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Mirror Symmetry Breaking, Origin of Biochirality and Prebiotic Evolution

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These are preliminary lecture notes, intended only for distribution to participants.

Mirror Symmetry Breaking, Origin of Biochirality and Prebiotic Evolution.

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Outline of lectures.

Lecture 1.

What is the Biochirality?

Lecture 2.

How many scenarios for the origin of Biochirality can be?

Lecture 3.

Could Biochirality result from the action of any asymmetric factor?

Lecture 4.

The equation for the origin of Biochirality.

Problems and Approaches

The self-replication of polymeric systems is known to be one of the most important features of Life. However from the physical standpoint, the self-replication is a non-trivial phenomenon. This can be illustrated in the following manner.

Let the primary structure of the polymeric chain contains N units of m types. The total number of polymers differing by the sequence of units in the chain is equal to $P=m^N$. Here the dependence of P on m is unessential, but the rapid growth of P with N is of a principle importance. For polymers with N more than 100 the number P is the number being anomalously high for chemistry. For example, for enzymes with m=20 and N>100 it is more

than 10^{130} . This number is greater than the number of electrons in Universe!. For nucleic acids with m=4 and with N of the order of 10^6 , the quantity P reaches the value of 10^{100000} .

Therefore the self-replication of polymers is the assembly resulting in the formation of the given chain among the tremendous number of possible chains.

As a result two questions arise, i.e. how to realize the only required sequence among all possible sequences and whether it is possible to make such choice in the framework of abiogenic "stochastic" chemistry.

The probability of the stochastic assemble of some given structure is proportional m^{-N} and, hence, it is exponentially small. While for rather short chain assembling some hopes may exist, the reproduction of such long chains as DNA kills illusions. Therefore the self-replication of polymers seems to be unlikely from the standpoint of the abiogenic chemistry. However the probability of self-replication in biology is practically equal to unity.

What tools has Nature to realize such a high accuracy of the self-replication? The answer is also well known. In biological systems the self-replication is realized by special macromolecules - enzymes, which ensure the exclusive precision of the assembly of polymeric chains.

The functionality of enzymes looks like the functionality of very precise automatic machines. In this sense we are dealing with chemical transformations governed by strictly defined rules, i.e. with the so-called algorithmic chemistry.

Now we can formulate the main problem of prebiotic evolution as the elucidation of conditions necessary for the transition from stochastic chemistry to algorithmic one.

Encountering such a problem one should try to find properties common to

all objects under consideration. In this context another question becomes important. Do any properties general for all biopolymers exist? Fortunately, we know these properties. The first is homochirality. Enzymes are constructed only from "left-handed" amino acids and nucleic acids consist of only "right-handed" sugars. This property of biopolymers is the structural manifestation of Biochirality. The second important property is the absolute enantioselection which is the functional manifestation of Biochirality.

These properties are so exited that following Louis Pasteur Biochirality is often considered as "the demarcation line between living and non-living matter". From this point of view, the background of living matter is the self-replication of homochiral polymers. Whatever the pathway of evolution might be, it has led to homochiral structures possessing an absolute enantioselection.

From the first glance, it seems that the problem of the origin of Biochirality is similar to the problem of the origin of self-replicating complex systems. But we can hope that the Biochirality can play a role of the Ariadna's thread in the labyrinth of the prebiotic evolution, because this phenomenon relates to symmetrical properties of complex chemical compounds and their functions. Indeed, the symmetry conservation or the symmetry breaking implies the existence of a corresponding physical law.

Let us try to do the first step in this labyrinth by formulating conditions for the origin of homochiral polymers. Obviously we are interested in such conditions which allow to obtain the large amount of homochiral polymers, i.e in conditions of polymeric takeover of organic medium.

The latter process depends on the interplay of two factors. The first one is the relation between the content of L- and D-isomers in the medium (the

so-called chiral polarization). The second factor takes into account the difference in probabilities of the incorporation of L- or D-isomer into the chain (the so-called enantioselectivity of polymerization).

If we consider necessary conditions for the assembling of a homochiral chain, we shall obtain a very simple condition of the type "all or nothing". The polymeric takeover of organic medium by a long homochiral chains could be possible either in chiral pure medium (for any enantioselectivity) or for an extremely high enantioselectivity (in an environment with any chiral polarization). The high stereoselectivity which allows to construct a chain in any environment practically without mistakes is strictly speaking algorithmic chemistry.

This result is the direct consequence of the fact that N is a large number, for example one hundred, two hundred or even more. Therefore we are dealing with the problem of the choice of the only required sequence of units among the tremendous number of all possible sequences.

Thus Ariadna's thread led us to two different scenarios of prebiotic evolution.

The first of them denoted as abiogenic scenario (A) includes the stage of the strong mirror symmetry breaking, which has preceded by primary polymeric takeover. It was just a particular medium that provided the formation of homochiral polymers and their evolutionary changes towards the formation of specifically active structures. In other words, the transition from the conventional chemistry to algorithmic one was realized in chirally pure medium.

The second scenario denoted as biogenic one (B) implies that initially polymeric takeover in racemic medium has led to the heterochiral or achiral polymers formation. After that, in the course of their evolution, the transition from the conventional chemistry to algorithmic one has been

realized and specifically active structures have originated. The evolution of the latter could lead, at least in principle, to the appearance of the absolute enantioselectivity and to the self-replication of homochiral polymeric structures.

As a result the problem of the choice of the scenario for the prebiotic evolution reduces to the question, what has originated earlier: homochiral structures or functions of biochemical level of complexity?

If we choose scenario A, we must explain how the mirror symmetry has been broken and how the chirally pure medium has been formed. If, in opposite, we choose scenario B, we should have an answer to the question, whether heterochiral or achiral protoenzymes could exist. However, it can be shown that a random sequence of L and D units leads to the destruction of the secondary and tertiary structures and, hence, such heterochiral chains cannot form an ordering patterns of biochemical functions. Moreover, it can be shown that chains with regular sequences of L- and D-isomers or any special achiral polymers could not takeover the organic medium due to a strong kinetic limitation for such process in abiogenic conditions.

Consider the scenario A. The key question for this variant is how a chiral purity of medium could appear at the chemical stages of evolution. In the discussion of this question one should take into account that the chiral purity had to appear not only at the beginning of evolution, but had to be maintained in the course of the entire transition from abiogenic chemistry to algorithmic one.

In general, there are two possibilities for strong mirror symmetry breaking.

The first one is asymmetric actions, for example circularly polarized radiations, mineral asymmetric catalysts and so on.

The second possibility is the formation of a chirally pure medium due to

the bifurcation with symmetry breaking, i.e due to the spontaneous mirror symmetry breaking.

From the standpoint of the formation of the initial chirally pure medium, we have no reasons to reject any of these two possibilities. But these two ways of symmetry breaking are distinguished by their abilities for the stabilization of chirally pure state in the course of prebiotic evolution. As will be shown, only chemical processes with spontaneously mirror symmetry breaking can guarantee the stability of ϵ chirally pure medium in the course of the formation of structures and function by biochemical level of complexity.

Finally, we discuss some examples of chemical processes which could be important for the strong mirror symmetry breaking in organic medium and for the origin of Biochirality.

Summing up, we conclude that Biochirality is in fact the Ariadna's thread which does help us to pass through the labyrinth of prebiotic evolution. In addition, this thread does allow to give a sketch of the prebiotic evolution scenario. Certainly one cannot state that it is impossible to imagine another scenario for the prebiotic evolution. But if somebody would like to offer another version, please, find another Ariadna's thread.

Useful Introductory References

- 1. Avetisov, V.A. & Goldanskii, V.I., BioSystems 25, 141-149 (1991)
- Avetisov, V.A., Goldanskii, V.I. & Kuz'min V.V., Physics Today
 44, 33-41 (1991)
- Avetisov, V.A., Goldanskii, V.I., Grechukha, S.N. &
 Kuz'min, V.V., Chem. Phys. Lett. 184, 526-530 (1991)
- 4. Barron, L.D., J.Am. Chem. Soc. 108, 5539-5542 (1986)
- 5. Bonner, A.W., Origins Life Evol. Biosphere 21, 59-111 (1991)
- Feng, Q., Park, T.K. & Rebek, J., Science 254, 1179-1180
 (1992)
- 7. Frank, F., Biochem. Biophys. Acta 11, 459-463 (1953)
- 8. Goldanskii, V.I. & Kuz'min, V.V., Sov. Phys. Uspekhi 32, 1-29 (1986)
- 9. Goldanskii, V.I., Anikin, S.A., Avetisov, V.A. & Kuz'min, V.V., Comments Moll. Cell. Biophys. 4, 79-98 (1987)
- Goldanskii, V.I. & Kuz'min, V.V., J. Brit. Interplanet. Soc. 43, 31-37 (1990)
- 11. Goldanskii, V.I. & Kuz'min, V.V., Nature 352, 114 (1991)
- 12. Hurst, L.D. & Dawkins, R., Nature 357, 198-199 (1992)
- 13. Joyce, G.F., Inoue, T. & Orgel, L.E., J.Mol.Biol. 176, 279-306
 (1984)
- 14. Joyce, G.F., Visser, G.M., van Boeckel, C.A.A., van Boom, J.H., Orgel, L.E., & van Westrenen, J., Nature 310, 602-604 (1984)
- 15. Joyce, G.F., Shwartz, A.F., Miller, S.L. & Orgel, L.E., Proc. Natl. Acad. Sci. USA 84, 4398-4402 (1987)
- 16. Joyce, G.F., Nature 338, 217-224 (1989)
- 17. Kondepudi, D.K. & Nelson, G.W., Physica 125A, 465-496 (1984)

- 18. Kondepudi, D.K. & Nelson, G.W., Nature 314, 438-441 (1985)
- Kondepudi, D.K., Kaufman, R.J., & Singh, N., Science 250, 975-976 (1990)
- 20. Mason, S.F., Nature 311, 19-23 (1984)
- 21. Morozov, L.L., Origins Life 9, 187-218 (1979)
- 22. Morozov, L.L., Kuz'min, V.V. & Goldanskii, V.I., Sov. Sci. Rev.

 D Physicochem. Biol. 5, 357-405 (1984)
- Nowick, J., Feng, Q., Tijivikua, T., Ballester, P. & Rebek, J.,
 J. Am. Chem. Soc. 113, 8831-8839 (1991)
- 24. Nicolis, G. & Prigogine, I., Proc.Natl.Acad.Sci.USA 78, 659-663 (1981)
- 25. Salam, A., J., Mol. Evol. 33, 105-113 (1991)
- 26. Von Kiedrowski, G., Wlotzka, B., Helbing, J., Matzen, M. & Jordan, S., Angewandte Chemie 30, 423-426 (1991)