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Multiple conformations in polyampholytes

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Abstract. We study the configurational statistics of a ring polyampholyte chain made of N randomly charged monomers with elementary charge $\pm q_{\mathrm{o}}$. To a large extent, the overall structure of a polyampholyte is controlled by a total sum Q of all charges. When the total charge is smaller than $Q_1 \approx \sqrt{N} q_{\mathrm{o}}$, the polyampholyte has a compact globular structure. At charges larger than $Q_2(\sim Nq_{\mathrm{o}})$, the configuration has the form of a ring of small globules (beads) connected by strings. Between Q_1 and Q_2 we find a remarkable diversity of meta-stable configurations having the shapes of irregular clusters of small globules connected by the strings. We estimate the number of these configurations and the energy barriers between them. Between Q_1 and Q_2, the minimum energy configurations are completely controlled by randomness in the charge distribution along the chain. There are hysteresis effects in the shapes of the clusters. As the total charge increases, the linearly extended configurations become dynamically more preferable. When the charge decreases, the circular shapes are preferred. We remark on the probable connection with the multiple phase transitions observed in polyampholyte gels.

PACS. 36.20.Ey Conformation (statistics and dynamics). – 36.20.-r Macromolecules and polymer molecules. – 61.25.Hq Macromolecular and polymer solutions; polymer melts; swelling

1 Introduction

Polyampholytes (PA) are charged polymers which have positive and negative charges distributed randomly along their backbones [1]. The strength of the electrostatic interaction and the relative ratio of positive and negative charges depend on the dielectric constant and the pH of the solvent. The interplay of the long range electrostatic interactions and the short range forces can produce sharp structural transitions upon changing certain properties of the solvent [2–12]. The interest in the properties of PA is due not only to their rich structural properties, but also to the obvious relevance to the protein folding problem [13–15].

Recently, Kantor and Kardar studied the conformational properties of a *linear* PA chain. Consider a linear polyampholyte chain consisting of N monomers of size a. Each monomer carries either positive or negative elementary charge $\pm q_{\mathrm{o}}$. The overall shape of a randomly charged linear polyampholyte chain depends on the magnitude of the net charge Q on the molecule [16,17]. If this charge is less than the critical charge Q_{R}, the molecule has the shape of a compact globule, for which positive and negative charge groups nearly compensate each other. The globule has a spherical shape in order to minimize its external surface. When the net charge exceeds the critical value $Q_{\mathrm{R}} \sim \sqrt{N} q_{\mathrm{o}}$, the globule splits into two. This new configuration has a larger surface area, but the separation of two resulting globules reduces the energy of electrostatic repulsion. This splitting is analogous to the classical instability of a charged droplet described by Rayleigh [18]. Because both smaller globules are made of the single polymer chain, they can not move too far apart from each other and remain connected with a string (the stretched part of the polymer chain). At larger charges each globule can again split, therefore forming a linear chain of globules connected by strings. The number of globules n is controlled by the net charge Q. The optimal number of globules is approximately $n = \frac{24}{5} Q^2 / Q_{\mathrm{R}}^2$ where Q_{R} is Rayleigh charge $Q_{\mathrm{R}}^2 \equiv 16\pi\gamma R^3$ ($\gamma \approx q_{\mathrm{o}}^2/a^3$: surface tension, R: radius of the globule) [16,17].

The randomness in the distribution of charges along the chain results in fluctuations of the charge in each globule. These fluctuations ($\sim {N_{\mathrm{b}}}^{1/2}$, where N_{b} is the number of monomers in a globule) are of the order of Q_{R} for a globule. Therefore, the fluctuations caused by the randomness are always important in the size distribution of globules. There is another factor which affects the statistics of the size distribution of globules. For the globules on a linear chain, the effects of electrostatic repulsion are strongest in the middle of the chain, and weakest near the chain ends. As a result, the size of globules and the distance between them depend on the position of these globules on the chain. The combined effects of randomness and position dependence make any analytical and numerical study of the globule distribution in the linear configurations very difficult.

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In this work we consider the configurational properties of *circular* chains. There are two motivations. First, a ring has an additional symmetry compared to the linear chain, since all monomers have the same structural connections to the rest of the chain. The effects of different string tensions discussed above can be eliminated. This allows the study of the asymptotic size distribution of globules on smaller chains than in the linear case. Second, the process of clusterization of the circular polymer might provide an insight into the micro-phase separation in polyampholyte networks (gels). As a first approximation, these networks can be thought of a collection of cross-linked polyampholyte rings. In the same way as different parts of the ring can be mutually attractive, different chains inside the elementary cell of a polymer gel network can be attractive and form a secondary network of compact globules connected with single or double strings.

2 Ring polymer

2.1 Mean field estimates

We study a cicular polyampholyte consisting of N monomers. First, we neglect effects caused by disorder and assume that the distribution of charges along the circular chain is almost homogeneous. The total charge on any fragment of a polymer of length m is mQ/N. This is similar to the case of a homogeneously charged polyelectrolyte in a bad solvent [19], where the monomers are attracted to each other due to short range interactions, but repelled due to long range electrostatic interactions. The only difference to [19] is the circular form of the chain. The configuration of a polymer is controlled by the overall charge. If this charge is small, the polymer is in a compact globular configuration. If the charge is large, it will be in an extended multi-globule configuration. There are two major possibilities of transitions. One possibility is that the extended configuration is linear, similar to the configurations of a linear chain (see Fig. 1 ($a \to b' \to c'$)). Another possibility is that the multi-globule configurations will have a circular necklace shape as shown in Figure 1 ($a \to b \to c$). The difference in the energy of these configurations depends on the microscopic details of the model.

Consider the energy of three globule configurations of a linear and a circular polymer (see Figs. 1c and c′). There are three major contributions to the energy of this configuration: The surface energy of the globules, the surface energy of strings and the coulomb energy of the interacting globules. Since the surface energies of globules of both configurations are about the same, we will compare only remaining two contributions. In this discussion, we can neglect the contribution of entropy because it is much smaller than the other energies.

$$E_{\text{linear}} = \frac{5}{2}\frac{(Q/3)^2}{R} + 2\sigma_2 R,$$
$$E_{\text{circular}} = 3\frac{(Q/3)^2}{R} + 3\sigma_1 R. \tag{1}$$

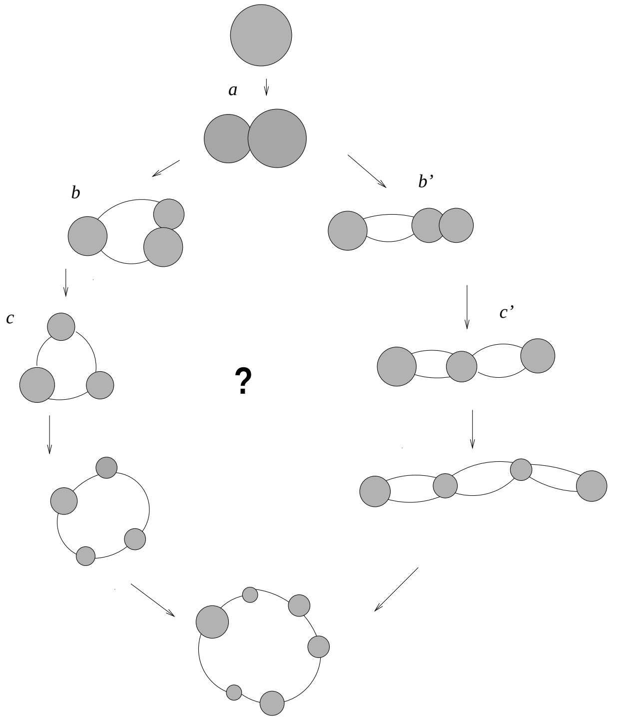

Fig. 1. Illustration of the transitions of a ring polymer. When the charge of the polymer increases, new configurations can be formed following linear of circular sequences. If randomness is present, there is a mixture of linear and circular patterns.

Here $Q/3$ is the charge on the globules, R is the distance between them, σ_2 (σ_1) is the linear tension of a double (single) folded string. This tension is the energy needed to pull a unit segment of the string out of the globule. Minimizing both energies with respect to R we find:

$$E_{\text{linear}} = 2\sqrt{5}Q\sqrt{\sigma_2},$$
$$E_{\text{circular}} = 6Q\sqrt{\sigma_1}. \tag{2}$$

If the double folded string tension σ_2 satisfies the following inequality,

$$\sigma_2 > 9/5\sigma_1 \tag{3}$$

the circular configuration will have a lower energy compared to the linear configuration. If the reverse inequality holds, the linear configuration is preferred. The ratio 9/5 is special to the three globule configuration. If the number of globules n is large ($n \gg 1$), the energies of linear and circular configurations are:

$$E_{\text{linear}} = \frac{(Q/n)^2}{R}\, n\, \text{Log}(n) + (n-1)\sigma_2 R,$$
$$E_{\text{circular}} = \frac{(Q/n)^2}{R}\, n\, \text{Log}(n) + n\sigma_1 R. \tag{4}$$

In this case, we have the inequality $\sigma_2 > \sigma_1$ as the condition of lower energy of the circular configuration. As n increases, the energy difference δE between linear and circular configurations converges to $c(n)Q$, where $c(n)$ is a function of the number of globules and σ_1, σ_2.

$$c(n) = 2(\sqrt{\sigma_2} - \sqrt{\sigma_1})(\mathrm{Log}(n))^{1/2}. \tag{5}$$

We expect that the maximum energy needed to pull out a double folded string is about twice the energy needed to pull out a single string: $\sigma_2 \sim 2\sigma_1$, the actual ratio depends on the details of the short range interactions of monomers on the two strings. If the monomers are interacting through saturating forces (with formation of H-bonds), it might happen that the unit energy of the double string σ_2 can be even less than that of a single string σ_1.

Summarizing, for charges $Q > Q_{\mathrm{R}}$ the minimum energy configuration can be linear or circular, depending on details of the model. The most likely scenario is that with a small number of globule n the preferable configuration is linear, while for large n it is circular. In the limit case when the electrostatic repulsion between monomers dominates over all other interactions, the minimum energy configuration is always an open ring.

2.2 Effect of a random charge distribution, phase diagram

The randomness in the charge distribution creates a fluctuation of the net charge in each globule. Consider a n globule configuration. The typical charge fluctuation in each globule is $\sim q_{\mathrm{o}}(N/n)^{1/2}$. The fluctuation in electrostatic energy per globule with radius $r \sim (N/n)^{1/3}a$ is of the order of $\delta E_{\mathrm{fluct}} \sim q_{\mathrm{o}}^2/a(N/n)^{2/3}$. If the energy $\delta E_{\mathrm{fluct}}$ is comparable to the difference between the energies per globule in linear and circular configuration

$$\delta E/n = (E_{\mathrm{linear}} - E_{\mathrm{circular}})/n,$$

the effects of randomness will completely control the local arrangement of globules. Setting $\delta E_{\mathrm{fluct}}$ equal to $\delta E/n$, we have

$$c(n)Q/n \approx q_{\mathrm{o}}^2/a(N/n)^{2/3} \tag{6}$$

where $n \sim Q^2/N$. This equation represents a line in the phase diagram plotted in coordinates Q^2/Q_R^2 $(= n)$ and N. In the $n \gg 1$ limit,

$$N \approx c(n)^3\, Q^2/Q_R^2 \tag{7}$$

with $c(n)$ given by equation (5). The equation (6) provides an upper bound for the region in the phase diagram where the effects of randomness are dominant (Fig. 2). Above this line (region I) the minimum energy configuration is circular or linear, depending on the microscopic details of the model. The dashed vertical lines in the region I of the phase diagram separate regions with different optimal numbers of globules n. In this region there are also numerous meta-stable configuration of various shapes. The energy difference between the different topological configurations is of the order $\sim \delta E/n$. Below the line given by equation (6) (region II), the ground state energy configurations are completely random. In addition, there are many meta-stable states with similar energies. The lower bound of region II is given by the equation

$$Q_2 = c_2 N. \tag{8}$$

Here c_2 is a model dependent constant. Below this line (region III) the charge on the chain is so strong that the only stable configurations are open rings (see Fig. 2).

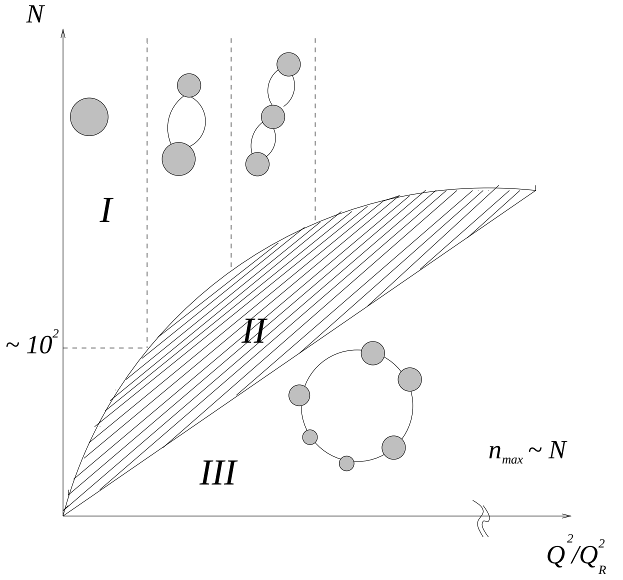

Fig. 2. Phase diagram of a circular polymer. In regions I and II meta-stable states are observed. In region I, the ground state is either linear or circular depending on the model. In region II, the ground state is controlled by randomness. In region III (strong net charge limit $Q > c_2 N q_0$), only open ring configurations are observed.

2.3 Meta-stable configurations and barriers

In regions I and II of the phase diagram there are many configurations which do not have the lowest energy but are relatively stable. Some of them can be relatively easy transformed into another (soft mode). The simplest way to obtain a slightly different configuration is to make cyclic shift of the chain between each pair of nearest globules by one or two monomers. This transformation preserves the topology of the overall structure of globules connected by strings. The difference in energy of the new configuration is of the order of $\sim q_0(Q/n)/a$. There are about N such states for each topologically distinct configuration. Another type of transformation is related to a change in topology. The typical barrier between two such configurations can be estimated from the energy needed to bring two globules together and then regrouping them (see Fig. 1). This energy is of order $E_{\mathrm{b}} \sim (Q/n)^2/a(N/n)^{1/3}$. An estimate of the number of configurations with different topology can be made by evaluating the number $\aleph$ of connected clusters consisting of n globules. This is the well known "animals" problem [20], and the number of configurations is: $\aleph \sim n^{-\alpha}\mathrm{e}^{\lambda n}$, where the exponent $\alpha = 3/2$ for three dimensions and λ is a constant of the order of one.

2.4 Hysteresis

If the overall charge of the chain is increased (due to changes in solvent properties), the formation of linear structures is more preferable. Consider the transition from two to three globules. This transition might occur by splitting one of the globules leading to the formation of circular or linear three globule configuration as shown in Figures 1c and c$'$. Because of the electrostatic repulsion between the globules, the splitting of the globule in parallel direction is dynamically more preferable (Figs. 1a $\to$ b$'$) than the splitting in perpendicular direction (Figs. 1a $\to$ b).

The linear configurations formed in this way may not be the ground state. However they are meta-stable and dynamically preferable. The time required to overcome the energy barrier between linear and circular configurations is proportional to $\mathrm{e}^{E_\mathrm{b}/k_\mathrm{B}T}$. Depending on the temperature and the size of the globules, the transition from one topology to another cannot be observed during reasonable time.

In the reverse situation, when the total charge decreases from a large value, the formation of a circular configuration is dynamically more preferable.

2.5 Monte Carlo simulation

Our model and the details of the Monte Carlo simulation are very similar to that of Kantor and Kardar [16,17] for a linear chain. We consider a ring polymer as a flexible chain of N randomly charged monomers. Each monomer has charge $+q_0$ with probability p and charge $-q_0$ with probability $1-p$ independent of all the others. A typical random sequence of N monomers has a total excessive charge of about $(2p-1)q_0$. We characterize the sample system by chain length N, temperature T and net charge Q. At a given net charge, several quenched configurations are tested. The interaction between a monomer pair i, j is the electrostatic interaction $U_{i-j} = q_i q_j / r_{i-j}$. During the simulation the monomers are placed on a cubic lattice. Each site can be occupied by only one monomer, and the length of the link between two subsequent monomers was allowed to vary from 1 to 4 lattice units. The Monte Carlo simulation creates new configuration by attempting to move each monomer in a randomly created sequence. The new configuration is accepted with probability $\mathrm{e}^{-\Delta E/k_\mathrm{B}T}$, where ΔE is the energy difference between the old and new configurations.

We run the simulation in the temperature range $0.1 \sim 1$ measured in q^2/ak_B units and chain sizes N from 16 to 128. Most of the simulations were performed at temperature $T = 0.1$ with $N = 96$. The temperature is chosen in such a way that the system arrives at the equilibrium state in a reasonable MC time, but low enough to see clear transition patterns. The specific transition patterns are different for the various models. For example, the more we increase the maximum allowed distance between the subsequent monomer, the more linear configuration will be preferable.

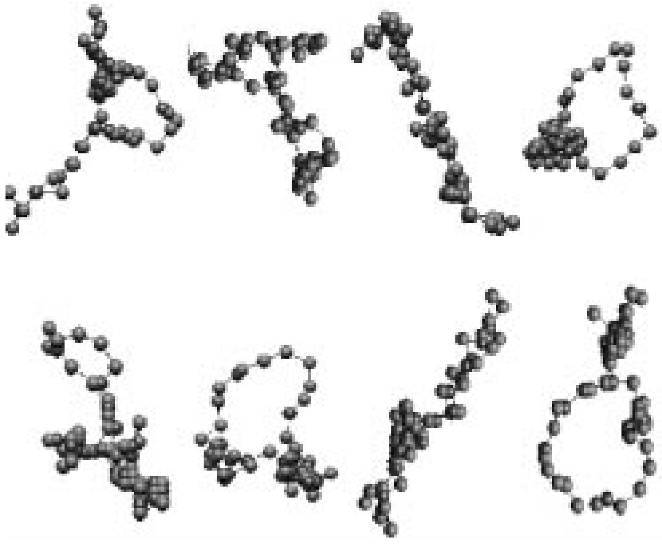

Fig. 3. Different meta-stable configurations of a single chain with fixed random charge distribution.

We found a very rich configurational diversity. This is caused by the randomness in the charge distribution. In a linear polymer, the randomness in the charge distribution contributes only to the size distribution of the globules. In a ring polymer, there are additional possibilities to combine two remote parts of the chain containing complementary charged monomers. The transitions have different patterns for various polymer sizes. As a rule, the effect of randomness in configurations and transitions with the same number of globules n is more pronounced for small N. For $N < 10^2$, the transition of splitting one globule was highly irregular for different sequences, but for $N \geq 10^2$ the transition occurs at $Q \approx Q_\mathrm{R} = \sqrt{N}$, as predicted by mean field theory. For the chain length $N = 128$, the 2-globule to 3-globule transition was affected by randomness in the charge distribution (see phase diagram Fig. 2). If we increase the excess charge at fixed N, the number of globules increases. In this case each globules contains less monomers, and we found very irregular cluster shapes. Some sample configurations are shown in Figure 3.

For each particular charge distribution, different metastable configurations can be accessed by repetition of the cooling and heating procedures described below. The easiest way to distinguish different configurations is by direct observation. It is very difficult to assign any quantitative parameters for the different configurations.

In Figure 4, we plot the 4th moment of the polymer size $\langle R_\mathrm{g}^4 \rangle \equiv \frac{1}{N^4} \sum_{i,j} (x_i - x_j)^4$ while the system undergoes the heating and cooling cycles. In the beginning of each interval (1/5 of the interval), the system is heated to $T = 10$ and configurations become nearly Gaussian. ($\langle R_\mathrm{g}^4 \rangle$ goes down for this configurations!) Then we drop the temperature to $T = 0.1$ to ensure the relaxation to the local energy minimum. We can differentiate the configurations by the value of R_g^4. There are large scale plateaus which include small scale fluctuations. The linear stretched configuration has the largest R_g^4 (shown as the highest plateau),

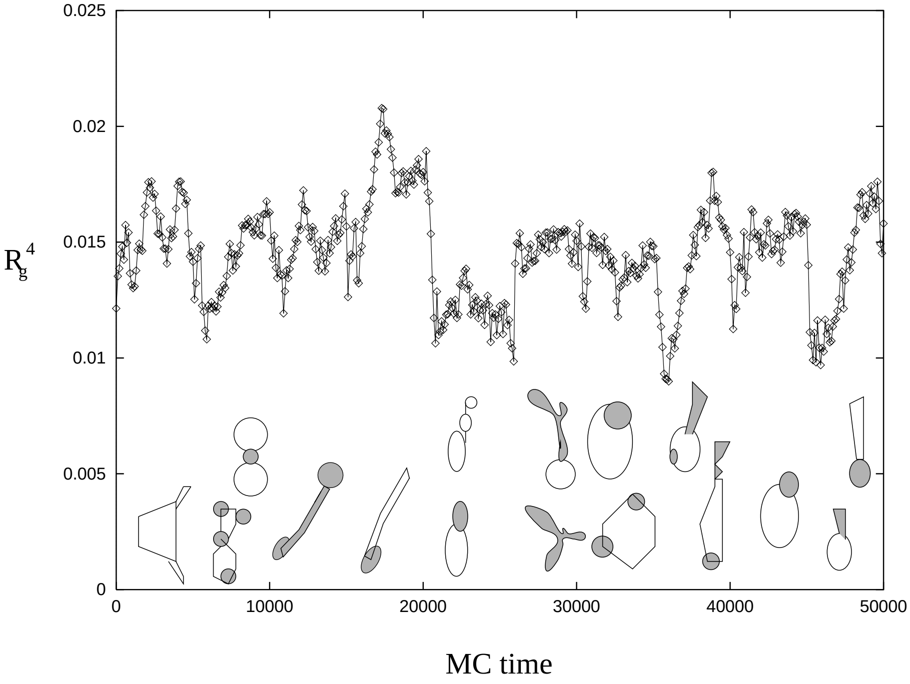

Fig. 4. Plot of R_{g}^4 *versus* Monte Carlo time. In the beginning of each cycle for the first 10^4 steps the temperature is increased to $T = 10$. Then the system is at $T = 0.1$ for the rest of the cycle. R_{g}^4 has plateaus at various levels indicating different meta-stable configurations shown below the graph.

the circular open shape has smaller R_{g}^4 (middle plateau). The configuration with a large collapsed part or a Gaussian configuration has the smallest value of R_{g}^4. After each heating and cooling process, we reach a different configuration and a different level of plateau. The large scale jumps imply the change from a circular to a linear configuration or *vice versa*. The small fluctuations are due to the shift in monomer level. With chain length $N = 64$, the longest relaxation time we observe to reach to the local minimum is of order $N^2 \approx 3000 - 4000$ time units.

Upon increasing the net charge ($Q > Q_2$), we observe a ring configuration with different sizes of globules as a dominant configuration. We define Q_2 as the minimum net charge which allows exclusively ring configuration. Q_2 is proportional to the polymer size N, $Q_2 = c_2 N$. The model dependent constant c_2 is approximately 0.6 in our model.

3 Conclusions

We find that ring polyampholytes have remarkable rich configurational properties as a result of competition between tendencies to form linear or circular structures. The different parts of a ring may be attracted to each other forming a compact globule, so the configuration has the form of a random cluster of such globulae. There are many different meta-stable configurations of this type for the same chain and their energies are about equal. We find the region of the phase diagram where the effects of randomness in the distribution of charges along the chain are most important. We suggest that similar multiple conformation phenomena might be observed in a polyampholyte gel. In the same way as different parts of a circular chain attract, producing various configurations, the different parts of the strands inside a gel can attract. Local rearrangement of such configurations may involve strands from adjacent elementary cells and may be thermodynamically unlikely. We expect that under the change of the external conditions (temperature, pH, salt concentration, *etc.*) the rearrangement will happen in abrupt steps which could involve the whole sample. Nevertheless, our attempt to link the multilevel volume phase transition observed in polyampholyte gels [12] using the analogy with single chain phenomena should be considered with caution. In our approach we neglected the possibility of screening effects due to the presence of counterions, ions of salt and other polyampholyte molecules. The future development should incorporate these effects of screened interaction as well as the thermodynamical contributions of other ions.

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