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Physics

STRAIGHT CALCULATION OF HELIX–COIL TRANSITION PARAMETERS IN HETEROPOLYMERS

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The main goal of this paper is the investigation of helix–coil transition in heteropolymers by means of straight calculation of partition function, free energy, helicity degree and other characteristics of transition on the bases of generalized model of polypeptide chain. Product of random matrices was applied to solve the problem for the comparison with constrained annealing method in the future.

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***Keywords*:** generalized model of polypeptide chain, free energy, average length of helix region.

Introduction. Helix–coil transition phenomenon in biopolymers has been investigated since 1960*s* [1–7] till nowadays [8–15]. Various modifications of Zimm–Bregg model [16–19] are used mostly. Authors were some theoretical models both for polypeptides [20–22] and polynucleotides [9–13]: without usage of mean field approximation. Moreover, some models have been applied to describe melting of heteropolymers and many important results [1–19] are obtained on their bases. In our previous papers [23–27] microscopic model describing helix–coil transition was represented. This model is based on Potts model with multi-particle interactions and has been called generalized model of polypeptide chain (GMPC). Several fundamental results are achieved for homopolymers in the frame of this model. On the basis of GMPC and application of micro-canonic method we obtained some interesting results for the case of heteropolymer [28]. Not long ago, the helix–coil transition problem for polymers with heterogeneity by base formation energies was examined with the help of constrained annealing method [29] by our team. All the results were reached for a system with bimodal heterogeneity [30]. The aim of this research appears to be investigation of helix–coil transition in heteropolymers by means of straight calculation of partition function, free energy, helicity degree, average length of helicity state and other characteristics of transition to find out details of transition and deference between homo- and heteropolymers in the frame of GMPC.

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Generalized Model of GMPC [23–28, 30]. Hamiltonian of this model is as follows:

$$\beta H = J\sum_{i=1}^{N}\delta_i^{(\Delta)}, \tag{1}$$

where $\beta = T^{-1}$ is inverse temperature; N is number of repeated units; $J = U/T$ is reduced energy of intramolecular hydrogen bond. $\delta_j^{(\Delta)} = \prod_{k=\Delta-1}^{0}\delta(\gamma_{j-k},1)$, $\delta(x,1)$ is kronecker symbol, $\gamma_i = 1,2,\ldots,\ Q$ is spin variable, which varies from 1 to Q and describes conformations of l-th repeated unit. Number 1 conformation represents helicity state, and the others correspond to coil conformation.

Kronecker symbol δ leads to J energy release only when Δ repeated units in succession are in helical state.

The transfer-matrix corresponding to Hamiltonian appears as:

$$\hat{G}(\Delta) = \begin{pmatrix} \exp^J & 1 & 0 & \cdots & 0 & 0 & 0 \\ 0 & 0 & 1 & \cdots & 0 & 0 & 0 \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & 0 & \cdots & 0 & 0 & Q-1 \\ 1 & 1 & 1 & \cdots & 1 & 1 & Q-1 \end{pmatrix}. \tag{2}$$

It has following properties:

1) element $(1;1)$ is equal to $\exp^J$;

2) upper first pseudo-diagonal is equal to 1;

3) the last row is equal to 1;

4) $(\Delta-1,\Delta)$ and (Δ,Δ) elements are equal to $Q-1$;

5) other elements take zero.

Let us emphasize that the following characteristics reflects in GMPC:

1. Conformational freedom of each repeated unit by means of $Q-1$ parameter;

2. Scale of constrains imposing with the first hydrogen bond by means of Δ parameter;

3. Energy of one hydrogen bond by means of $W = \exp^J$ parameter, which appears to be statistical weight of hydrogen bond formation.

Model of Heteropolymer. In the frame of GMPC Hamiltonian of heteropolymeric system will appear as follows:

$$-\beta H = \sum_{i=1}^{N} J_i\delta_i^{(\Delta)}, \tag{3}$$

where the energy of hydrogen bond depends on the type of repeated unit on the contrary to homopolymeric model. As it has been already mentioned, $\delta_j^{(\Delta)} = \prod_{k=\Delta-1}^{0}\delta(\gamma_{j-k},1)$, where $\gamma_i = 1,2,...,Q_i$. In this paper we are going to discuss GMPC with bimodal heterogeneity both by energies of helicity structure's formation, and by number of conformations of repeated units. Let us insert a new variable

σ_i, which takes value 1 with probability X and -1 with probability $(1-X)$. Therefore, we will work with two-component heteropolymer with various values of intramolecular hydrogen bond's energies: $J = J_0 + \Delta J\sigma,\ J_A = J_0 + \Delta J$ and $J_B = J_0 - \Delta J$.

We will do the same with parameter Q. Let us insert $K = \log(Q-1)$ for the convenience. Hence, $K = K_0 + \Delta K\sigma,\ K_A = K_0 + \Delta K$ and $K_B = K_0 - \Delta K$.

As a consequence, the primary structure of a biopolymer will appear as sequence of ±1 numbers.

Calculation of Partition Function and Average Characteristics of Heteropolymer. According to [4, 23, 24], partition function determines as

$$Z = Tr\prod_{i=1}^{N}\hat{G}_i, \tag{4}$$

where $\hat{G}_i$ defines in relation to primary sequence as transfer-matrix

$$\hat{G}_i = \hat{G}(J_0 + \Delta J\sigma_i, K_0 + \Delta K\sigma_i).$$

For given variables $X, N, J_0, \Delta J, K_0, \Delta K$ and for each realization of random sequence it is possible to obtain expression for $Z_N(\{\sigma_i\})$ and reduced free energy:

$$f_N(\{\sigma_i\}) = \frac{\ln Z_N(\{\sigma_i\})}{N} = -\frac{F_N}{NKT}. \tag{5}$$

To calculate free energy $\langle\delta_i^{(\Delta)}\rangle$ we use the following expression:

$$\theta_N = \frac{1}{NZ}\sum_i \delta_i^{(\Delta)} \exp^{-\beta H}. \tag{6}$$

Taking into account the expression (6), for hamiltonian we get

$$\theta_N = \frac{1}{NZ}\cdot\frac{\partial Z}{\partial J_0}. \tag{7}$$

With the help of partition function expression in terms of transfer-matrix, we will obtain

$$\theta_N = \frac{1}{NZ}\sum_i Tr\prod_{k=1}^{i-1} G_k G_i' \prod_{k=i+1}^{N} G_k. \tag{8}$$

For calculation of such sums we have used method of supermatrices [4]. The supermatrix we have inserted has dimensions $(2\Delta\times 2\Delta)$ and can be expressed as

$$\hat{M}_i = \begin{pmatrix} \hat{G}_i & \hat{G}_i' \\ O & \hat{G}_i \end{pmatrix}, \tag{9}$$

where O is null matrix $(\Delta\times\Delta)$. $\hat{G}_i' = \dfrac{\partial \hat{G}_i}{\partial J_0}$, consequently, the matrix has only one nonzero element: $\hat{G}_{i,11}' = \exp^{J_i}$, all the others elements of matrix are equal to zero. Therefore,

$$\theta_N = \frac{Tr[E,O]\prod\limits_{i=1}^{N}\hat{M}_i\begin{bmatrix} O \\ E \end{bmatrix}}{NTr[E,O]\prod\limits_{i=1}^{N}\hat{M}_i\begin{bmatrix} E \\ O \end{bmatrix}}, \tag{10}$$

where E is identity matrix $(\Delta \times \Delta)$. It's possible to calculate the average length of helical region in the same way: $\nu = \dfrac{\theta_N}{\eta_N}$, where η_N is number of helical regions or number of bounds between helical and coil regions:

$$\eta_N = \langle \delta_i^{(\Delta)} (1 - \delta_{i+1}) \rangle. \tag{11}$$

Consequently:

$$\nu_N = \left(1 - \frac{\langle \delta_i^{(\Delta)} \delta_{i+1}^{(\Delta)} \rangle}{\langle \delta_i^{(\Delta)} \rangle} \right)^{-1}. \tag{12}$$

Let us introduce supermatrix $N_{i,i+1}$, which appears as

$$\hat{N}_{i,i+1} = \begin{pmatrix} \hat{G}_i & \hat{G}'\hat{G}'_{i+1} \\ 0 & \hat{G}_{i+1} \end{pmatrix}.$$

Hence

$$\langle \delta_i^{(\Delta)} \delta_{i+1}^{(\Delta)} \rangle = \frac{1}{NZ} Tr \left[\; O, \quad E \; \right] \prod_{i=1}^{N-1} \hat{N}_{i,i+1} \begin{bmatrix} 0 \\ E \end{bmatrix} \tag{13}$$

and finally

$$\nu_N = \left(1 - \frac{Tr \left[\; E, \quad O \; \right] \prod\limits_{i=1}^{N-1} N_{i,i+1} \begin{bmatrix} 0 \\ E \end{bmatrix}}{Tr \left[\; E, \quad O \; \right] \prod\limits_{i=1}^{N} M_i \begin{bmatrix} 0 \\ E \end{bmatrix}} \right)^{-1}. \tag{14}$$

It is possible to obtain other characteristics of transition using the same method.

Results and Discussion.

Reduced Free Energy. The behavior of reduced free energy depending on chain length is shown on Fig. 1 according to expression (5).

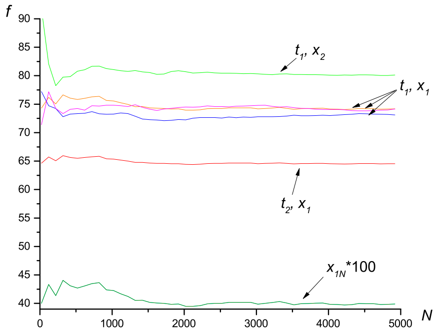

Fig. 1. Dependence of reduced free energy $f_N = -F_N/NKT$ and $x_N = N_A/N$ from the length of the chain for two values of x: $x_1 = 0.4$, $x_2 = 0.5$ and for two reduced temperatures: $t_1 = 0.213$, $t_2 = 0.225$, $u_A = 1$, $u_B = 0.8$, $Q_A = 71$, $Q_B = 51$, $N = 5000$.

As indicated in Fig. 1, in case of short chain length the value of reduced free energy strongly depends on realization, yet for length about 5000 repeated units the dependence flattens with reducing fluctuations. This behavior doesn't change qualitatively when temperature changes and when changes the value of x. The behavior of type A repeated units' fraction x_N, which obviously varies from a priori probability x, is shown on the same figure. We should particularly note the coincidence between qualitative behavior of free energy and x_N, which indicates that the fluctuations of free energy for quite long chains is mostly due to x_N. According to the results presented in Fig. 1, we will gain all other results for chain with $N = 5000$ repeated units.

Helicity Degree. In Fig. 2 the denaturation curves for various realizations of heteropolymer are presented. Curves of both homopolymers are represented for comparison.

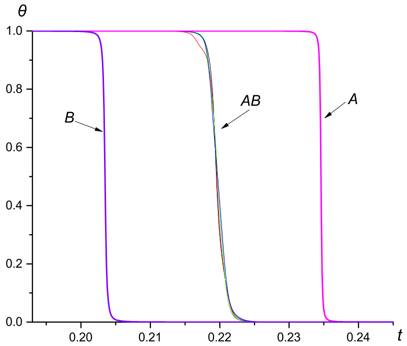

Fig. 2. Denaturation curves of heteropolymer (AB), homopolymers A, B when $x = 0.5$ for various realizations of primary sequence: $u_A = 1,\ u_B = 0.8,\ Q_A = 71,\ Q_B = 51,\ N = 5000$.

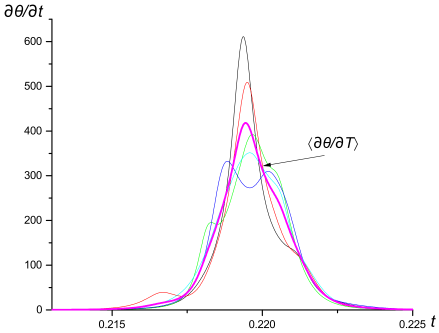

Fig. 3. Differential melting curves (DMC) for various realizations of primary sequence when $x = 0.5$ and average DMC over all realizations: $u_A = 1, u_B = 0.8, Q_A = 71, Q_B = 51, N = 5000$.

One can clearly see from curves broadening of heteropolymeric curve compared to homopolymeric ones. Although, curves slightly vary from one realization to another, qualitatively they behave the same way. We should especially pay attention on reduced fluctuations near the transition point. Helicity degree is self-averaging parameter, as it is order parameter. As a consequence, its qualitative behavior should not change strongly due to realizations. Differential melting curves (DMC) are represented in Fig. 3 for various realizations of primary structure. Figure obviously shows that DMC of various realizations differs from each other qualitatively and appear to be characteristics both for composition and features of sequence. It will require detailed analysis of correlation characteristics for various realizations.

Portion of Junctions between Helix and Coil Regions. Dependences of portion of junctions from helicity degree are shown on Fig. 4. Such dependence has been chosen to gain multipurpose results, connected with partition of macromolecules to helix and coil regions. It is demonstrated that all curves have maximum near $\theta = 0.5$.

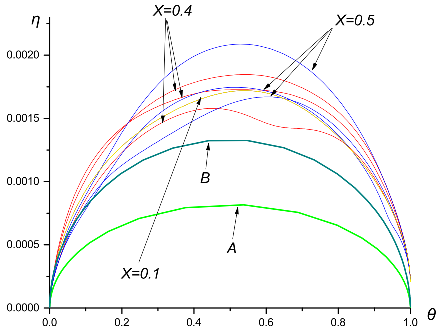

Fig. 4. The dependence of portion of junction η from helicity degree θ: $u_A = 1$, $u_B = 0.8$, $Q_A = 71$, $Q_B = 51$, $N = 5000$.

Strong quantitative dependence of curves from realizations has been observed. This indicates that number of boundaries appears to be feature for transition characteristic as well as for very sequence. Moreover, the scattering is maximal for $x = 0.5$, naturally, as realizations vary more for this value. Heteropolymeric curves always locate upper than homopolymeric ones. This indicates that probability of junction formation in heteropolymers is higher than in corresponding homopolymers. To clarify the last outcome, portion of junctions has been calculated for regular heteropolymers, when $x = 0.5$. Heteropolymers like $ABABAB\ldots$, $AABBAABB\ldots$, $AAAAABBBBB\ldots$ has been investigated. Calculations have shown that portion of junctions of such heteropolymers slightly differs from B homopolymer, i.e. regular heteropolymer behaves like homopolymer also at level of splitting into regions. Therefore these results are not demonstrated on Fig. 4.

Average Length of Helix Region. The behavior of average length of helix region ν from helicity degree is represented on Fig. 5. In the respect of dependence of ν from realizations slighter shift has been observed. Furthermore, there is almost no dependence from x to observe.

Such behavior explains applicability of Zimm–Bragg model to heteropolymers, which is based on splitting macromolecules into helix and coil regions.

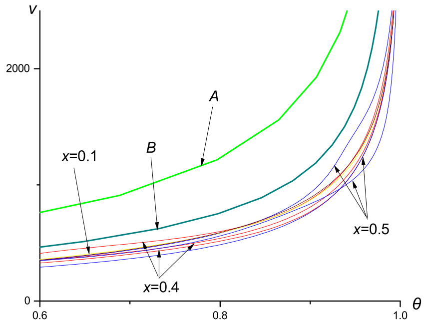

Fig. 5. The dependence of average length of helix region ν from helicity degree θ:
$u_A = 1$, $u_B = 0.8$, $Q_A = 71$, $Q_B = 51$, $N = 5000$.

Conclusion. Series of averaged characteristics of biopolymer in helix–coil transition area has been obtained by means of direct calculation of partition function on the bases of GMPC. It is indicated that 5000 repeated units of chain length allow us to obtain thermodynamic limit, which is more by several orders than the results for homopolymers and regular heteropolymers. For smaller lengths strong dependence from realization has been observed. The same is true for helicity degree. However, DMC shows qualitative shift by realizations for length of 5000 repeated units and more. This follows directly from the fact, that helicity degree is self-averaging parameter, while DMC is not, as well as portion of junctions. Some generality in the behavior of helix region average length needs to be investigated in the future for application of homopolymeric models and heteropolymers, particularly the constrained annealing approach.

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