

Generalized Model of Polypeptide Chain for Helix–Coil Transition in Two-Component Solvent

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Abstract—Within the frameworks of Generalized Model of Polypeptide Chain (GMPC) the influence of the ligands interacting by different ways in the helix–coil transition is studied. It is shown that the model is reduced to the base model by converting the energy and the entropic parameters. In contrast to the case of the pure solvent, both the competitive and the noncompetitive interactions affect to these parameters. As a result, the temperature curve of melting shows more transitions. The influence of polyethylene glycol on the helix–coil transition in the polyalanine is discussed.

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1. INTRODUCTION

The experimental studies of the helix–coil transitions in biopolymers are usually carried out in aqueous solutions in the presence of other chemical compounds. As is well known, the polymers also show the biological activity *in vivo* in a complex aqueous surroundings as well. For the formation of hydrogen bonds, the water may compete with the repeating units of biopolymers and do not compete and be bonded with the repeating units directly, changing the picture of intramolecular interactions. The other substances dissolved in water may act in a similar manner. Almost all biological phenomena are related to the interactions of macromolecules with the ligands. In previous works we had considered different models that take into account the variety of the biopolymer–solvent interactions. The result is a number of interesting effects of influence of various mechanisms on transition effects parameters such as the degree of helicity, the correlation length, heat capacity, etc., showing the diversity of the model by transitions which include both the melting and the arrangement.

The aim of the present work is to study the influence of ligands interacting by different ways with the biopolymer on the parameters of the helix–coil transition.

2. HAMILTONIAN OF THE BASE MODEL AND HAMILTONIAN IN TWO-COMPONENT SOLVENT

As in our previous publications devoted to the helix–coil transition [1–5], the investigations have been carried out within the frameworks of GMPC. The Hamiltonian of base GMPC is as follows:

$$-\beta H = J \sum_{i=1}^N \delta(\gamma_{i-\Delta+1}, 1) \delta(\gamma_{i-\Delta+2}, 1) \dots \delta(\gamma_{i-1}, 1) \delta(\gamma_i, 1) = J \sum_{i=1}^N \delta_i^{(\Delta)}. \quad (1)$$

Here $J = U/T$ is the binding energy of hydrogen reduced to the temperature, $\delta(\gamma_i, 1)$ the Kronecker symbol, γ_i a variable describing the conformation of one repeating unity which obtains the values from 1 to Q . The product of Kronecker symbols $\delta_i^{(\Delta)} = \prod_{k=\Delta-1}^0 \delta(\gamma_{j-k}, 1)$ is equal to unity, and the released energy J , if Δ is a series of the neighboring repeating units in the spiral conformation, is denoted by us as $\mathcal{N}1$.

Consider the biopolymer interacting with the solvent and consisting of two types of low molecular weight compounds. One of the components is called the solvent (S), and the other (L) is the ligand. These notations are used to differ the parameters corresponding to the solvent and the ligand. Let the solvent and the ligand interact with the chain both by competitive and noncompetitive methods. Consider the most general case when there are several binding site of the ligand or the solvent. We proceed from the assumption that the ligand and the solvent are arranged evenly around each of the binding site. Let the number of molecules capable to interact with the each binding site is equal to n , the p of them being the molecules of the ligand, and $(n - p)$ of the solvent. In this case $p/n = c$, where c is the concentration of the ligand. We introduce the variable f which represents the number of molecule located near the binding site, and the $\delta(f < p)$ function that becomes a unity, if the molecule of ligand interacts the with the binding site, and vanishes, if the molecule of the solvent interacts with one; then $\delta(f > p) = 1 - \delta(f < p)$.

In these notations the Hamiltonian of the polymer – two-component solvent system is written as follows:

$$-\beta H = -\beta H_0 - \beta H_S \times \delta(f > p) - \beta H_L \delta(f < p), \quad (2)$$

where βH_0 is the Hamiltonian of the base model without the solvent. We introduce the variables l for ligand molecules and s for the solvent molecules as follows:

$l_{i,st,k}$ is the variable that indicates the orientation of the ligand molecules which are in the vicinity of the k -th binding site in the spiral structure, that is, the i -th repeating unit is related to the hydrogen bond; this hydrogen bond being originated, if the molecule of ligand is in the $\mathcal{N}1$ orientation;

$l_{i,h,k}$ is the variable that indicates the orientation of the ligand molecule which are in the vicinity of the k -th binding site in the spiral conformation, that is, the i -th repeating unit is in the $\mathcal{N}1$ conformation regardless of whether it is related or do not related to the hydrogen bond;

$l_{i,dst,k}$ is the variable that indicates the orientation of the ligand molecule, which is in the vicinity of the k -th binding site with the broken hydrogen bonds;

$l_{i,c,k}$ is the variable that indicates the orientation of the ligand molecule, which are in the vicinity of the k -th binding site in the coiled conformation, that is, the i -th repeating unit is not in the conformation 1.

For the solvent molecules the similar notations are introduced. Then we have:

$$\begin{aligned} -\beta H_S = & \sum_{i=1}^N \sum_{k=1}^{m_{st}^S} I_{k,st}^S d_i^{(D)} d(s_{i,st}^k, 1) + \sum_{i=1}^N \sum_{k=1}^{m_c^S} I_k^S (1 - d_i^{(D)}) d(s_{i,k}, 1) \\ & + \sum_{i=1}^N \sum_{k=1}^{m_h^S} I_{k,h}^S d_i^{(1)} d(s_{i,h,k}, 1) + \sum_{i=1}^N \sum_{k=1}^{m_c^S} I_{k,c}^S (1 - d_i^{(1)}) d(s_{i,c,k}, 1), \end{aligned} \quad (3)$$

$$\begin{aligned} -\beta H_L = & \sum_{k=1}^{m_{st}^L} I_{L,st}^k \delta_i^{(\Delta)} \delta(l_{i,st}^k, 1) + \sum_{k=1}^{m_c^L} I_L^k (1 - \delta_i^{(\Delta)}) \delta(l_{i,c}^k, 1) \\ & + \sum_{k=1}^{m_h^L} I_{L,h}^k \delta_i^{(1)} \delta(l_{i,h}^k, 1) + \sum_{k=1}^{m_c^L} I_{L,c}^k (1 - \delta_i^{(1)}) \delta(l_{i,c}^k, 1), \end{aligned} \quad (4)$$

3. PARTITION FUNCTION AND PARAMETER TRANSFORMATION

For the model described above the partition function takes the form

$$Z = \sum_{\{\gamma\}} \sum_{\{s\}} \sum_{\{l\}} \sum_f e^{-\beta H} . \tag{5}$$

We sum (5) over f and then obtain the expression

$$Z = n^N \sum_{\{\gamma\}} \prod_{i=1}^N e^{-\beta H_0} c \sum_{\{S\}} \sum_{\{L\}} e^{-\beta H_L} + n^N \sum_{\{\gamma\}} \prod_{i=1}^N e^{-\beta H_0} (1-c) \sum_{\{S\}} \sum_{\{L\}} e^{-\beta H_S} , \tag{6}$$

where each of the terms related to the solvent and the ligand can be transformed as it was done in [6, 7]. It was taken into account that each type of interaction between the polymer and the solvent and polymer-ligand occurs in several binding sites. Since the first sum in the formula (8) is independent on $\{S\}$, and the second sum is independent on $\{L\}$, the product of all $q_{\{s_i\}}$ originates for the first sum and the product of all $q_{\{l_i\}}$, for the second sum, respectively. Then, taking all $\{q_l\}$ and $\{q_s\}$ as a common, the partition function can be reduced to the linear form by concentration and one will consist of two subsums $\sum_{\{l\}}$ and $\sum_{\{s\}}$:

$$Z = \sum_{\{\gamma\}} \prod_i c \sum_{\{l\}} \frac{e^{-\beta H_L}}{\prod_{\{q_l\}}} + \sum_{\{\gamma\}} \prod_i (1-c) \sum_{\{s\}} \frac{e^{-\beta H_S}}{\prod_{\{q_s\}}} . \tag{7}$$

We carry out the summation over all the variables orientation of molecules of solvent and ligand. Because the each type of interaction contains terms in the Hamiltonian with the independent variables, then each of the subsums $\sum_{\{l\}}$ and $\sum_{\{s\}}$ has the products of $q_j \left(1 + \left[\left(\frac{e^{J_j} - 1}{q_j} + 1 \right) - 1 \right] \delta \right)$ -type, where $\delta_i^{(\Delta)}, 1 - \delta_i^{(\Delta)}, \delta_i^{(1)}, 1 - \delta_i^{(1)}$ should be understood as δ . Using the obvious equality $\prod_j (1 + (A_j - 1)\delta) = 1 + \left(\prod_j A_j - 1 \right) \delta$, up to a constant we obtain the expression

$$\begin{aligned} Z = & c \sum_{\{g\}} \prod_i e^J \delta_i^{(\Delta)} \left[1 + \left(\prod_{k=1}^{m_{st}^L} \left(\frac{e^{J_{st,k}^L} - 1}{q_k^L} + 1 \right) - 1 \right) \delta_i^{(\Delta)} \right] \\ & \times \left[1 + \left(\prod_{k=1}^{m_{st}^L} \left(\frac{e^{J_{dst,k}^L} - 1}{q_k^L} + 1 \right) - 1 \right) (1 - \delta_i^{(\Delta)}) \right] \left[1 + \left(\prod_{k=1}^{m_h^L} \left(\frac{e^{J_{h,k}^L} - 1}{q_k^L} + 1 \right) - 1 \right) \delta_i^{(1)} \right] \\ & \times \left[1 + \left(\prod_{k=1}^{m_c^L} \left(\frac{e^{J_{c,k}^L} - 1}{q_k^L} + 1 \right) - 1 \right) (1 - \delta_i^{(1)}) \right] \\ & + (1-c) \sum_{\{g\}} \prod_i e^J \delta_i^{(\Delta)} \left[1 + \left(\prod_{k=1}^{m_{st}^S} \left(\frac{e^{J_{st,k}^S} - 1}{q_k^S} + 1 \right) - 1 \right) \delta_i^{(\Delta)} \right] \\ & \times \left[1 + \left(\prod_{k=1}^{m_{st}^S} \left(\frac{e^{J_{dst,k}^S} - 1}{q_k^S} + 1 \right) - 1 \right) (1 - \delta_i^{(\Delta)}) \right] \left[1 + \left(\prod_{k=1}^{m_h^S} \left(\frac{e^{J_{h,k}^S} - 1}{q_k^S} + 1 \right) - 1 \right) \delta_i^{(1)} \right] \\ & \times \left[1 + \left(\prod_{k=1}^{m_c^S} \left(\frac{e^{J_{c,k}^S} - 1}{q_k^S} + 1 \right) - 1 \right) (1 - \delta_i^{(1)}) \right] . \end{aligned} \tag{8}$$

After multiplication in (8) the subsum is converted into the form

$$\sum_{\{j\}} \prod_i \left[\delta_i^{(1)} + (Q-1) \frac{cD_{dst}^L D_c^L + (1-c)D_{dst}^S D_c^S}{cD_{dst}^L D_h^L + (1-c)D_{dst}^S D_h^S} (1 - \delta_i^\Delta) \right. \\ \left. + \left(e^J \frac{cD_{st}^L D_h^L + (1-c)D_{st}^S D_h^S}{cD_{dst}^L D_h^L + (1-c)D_{dst}^S D_h^S} - 1 \right) \delta_i^{(\Delta)} \right], \quad (9)$$

where the following notation is used $D_j = \prod_k \left(1 + \frac{e^{J_{j,k}} - 1}{q_{j,k}} \right)$.

Thus, the considered model is reduced to the base model with the redefinition of energy and entropy parameters of the theory with the complex dependence on the concentration according to the expression:

$$\tilde{Q} - 1 = \frac{cD_{dst}^L D_c^L + (1-c)D_{dst}^S D_c^S}{cD_{dst}^L D_h^L + (1-c)D_{dst}^S D_h^S} \times (Q-1), \quad (10)$$

$$\tilde{W} = e^J \times \frac{cD_{st}^L D_h^L + (1-c)D_{st}^S D_h^S}{cD_{dst}^L D_h^L + (1-c)D_{dst}^S D_h^S}. \quad (11)$$

4. RESULTS AND DISCUSSION

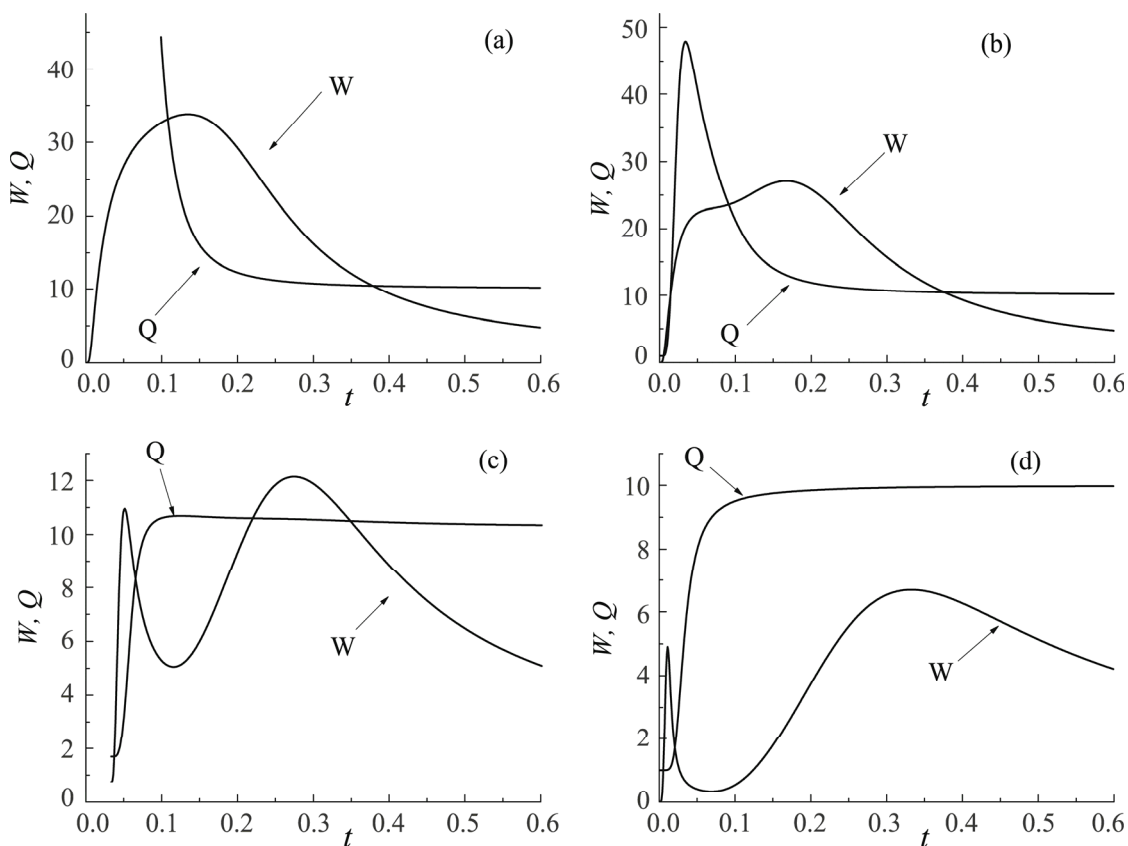
As seen from the equations (10) and (11), unlike the case of the pure solvent where the competitive interaction affects only the energy parameter \tilde{W} and the noncompetitive interactions affects only the conformational parameter \tilde{Q} , in the case of two-component solvent the mixing of these parameters is observed: the noncompetitive interaction with the helix enters both expressions for \tilde{W} and \tilde{Q} . The same takes place in the case of the competitive interaction. It becomes clear from the obtained formulas (10) and (11) that the system in two-component surroundings (solvent–ligand) has a more varied behavior than in the single component surroundings considered by us earlier [6, 7].

The figure shows the behavior of \tilde{W} and \tilde{Q} at certain ratio of energies of intra- and intermolecular interactions at different concentrations of ligand molecules. To illustrate, we show the case where the number of binding sites of ligand and solvent molecules is equal to one, the intermolecular interactions with solvent and ligands are energetically more favorable as compared with the intramolecular, and for noncompetitive interactions with the ligand the helical conformations, and with the solvent the coiled conformations are more beneficial. It can be seen that the two-component solvent may reveal the greater number of transitions (the helix–coil and the coil–helix) than a single component solvent. With the change of the concentration of ligand molecules the number of transitions is changing, the maximum number of transitions being occurred at the intermediate values of concentration.

Consider the behavior of the temperature of the helix–coil transition T_m . It is determined from the $\tilde{W} = \tilde{Q}$ relationship. Using the formulas (10) and (11), this condition takes the form

$$cD_{dst}^L \left[\frac{e^J D_{st}^L}{D_{dst}^L} - \left(1 + (Q-1) \frac{D_c^L}{D_h^L} \right) \right] + (1-c)D_{dst}^S \left[\frac{e^J D_{st}^S}{D_{dst}^S} - \left(1 + (Q-1) \frac{D_c^S}{D_h^S} \right) \right] = 0. \quad (12)$$

One can see from the formula (12), for the pure ligand and solvent the transition point is determined from the expressions in square brackets. Thus, the transition point for ligand–solvent mixture is between the points of helix–coil transition of pure solvent and ligand, i.e. the concentrational behavior of the



Temperature dependences of energy and entropy parameters at the values of concentrations of ligand molecules: (a) $c = 0$, (b) $c = 0.022$, (c) $c = 0.28$ and (d) $c = 0.88$.

transition point is a monotonic from the point of transition of pure solvent to the point of transition of pure ligand.

It was shown in our earlier studies [6, 7], since the water is a competitor for the formation of the hydrogen bond, the point of the helix–coil transition in the aqueous surroundings is below the transition point of the base model defined by the relationship $e^J = Q$. Just this result enables one to interpret the experiments with the stabilizing effect of polyethylene glycol (PEG) on the helical structure of the polypeptide.

In work [8] the helix–coil transition in polyalanine in the presence of PEG has been studied experimentally. It was shown that although the PEG has not reacted with the polypeptide, it stabilizes the helical structure. The mechanism of this effect stated by us earlier in the frameworks of the theory of single-component solvent had the complicated explanation [9]. In the frameworks of the model presented in this work, we can get this result

$$(1 - c)[\tilde{W}_s - \tilde{Q}_s] - c[\tilde{W}_L - \tilde{Q}_L] = 0, \tag{13}$$

Since the PEG does not interact with the polypeptide, all D^L -s are equal to unity, and the expression to determine the transition point takes the form

$$(1 - c)D_{dst}^S \left[\frac{e^J D_{st}^S}{D_{dst}^S} - \left(1 + (Q - 1) \frac{D_c^S}{D_h^S} \right) \right] + c[e^J - Q] = 0. \tag{14}$$

5. CONCLUSION

As already was mentioned, the temperature of helix–coil transition of the base model is higher than in the aqueous surroundings. Therefore, with the increase in PEG concentration the transition point should increase. This result can be interpreted as follows: the water competes for the hydrogen bonding, and the ligand, though it does not react but occupies the seat, impedes to competition, which results to the stabilization.

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