MOLECULAR SELF-ASSEMBLY

Molecular Self-Assembly as a Trigger of Life Origin and Development

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Abstract

The origin and reason for the homochirality of living cells go with the problem of a relatively narrow spectrum of the actual biological monomers compared to the whole theoretically possible spectrum of amino acids or carbohydrates. A limited number of bio-monomers implies some special feature differing from all other similar molecules that are not present in the living cell. Here we propose one of the candidates for such a peculiarity: the ability to form highly elongated helical supramolecular structures (strings) when precipitating from homochiral solutions. The strings' forming can be accompanied by spontaneous splitting and/or chiral purification of the initially racemic mixture. Our previous theoretical reasoning was based mainly on the biomimetic systems, while now we describe the strings forming in homochiral amino acid solutions.

Keywords Origin of Life · Self-Assembly · Chirality

The description of the early stages of chemical evolution faces two significant problems, including relatively small diversity of the biological monomer compared to a wide range of organic compounds emerging in the corresponding reactions and chirality of biomolecules (Schwartz 2007; Kuhn 2008; Kitadai and Maruyama 2018). The segregation of both enantiomers and chemical species can occur due to the amplification of some initial asymmetry, which requires the oligomers to be capable of replication. If the replication of the homochiral oligomers appears to be faster than that of their racemic analogs, the concentration of the former will increase and the latter – decrease (Joyce et al. 1984; Bolli et al. 1997; Kuhn 2008; Avalos et al. 2010). However, the origin of the initial chirality is unclear, and this problem is difficult enough to discuss the extraterrestrial hypothesis (Pizzarello and Weber 2004; Breslow and Cheng 2009; Glavin and Dworkin 2009).

Besides the chiral catalysis capable of symmetry breaking (Avalos et al. 2010), there are several other mechanisms, including Prigogine's theory for far-from-equilibrium systems (Nicolis

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and Prigogine 1981; Frank 1953; Mauksch et al. 2007; Mauksch et al. 2009). This scheme realizes in the process of $NaClO_3$ chiral crystallization under stirring. The phenomenon was explained by the "secondary" nucleation forming under the influence of the existing "mother" crystal imposing the symmetry of crystallization (Kipping and Pope 1898; Kondepudi et al. 1990). Together with the conglomerates' resolution in the same system (Viedma 2005; Viedma 2007), the latter effect allowed supposing the key initial steps of chemical evolution were heterogeneous (Avalos et al. 2010). This supposition is in tune with the hypothesis on the putative role of molecular self-organization in the prebiotic evolution on Earth (Eigen 1971).

The chemical reactions that could have been a source of the initial biological compounds on the young Earth seem to be found and well-described (Orgel 2004; Schwartz 2007; Kitadai and Maruyama 2018). The best candidate for the abiotic source of the carbohydrates is the formose reaction, which is a condensation of formaldehyde under alkali conditions and in the presence of metal ions (Butlerow 1861; Orgel 2004; Schwartz 2007; Kim et al. 2011; Ritson and Sutherland 2012; Kitadai and Maruyama 2018; Zlenko et al. 2020). The formose reaction brings a wide range of carbohydrates, including ribose and some hexoses common for living cells (Breslow 1959; Decker et al. 1982; Kim et al. 2011). The abiotic synthesis of the amino acids could have been proceeding through the Miller-Urey reaction, which is a reaction of methane, ammonia, hydrogen, and water in a gas phase under the electrical discharge (Miller 1953; Miller and Urey 1959; Schwartz 2007; Kitadai and Maruyama 2018). The natural biological amino acids (a glycine in the original work) were found among the products of this reaction, in some cases in significant concentration (Miller 1957). The ways of probable prebiotic synthesis of purines and pyrimidines are more complicated (Orgel 2004) but not impossible as it was demonstrated, for example, by Juan Oro for adenine (Oro 1960; Oro and Kimball 1961; Oro and Kimball 1962). However, the segregation of some "privileged" molecules (presented in the modern cells) and the emergence of the initial chirality remains unclear (Burton et al. 2012). The latter problem finds some theoretical explanations, whereas the former stays completely mysterious. Indeed, there are no reliable reasons why the α-aminopropanoic acid (alanine) is always present in living cells, while, for example, α-aminobutanoic acid is not?

Recently we have formulated a hypothesis describing the spontaneous self-segregation (and purification) of chirally pure monomers having some special properties (Zlenko et al. 2019; Stovbun et al. 2019; Zlenko et al. 2020). Some low-molecular-weight substances are capable of self-assembly into highly-elongated fibers (we called them "strings") when precipitating from the chirally pure solutions while forming the isometric (i.e., not elongated) aggregates or crystals from the racemic solutions (Stovbun et al. 2018; Zlenko et al. 2019). Moreover, in a bit chirally asymmetric mixtures, the racemic part of the solution precipitated first (under cooling or evaporation), while the rest of the system became chirally pure and precipitated in the form of the strings (Breslow and Cheng 2009; Zlenko et al. 2019).

Being segregated from others, the special molecules would concentrate in some locations, whether it would be a puddle or pond, and form a piece of a chirally pure world inhabited by some unique molecules highly capable of self-assembly. Given that the strings are helical and tend to form superhelices, one can suppose they resemble the DNA double-helix or α-helices in proteins (Stovbun et al. 2018; Zlenko et al. 2020). The only but significant difference is that the strings are noncovalent structures, while the natural macromolecules are always polymers. However, it could be supposed that polymerization of the initial pra-monomers has occurred and fixed by Natural Selection after the string-like structures' formation and fixing, as it actually occurs in the course of the DNA synthesis. Indeed, the nucleotides arrange along the single-stranded DNA spontaneously according

to the complementary rules, while polymerase only fixes their position chemically (Kissel et al. 2012; Stovbun et al. 2019).

All of the advantages of the described hypothesis are poisoned by the substances we have used in the experiments, as the results were obtained using solutions of trifluoroa-cetylated *α*-aminoalcohols (TFAAAs) in organic solvents (Stovbun et al. 2018). TFAAAs are neither biological monomers nor any other part of living cells. Therefore, it was crucial to determine if modern natural amino acids can form strings. If so, our hypothesis can be considered rational. Carbohydrates can form helical string-like fibers, at least in the mixtures (Stovbun et al. 2019).

The phenomenon of strings forming was demonstrated earlier for phenylalanine in human serum by Adler-Abramovich et al. (2012). Still, the main goal of that work was an investigation of the strings' toxicity and their role in the pathogenesis of phenylketonuria. Therefore, the authors did not outline the potential role of self-ordering in the phenylala-nine solutions in prebiotic evolution. Breslow and Cheng (2009) have shown that even a relatively small (~ 1 %) enantiomeric excess (EE) in the racemic phenylalanine solution can be amplified up to ~ 90 % in only two successive evaporations leading to precipitation of racemate. Therefore, phenylalanine behaves in this experiments exactly like TFAAAs, which are also capable of spontaneous chiral purification in only one heating-cooling cycle (Zlenko et al. 2019).

In our experiments, a small (~ 30–50 μL) droplet of a relatively weak (0.1–1.0 %) amino acid solution was plotted on the glass mount and then evaporated at the room temperature. To decrease the evaporation rate and obtain larger morphological structures, we placed the specimens in an airtight plastic box. The optical microscopy of the obtained specimens revealed strings in xerogels of only two amino acids: L-phenylalanine and L-valine (Fig. 1). At the same time, there were only conventional crystals and dendrites in xerogels of other amino acids. Therefore, at least two of twenty amino acids can form supramolecular strings under evaporation.

The phenomenon of the physical (i.e., noncovalent) gel forming in the solutions of low-molecular-weight substances is not so rare. In the most common case, such gelator molecules have a rod-like shape (Smith 2009; Raeburn et al. 2013). The rod-shaped gelator molecules can interact by their side surfaces, forming long and usually coiled fibers (Tachibana et al. 1979; Terech and Weiss 1997; van Gestel et al. 2006;
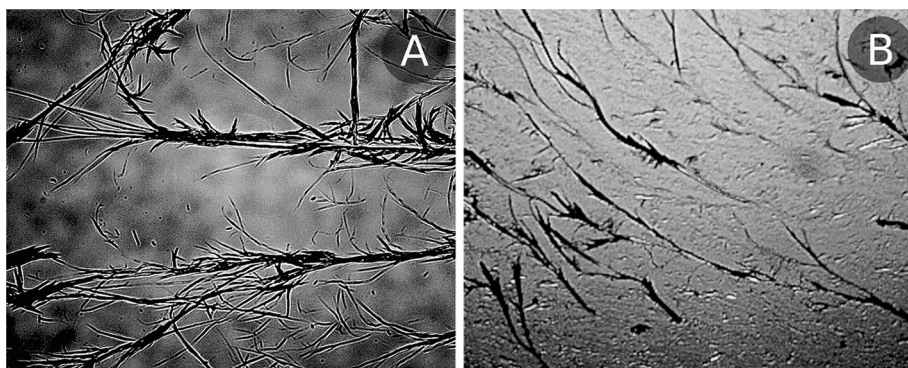
Fig. 1 The optical micrographs (*x*400) of the amino acid xerogels demonstrating strings on the glass sur-face. A. L-phenylalanine (0.1 %); B. L-valine (1 %)

Liu et al. 2015). For example, such rod-shaped gelators can be the derivatives of fatty acids (de Loos et al. 2005; Tachibana et al. 1979; Terech and Weiss 1997; Liu et al. 2015; Terech et al. 1994; Côte et al. 2009; Placin et al. 2001) or long-chain N-alkyl perfluoroalkanamides (George et al. 2003). The gelator molecules can also be disk-shaped and self-assemble into long stacks (de Loos et al. 2005; George and Weiss 2006; van Gestel et al. 2006; Liu et al. 2015; Godquin-Giroud et al. 1984). The disk-shaped cores of such gelators can be porphyrins (Godquin-Giroud et al. 1984), phthalocyanines (van Nostrum et al. 1995), or crown ethers (Terech and Weiss 1997; van Nostrum et al. 1995), for example. However, the low-molecular-weight organic gelators with isometric molecules, without special (long or short) axes in their structure, are much rarer. Among them, one can find the derivatives of choles-terol (George and Weiss 2006; Terech and Weiss 1997), carbohydrates (Yamasaki and Tsutsumi 1994; Wilder et al. 2002; Gronwald and Shinkai 2001), mentioned above phenylalanine (Adler-Abramovich et al. 2012; Breslow and Cheng 2009), and TFAAAs (Stovbun et al. 2018). The latter, to our knowledge, is a sole example of the non-biological low-molecular-weight substances having isometric molecules and able to supramolecular self-ordering. Therefore, such ability seems peculiar for the bio-molecules or at least occurs queerly frequently among them.

Although we did not find the strings in xerogels of all amino acids, the hypothesis on the initial selection of the capable of self-ordering substances can still be exculpated. Following it, one has to accept that Natural Selection fixed the self-ordering ability long before the biomolecules became really polymer molecules. Therefore, the selection pres-sure maintaining the self-ordering ability had to vanish after the "anagenesis of polymeri-zation." Therefore, nowadays, several billion years after this anagenesis, we can find only the remote offsprings of the initially selected molecules. Most of the initially selected mol-ecules probably changed beyond recognition and lost the ability to self-assemble. However, we still observe such molecules among the modern amino acids and carbohydrates, which are extremely rare outside the living cell.

The ability to self-assemble into long helical fibers by biological proto-monomers can be considered as a preadaptation predetermined the direction of all of the further molecular evolution on Earth. Indeed, the superhelical structure of modern macromolecules plays a significant role in their structure and functioning. The biopolymer helices, such as DNA double helix, or protein alpha-helices, can twist around each other and form thicker helices having the opposite twisting sign (Tverdislov et al. 2017; Malyshko et al. 2020; Tverdislov and Malyshko 2020). This provides for the novel and potentially more complex structures' formation, which can be a substrate for Natural Selection.

Coiling long enough and rigid helices always generate some torque forcing their rota-tion and forming hairpins (Cole and Bystroff 2009; Zlenko et al. 2020). The latter can serve as paddles capable of hooking other helices and spooling them to the one bearing the hair-pin and rotating. Therefore, multiple hairpins on many different growing seperhelices can hook and spool them to each other, forming a complex three-dimensional clew, which was observed experimentally for the case of spontaneous spatial concentration of the TFAAA gels (Zlenko et al. 2020). The latter clew can be considered as a foretype of the globule, while the process of its formation can be treated as a foretype of the macromolecules' fold-ing (Zlenko et al. 2020). Therefore, the helical strings' forming ability is probably the most significant peculiarity of the biological monomers (or their ancestors), providing for the actual difference between the living and non-living matter on Earth. According to our hypothesis, it has provided for the initial selection and segregation of only a few kinds of

monomers, their chiral purification, and provided a broad road to the structure complication in the future.

Declarations

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