

Conformations of Polyampholytes

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Polyampholytes are polymers composed of positive and negative charges randomly quenched along the chain. We examine configurations of such macromolecules by Monte Carlo simulations and analytical arguments. Polyampholytes with an overall constraint of charge neutrality are found to collapse into compact globules. Without such a constraint, on lowering temperature, the chain initially reduces its size and then becomes stretched due to a net charge imbalance. Experimental preparation conditions (water or organic solvent) determine if the polymer is overall neutral or randomly charged.

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A challenging topic of much current interest is the extent to which the complexity of biological systems can be mimicked by relatively simple physical models. For example, there have been several attempts to unravel the structure and folding of proteins [1] using concepts from the statistical mechanics of random systems and spin glasses [2–4]. Typically the macromolecule is represented as a linear sequence of monomers subject to a variety of interactions which ultimately determine its overall shape. One of the simplest examples is the polyampholyte (PA), composed of a random sequence of positive and negative charges [5]. Such polymers were first considered theoretically by Edwards, King, and Pincus [6] as an example of a “microelectrolyte.” Two recent studies of this problem, however, have led to opposite conclusions on whether the configuration of a typical PA is stretched [7] or compact [8]. Resolving this discrepancy may also be relevant to observations on polyamphiphilic gels [9], and experiments on dilute PAs [10].

Motivated by the above, we reexamine the conformations of PAs, and find a behavior very sensitive to the presence of constraints and the choice of ensemble. A polymer constrained to have zero net charge collapses to a compact configuration upon reducing temperature. On the other hand, if L monomers are randomly assigned positive or negative charges, $\pm q_0$ with equal probability, the resulting polymer typically has a small overall charge

of order of $q_0\sqrt{L}$. Independent of its sign, this deviation from neutrality is sufficient to stretch the chain to an extended state at low temperature. The size of the polymer in the latter case has an unusual nonmonotonic dependence: It first decreases upon reducing temperature before becoming extended below a characteristic point. In an annealed ensemble the constraint of charge neutrality is automatically enforced due to the lower energy of neutral polymers. By contrast, the quenched ensemble is dominated by polymers of charge $\pm q_0\sqrt{L}$. The two different types of PA may indeed result from different preparation conditions. Consider a PA prepared by polymerizing a dilute solution with equal concentrations of positive and negative monomers. If the electrostatic interactions are strongly screened by addition of salt, there is no energetic incentive for overall neutrality. Otherwise, in the absence of screening, the energetics favors neutral PAs.

The PA is modeled by a linear sequence of charges $q_i = \pm 1$, whose locations in space are labeled by a set of vectors \mathbf{r}_i . It is convenient to also adopt a continuum description in which monomer configurations are described by $\mathbf{r}(x)$, where x is the internal label for the position of a monomer along the chain, and for generality \mathbf{r} is assumed to be a d -dimensional vector. Each PA is specified by a particular charge density $q(x)$, which is quenched along the chain and on average zero. The Hamiltonian for the polymer now takes the form

$$\frac{\mathcal{H}}{k_B T} = \frac{K}{2} \int_0^L dx \left(\frac{d\mathbf{r}}{dx} \right)^2 + \frac{1}{2} \int_0^L \int_0^L dx dx' \left[\frac{q(x)q(x')}{k_B T |\mathbf{r}(x) - \mathbf{r}(x')|^{d-2}} + v \delta^d(\mathbf{r}(x) - \mathbf{r}(x')) \right]. \quad (1)$$

The first term is the entropic elasticity of the polymer with a force constant K . The second term represents the two-body interactions between the monomers, composed of a long-ranged electrostatic component, and a short-ranged steric repulsion of strength v . We first briefly summarize the competing arguments for typical conformations that result from this Hamiltonian.

Elaborating on earlier arguments [6], Higgs and Joan-

ny [8] suggest that the polymer collapses to a state with a radius of gyration, R_g , significantly smaller than its value in the absence of the charges. This collapse is assumed to result from an attractive interaction due to screening of the long-range electrostatic forces. The screening length l is related to the density $n \approx L/V \approx L/R_g^d$ by $l \sim (k_B T / n q_0^2)^{1/2}$. The magnitude of the attractive part of

the free energy is then estimated from the Debye-Hückel (DH) theory [11] of electrolytic solutions as

$$F_e \approx -k_B TV/l^d \approx -q_0^2 L^{d/2} R_g^{-d(d/2-1)} (k_B T)^{1-d/2}.$$

This attraction reduces the polymer size, until the pressure of excluded-volume interactions prevents further collapse. For future reference we present the temperature dependence of R_g in $d=3$ using scaling arguments: Typical electrostatic energies for the polymer scale as $q_0^2 L/R_g$. This is obtained, for example, by considering the interaction of two halves of the chain, each with a nonbalanced charge of order $q_0\sqrt{L}$, while the typical distances are of order of R_g . At very high temperatures interactions are not important and $R_g \approx aL^{\nu_0}$, where a is a typical microscopic length. For a neutral self-avoiding chain in $d=3$, $\nu_0 \approx 0.59$. Electrostatic interactions become important when $q_0^2 L/R_g \approx k_B T$, at a temperature $T_0 = q_0^2 L/R_g k_B \approx (q_0^2 L/ak_B) L^{-\nu_0}$. The temperature variations of R_g should depend on the dimensionless variable $z \equiv T/T_0$, i.e., $R_g = aL^{\nu_0} G(z)$, with $G(z) \approx \text{const}$, for $z \gg 1$, and $G(z) \approx z^\alpha$, for $z \ll 1$. The exponent α depends on the state of the PA at low temperatures. The assumption of a compact polymer [8], i.e., $R_g \sim L^{1/3}$ in $d=3$, then implies $\alpha = (\nu_0 - \frac{1}{3})/(1 - \nu_0)$.

By contrast, Kantor and Kardar [7] study the PA using a scaling approach similar to the treatment of homogeneously charged polymers [12,13]. First note that under a rescaling $x \rightarrow \lambda x$ and $\mathbf{r} \rightarrow \lambda^{\nu} \mathbf{r}$, charge correlations scale as $\langle q(x)q(x') \rangle \rightarrow \langle q(x)q(x') \rangle/\lambda$, where $\langle \rangle$ denotes the average over all quenched configurations. [This follows from $\langle q(x)q(x') \rangle \propto \delta(x-x')$.] Thus, in d dimensions, the elastic and electrostatic terms are respectively rescaled by λ^{ν_K} and λ^{ν_C} , with the bare dimensions $\nu_K = 2\nu - 1$ and $\nu_C = 1 - (d-2)\nu$. The Gaussian chain with $\nu = \frac{1}{2}$ becomes unstable to interactions for dimensions $d \leq 3$. Charge conservation [13] implies that Coulomb interactions are not renormalized for uniformly charged polymers. The *exact* exponent ν is thus obtained by setting the bare dimension of the interaction to zero. Assuming a similar nonrenormalization for randomly charged polymers, Kantor and Kardar conclude that $\nu = 1/(d-2)$ from $\nu_C = 0$. The PA in $d=3$ is thus fully stretched with $\nu = 1$ according to this argument, which in essence states the following: When individual charges are uncorrelated, the total charge is of order of $q_0\sqrt{L}$, resulting (in $d=3$) in an electrostatic energy of order of $q_0^2 L/R_g$. Equating this energy to $k_B T$ then gives $R_g \sim L$.

The disagreement between these two conclusions is quite extreme, in that one predicts a compact configuration and the other a stretched state. In fact, neither solution is exact: One [8] employs the DH theory whose applicability to a polymer, even in the dense state, has not been established, while the other [7] substitutes dimensional arguments for a true renormalization-group (RG) treatment. We also note a very important conceptual distinction between the two: The DH approach implicitly

assumes that the polymer is overall neutral (or at least very close to neutrality), while the scaling results rely on typical excess charges of order of $\pm q_0\sqrt{L}$ in the various quenched configurations. Since the number of random charges grows as L , the naive expectation is that imposing the constraint of neutrality should not affect the large- L asymptotic behavior. Indeed, if we randomly scatter exactly $L/2$ charges $-q_0$ and $L/2$ charges q_0 on L monomers, we expect (in the discrete case) $\langle q_i q_j \rangle = q_0^2 [\delta_{ij}(1+1/L) - 1/L]$, where i and j are the discrete indices of the monomers. Although the additional correlations due to the neutrality constraint decay as $1/L$, it has important consequences that are explored in the remainder of this paper.

We performed Monte Carlo (MC) simulations for randomly charged chains of $L=4, 8, 16, 32$, and 64 monomers. The monomer positions were discretized to a cubic lattice ($d=3$), and the polymer connectivity was implemented by restricting the maximal distance between neighbors to 4. Such nearest-neighbor "square well" potentials have been previously used in continuum simulations of tethered surfaces [14] and discrete simulations of linear polymers [15]. The excluded-volume interaction is implemented by not allowing two monomers to come closer than $\sqrt{2}$ lattice constants to each other, and the electrostatic interaction $\mathcal{U} = \sum_{(i,j)} U_{ij}(|\mathbf{r}_i - \mathbf{r}_j|)$ by assigning energy $U(r) = c' q_i q_j / (c+r^2)^{1/2}$ to every pair of charges at a distance r from each other. (We set $c=2$, $c'=4$, and $q_i = \pm 1$ dependent on the quench.) In a single MC time step, an attempt is made to move every monomer by one lattice spacing in a randomly chosen direction, and the resulting configuration is accepted or rejected according to its Boltzmann weight. For each quenched configuration of $\{q_i\}$, the PA is first equilibrated at a temperature $T \gg T_0$, and then cooled through a sequence of lower temperatures by halving T each time, over a range of three decades. At each T , 2500 L MC time steps are performed. The high- T equilibration time τ is estimated as the time the polymer requires to diffuse its own radius of gyration $R_g \sim L^{\nu_0}$, leading to $\tau \approx L^{2\nu_0+1}$. Thus, even for the longest chains, our equilibration time exceeds τ by a factor of 20. We also expect to have good equilibration at lower temperatures, except possibly at almost vanishing temperatures where the polymer freezes into a minimal energy configuration. The procedure is repeated for different quenches (twenty quenches for $L=4, 8$, and 16 , ten quenches for $L=32$, and five quenches for the longest chain), and the results are averaged over the quenches.

We first describe results for exactly neutral polymers constructed by assigning a charge of $+1$ to half of the monomers and -1 to the rest. The temperature dependences of R_g for different values of L are presented in Fig. 1. In accordance with the expected data collapse, we scaled R_g and T with appropriate powers of L , using the (*effective*) exponents ν and a as fitting parameters (β

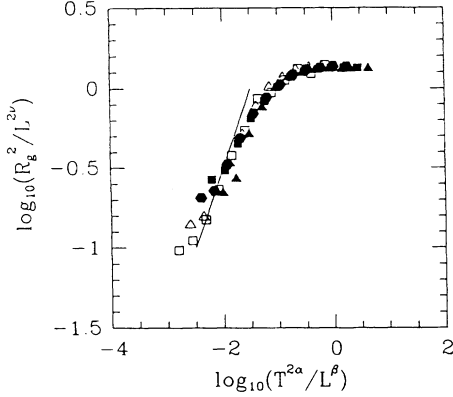


FIG. 1. The scaled R_g^2 is plotted against scaled temperature T for polymers that are overall neutral. Distances are measured in lattice constants while the temperature is in units of electrostatic energy divided by k_B . Open squares, open triangles, solid hexagons, solid squares, and solid triangles correspond to $L=64, 32, 16, 8,$ and 4 , respectively. The straight line indicates the expected slope for compact conformations.

$=2\nu-\alpha$). The best fit is obtained for $\nu=0.55$ and $\alpha=0.40$, with uncertainties of about ± 0.02 . It is immediately obvious from Fig. 1 that the neutral PA indeed collapses at low temperatures as predicted by Higgs and Joanny [8]. While the data collapse is quite reasonable, we note several deviations from the expected behavior: ν is smaller than its known value of about 0.59. This result is not particularly surprising for relatively short chains with a moderate excluded-volume interaction, due to the crossover between Gaussian and self-avoiding behaviors. Similarly, $\alpha=0.40$ corresponds to a collapsed state in which $R_g \sim L^{0.37}$. It is again likely that the exponent of 0.37 (instead of 1/3) also represents a *crossover*.

Very different results are obtained when the charges are selected randomly without regard to overall neutrality, as depicted in Fig. 2. As temperature decreases below T_0 the radii first contract and then reexpand. Actual pictures of polymer configurations indicate the following: At

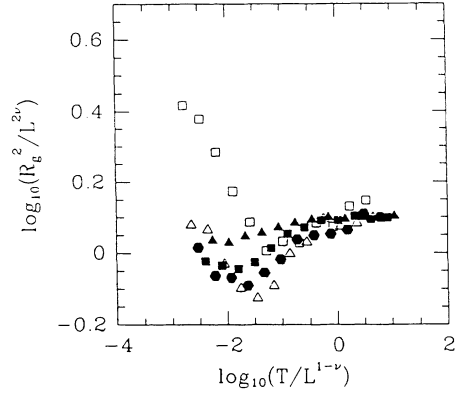


FIG. 2. Same as Fig. 1, but for polyampholytes without the constraint of overall charge neutrality. (In this plot $\nu=0.57$.)

T somewhat smaller than T_0 positive and negative charges start to pair up, thereby reducing the chain size. At lower T the “excess charges” can only reduce their energy by stretching the entire chain: The chain “unfolds” into a stretched linear or branched object with folded “double strands.” On average, at very low temperatures $R_g \sim L$ as predicted by Kantor and Kardar [7]. A visually compelling illustration of the importance of neutrality is presented in Fig. 3 which depicts the compact configuration of a neutral PA, and the stretched conformations obtained by breaking the same polymer in half (the two halves typically have opposite nonvanishing charges).

An unusual aspect of the numerical results is the non-monotonic variation in size of the unconstrained PA with temperature. While stretching of the PA due to excess charge is not surprising, its initial collapse at higher temperatures is unexpected. Fortunately, some insight into the high-temperature behavior can be obtained by perturbation theory. We start with the Hamiltonian in Eq. (1) with $\nu=0$, and treat the electrostatic interactions perturbatively. To the first order in the interaction, the averaged end to end distance $R(L)^2 = |r(L) - r(0)|^2$ in $d=3$ is given by

$$\langle R(L)^2 \rangle = \frac{3L}{K} \left[1 + \left(\frac{K}{2\pi} \right)^{1/2} \int_0^L \int_0^L dx dx' \frac{|x-x'|^{1/2}}{3Lk_B T} \langle q(x)q(x') \rangle \right]. \quad (2)$$

If there is no constraint of overall charge neutrality, $\langle q(x)q(x') \rangle = 0$, and there is no correction to the polymer size at this order. By contrast, if the polymer is constrained to be neutral, $\langle q(x)q(x') \rangle = -q_0^2/L$, leading to a reduction in polymer size,

$$\langle R(L)^2 \rangle_{\text{neutral}} = \frac{3L}{K} \left[1 - \frac{8\sqrt{3}}{45\sqrt{2\pi}} \frac{T_0}{T} \right], \quad (3)$$

where $T_0^2 = LKq_0^4/3k_B^2$. To see the first correction to the size of the unconstrained PA, perturbation theory must

be carried to second order and the final result is

$$\langle R(L)^2 \rangle_{\text{random}} = \frac{3L}{K} \left[1 - \left(\frac{1}{2} - \frac{1}{\pi} \right) \left(\frac{T_0}{T} \right)^2 \right]. \quad (4)$$

This correction again reduces the size of the PA at high temperatures, in agreement with the numerical results. However, we note that whereas the reduction in size of the neutral polymer starts at order of $1/T$, that of the unconstrained polymer begins at order of $1/T^2$. Clearly

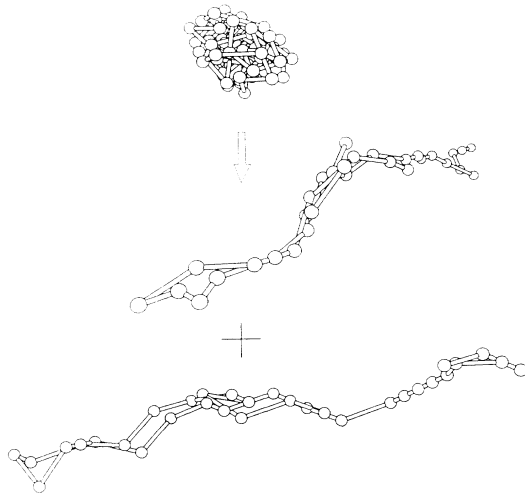


FIG. 3. The low-temperature configurations of a neutral polymer, and its two halves.

higher-order terms in the latter case must be of opposite sign to lead to the eventual stretching of the polymer. This suggests that reorganizing the perturbative results into a rigorous RG may be difficult for this problem. Such an RG has been attempted for the case where the interactions due to random charges are short ranged [16].

Finally we point out the delicate role played by the choice of ensemble in this problem. Higgs and Joanny [8] examine the behavior of *unconstrained* PAs in an annealed approximation, and again find collapsed states. In most cases annealed approximations give results that are qualitatively, if not quantitatively, similar to the quenched system. However, in this example, quenched polymers are stretched while the annealed ensemble yields compact states. This is because the annealing procedure automatically selects neutral polymers because of their much more favorable electrostatic energy. Typical members of the quenched ensemble are given negligible weight due to the Coulomb energy of their excess charge. As stated earlier these considerations are relevant to the preparation conditions for the PA. In an organic environ-

ment the monomers tend to form neutral PAs, while in an ionic solvent, the screening of charges favors PAs with a typical excess charge. These conclusions will hopefully be verified by ongoing experiments [10].

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