Simple Models of Polypeptides – Conformational Properties. A Monte Carlo Study

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Summary: A simple model of polypeptide chains was studied by means of Monte Carlo method. The chains were built on the (310) hybrid lattice and were represented by united atoms centered on alpha carbons. The residues interacted with the long-range potential. The model chain consisted of two kinds of residues only: hydrophobic and hydrophilic forming a helical pattern -HHPPHPP-. The classical sampling Metropolis and new Replica Exchange simulation methods were applied to study the model chains. It has been found that at low temperatures the model chain formed dense and partially ordered but not unique structures. The characteristics of the coil-to-globule transition was determined.

Introduction

The phase transition of the flexible polymeric chains from a random coil to a dense globule has been extensively investigated. For a homopolymeric chain the transition is continuous and the low-temperature structures do not exhibit any global ordering. In the case of natural proteins a transition from the random coil-like state to a dense globule is a more complicated process.[1-2] The recent computer simulations demonstrated that a simple lattice models without any specific interactions could mimic the conformational transitions of globular proteins in both the topology and thermodynamics of the process as well as a "all-or-none" character of the transition.[2-3] However, the role of tertiary interactions in forming secondary structures is still far from understanding.[1]

The model and the simulation algorithm

The residues in the polypeptide chain were represented by alpha carbons only. The positions of residues were limited to a hybrid (310) lattice with a high coordination number $z = 90$. On this lattice one can represent a polypeptide chain with the accuracy of 0.6-0.7 Å with respect to real one.[2, 4-6]

The residues forming the chain interacted by a contact potential. The potential has a form of a square well with a short-distance repulsive part $\epsilon_{rep} = 5$ and long-distance part: $\epsilon_{HH} = -2$, $\epsilon_{PP} =$

 CCC 1022-1360/00/$ 17.50+.50/0

-1, $\epsilon_{HP} = 0$. In this paper we studied model chains consisting of the typical helical pattern, *i.e.* containing septets (-HHPPHPP-), where P denotes the hydrophilic (polar) and H is a hydrophilic (polar) residue.[4]

The classical Metropolis-type Monte Carlo sampling algorithm (MS) was employed. The model chain underwent a series of local micromodifications. For the hybrid (310) lattice the following set of local chain conformational changes was used [4]: (i) 2-bond kink motion, (ii) 3-bond motion and (iii) chain ends motion. The Replica Exchange Monte Carlo (RE) algorithm was also used - 20 separate but interchangeable replicas were simulated using the same set of micromodifications and within the same temperature range.[7]

Results and discussion

The simulations were carried out for model chains consisting of N = 10, 30, 60 and 100 residues. In Figure 1 changes of the mean square radius of gyration of the model chain $< S^2 >$ with the temperature T (for different chain lengths) are presented. The size of the system decreases gradually and smoothly with the decrease of the temperature T. One can observe that the location of the transition to the collapsed state shifts towards the higher temperatures for longer chains. RE simulations show that MS simulations apparently quench the system especially for longer chains.

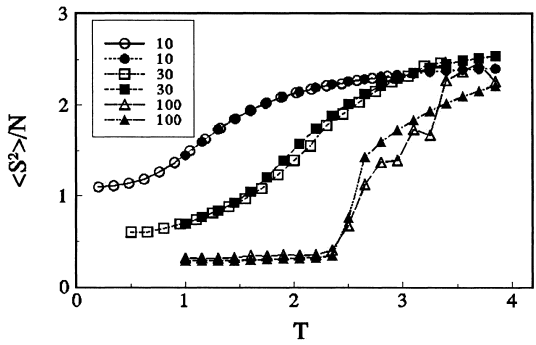

Figure 1. The mean-square radius of gyration versus the temperature for different chain lengths. Open symbols correspond to MS and solid symbols to RE method respectively. The length of the chain is given in the inset.

The mean energy also changes with the temperature gradually, what is presented in Figure 2. There are almost no differences between MS and RE results. As one can observe, RE method

gives a smoother than MS method curve for longer chains.

The coil-to-globule transition temperature T_c can be estimated from the location of the peak on the heat capacity plot. Figure 3 shows the heat capacity C_v/k versus the temperature T for some chain lengths. RE method gives smoother curve with one well-defined peak only, which shows the value of the coil-to-globule transition temperature.

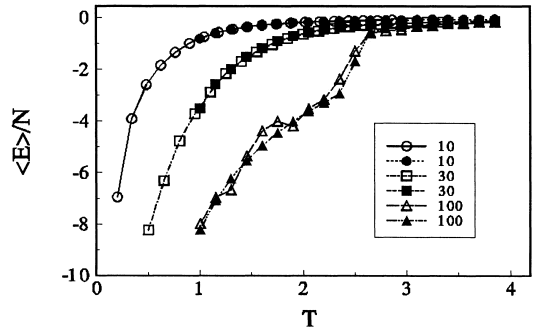

Figure 2. The mean energy versus the temperature for different chain lengths; (Symbols: see Figure 1).

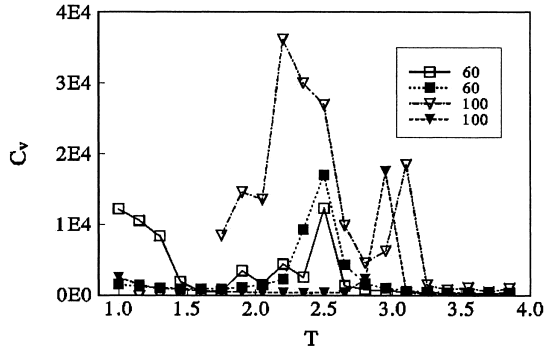

Figure 3. The heat capacity versus the temperature for different chain lengths. Values for $N = 60$ are multiplied by the factor 10; (Symbols: see Figure 1).

The amount of secondary structure (helices) in the system can be expressed in the term of helicity, i.e. the percentage of the residues forming the helical structures of the chains. In the Figure 4 we present the helicity against the temperature T for different chain lengths. In general the helicity increases with the decrease of temperature approaching values close to those for random sequences.[4]

The representative structures of high-temperature and low temperature chains are given in Figure 5. One can observe that a hydrophobic core is formed inside the collapsed chain as well as the increase of a number of helical conformations.

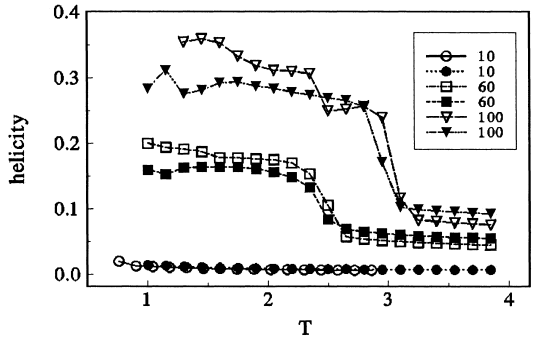

Figure 4. Mean helicity vs. the temperature for different chain lengths; (Symbols: see Figure 1).

Figure 5. Snapshots of the chain configuration at the temperatures (N = 60). Solid circles correspond to hydrophobic and open circles to hydrophilic residues respectively. T = 3.85 (left) and T = 1.00 (right).

Acknowledgment

This work was supported by the University of Warsaw grant BW-1522/18/2001.

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