Chiral purity of nucleotides as a necessary condition of complementarity

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This work discusses the question about the role of chiral purity (homochirality) of nucleotides in the formation of complementary replicas. A qualitative answer to this question can be obtained from molecular models constructed to simulate the chiral defect in the polynucleotidic chain. It shows the necessity of homochirality of nucleotides for the complementarity preservation. The necessity of the strong mirror-symmetry breaking in the abiogenic formation of the self-replicating oligonucleotide structures is discussed in the context of prebiological evolution.

Polynucleotide *Chiral purity* *Complementarity*

1. INTRODUCTION

The complementarity of nucleotide pairs is known to be the key property that ensures the mechanism of preservation and transmission of genetic information on the molecular level. Another, no less important property of polynucleotides is their chiral purity. Indeed, the nucleotides which form DNA and RNA contain only dextro-(D) isomers of sugars.

In this note we would like to draw attention to the fact that the complementarity of the polynucleotides is possible only in the case of their chiral purity.

It seems apparent that replacement of a unitary naturally occurring (D) nucleotide in DNA or RNA by its mirror (L) isomer will lead to the formation of a structure with a greater energy. This raises the question whether it is possible to preserve the complementarity of such a chirally deficient pair in the double-stranded structure, and, moreover, is such a defect local or does it destroy a large domain of the polynucleotide chain? A qualitative answer to these questions can be obtained from molecular models constructed to simulate this situation. Corey-Pauling-Koltun (CPK) spaced molecular models are most suitable for a qualitative investigation of these questions.

2. EXPERIMENTAL

For the sake of comparison fragments of double-stranded (poly-A and poly-T) nucleotide structures have been constructed. Each fragment comprising five complementary pairs A-T. In the first fragment both strands were chirally pure. It is natural that such a structure is regular (see fig.1) and forms a fragment of the usual double helix. (For the model of the B-form double helix see fig.2.) The second fragment differed from the first in that in one of the strands the T-nucleotide in the third unit was replaced by its mirror isomer. Such a nucleotide, in contrast to the naturally occurring one, contains L-sugar. This nucleotide was inserted in such a manner that the bonds 3′-5′ were preserved and, thus, the integrity of the poly-T strand preserved (see fig.3).

The model of the B-form containing a chiral defect is shown in fig.4. In such a structure the position of the pyrimidine ring of the naturally non-occurring T-nucleotide proves to be turned with respect to the normal position of the nitrogen

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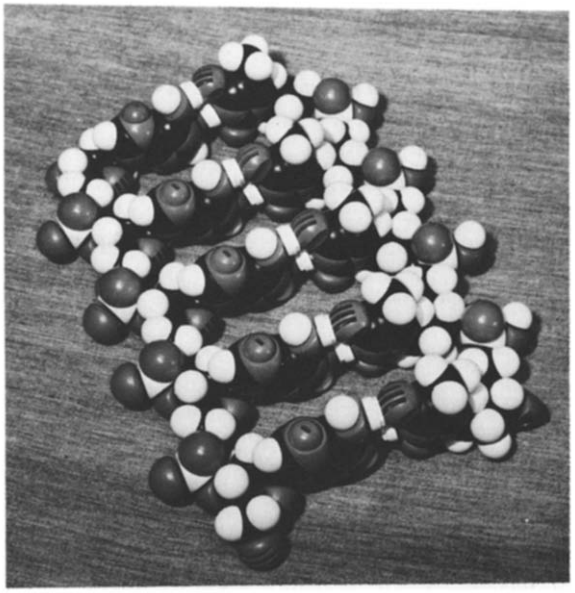

Fig.1. CPK molecular model of the naturally occurring (homochiral structure) fragment of A-T structure.

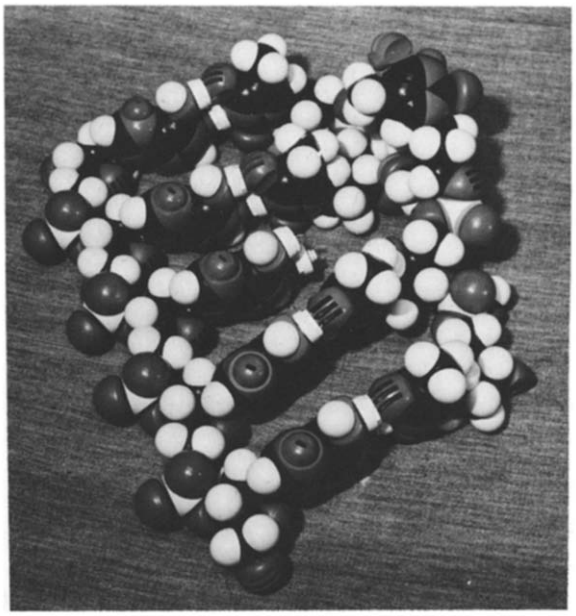

Fig.2. CPK molecular model of a fragment of the B-form of A-T double helix.

base in the double bond through an angle of $\simeq 100°$. This rules out the possibility of the formation of hydrogen bonds between the bases A and T of the third pair and, hence, removes the main cause of the origin of complementarity since in this case the combination of the nucleotide bases of the deficient pair may be arbitrary. This situation takes place in the A-form containing a chiral defect too.

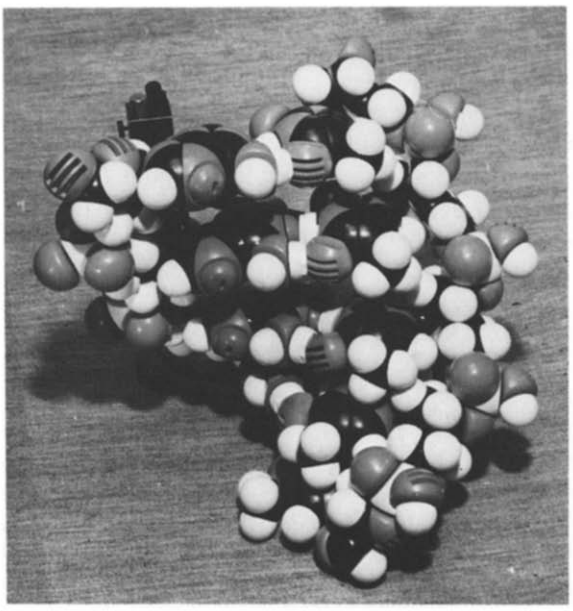

Fig.3. CPK molecular model of the chirally-deficient A-T structure.

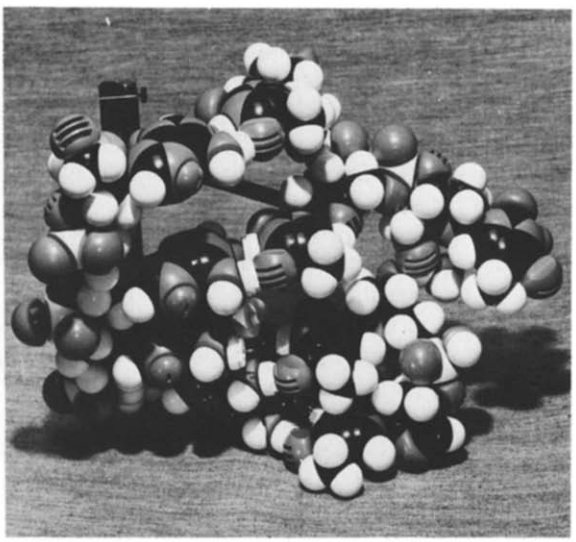

Fig.4. CPK molecular model of the B-form of A-T structure consisting of the chiral defect.

3. RESULTS AND DISCUSSION

It is easy to understand what will happen upon insertion into a homochiral structure of a unit consisting of a pair of nucleotides, the chirality of both partners of which is opposite to the chirality of other nucleotides. In this case the formation of hydrogen bonds between the bases of the inserted foreign pairs will not take place either.

Thus, the chiral purity of the polynucleotides is a necessary condition of complementarity.

The problem discussed concerning the connection between the chiral purity and complementarity may seem artificial to the biochemist. The mechanism of DNA and RNA replication, existing in living organisms, is stereospecific to such an extent that the occurrence of a chiral defect is practically excluded.

Yet, in the absence of such a mechanism of replication this problem becomes quite topical. It is apparent that the above-discussed possibility of formation of a chiral defect can take place during the process of matrix oligomerization of the nucleotides. This situation is characteristic of prebiological evolution, in an abiogenic formation of polynucleotides [1]. Recently it was shown (review [2]) that RNA (highly probable ancestor of modern nucleic acids) possesses autocatalytic activity and the ability to self replicate.

It was shown experimentally in [1] that the process of matrix oligomerization of the nucleotides was strongly dependent on the ratio of mirror isomers in the initial medium. On the basis of these results an estimation was given in [1] of a minimum degree of chiral polarization of a medium containing nucleotides, in which, as a result of matrix oligomerization homochiral replicas of any essential length n might form (n being the number of monomeric units in a replica). This minimum degree of chiral polarization is a parameter describing the relative excess of one of the mirror isomers. An analysis of a sufficiently simple and natural kinetic model of the replication process led us to conclude that under the best conditions, i.e. in a chirally pure medium, the process of matrix oligomerization enables the formation of chirally pure nucleotide replicas with a length $n \sim 300$. In a racemic medium (with an equal content of L- and D-isomers) the length of complementary replicas cannot exceed $n \sim 10$.

These results lead to a conclusion of great importance for the problem of the origin of life: the chiral purity of the biosphere is conditioned by the strong mirror-symmetry breaking of the organic medium, that had occurred in the course of the prebiological (chemical) evolution, i.e. at the stage preceding the appearance of self-replicating structures.

These conclusions [3] are made on the basis of a kinetic analysis of the process of matrix oligomerization of nucleotides on a homochiral matrix, carried out in [1]. Yet, the question whether the process of self-replication of heterochiral polynucleotides could proceed at all – now from the standpoint of the structure of the initial substances and reaction products – still remained to be answered. The considerations about the interconnection of chiral purity and complementarity set forth above allow us to give a negative answer to this question. Indeed, in the absence of complementarity the mechanism of preservation and transmission of biologically important information on the molecular level is not deemed possible and, therefore, the very possibility of evolution of biomolecular structures and systems disappears.

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