neutron scattering. *Scientific Reports* 6:37138. doi:[10.1038/srep37138](https://doi.org/10.1038/srep37138)