CONFORMATION-DEPENDENT SEQUENCE DESIGN: EVOLUTIONARY APPROACH

A.R. Khokhlov[1,2], A.V. Chertovich*[1], E.N. Govorun[1], V.A. Ivanov[1] and P.G. Khalatur[2,3]

[1] *Physics Department, Moscow State University, 119992 Moscow, Russia*
[2] *Department of Polymer Science, University of Ulm, 89069 Ulm, Germany*
[3] *Department of Physical Chemistry, Tver State University, 170002 Tver, Russia*

The concept of evolution of primary sequences of biopolymers attends large interest of biologists, chemists and physicists for a long time. The progress in this field will help a lot both in understanding of biological evolution and in creation of synthetic "functional" copolymers.

In the present investigation a new modification of the so-called conformation-dependent sequence design scheme is proposed. The simultaneous evolution of sequences (sequence annealing) and conformations is studied for *HP*-copolymers consisting of hydrophobic (*H*) and hydrophilic (or polar, *P*) units. The formation of a stable core-shell structures with a dense hydrophobic *H*-core surrounded by polar *P*- loops is obtained in computer simulations if we switch on the attraction between *H*- units. Annealing of the sequences is performed according to conformation-dependent scheme, i.e., the types of two randomly chosen monomer units are exchanged if they happen to be found in the "non-favorable" surrounding of units of the other type.

The state of the system is characterized by the location in the ordinary "conformational" $3d$ space and by the specific sequence in the "space of sequences". We measure the information entropy and other statistical characteristics of sequences. The design procedure leads to the final state, which depends on the set of interaction parameters and on the intensities of rearrangement in conformational space and in the space of sequences. These intensities are characterized by the thermodynamic temperature (T_{conf}) and by the sequence rearrangement temperature (T_{seq}) correspondingly.

We show that there are two asymptotic cases for the relation between the intensities of conformational changes and sequence evolution: 1) fast sequence evolution and slowly changing conformation ($T_{conf} \gg T_{seq}$) bring the system to the formation of completely random *HP*-copolymer in the globular conformation, 2) fast conformational evolution and slow dynamic in the space of sequences ($T_{conf} \ll T_{seq}$), when the most favorable conformation of the system should have hydrophobic core with very few polar loops. The main point of our interest is an intermediate situation ($T_{conf} \sim T_{seq}$), where the non-trivial set of sequences and conformations in the final state is expected.

This model can be considered as a "toy" model of the evolutionary process: the rearrangement of unit types corresponds to random mutations in sequences of biopolymers. The proposed method can be easily extrapolated to more complex external conditions and interactions of units.

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Phone: 939-4756, fax: 939-2988; e-mail address: chertov@polly.phys.msu.su