Effect of a net charge on the conformation of polyampholytes

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We investigate polyampholyte chains with random sequences of positive and negative charges using simple scaling arguments. We show that Coulomb interactions between charges of opposite signs in a single chain lead to formation of a globule. Due to a net charge the globule might be strongly elongated depending on the value of the net charge. This effect is especially pronounced for chains with long-range correlations in the sequence of charges. When the net charge is strong enough the radius of gyration may even grow as the temperature decreases.

The problem of polyampholytes has recently received much attention [1–7]. Polyampholytes are linear molecules composed of positively and negatively charged monomers. If the overall charge per monomer is nonvanishing in the thermodynamic limit, then electrostatic repulsion due to this overall charge results in a completely stretched rodlike conformation of the chain [8]. The case in which, in the thermodynamic limit, the net charge per monomer vanishes is more subtle. This happens when the sequence of charges is random with equal probability of positive and negative charges. It was shown [1] that electrostatic interactions in such statistically neutral chains result in the collapse of those chains. A detailed analysis of the collapse by means of scaling arguments and the so-called "uniform expansion method" was done by Higgs and Joanny [3]. Their analysis was based on the assumption that the equilibrium distribution of charges in space is similar to that in a simple ionic solution. Accordingly, the contribution of Coulomb interactions can be estimated from the Debye-Hückel theory. The same result was obtained [7] within the framework of the random phase approximation.

It should be mentioned that the approaches used in Refs. [3,7] do not distinguish between the quenched and the annealed sequences. In particular, they do not take into account the effect of the random net charge. At the same time, it was shown [4] numerically and by means of scaling arguments that electrostatic repulsion due to a net charge imbalance must not be neglected and may lead to a stretched rather than a collapsed state.

In this paper we address the problem in more detail. Our conclusion is that the presence of charges of opposite signs does result in a globular state. At the same time, the globule may be strongly elongated due to a random charge imbalance, the shape of the globule being strongly dependent on the value of the net charge.

The model under consideration is a linear chain composed of a random sequence of N positive and negative charges $\pm q_0$ occurring with equal probability. The size of a charged monomer is a. If the sequence of charges is uncorrelated, then the random overall charge Q is of the order of $q_0 N^{1/2}$. We also study random sequences with long-range correlations similar to those that have been found in DNA [9] and protein [10] sequences. For such sequences the net charge

$$Q \sim q_0 N^{\alpha} \tag{1}$$

with $0 \le \alpha \le 1$. In the absence of long-range correlations $\alpha = 1/2$, while $\alpha < 1/2$ corresponds to anticorrelations and $\alpha > 1/2$ corresponds to positive correlations. In particular, $\alpha = 1$ corresponds to polyelectrolytes.

The important dimensionless parameter in the problem is

$$u \equiv q_0^2 / a k_B T, \tag{2}$$

where T is the temperature and k_B is the Boltzmann constant. It is seen that the parameter u is just the energy of the Coulomb interaction of neighboring charges along the chain, divided by $k_B T$. If $u \gtrsim 1$, then Coulomb interactions are strong, while $u \ll 1$ corresponds to weakly charged polyampholytes or to high temperatures.

Consider, first, the case of strong electrostatic interactions when $u \gtrsim 1$. In this case a globular state with maximal density $\rho \sim a^{-3}$ seems to be the most favorable. Indeed, in such a globular state each charge is surrounded mainly by charges of the opposite sign. As a result charges are effectively screened on the microscopic scale a and electrostatic interactions are effectively short range. Therefore the free energy of the globule is additive, i.e., it is proportional, in the thermodynamic limit, to the number of charges N. In fact, such a dense globular state was observed in the computer simulation of neutral polyampholyte chains [4]. It should be mentioned also that if the chain is not too flexible, then there must be a frozen phase at low enough temperature as in the case of short-range interactions [11]. In this phase only a few conformations dominate in equilibrium.

These arguments resolve the question when the chain is neutral ($Q = 0$). If $Q \ne 0$, then this extra charge Q is not screened and its contribution to the energy of a globule can be estimated as $E_e \sim Q^2/R$, where R is the size of the globule. If the globule has a spherical shape, then $R \sim (N/\rho)^{1/3} \sim a N^{1/3}$ and $E_e \sim Q^2/a N^{1/3}$. Therefore the energy E_e of Coulomb repulsion of the net charge becomes of order N only when $Q \sim q_0 N^{2/3}$, i.e., when $\alpha = 2/3$. Thus one might think that when $\alpha < 2/3$ the net charge is negligible and only when $\alpha > 2/3$ does the Coulomb repulsion caused by the net charge destroy the globule.
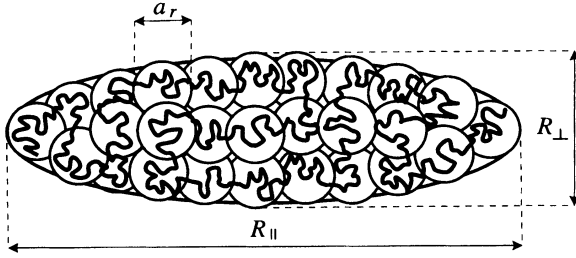
FIG. 1. Elongated globule. $R_\parallel$ is the length of the globule and $R_\perp$ is its width. The globule is formed by tightly packed blobs. a_r is the size of a blob.

This conclusion is wrong. In fact, the net charge cannot be neglected when $\alpha \geq 1/2$, in particular, in the case of uncorrelated sequences. The Coulomb repulsion due to the net charge does not destroy the globular state but it makes the globule elongated (to be compared with [13]).

More exactly, let us consider a strongly elongated globule with length $R_\parallel$ and width $R_\perp \ll R_\parallel$ (see Fig. 1). Since the density inside the globule $\rho \sim a^{-3}$ and its volume $V \sim R_\perp^2 R_\parallel$, we have $R_\perp^2 R_\parallel / a^3 \sim N$ and $R_\perp \sim (a^3 N / R_\parallel)^{1/2}$. The main contribution to the free energy of such a globule is of order N and it is the same as for a spherical globule. The difference is only due to the surface tension and the electrostatic repulsion caused by the net charge. A simple estimate of the corresponding contributions to the free energy is possible.

Since in a dense globular state Coulomb interactions between all charges but the net charge are screened and, therefore, are effectively short range, the surface-tension coefficient σ can be estimated as $\sigma \sim q_0^2 / a^3$. The surface area of a strongly elongated globule is of order of $S \sim R_\perp R_\parallel \sim (a^3 N R_\parallel)^{1/2}$ and the surface free energy $F_s \sim \sigma S \sim q_0^2 (N R_\parallel / a^3)^{1/2}$.

Now we estimate the contribution to the free energy due to the net charge. Coulomb repulsion of this charge results in a homogeneous distribution of the net charge inside the globule (more precisely, on the surface of the globule, see below). The homogeneity of the distribution makes it possible to estimate the energy of the electrostatic repulsion E_e due to the net charge. Neglecting logarithmic corrections we have $E_e \sim Q^2 / R_\parallel$.

Thus the nonadditive part of the free energy

$$F = F_s + E_e \sim q_0^2 (N R_\parallel / a^3)^{1/2} + Q^2 / R_\parallel \qquad (3)$$

as a function of the length $R_\parallel$ reaches the minimum at

$$R_\parallel \sim a (Q/q_0)^{4/3} N^{-1/3}, \qquad (4)$$

the width being

$$R_\perp \sim a (Q/q_0)^{-2/3} N^{2/3}. \qquad (5)$$

Let us note that this estimate is valid when $R_\perp \ll R_\parallel$. This implies a limitation on the value of the net charge Q: $Q \gg q_0 N^{1/2}$. In other words, if the net charge is small ($Q \lesssim q_0 N^{1/2}$), then the shape of the globule is close to spherical. In contrast, when $Q \gg q_0 N^{1/2}$ the globule is strongly elongated. Taking into account that $Q \sim q_0 N^\alpha$, we

come to the conclusion that the random net charge must not be neglected for $\alpha > 1/2$ and it strongly elongates the globule in this case with

$$R_\parallel \sim a N^{(4\alpha - 1)/3} \qquad (6)$$

and

$$R_\perp \sim a N^{2(1-\alpha)/3}. \qquad (7)$$

In particular, at $\alpha = 1$, i.e., for polyelectrolytes, $R_\parallel \sim aN$ and $R_\perp \sim a$ which means that a chain is completely stretched as it should be in the case of strongly interacting polyelectrolytes.

Thus, when $\alpha > 1/2$ a polyampholyte globule is strongly elongated. The degree of the elongation can be described by the ratio of the length to the width of the globule $A \equiv R_\parallel / R_\perp$. For the polyampholyte globule

$$A \sim N^{2\alpha - 1} \gg 1 \qquad (8)$$

when $\alpha > 1/2$. At the same time, the most interesting case of uncorrelated sequences corresponds to $\alpha = 1/2$. In this case the minimization of the nonadditive part of the free energy with respect to $R_\parallel$ formally gives $R_\parallel \sim R_\perp \sim aN^{1/3}$ and $A \sim 1$. However, the assumption that $R_\perp \ll R_\parallel$ is not valid and a more delicate consideration is required.

First of all, we notice that due to changes in the chain conformation the net charge can move inside the globule. In this sense a polyampholyte globule behaves as a conductor with respect to this charge. In fact, the movement of the charge leads to a certain loss of the free energy. In order to estimate this loss, we notice that in an ordinary conductor an overall charge is on the surface of the conductor. Placing a net charge on the surface of a polyampholyte globule can be considered in terms of [12] as a somewhat weak separation between negative and positive charges. The loss of the entropy due to a weak separation was calculated [12]. In the case of a polyampholyte with $Q \sim q_0 N^{1/2}$ this gives the value of order of $N^{1/3}$, the polymeric bonds being unimportant. Thus the loss of the free energy caused by placing a net charge $Q \sim q_0 N^{1/2}$ on the surface of a polyampholyte globule is of order of $N^{1/3}$. At the same time, the nonadditive part of the free energy is of order of $N^{2/3}$. Therefore a polyampholyte globule does behave as a conductor with respect to a random net charge.

The problem of a charged conducting droplet is a classical one [14]. If the overall charge Q of the droplet does not exceed a certain threshold Q^*, then the spherical shape of the droplet is stable under small deformations. When Q exceeds Q^* the spherical shape becomes unstable. However, at even lower (than Q^*) overall charge the spherical shape becomes globally unstable; dividing the original droplet into two equal droplets with equal charges and separating them from each other at infinite distance is more favorable. In other words, in equilibrium, a charged conducting droplet always has a spherical shape and breaks into smaller droplets when its charge increases.

For a polyampholyte globule this breaking is impossible because all charges are connected by polymeric bonds into one chain. Therefore, when $Q > Q^*$, such a globule cannot do anything but elongate. One can calculate the value of the threshold Q^* exactly [14] but for our consideration a simple

estimate is enough. The fact that at $Q=Q^*$ the energy of the electrostatic repulsion E_e is comparable to the surface free energy F_s [14] provides such an estimate. For polyampholytes it gives $Q^* \sim q_0 N^{1/2}$. At the same time, for polyampholyte chains without long-range correlations ($\alpha = 1/2$) the random net charge Q has a Gaussian distribution with a zero average and with the standard variance $\delta Q = q_0 N^{1/2} \sim Q^*$. Therefore a net charge Q exceeds the threshold Q^* with a finite (in the thermodynamic limit) probability. Accordingly, a finite fraction of random polyampholytes form elongated globules with $A \gtrsim 1$ and the other (also finite) fraction form spherical globules.

Thus, even for uncorrelated sequences one cannot neglect a net charge imbalance, because it can change the shape of a polyampholyte globule. In addition, this effect is not self-averaging in the sense that at $\alpha \gtrsim 1/2$ the shape of a globule (the value of A) strongly depends on the specific sequence. Thus, for example, the radius of gyration strongly changes from sequence to sequence, even in the thermodynamic limit $N \to \infty$. That means that averaging over random sequences of the radius of gyration does not cover the problem. It should be noted that with respect to the free energy the system is self-averaging, because the main contribution to the free energy is of order of N and it does not depend either on the shape of the globule or the net charge.

Until now we considered the case of strong electrostatic interactions when $u \equiv q_0^2/ak_B T \gtrsim 1$. Let us now consider the opposite case of weakly charged polyampholytes in which $u \ll 1$. In such a case it is convenient to introduce the new renormalized monomer consisting of g original monomers neighboring on the chain. The charge of such a renormalized monomer $q_r(g) \sim q_0 g^\alpha$ and its size $a_r(g) \sim a g^\nu$, where $\nu = 1/2$ in a θ solvent and $\nu \approx 3/5$ in a good solvent. Accordingly, the renormalized dimensionless parameter

$$u_r(g) \equiv q_r^2(g)/a_r(g)k_B T \sim u g^{2\alpha - \nu}. \qquad (9)$$

This consideration is valid only up to $u_r(g) \lesssim 1$.

If $\alpha \leq \nu/2$, which corresponds to strong enough anticorrelations in sequences of charges, then for any g the renormalized parameter $u_r(g) \ll 1$, that is, electrostatic interactions are negligible on all scales. Thus the conformation of a polyampholyte is not perturbed by charges.

In contrast, at $\alpha > \nu/2$ the parameter $u_r(g)$ grows with increasing g and becomes of order 1 when

$$g \sim g^* = u^{1/(\nu - 2\alpha)} \gg 1. \qquad (10)$$

That means that electrostatic interactions between the renormalized monomers become strong and we come back to the problem, considered above, of strong electrostatic interactions, but instead of real monomers we have renormalized monomers (blobs). As we showed before, such a chain forms a globule of tightly packed (renormalized) monomers (see Fig. 1). Therefore the density ρ of such a globule is equal to the density of the original monomers inside the blob:

$$\rho \sim g^*/a_r^3(g^*) \sim a^{-3} u^{(3\nu - 1)/(2\alpha - \nu)}. \qquad (11)$$

This result for $\alpha = 1/2$ coincides with the result obtained in [3] by means of the Debye-Hückel theory.

The result also shows that with increase of electrostatic interactions (decrease of temperature) the density of the globule increases. It is not clear, however, what happens to the shape and the size of the globule. When $\nu/2 < \alpha < 1/2$ the globule is spherical and it just collapses as temperature decreases. In order to analyze the behavior at $\alpha > 1/2$ we just use the results for $R_\parallel$, $R_\perp$, and A obtained for the case of strong interactions. These results are valid now for blobs, in particular,

$$A \sim N_r^{2\alpha - 1}(g^*) \sim (N/g)^{2\alpha - 1}, \qquad (12)$$

which means that with decreasing temperature the globule becomes more elongated. Accordingly, the width of a globule $R_\perp$ always decreases, while the length

$$R_\parallel \sim a_r(g^*) N_r^{(4\alpha - 1)/3}(g^*)$$
$$\sim a N^{(4\alpha - 1)/3}(g^*)^{\nu + (1 - 4\alpha)/3}$$
$$\sim a N^{(4\alpha - 1)/3}(q_0^2/ak_B T)^{(\nu + (1 - 4\alpha)/3)/(\nu - 2\alpha)}. \qquad (13)$$

It is seen that if $1/2 < \alpha < \alpha^* \equiv (3\nu + 1)/4$, then with decrease of temperature (decrease of g^*) the length of a globule decreases as well. In contrast, when $\alpha > \alpha^*$ with decreasing temperature the length of the globule and, therefore, the radius of gyration grow in spite of the growth of the density inside the globule.

In conclusion, we have investigated the effect of a random charge imbalance on the behavior of a single polyampholyte chain composed of a random sequence of positive and negative charges with equal probability. The Coulomb attraction between charges of opposite signs leads to globularization of a chain. Nevertheless, a random charge imbalance can result in strong elongation of the globule. This effect is drastic for polyampholytes with positive long-range correlations in a sequence of charges. An unusual behavior when the radius of gyration grows as temperature decreases is possible for such chains. The degree of the elongation strongly depends on the value of the net charge, i.e., on the specific sequence, even for very long chains.

The strong elongation predicted by us can be verified experimentally using, for example, small-angle scattering. The results of scattering experiments on polyampholytes are reported [15]. Here one comes across the solubility problem which is vital for real experiments. We think that the solution of the single chain problem presented in the present paper may help to approach the solubility problem. The corresponding work is in progress.

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