POSSIBLE MECHANISM FOR ORIGIN OF CHIRAL SPECIFICITY DURING ORIGINS OF LIFE

R. BALASUBRAMANIAN

Department of Crystallography and Biophysics, University of Madras, Guindy Campus, Madras – 600 025, India*

(Received 10 January 1983; in revised form 16 June, 1983)

Abstract. We have earlier (*Origins of Life* **10** (1980), 15–30) proposed a conformational theory for the origin of nucleic acid-directed adaptor-mediated ordered and proliferative synthesis of proteins and hence origin of life. Conjunction of L-amino acids and beta-D-ribonucleotides emerges as a natural consequence of a template fitting interaction in this theory of the origin of the genetic decoding apparatus. Here we propose an interesting new concept for the origin of chiral specificity, by showing that two autonomously developing systems of protein-synthesizing machinary, one manufacturing L-peptides (L-system) and the other, D-peptides (D-system) could have arisen and during early stages of evolution L-system could have developed a *killer enzyme* to destroy the D-system, causing the presently existing chiral specificity in all the evolved organisms on Earth. It would be interesting to look for such 'killer enzymes' in the present-day organisms. Of course, the existence of D-amino acid-containing antibiotics gives some credence to this theory.

Since nucleic acid-directed protein synthesis lies at the root of all biochemical processes, nucleic acids and proteins, assume a fundamental importance in biological organisms. The striking features of these important biomolecules are that the nucleic acids are made of beta-D-ribonucleotides, and proteins of L-amino-acids. Such specifities in the enantiomers in the molecular processes of biology have, naturally, evoked much interest. Wald [1] has elegantly discussed the idea that the selection of enantiomers went hand in hand with the origin of life, which is more acceptable than the concept of a prior selection of asymmetry in the monomers of the biopolymers. But the idea of preferential synthesis/destruction of a particular enantiomer during chemical evolution, due to various possible natural causes has always had a great appeal to researchers, and several theoretical and experimental studies have been reported in the literature (see the recent book edited by Walker [2]). There are also more recent experimental (Edwards *et al.* [3]) and theoretical (Gladyshev and Khasavor [4]) studies reported in the literature.

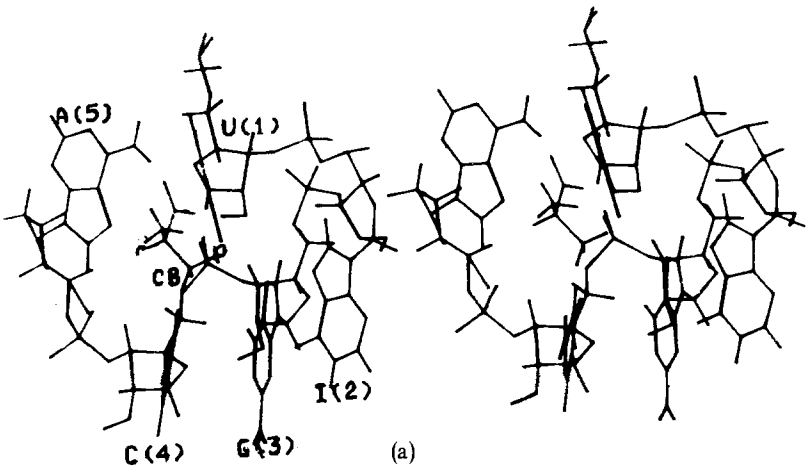
As discussed by Miller and Orgel [5], and more recently by several researchers, as seen in a Newsletter [6] and proceedings (Thiemann [7]) the differential chirality induced by physical agents may not be sufficient to achieve chiral selection during the early stages of evolution of life; in addition the rate of recemization is probably high enough to overcome any preferential incorporation of chirality in the primitive living organisms.

Recently we have proposed a molecular interactions theory involving nucleotides and amino acids leading to a primitive mechanism of nucleic-acid-directed, adaptor-

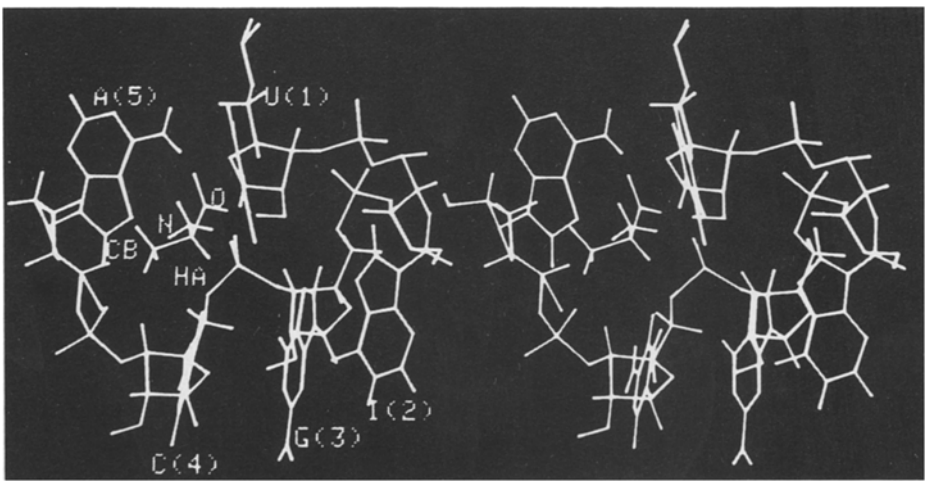
* Contribution No. 616 from this department.

Origins of Life **13** (1983) 109-112.0302-1688/83/0132-0109$00.60.

mediated ordered and proliferative synthesis of proteins that might have served as the link between chemical and biological evolution (Balasubramanian *et al.* [8-11]). Describing it very briefly, a penta-nucleotide conformer of beta-D-ribonucleotides is able to nestle an L-amino-acid in a sort of a cleft in its structure. This can act as a primitive tRNA or adaptor molecule that would base-pair with codons on primitive mRNA molecules (PIMs) to trigger off an ordered and repeated synthesis of L-peptides. Our earlier studies (Balasubramanian *et al.* [9]) and recent computer



(a)



(b)

Fig. 1. Stereo diagram of molecular model of the genetic decoding apparatus (primitive tRNA or PIT) showing an amino acid nestled in a beta-D-ribonucleotide conformation. In the stereoview the middle triplet of nucleotides (I(2), G(3) and C(4)) are seen in a helical stacked conformation with their base-pairing direction towards the viewer. The amino acid can be seen 'floating' (held by hydrogen bonds) in a sort of a cleft formed by the pentanucleotide. The group C-Beta(H3) is seen projecting towards the middle bases (G(3) and C(4)) for intimate interaction ('recognition')

(a): — L-ala is nestled in the PIT

(b): — D-ala is shown nestled in the same PIT, in order to show that the amino-acid side-chain group C-Beta (H3) (Marked as CB) is sticking out of the cleft.

calculations show that D-amino-acids do not fit into the model (see Figure 1 and its legend) for a close-packed interaction as the amino-acid side-chain sticks out of the cleft; moreover this cleft serves as a discriminating site for the specificity of the anticodon for the corresponding amino acid, as in the genetic code (for more elaborate discussions see Ref. 8 to 13).

Thus in the possible origin of this genetic decoding apparatus (primitive tRNA) the coexistence or conjunction of L-amino-acids and beta-D-ribonucleotides becomes a necessity, because of their cooperative template-fitting interaction; of course, the mirrored combination of optical antipodes of our primitive decoding complex could also trigger off ordered synthesis of proteins containing D-peptides.

At this stage, thus there can exist two independent and autonomously developing systems of protein-synthesizing machinery, one of which could manufacture L-peptides and the other D-peptides, separately. The sequences of amino acids in these polypeptides would be determined by the chance sequences of RNAs (PIMs) available at that time of prebiotic evolution. Some of the so-produced, ordered polypeptides may happen to be 'enzymatically' active. Such of these systems of primitive enzymes that support self-sustaining cycles of chemical reactions would survive in the Darwinian sense (in the environment of 'prebiotic soup'). The interesting feature of the system is that it is capable of evolving. Natural mutations on the sequences of PIMs and the errors in the primitive translation would bring in new sequences in polypeptides and the process of the survival of the fittest would lead to more and more sophisticated systems and towards the present day protein-synthesizing machinery which is very efficient and error-free. During these stages the two enantiomorphic systems producing L-peptides and D-peptides (called L-system and D-system respectively for further discussions) might take up two entirely different paths in evolution, since each one is dependent on the chance sequence of its own corresponding enantiomorphic PIMs.

At one stage, let us suppose that the L-system develops an enzyme that is capable of hydrolyzing or cleaving all D-peptides. Let us call this a D-peptidase. (The possibility of the existence of such enzymes is vouchsafed by the fact that enzymes are known, not only as chemically but sterically (enantiomorphically) specific: see for example Gladyshev and Khasavov, p. 235). Then the L-system attains an evolutionary supremacy over the D-system, which would not be able to survive because of the destructive actions of D-peptidase, which acts as a 'killer enzyme' for D-system. (These of course should not be confused with the present-day proteinases that hydrolyze L-peptides in living organisms. These proteinases are first synthesized as non-active proenzymes and then activated by other enzymes at proper stages and proper places in the present-day biological organisms *so that they cannot trigger a self destruction in these organisms* by hydrolyzing all the proteins in their body).

At some stage, it would have been possible that the D-system develops L-peptidases and this would have led to the establishment of D-systems of living organisms. It may be noted that since both the systems are independent (and autonomous), the probability of both the systems developing such stereo-specific peptidases for the antipode *at the same time* is very small and whichever system happened to bring forth

such a killer enzyme for the other system survived to outlast the other system in the evolutionary race.

Since this hypothesis is based on a mechanism of active destruction of the system of opposite chirality, this turns out to be a specific and forceful rationale for the establishment of biological organisms of a given chirality in a biosphere. It is also testable in the sense that one could look for such enzymes in the primitive or archaic organisms. Here it may be noted that the enzyme in question need not necessarily be the one that hydrolyzes D-peptides. An enzyme that destroys β-L-nucleotides or even D-amino acids could serve the purpose of establishing L-system on Earth, since the primitive decoding apparatus (Balasubraznian, 1980) for D-peptides consists of β-L-nucleotides capable of nestling D-amino acids. (exact mirror image of β-D-nucleotides and L-amino acid complex)

It is possible that, such enzymes that existed during prebiotic or early biotic stages of evolution might have become obsolete in the present-day organisms (even in archaic bacteria). But evolution has a tendency to preserve many of its archaic processes and there is a good chance that these enzymes are still available in present-day living organisms.

Another interesting aspect of our postulate is that the concept of a 'killer enzyme' of L-systems for destroying the D-system, can be stretched even to higher levels of organization during the early stages of evolution. The D-system might even have survived the chance supermacy of L-system to the level of micro-organisms. Even at this stage of evolution of the D-system, the L-killer-enzymes could have destroyed the D-system by attacking various components of the cells of D-system. The existance of antibiotics for the presently existing L-system gives credence to it, and it should be noted that the present day peptide antibiotics contain D-amino-acids that are inevitable for their biological function (see Davies, 1977).

References

[1] Wald, G.: 1957, *Ann. N.Y. Acad. Sci.* **69**, 352–368.
[2] Walker, D.C.: 1979, *Origins of Optical Activity in Nature*, Elsevier Sci. Publish. Co.
[3] Edwards, D., Cooper, K., and Dougherty, R. C.: 1980, *J. Amer. Chem. Soc.* **102**, 381.
[4] Gladyshev, G. P. and Khasavov, M. M.: 1981, *J. Theoret. Biol.* **90**, 191–198.
[5] Miller, S. L. and Orgel. L. E.: 1974, *The Origins of Life on the Earth*, Prentice-Hall, Inc., New Jersey.
[6] Newsletter No. 3: 1980, 'The Origins and Early Evolution of Life', Orleans University, Cedex.
[7] Proceedings of the 2nd International Symposium, University of Bremen, July 16–18, 1980, *Origins of Life*, **11** No. 2 1981,
[8] Balasubramanian, R.: 1979, *Indian J. Biochem. Biophys.* **16**, 442–444.
[9] Balasubramanian, R., Seetharamulu, P., and Raghunathan, G.: 1980, *Origins of Life* **10**, 15–30.
[10] Balasubramanian, R. 1980 in 'Proceedings of the Workshop on Origin and Evolution of Life and Intelligence in the Universe' held in Bombay, Jan. 14–16, 1980) (Ed. Chadha, M. S., Chitre, S. M., Daniel, R. R.) ISRO, India.
[11] Balasubramanian, R.: 1981, *Trends in Biochem. Sci.* **7**, 9–10.
[12] Balasubramanian, R. and Seetharamulu, P.: 1980, *Madras Univ. J.* B43, 54–58.
[13] Balasubramanian, R.: 1982, *BioSystems* **15**, 99–104.
[14] M. and Webb, E. C.: 1979, *Enzymes*, 3rd Edition, Longman Group Limited, London.
[15]Davies, J. S.: 1977, in B. Weinsten (ed.), *Chemistry and Biochemistry of Amino Acids, Peptides and Proteins*, Vol. 4, pp. 1–27 Marcel Dekker, Inc., New York and Basel.