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Helix transition in di-block polyampholyte

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Abstract

Molecular dynamics simulations are applied to study the structural organization of a bead–monomer model of di-block polyampholyte. Di-block polyampholyte is formed of two consecutive blocks of equal length, each containing charges of one sign only. The ground state of the model studied has been found to be a double-stranded helix. The folding (freezing) into the ground state is not an all-or-none process but proceeds via an intermediate molten-globule phase. In the intermediate phase, the molecule is subject to considerable structural fluctuations and its size is small compared with both the high-temperature and ground-state conformations. Also at the stage of the coil-to-globule transition the twist of the native helix is fixed. In the globular state below the collapse transition, the chain cannot change its twist spontaneously. By applying finite-size analysis to the helicity distribution function at the freezing temperature we find that the molten-globule–helix transition is of first order.

1. Introduction

Polyampholytes are polymers containing charged monomers of both signs as well as neutral monomers. Despite providing an interesting problem of polymer physics in their own right, polyampholytes owe much of the interest seen in recent years to the protein-folding problem. This is because some of the protein amino acid residues can carry electric charges at neutral pH conditions which places proteins into the class of polymers with long-range (LR) interaction between monomers, i.e. polyampholytes. The work on polyampholytes to date has focused on structural organization of these systems in dilute solutions. Depending on whether a polyampholyte chain is neutral or bears a net electric charge, its conformations at low temperatures can be either compact [1] or semicompact [2, 3]. Charged chains with net electric charge not exceeding $\sim e\sqrt{N}$, where e is the electron charge and N is the number of the chain's monomers, are believed to behave like globally neutral chains, while for the

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systems with larger net charge, two conflicting theories have been presented: the elongated-globule model [4] and the necklace model [5]. In a recent MC simulation the controversy over the shape of collapsed charged polyampholytes was resolved in favour of the necklace model [6]. The main findings of [6], which seems to contain the most extensive and reliable simulation of polyampholyte chains to date, can be summarized as follows. Long enough globally neutral polyampholyte chains collapse into maximally compact conformations with $R_g \sim N^{1/3}$ at low temperatures in full accord with the theory of Higgs and Joanny [1], where by R_g we denote the radius of gyration. Statistically neutral chains, i.e. an ensemble of non-neutral quenched chains whose charge is drawn from a Gaussian distribution of zero mean, are prevented from acquiring maximally compact states by charge fluctuations. Instead they collapse into semicompact states with a larger gyration radius $R_g \sim N^{1/2}$. In this paper we shall be concerned with the freezing in compact globules of neutral polyampholytes at low temperatures.

The term ‘freezing’ [7] designates the transition of a polymeric chain from a state where it spans over a large number of conformations $O(e^N)$ into the state where the chain statistics is dominated by one (or a few) $O(1)$ conformations. An outstanding example of a freezing transition in polymers is the folding of a protein. Most attention in the studies of heteropolymer freezing transitions has been devoted to polymers with short-range (SR) potentials between monomers for which a number of theories [8–14], partly confirmed in computer simulations [15–17], have been presented. In general, it is believed that the structural statistics of short-range heteropolymers with random-sequence links is satisfactorily described by the random-energy model (REM) [14]. When it comes to polymers with monomers interacting via long-range potentials the situation is rather different, since the theories developed for the SR case do not universally hold true in the LR case. The difficulties of the theoretical description of freezing in polyampholytes were highlighted by Pande *et al* [11] who demonstrated that the REM is not applicable in these systems. Another important aspect that sets apart collapses in the SR and LR cases is the impact of the monomer sequence on the chain’s conformational statistics. In polyampholytes, sequence specificity fully determines the conformation space accessible to the system at all temperatures, in contrast to the case for SR polymers where the self-averaging breaks down below the collapse transition only. Considering the difficulties faced by the theoretical treatment of the freezing phenomenon in polyampholytes and the importance of this phenomenon in the context of the protein-folding problem, molecular dynamics simulation studies of the low-temperature conformation space of polyampholytes seem highly desirable. Issues of particular interest in such studies are the sequence–structure relationships and the exact mechanism of freezing, i.e. the way in which freezing proceeds. Does the freezing look like an all-or-none process or does it go through an intermediate molten-globule phase [7, 18]? To shed light on the questions raised for a specific charged monomer sequence is the aim of the present paper. We consider a polymeric chain consisting of two equal blocks of positively and negatively charged monomers. This kind of polyampholyte—di-block polyampholyte—was studied earlier by Imbert *et al* [19]. In a MC simulation of the bond-fluctuation model, the authors found that the di-block polyampholyte undergoes a so-called zipping transition at a sufficiently high temperature. The two oppositely charged parts of the chain zip together to form a supercoil whose repeated units are formed by dipoles of opposite charges. It was also found that the supercoil structure can be further compacted by a decrease of temperature, but the details of the resultant low-temperature phase were not studied. Such a study was undertaken later in a paper by Hiwatari and co-workers [20] for an off-lattice model of polyampholyte. However, because of the problems encountered in bringing a rather long chain containing 60 monomers into proper thermal equilibrium, a detailed study of the frozen conformations of di-block polyampholytes failed to emerge.

In order to avoid the equilibration problem, in the present paper we study shorter chains made up of 20, 30 and 40 monomers with the same off-lattice model as in reference [20]. In section 2 we give a short description of the physical model employed. It is important to stress here that the polyampholyte studied is a purely theoretical model that has no immediate prototype in polymeric materials. As stated above, our primary concern in studying this model is the sequence–structure relationship in the presence of long-range interactions. In section 2 we also give the details of our computer simulations. Section 3 concerns the main results that we obtained in this paper. We find that the ground state of short di-block polyampholytes is a double-stranded helix conformation. On its folding path towards the ground state the polyampholyte passes through an intermediate random-globule phase. The molten-globule state is marked by a degree of similarity to the ground-state helix, but further setting in of order is hampered by large-scale conformational fluctuations. Both transitions—from coil to random globule and from random globule to helix—are observable in the specific heat at constant volume C_v , as separate maxima. In order to determine the nature of the freezing transition we performed a finite-size scaling analysis of the critical helicity distribution function. According to the Wilding and Bruce [21] criterion, the helix transition in di-block polyampholytes with the model parameters adopted is of first order. This compares favourably with the theoretical predictions [7]. In section 4 we summarize our work in concluding observations.

2. Model and computer simulations

To study low-temperature structural properties of di-block polyampholytes we considered a bead model of polymer containing N monomers. Charged spherical beads interact via a soft-core potential:

$$U^{sf}(|\vec{r}_i - \vec{r}_j|) = 4\epsilon \left(\frac{\sigma}{|\vec{r}_i - \vec{r}_j|} \right)^{12} \quad (1)$$

designed to provide for the excluded-volume effect. Here \vec{r}_i denotes the position of monomer i , while σ and ϵ are parameters characterizing the space scale and the strength of the soft-core force. In order to avoid following relatively fast internal motions arising from strong covalent forces, such as bond-length vibrations, distances between adjacent monomers of our model were kept constant. The length of the covalent bonds was chosen to be σ . The charges on the chain are arranged into two blocks with the same number of particles. One block containing $N/2$ positively charged monomers is followed along the chain by the other block made up of the same number of negatively charged monomers. The Coulomb potential acting between the units is given by

$$U^c(|\vec{r}_i - \vec{r}_j|) = \frac{q_i q_j}{|\vec{r}_i - \vec{r}_j|} \quad (2)$$

where we set the dielectric constant of the medium to 1 since we consider a single chain in vacuum. The positively and negatively charged monomers were assigned charges e and $-e$ respectively. The other parameters involved in equation (1), namely $\sigma = 3.4$ au and $\epsilon = 0.25 \times 10^{-2}$ au, were adopted from reference [20].

For the above model we performed several molecular dynamics simulations with $N = 20$, 30 and 40. The choice of the number of simulated monomers was motivated by the following considerations. It is well known that in polymer models (both lattice and off-lattice) the presence of different types of conflicting interaction, such as attractive Coulomb forces and rigid bond-length constraints, leads to the ubiquitous problem of multiple potential energy minima. The potential energy surface of a constrained polymer possesses many local minima which

act as kinetic traps in molecular dynamics simulations, thereby making proper thermalization of the system problematic. Among the methods specifically designed to tackle the multiple-minima problem, the multicanonical algorithm [22, 23] is the most widely used. The strength of the multicanonical scheme lies in the reduction of the barrier separating two free-energy minima, which results in enhanced exploration of the conformation space. Another asset of the multicanonical method is that it allows one to calculate various thermodynamic quantities as functions of temperature from one simulation only. Obviously, this property is essential in cases where an accurate location of phase transition temperatures is needed, in that it can save a great deal of computational time. In reference [20] some of the present authors applied the multicanonical molecular dynamics (MMD) method to the present polyampholyte model containing 60 monomers. Unfortunately, the time needed to equilibrate the chain in the transition temperature region turned out to be far beyond the capacity of currently available computational facilities even in the multicanonical ensemble. The failure to explore low-temperature conformations of the 60-monomer chain in [20] led us to consider shorter di-block polyampholytes. Since the number of the potential energy minima of the chain grows exponentially with the number of embedded particles, reducing the size of the system, besides the obvious advantage of cutting down on the cost of one time integration step, also reduces the molecule's relaxation time. By experimenting with the number of chain monomers, we found that $N = 20$ is the optimal value which allows reliable canonical and multicanonical ensemble sampling within reasonable computational time. All of the results reported in this paper have been obtained for the 20-monomer polyampholyte with a few exceptions following later in the text, where 30 and 40 monomers were considered. For the 20-mer we performed standard constant-temperature (NVT) MD simulations at a range of temperatures covering the transition point region. An additional MMD simulation was also performed for this system to better locate the transition points and to check on the consistency of the canonical simulations. Most of the NVT runs lasted over 20×10^6 time steps, which is large enough to account for the slow fluctuations taking place at low temperatures. The main quantity of interest in this study—the specific heat C_v —is a sufficiently smooth function of temperature for transition points to be identifiable. The multicanonical simulation consisted of a preliminary NVT run and five subsequent MMD iterations each 20×10^6 time steps long. The resulting potential energy distribution function had a flat part consisting of the energy region of the observed structural transitions. For more details on the integration algorithm used in this study, the multicanonical recursive procedure and the bond-constraint method, we refer the reader to our previous publication [20].

3. Results and discussion

In this section we report the results of our molecular dynamics simulations for the model of di-block polyampholyte studied here. In figure 1 we present the specific heat at constant volume C_v and the radius of gyration R_g generated by NVT and multicanonical simulations as functions of temperature. In this figure and throughout the paper, temperature is given in reduced units, $\sigma k_b T / e^2$. The usual plasma coupling constant Γ is related to the temperature as $\Gamma = 1/T$. In figure 1(a) the multicanonical specific heat was obtained from the canonical energy distribution function $P(E)$, reweighted according to the single-histogram method [24]. It is seen that the MMD reweighted data and the results of direct NVT simulations for C_v are in very good agreement. At $T > 0.5$ the specific heat is a smooth slowly decreasing function of temperature while at lower temperatures we find two distinct maxima at $T_1 = 0.032$ and $T_2 = 0.067$, signalling structural transitions in the system. From the previous study on di-block polyampholytes [19] it is known that this system has an unusual collapse scenario different

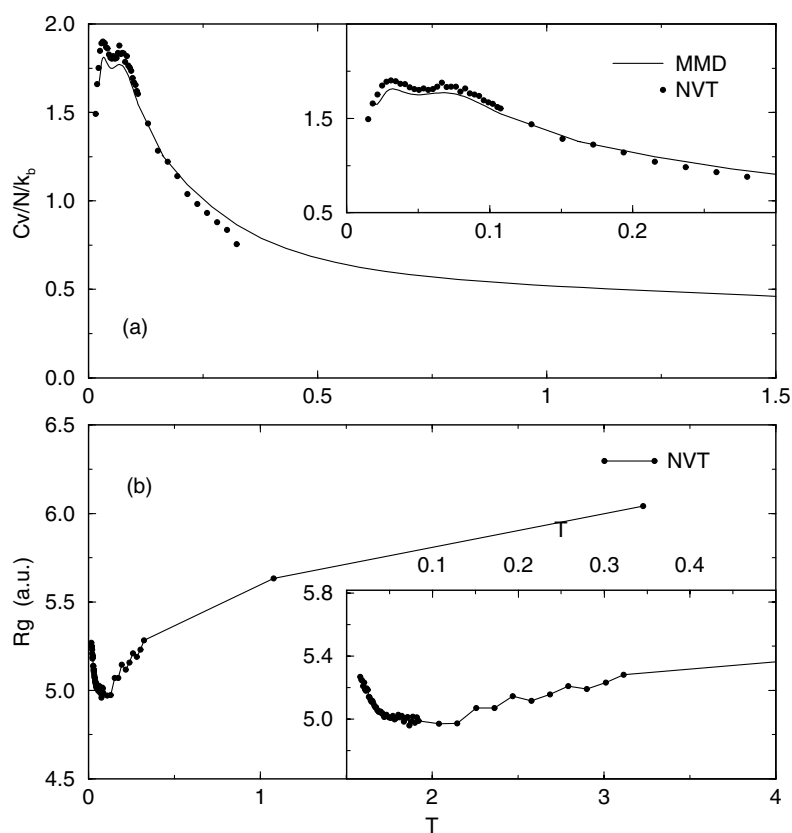


Figure 1. The specific heat at constant volume C_v (a) and radius of gyration R_g (b) for the 20-monomer di-block polyampholyte as obtained from canonical and multicanonical MD simulations.

from those for other charged copolymers, for example alternating polyampholytes [25]. At quite a high temperature, which we estimate to be $T_z \sim 2.65$ for the 20-mer considered, the chain starts to bring its two oppositely charged halves together. This so-called zipping transition leads at $T < T_z$ to the formation of a supercoil structure—a polymer chain whose repeated units are dipoles made up of pairs of one positive and one negative charge. Further cooling of the system causes a collapse of the newly formed supercoil into a compact globule. According to [19] this collapse takes place at $T \sim 0.07$, which agrees very favourably with the position of the second maximum of C_v of our model, T_2 . That the chain collapses at $T \sim T_2$ is also clear from the temperature evolution of R_g in figure 1(b). Starting from $R_g \sim 6$ au at $T \sim 2-3$, the radius of gyration rapidly drops by about 20% to reach 5 au at $T \sim T_2$. In the vicinity of the collapse transition, R_g stays constant for a while and then grows again and reaches 5.4 au at the lowest temperature studied. The growth of the gyration radius at temperatures near T_1 is rather surprising since, obviously, one would expect a chain to shrink upon cooling, not to expand. Upon visual inspection of the simulated model, we find that the chain finds itself in double-stranded helix conformations at $T < T_1$ as shown in figure 2. That the double-stranded helix conformation is the ground state of the present model was verified by a series of simulated annealing runs starting at $T \sim T_1$ from different initial configurations. All the simulated annealing runs converged to the single structure shown in figure 2 when the temperature was gradually decreased to $T \sim 0$.

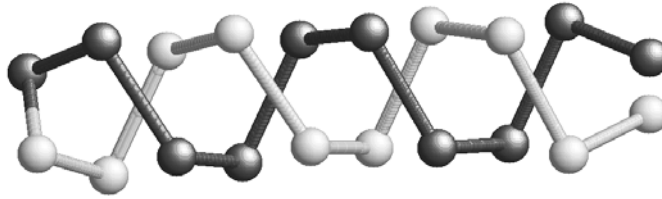


Figure 2. The gross appearance of the double-stranded-helix ground-state conformation as found in the MD simulations of di-block polyampholyte. Black balls represent positively charged monomers and grey ones negatively charged monomers.

Having determined the ground state of the chain, the question of a quantitative description of the freezing into this ground state arises, in particular as regards the nature of this transition. In order to distinguish between the ordered helical phase at $T < T_1$ and the disordered random-globule phase at $T > T_1$, one needs to introduce an order parameter. Following Hansmann and Okamoto [26] we adopt helicity for this purpose. Its definition relies on the observation that, unlike coil or random-globule states, a helical conformation is characterized by some specific values of the bond and torsion angles. If we denote by ξ_1 the angle between two consecutive bonds $(i, i + 1)$ and $(i + 1, i + 2)$ and by ξ_2 the next angle for monomers $i + 1, i + 2$ and $i + 3$, and if we further denote by ζ the angle between bond $(i + 2, i + 3)$ and the plane formed by monomers $i, i + 1$ and $i + 2$, then we call the quartet of monomers $i, i + 1, i + 2$ and $i + 3$ helical if $\xi_1, \xi_2 = 101 \pm 30^\circ$ and $\zeta = 56 \pm 17^\circ$. In this definition of a helical four-monomer segment the given acceptable deviations of the bond and torsion angles from their ground-state values account for the thermal fluctuations such that the helix is not considered broken. They were estimated from the widths of the distribution functions of ξ and ζ at $T < T_1$. We note that all the results and conclusions obtained in this work remain intact even after making small changes to the permissible deviations of the ξ s and ζ . Helicity is defined as the ratio of the number of helical four-monomer segments on the chain to the total number of such segments:

$$h = \frac{n_h}{N - 3}. \quad (3)$$

Clearly, in disordered conformations at $T > T_1$ the helicity will acquire small values of order 0, while in the ordered phase at $T < T_1$ it will approach unity (in sufficiently long chains). We also consider the susceptibility χ of the order parameter h defined in a manner that is standard for response functions:

$$\chi = N \langle \Delta h^2 \rangle. \quad (4)$$

Here angular brackets denote the ensemble average. We expect the susceptibility, like the specific heat, to have maxima at transition points where the structural fluctuations of the system are significant.

Information contained in molecular dynamics data for helicity and susceptibility can be used to establish the order of the freezing transition. A problem that emerges in MD studies of critical phenomena is that continuous and discontinuous phase transitions look alike in finite-size systems. Thermodynamic quantities expected to be discontinuous at first-order transitions, such as internal energy, are smooth functions of temperature for the two kinds of transition. This makes determination of the order of phase transitions from molecular dynamics ensembles a non-trivial computational problem whose successful solution requires application of the finite-size scaling theory [27]. According to this theory the maxima of the specific heat

and susceptibility of finite-size systems containing N particles scale as

$$\begin{aligned} C_v(N) &\sim N^{\alpha/(d\nu)} \\ \chi(N) &\sim N^{\gamma/(d\nu)} \end{aligned} \quad (5)$$

where α is the specific heat critical exponent, γ is the susceptibility critical exponent, ν is the correlation length critical exponent and d is the space dimensionality. It is generally believed that at first-order transitions the response functions scale as $\sim N$, i.e. α , γ and $d\nu = 1$ [28], while at discontinuous transitions the critical exponents have non-trivial values [29]. Provided that the dependence of C_v and χ on the number of particles is available from computer simulations, it is possible to carry out the scaling analysis on the basis of (5) in order to establish the nature of the transition. Such an analysis has been attempted in [26, 28] for the case of freezing coil–helix transition in alanine oligomers and in an off-lattice homopolymer model. Numerical implementation of relations (5) turned out, however, to be extremely sensitive to the statistical error contained in C_v and χ . A simple analysis of the data provided by Hansmann and Okamoto in references [26, 30] shows that as little as 10% error of the input quantity C_v may lead to as much as 100% error in the output critical exponent. Thus it appears that in order to be successful, this method needs an accurate calculation of the exponents in order to decide the order of a transition; this, in turn, entails unusually long computer simulations. It is this computational difficulty which prevented the authors of references [26, 30] from reaching an unambiguous conclusion regarding the order of the helix–coil transition.

Here, for the purpose of determining the order of a freezing transition, we propose to employ a less computationally demanding strategy based on the analysis of the order parameter distribution function $P(h)$ at criticality [21, 31]. Intuitively it is understood that in discontinuous transitions the order parameter distribution function should have two maxima corresponding to the average values of the order parameter in coexisting phases; in continuous transitions there is only one maximum, as in this case the difference between the two phases is smeared out. When one looks at this criterion for the distinction between first- and second-order transitions from the perspective of the free-energy profile $F(h)$, defined as $F(h) = -k_b T \ln P(h)$, the bimodal shape of the order parameter distribution function transforms into a two-minimum structure of $F(h)$ with each minimum corresponding to each phase at coexistence. Accordingly, the unimodal shape of $P(h)$ means one minimum for the free-energy profile.

In figure 3 we present the temperature dependence of the helicity distribution function $P(h)$ for the 20-monomer chain. One can readily see that at temperatures above freezing, $P(h)$ has one maximum positioned at small $h \sim 0.2$; the content of the helical segments of the chain is low and is a decreasing function of temperature in this region. As the temperature goes down, this maximum gradually fades away, giving place to another maximum centred this time around the large helicity $h \sim 0.7$. Clearly, in the ordered phase at low temperatures, four-monomer segments of the chain are predominantly found in the helical configuration. The temperature of the crossover from the ordered to the disordered phase can be identified as the point at which the two maxima of the distribution function have equal height. From figure 3 we find that the crossover occurs at $T = 0.031$ which coincides within numerical error with the temperature of the first maximum of C_v , T_1 . Thus the structural transition occurring in the system at $T = T_1$ may be identified as an order–disorder freezing transition from a random-globule phase to the helical phase. The critical helicity distribution function for the 20-monomer system is depicted in figure 4. In this figure we also present the data from our simulations performed for 30- and 40-monomer systems. The reason for this is as follows. It is understood that owing to finite-size effects the transition temperature T_c of some thermodynamic system of infinite extent $N \rightarrow \infty$ differs from the transition temperature

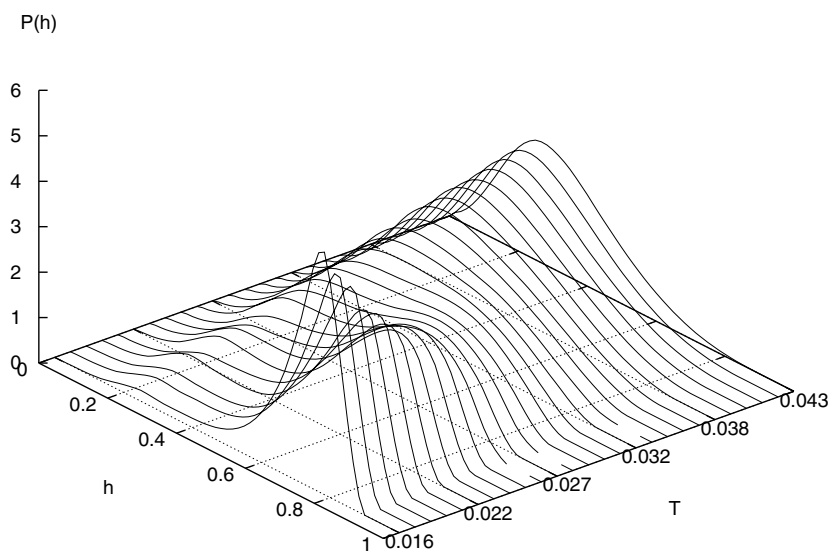


Figure 3. The temperature dependence of the helicity distribution function as obtained from NVT simulations of the 20-monomer polyampholyte. Lines in the graph represent a smooth interpolation between 17 values of helicity accessible to a chain of 20 units.

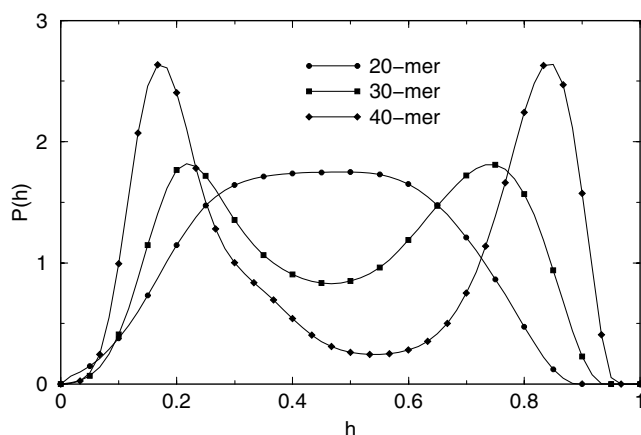


Figure 4. Critical distributions of helicity in 20-, 30- and 40-monomer polyampholytes. In the 30-mer the crossover occurs at $T = 0.026$ and in the 40-mer at $T = 0.021$. For information on how the lines were drawn in this figure, we refer the reader to the caption of figure 3.

$T_c(N)$ observed in a computer model of that system containing N particles. Naturally this holds true of both first-order and continuous phase transitions. When one is simulating an N -particle replica at thermodynamic conditions corresponding to the infinite-system critical point, the finite MD ensemble will find itself in the coexistence region and its critical order parameter distribution function will have two maxima. It follows, thus, that on extrapolating MD results to the thermodynamic limit one faces a problem as regards proper identification of the order of the transition, since a bimodal shape of the distribution functions does not provide enough evidence for the first-order nature of the transition. A clue as regards how to overcome this difficulty lies in the investigation of the dependence of the critical distribution function

on the number of underlying particles N [21]. At critical points the scaled order parameter distribution function $P^*(h^*)$ does not change with N . For some systems $P^*(h^*)$ can even be calculated analytically provided that the critical exponents are known [32]. Further, in the coexistence region, where the system undergoes a discontinuous transition, $P^*(h^*)$ acquires a more sharply peaked shape, characterized by higher and narrower maxima, as the number of particles grows. And finally, in the supercritical region the two peaks of $P^*(h^*)$ gradually merge into one maximum with the increase of N . The behaviour of the critical distribution functions described above was used by Wilding and Bruce to locate very accurately the liquid–vapour critical point in LJ fluids [21]. Returning to figure 4, we observe that helicity distribution functions exhibit trends consistent with the attributes of discontinuous transitions: the two maxima become sharply peaked as the number of simulated monomers grows. We note that, to accommodate the requirements of the discussion that follows, $P(h)$ in figure 4 is not given in scaled variables as originally prescribed in [21]. But it is clear from that figure that it is impossible to change the trend of the functions $P(h)$ with N by a simple scaling operation. In particular, it is impossible to superimpose $P(h)$ for the 30-mer on that of the 40-mer by simply multiplying the former by a constant factor. Hence all conclusions drawn on the basis of the observed N -trends of $P(h)$ remain intact. One can observe in figure 4 that the positions of the maxima of $P(h)$ corresponding to the helicity of the ordered and disordered phases are shifted towards 0 and 1 respectively for 30- and 40-monomer systems as compared to the 20-mer. In the limit of infinite N , one would find a finite jump in helicity at the transition point. All of the above considerations led us to conclude that the helix freezing transition taking place in the present model of di-block polyampholytes is of *first* order.

In figure 5 we show helicity and susceptibility as functions of temperature for all system sizes studied. The figure shows that the helicity is a monotonically decreasing function of temperature while the susceptibility has a maximum around the freezing temperature T_1 . As the number of chain monomers grows, the susceptibility peak becomes higher and narrower, while its position is shifted towards low temperatures. At the freezing point the chain spends equal amounts of time in conformations of ordered and disordered phases, i.e. with low and high helicity. As a result, the average helicity takes on values around 0.5 at $T \sim T_1$ as seen from figure 5. We would like to note here that the numerical data obtained for the 40-monomer polyampholyte are the least reliable ones, despite a great computational effort that we made to simulate this system. The 40-mer was simulated in runs of 200×10^6 time steps and the time spent on this simulation amounted to 60% of the total computational time of this work. The insufficient statistics for the 40-monomer chain is reflected in figure 5 in the remarkable scatter of h and χ and the notable deviations of h from its values in 20- and 30-particle ensembles. Another interesting aspect of the susceptibility is the presence of only one maximum, in contrast to the case for the specific heat where we saw two maxima. Clearly, the collapse transition at $T = T_2$ is by no means related to the helix formation in the frozen state.

Now we are in position to sketch a general picture of the basic physical processes, in particular the sequence of structural transitions, taking place in the single-chain di-block polyampholyte being studied. At sufficiently high temperatures the monomers have large enough kinetic energy to be able to approach each other very close. The potential energy of the system is then dominated by the repulsive soft-core contribution and the chain mostly populates extended-coil conformations. At $T \sim 2.65$ the attractive Coulomb force starts to take over, giving rise to the zipping transition. The chain is now in the state of the supercoil whose unit ‘monomers’ are formed by pairs of positive and negative charges, or dipoles. In the supercoil state the chain’s entropy gain coming from expansion is not balanced by the energy gain resulting from compaction. As a result, the system remains an extended random coil. At $T > T_2$ the system is subject to large-scale conformational fluctuations as shown in figure 6

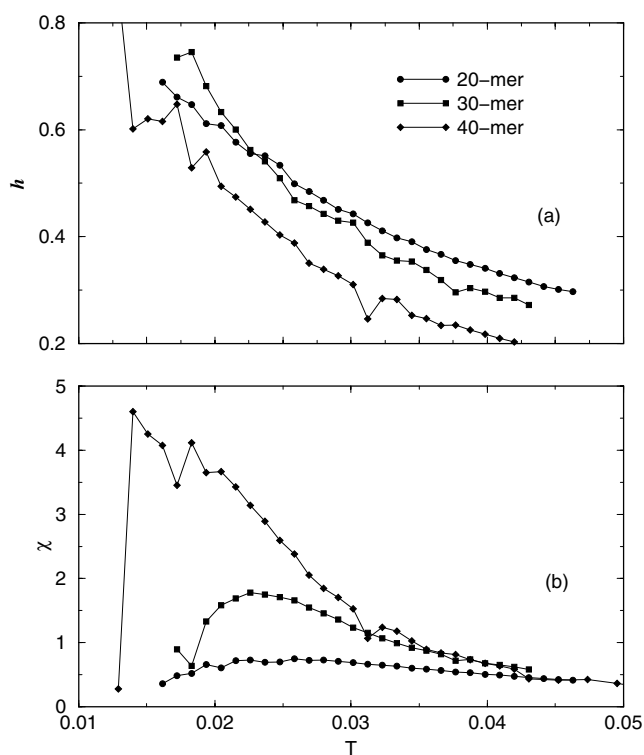


Figure 5. Helicity (a) and susceptibility (b) of the 20-, 30- and 40-monomer polyampholytes as obtained from *NVT* simulations.

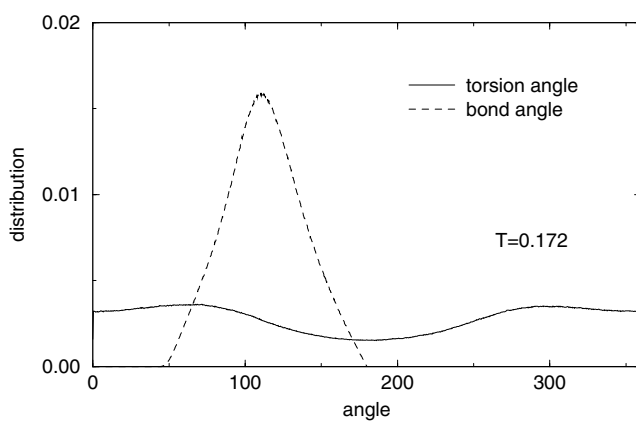


Figure 6. Distribution functions of the bond and torsion angles in the 20-monomer di-block polyampholyte above the collapse temperature at $T = 0.172$.

which shows the distribution functions of the bond and torsion angles of the 20-monomer system at $T = 0.172$. The bond-angle distribution is quite broad with one maximum peaked around 110° . At the top it reaches the upper possible limit of the bond angle, 180° , found in straight-line configurations of three-monomer segments, while at the bottom the distribution is limited by angles around 50° . The lower bound is connected with the effect of the soft-core

potential which prevents second-neighbour monomers from coming into too close contact. The torsion-angle distribution looks rather flat over the whole range of angles except for two broad maxima located symmetrically around 60° and 300° . The symmetry of the positions of the maxima is brought about by the invariance property of the system Hamiltonian with respect to the mirror reflection operation $\vec{r}_i \rightarrow -\vec{r}_i$. It follows, thus, that properly equilibrated di-block polyampholyte will always have a symmetrical torsion-angle distribution. Values $\zeta < 180^\circ$ correspond to the right-handed configuration of the ground-state helix, as shown in figure 2, and values $\zeta > 180^\circ$ signify left-handed configurations.

Upon further decrease of temperature, the entropic and energetic parts of the free energy finally balance each other and the polymer collapses at $T = T_2$. This process is accompanied by a rapid decrease of the overall size of the system (see figure 1(b)). In the collapsed state the chain is characterized by a still large degree of conformational freedom as illustrated in figure 7 which shows the bond- and torsion-angle distributions at $T = 0.054$. To a large extent the situation in the globular state is similar to that found in the coil states in that both distributions are sufficiently broad. What makes the temperature $T = 0.054$ differ is the breakdown of the system's symmetry. Instead of having two maxima as in the previous figure, the torsion-angle distribution function now exhibits only one peak which corresponds to the right-handed helix configuration. One can claim that at $T < T_2$ the system stays in a non-equilibrium state since every conformation explored by the chain is related by the symmetry operation to its counterpart, which has the same statistical weight but which has not been visited in the simulation. In fact, all such pairs of conformations are separated by an insurmountable—on the present timescale—free-energy barrier at $T < T_2$. Returning to figure 7, we would like to emphasize the fact that the twist of the ground-state helix is fixed at the collapse stage and cannot be changed spontaneously below T_2 .

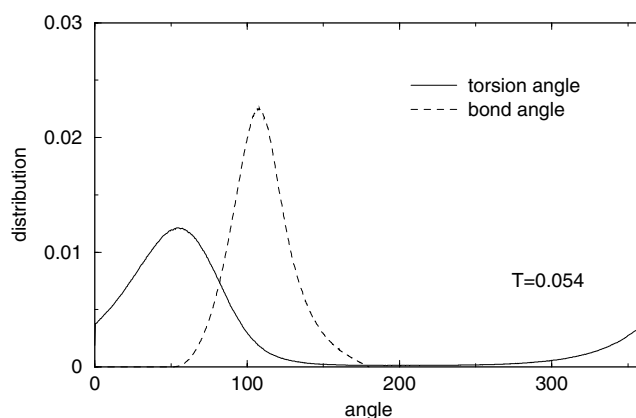


Figure 7. As figure 6, but for $T = 0.054$.

Following further decrease of temperature, the system freezes into the ground-state helix. The conformation space available to the chain dramatically shrinks to a few helix-like conformers at $T < T_1$. This is evident from figure 8 which shows the torsion- and bond-angle distributions at $T = 0.011$. Both distributions acquire sharply peaked shapes. Clearly, the chain cannot freely change its shape any longer and it is forced to remain in the vicinity of the ground state.

Finally in this paper, we would like to draw some parallels between the properties found in di-block polyampholytes and the statistical physics of unconstrained electrolytes which may

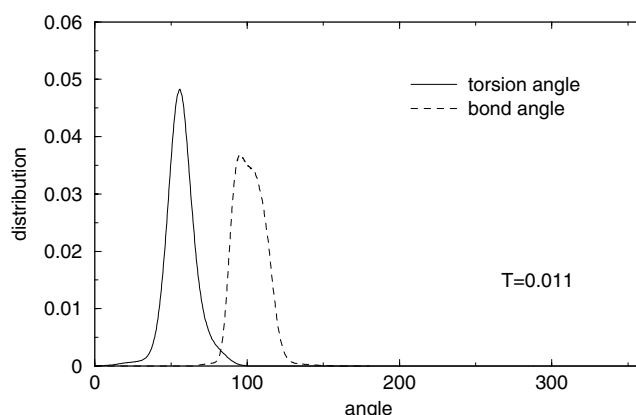


Figure 8. As figure 6, but for $T = 0.011$.

help us to better understand the role played by the chain connectivity in structural organization of polymeric systems. Depending on the applied external temperature, electrolytes can be found in three obvious phases: the gas phase at $T \sim 1$, the liquid phase at $T \sim 0.02$ and the solid phase at $T < 0.001$ [33]. Physical prototypes of all the above phases can be associated with dilute aqueous solutions of electrolytes, molten alkali halides and ionic crystals respectively. The mechanism by which electrolytes try to minimize their potential energy is the well-known screening effect: the particles rearrange themselves into alternating shells of opposite charges such that the resulting interaction potential between distant particles becomes effectively short ranged. It is understood that since an important prerequisite for the screening phenomenon to proceed is translational freedom of the particles, in polyampholytes the screening may well be hampered by the chain connectivity. The failure of the constrained system to optimize its electrostatic energy, or frustration, gives rise to a complicated shape of the potential energy surface with many local minima separated by energy barriers. The barriers naturally facilitate freezing of the chain: the higher the barrier, the easier it is for the chain to get trapped into one of the minima. Put another way, frustration caused by the chain connectivity is expected to raise the freezing temperature of the system. Our results are fully consistent with this speculation. The constrained polyampholyte studied freezes at temperatures $T \sim 0.01$ where ordinary electrolyte would remain in the liquid phase [33]. A similar conclusion about the implication of the bond-length constraints for the freezing properties of polyampholytes has also been reached in [34].

4. Conclusions

In this paper we reported on the molecular dynamics simulations of a bead model di-block polyampholyte. We found that the ground state of the model studied is a double-stranded helix. The chain on its folding path towards the ground state passes through an intermediate molten-globule phase. In the intermediate phase the molecule is smaller compared to both high-temperature and ground-state conformations, and it undergoes considerable structural fluctuations. Also at the stage of the coil-to-globule transition the twist of the native helix is fixed. Below the collapse transition the chain cannot spontaneously change its twist.

The transition temperatures of the coil-globule and globule-helix transitions are observable in the specific heat as two separate maxima. In addition, the freezing transition can

also be detected as a maximum of susceptibility. Finite-size analysis of the helicity distribution function at the temperature of freezing clearly demonstrates that the globule–helix transition is first-order-like.

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