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Mini Review

Possibility of Abiotic Genesis of Biochemistry

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Abstract

One of the first and primary life origin questions is how life can originate from primordial Earth chemistry. More than 60 years ago, Stanley Miller and Harold Urey conducted the famous Miller-Urey experiment where heated mixture of water, methane, ammonia and hydrogen; representing early compounds on Earth; produces several amino acids when passed through an electrical discharge representing lightning. This gave rise to the possibility of abiotic genesis of biochemistry. Over the next six decades, evidence supporting various primordial macrobiomolecules emerged; leading to the concepts of RNA, DNA and peptides being the first primordial macrobiomolecules. In this short review, possibility of each world originating separately, and coevolving were examined. Current evidence suggests that RNA world and peptide/amyloid world may originate independently and substantial possibility of interplay between these three worlds. Hence, RNA world, DNA world, and peptide/amyloid world may coevolve regardless of whether they originate independently. Thus, this calls for a reconciliation into a peptide-nucleic acid world.

Keywords: *Origins of Life; DNA World Hypothesis; RNA World Hypothesis; Peptide/Amyloid World Hypothesis*

Three types of primordial world

How life originates from primordial Earth chemistry is one of the earliest and biggest question in Biology. In 1923, a book by the Russian Biochemist, Alexander Ivanovich Oparin [1] titled 'The Origin of Life', suggested the emergence of heterotrophs in the anaerobic environment of primitive Earth. Oparin proposed the possibility of a heterotrophic world that was likely preceded by a prolonged period of abiotic syntheses and an accumulation of organic compounds forming what we call the primitive soup today.

While the heterotrophic theory of origin continues to be reshaped over the next few decades, evidence that supports various primordial macrobiomolecules emerged to suggest alternate possibilities to the theory of origin. A recent study by Fraccia., *et al.* [2] showed that short DNA fragments were capable of self-assembly and autocatalysis in liquid crystals. These properties had enabled an autocatalytic cycle which favours growth into larger DNA molecules, suggesting the possibility of a DNA world. Robertson and Joyce [3] had provided an overview of the RNA world where it explores the possibility of RNA being the origin of life. They showed that RNA nucleotides were able to undergo abiotic polymerisation to produce oligonucleotides, which could undergo self-replication to ensure genetic continuity. The peptide/amyloid world hypothesis by Maury [4] suggests that peptides and amyloids were the first molecular entities due to their abilities to self-assemble, self-replicate, transmit information, and evolve.

With the various theories suggesting that the origin of life is based on a single macrobiomolecule attributed mainly to their catalytic and informational properties. A recent study by Charles Carter [5] had proposed the possibility of a peptide/RNA world using urzymes (primitive enzymes) [6] enzymatic cores, as an ancestral predictive model. They showed that the two different biomolecule classes had likely descended as translational products from opposite stands of a single ancestral gene. Therefore, this calls for a reconciliation into the possibility of a peptide-nucleic acid world.

Formation of monomers

The first step to the formation of macrobiomolecules is the formation of required monomers - before DNA and RNA can be formed, deoxyribobases and ribobases must be formed respectively. Similarly, before peptides can be formed, amino acids must be formed. Hence, abiotic synthesis of macrobiomolecules require their respective monomers to be synthesized from their respective precursors (Figure 1). Thus, the question is whether such biomolecule precursorial monomers can be synthesized from their respective precursors in the primordial environment? It is expected that precursors for biomolecule formation are either simple organic compounds, such as methane, or inorganic compounds, such as carbon dioxide and nitrogen.

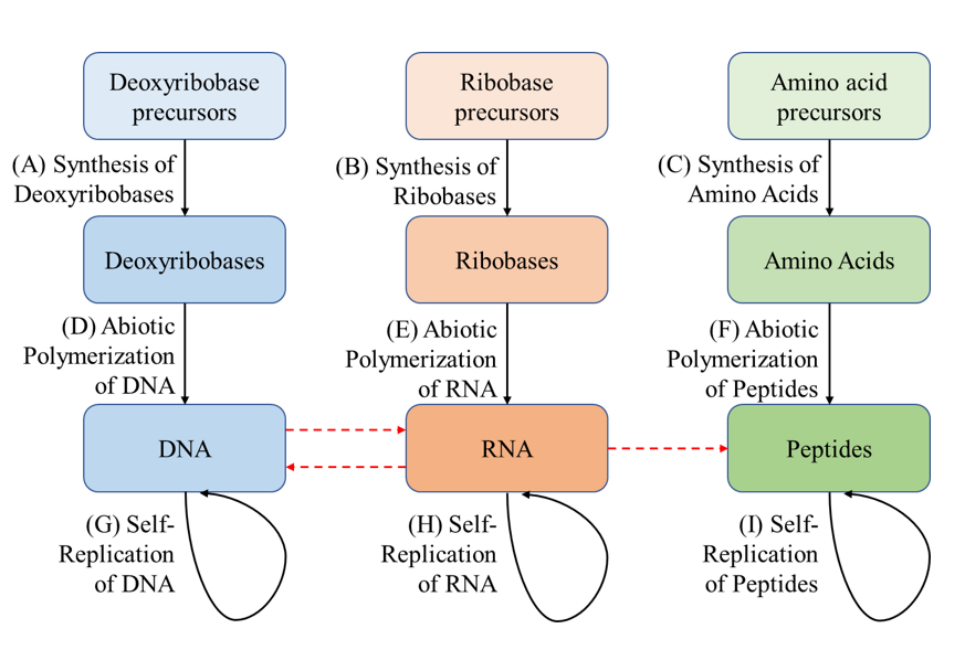

Figure 1: *Requirements of and interplay between DNA world, RNA world, and peptide/amyloid world.*

A spectrophotometric analysis of Milky Way Galaxy [7] suggests that the four basic elements of biomolecules are common - 73.90% hydrogen, 1.04% oxygen, 0.46% carbon, and 0.10% nitrogen. This is consistent with the expected earliest atmosphere of Earth [8] consisting primarily hydrogen and simple hydrides such as water vapor, methane and ammonia. Harries., *et al.* [9] suggests that the origins of nitrogen on Earth may be from the decomposition of ammonia. Further analyses of Titan [10], the only moon in the Solar System with a dense atmosphere, shows an abundance [11] of nitrogen (94.2%) and methane (5.65%). Hence, it is feasible to consider hydrogen, nitrogen, and hydrides as biomolecule monomer precursors.

In early 1950s, Stanley Miller and Harold Urey [12] conducted the famous Miller-Urey experiment where a mixture of water, methane, ammonia, and hydrogen was heated and its vapours passing through an electrical discharge to simulate lightning; and synthesized glycine, α-alanine, β-alanine, aspartic acid, and α-aminobutyric acid. Johnson., *et al.* [13] re-analyzed the vials left from the series of Miller-Urey experiments and identified 22 amino acids and five amines, in addition to what Miller and Urey had identified [12]. Neish., *et al.* [14] demonstrated that a mixture of 2% methane and 98% nitrogen exposed to an electrical discharge at -78°C with 880 Pascal (116% pressure on Earth surface), to mimic Titan's condition, is able to produce tholins. These tholin mixtures, at high ammonia solution (about 14 N) between -20°C to 20°C, yield all five nucleobases (adenine, thymine, cytosine, guanine, and uracil), as well as four amino acids (asparagine, aspartic acid, glutamine, and glutamic acid). Biscans [15] suggested possible abiotic synthetic routes of ribonucleobases. Both Miller-Urey's experiment and Neish., *et al.* are supported by a study [16] demonstrating room temperature aqueous Miller-Urey experiments, with or without initial ammonia, and Titan tholin hydrolysis experiments produce similar amino acid products. These experiments suggest that biomolecule precursors, such as amino acids and nucleobases, can be formed from biomolecule monomer precursors such as hydrogen, nitrogen, and hydrides.

Abiotic polymerization to macrobiomolecules

Given that biomolecule monomers can be formed from precursors, the next question is whether such monomers can abiotically polymerize into macrobiomolecules: such as chains of nucleic acids or peptides. Li., *et al.* [17] demonstrated that nucleobase monomers can form liquid crystals in water. At high concentrations of above 800 mg/ml, single nucleobase monomers can exhibit base-pairing [18] at temperatures below 30°C. Similarly, Fraccia., *et al.* [19] demonstrated spontaneous base-pairing in liquid crystals of tetrameric nucleic acids at 240 - 480 mg/ml below 30°C. Fraccia., *et al.* [2] had previously shown that self-assembly in liquid crystals provided the stability for autocatalysis and ligation of oligomeric deoxynucleic acids in the presence of a ligating agent, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide. It is not clear how polymerization of two nucleobases into a dinucleobase can occur in the absence of any ligating agents. On the other hand, Costanzo., *et al.* [20] showed that polymerization of cyclic nucleobases in water, yielding oligomers as long as 25 bases, is possible at low concentrations of 1 mM and moderate temperature between 40°C and 90°C in the absence of any enzymes and catalysts. Treating nucleosides in formamide and phosphate at 60°C for several hours can yield cyclic nucleobases suitable for polymerization [21]. Phosphate may be present in early Earth as mineral schreibersite [22] and formamide may be produced in early Earth from nitriles by radioactive compounds [23].

In terms of peptides, things are relatively simpler. Greenwald., *et al.* [24] demonstrated that short chains of alanine peptides consisting of 13 amino acids can originate from relatively low concentration (20 mM) of alanine monomers by volcanic gas carbonyl sulphide-catalyzed polymerization, suggesting that such possibility can occur at low concentrations. When the concentration of alanine was reduced to 10 mM, polymers of two to six polyalanines were observed. This suggests that abiotic amino acid polymerization into polypeptides is concentration dependent. However, the common theme in both nucleobase polymerization and amino acid polymerization is a cyclic change in temperature and concentration. This may suggest that polymerization may exist on coastal edge.

Catalytic properties of macrobiomolecules

Since abiotic polymerization of biomolecule precursors; deoxyribonucleobases, ribonucleobases and amino acids; to their respective macrobiomolecules; DNA, RNA and peptides; are likely possible; the next question is whether these macrobiomolecules can have catalytic properties. More specifically, can macrobiomolecules self-replicate (for example, a peptide catalysing the formation of itself from available free amino acids) or can macrobiomolecules cross replicate (for example, a peptide catalysing the polymerization of DNA from available free deoxyribonucleobases)? The answer is largely yes.

Firstly, we will consider the question of whether macrobiomolecules can have catalytic properties. Catalytic peptides are common known as enzymes in biology and about 84 thousand enzymes catalysing more than 5 thousand biochemical reactions had been identified

[25]. In 1982, Kruger., *et al.* [26] demonstrated that RNA may self-splice, which suggests that RNA can have catalytic properties, and term these RNA molecules as ribozymes. Breaker and Joyce reported the first DNA with catalytic properties, known as DNAzyme or deoxyribozyme, that can cleave RNA in 1994 [27]. These evidences suggest that macrobiomolecules can have catalytic properties.

Secondly, we consider whether macrobiomolecules can cross replicate. From the perspective of enzymes; there are enzymes for replicating RNA, which are known as RNA-dependent RNA polymerases [28] and replicating DNA, which are known as DNA-dependent DNA polymerases or more commonly known as DNA polymerases [29]. DNA polymerases enzymes involved in replication of DNA usually before cell division while RNA polymerases crucial enzymes for gene transcription. Hence, cross replications of DNA or RNA by peptides are well-known. From the perspective of ribozymes, peptidyl transferase centre of the ribosome has been considered as a type of ribozyme [30,31]. Ribozymes have also been shown to have ligase capabilities on nucleic acids [32]. Katzman., *et al.* [33] had demonstrated that class I RNA-ligase ribozymes can have DNA ligation capabilities. Hence, polymerization of peptides or DNA by ribozymes seems possible. From the perspective of deoxyribozyme, deoxyribozymes capable of 2'-3' RNA ligation was first reported by Flynn-Charlebois., *et al.* in 2003 [34]. Subsequently, 3'-5' ligation of two RNA molecules to form a linear RNA molecule was reported in 2005 [35]. Currently, deoxyribozymes capable forming amide bond between two amino acids or two peptides have not been found. However, formation of nucleopeptides by joining an amino acid to the 5'-end of a nucleotide by deoxyribozymes had been reported by Pradeepkumar., *et al* [36]. Zhou., *et al.* [37] reported the potential for deoxyribozyme-catalyzed hydrolysis of amide bond using a non-amino acid amide substrate. These studies suggest the possibility of deoxyribozyme use of amino acids as substrates [38]. More importantly, these studies demonstrated the ability of deoxyribozyme to polymerize RNA molecules despite polymerization of amino acids or peptides remains elusive [37]. Collectively, there are substantial evidence for cross replication by macrobiomolecules as five of the six possible cross replications had been demonstrated.

Finally, we consider whether macrobiomolecules can self-replicate. In 2002, Paul and Joyce [39] reported that R3C ribozyme, a RNA-dependent RNA ligase that catalyzes the formation of a 3'-5'phosphodiester bond between two RNA molecules [40], is able to replicate itself despite having difficulty achieving exponential growth. Subsequently, Robertson and Joyce [41] demonstrated exponential growth of a self-replicating ribozyme in 2014. These studies suggest that self-replicating ribozymes may be possible. Similarly, the possibility of self-replicating peptides has also been demonstrated. In 1996, Lee., *et al.* [42] demonstrated a case of self-replicating peptide in which a 32-residue leucine-zipper catalyses the amide-bond condensation of two constituent peptides of 15- and 17- residues. This is supported by Issac and Chmielewski [43] demonstrating a self-replicating peptide from two constituent peptides can result in near exponential growth. Maury [44] had presented a model for self-replicating amyloid proteins. Self-replicating proteins in the form of prions had been found in nature [45,46]. However, no self-replicating deoxyribozyme has been found to date. Despite so, DNA molecules have been shown to self-organize into nanostructures, which may be considered as self-replicating [47,48]. Hence, self-replication of ribozymes and peptides have been shown while self-replication of deoxyribozymes remains an elusive possibility.

Conclusion

Is there a real purpose to find the primordial macrobiomolecule or definitively decide whether the primordial world is an RNA world, DNA world, or peptide/amyloid world? This short review sets out to possibility of each world originating separately and coevolving together. Current evidence suggests a possibility that RNA world and peptide/amyloid world may originate independently whereas the origins of DNA world lacks several key pieces of evidence even though it may be inferentially possible. There are also substantial evidence suggesting the possibility of interplay between these three worlds as polymerization of monomers to macrobiomolecules appears to require similar conditions. This suggests that polymerization may occur in the same location, further increasing the probability of chemical crosstalk. Taken together, these evidences suggest that RNA world, DNA world, and peptide/amyloid world may coevolve regardless of

whether they originate independently as Liu., *et al.* [49] recently reported on the possibility of spontaneous emergence of self-replicating structures from mixtures of amino acid and nucleobases. This calls for a reconciliation into the possibility of a peptide-nucleic acid world [5].

Conflict of Interest

The authors declare no conflict of interest.

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