

Statistical mechanics of polyampholytes

Yacov Kantor

School of Physics and Astronomy, Tel Aviv University, Tel Aviv 69 978, Israel

Mehran Kardar

Department of Physics, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Hao Li

The James Franck Institute, University of Chicago, Chicago, Illinois 60637

(Received 16 April 1993)

Polyampholytes are polymers with a random sequence of positive and negative charges along their backbone. We examine the question of whether such polymers swell or contract due to Coulomb interactions, by Monte Carlo simulations and analytical arguments. We find that the answer depends crucially on whether the polyampholyte is neutral or charged, in turn reflecting its preparation conditions. If the monomers comprising the chain are assembled together in an organic solvent, the strong Coulomb forces ensure the neutrality of the resulting polymer. The neutral polymer in any environment then behaves as a "microelectrolyte" and compactifies to screen the charges. There is no such bias towards neutrality if the polymer is prepared in a solution where the Coulomb forces are screened. The typical polyampholyte will then have a net charge due to the random imbalance of positive and negative components. Such a net charge is actually sufficient to stretch the chain in an environment with no Coulomb screening. Even with a net charge, the polyampholyte initially contracts at high temperatures before stretching at lower temperatures. A perturbative analysis, valid at high temperatures, describes this initial contraction.

PACS number(s): 36.20.Ey, 64.60.Cn, 82.35.+t, 87.15.By

I. INTRODUCTION

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, such as spin glasses [2-4]. Typically in these models the macromolecule is represented as a linear sequence of monomers subject to a variety of interactions, which ultimately determine its overall shape. Such representation reduces the complicated description of the macromolecule to several parameters, which simplifies the problem, and enables application of a variety of techniques used in the statistical mechanics of polymers.

Spatial conformations of homogeneous polymers can be characterized by the critical exponent ν which relates the root-mean-squared size of the polymer to the number of monomers, L , via $R_g \approx aL^\nu$, where a is a microscopic dimension. For a flexible polymer in an athermal solvent, a is equal to the typical diameter of a monomer or to the distance between neighboring monomers on the chain. In such a system, and more generally in good solvents, the repulsive interaction between monomers is mainly steric (excluded volume) in origin. The resulting exponent ν is universal, depending only on the space dimension d ; in $d=3$ its value is $\nu=\nu_0 \approx 0.588$. In poor solvents the monomers prefer to be close to each other, resulting in compact configurations with $\nu=\nu_c=1/d$. Changing

temperature can cause a phase transition between swollen and compact conformations. At the transition, the so called θ point, $\nu=\nu_\theta=\frac{1}{2}$ [5].

The complexity of inhomogeneous macromolecules makes them considerably less susceptible to analytical treatment. One of the simplest examples is a polyampholyte (PA), composed of a random sequence of positive and negative charges [6]. Even such a chain, further restricted to short-range (point-contact) interactions and to one dimension, cannot be solved exactly. Some time ago we performed a numerical study of this problem [7], which indicated that the chain is swollen as compared to a regular random walk, i.e., its exponent ν is slightly larger than $\frac{1}{2}$ [8]. The conformation of PA's with true long-range Coulomb interactions was considered theoretically by Edwards, King, and Pincus [9] as an example of a "microelectrolyte," and later by Qian and Kholodenko [10]. 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 [11]. Resolving this discrepancy may also be relevant to understanding recent observations on polyamphiphilic gels [12], and experiments on dilute PA's [13].

Motivated by the above, we reexamined conformations of PA's and found that their behavior is very sensitive to the presence of constraints and the choice of ensemble [14]. 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 will typically have a small overall charge of order $q_0\sqrt{L}$. Independent of its sign, this deviation from neutrality is sufficient to stretch the chain to an extended configuration at low temperatures. The size of the polymer in this 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 with charge ranging from $-q_0\sqrt{L}$ to $+q_0\sqrt{L}$. The experimental preparation conditions will also favor one or the other type of PA. Suppose that the PA is prepared by polymerizing a dilute solution containing 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. However, if the Coulomb interactions are not sufficiently screened, the energetics favor neutral PA's. (There are some preliminary results from experiments on dilute solutions of PA's supporting this picture [13].)

The main results of this work have already appeared in a short communication [14]; here we provide a more detailed description. The rest of the paper is organized as follows. In Sec. II we introduce the basic model of polymers subject to unscreened Coulomb interactions, review the renormalization-group (RG) and numerical analysis of homogeneously charged polymers, and explain why the long-range nature of the force can simplify (in certain cases) its treatment. In Sec. III we introduce a model for polyampholytes and use dimensional analysis to estimate the exponent ν for the case of uncorrelated charges, as well as the case of charges with power-law correlations. The Debye-Hückel approximation for polyampholytes with vanishing total charge is described in Sec. IV, and numerical confirmations of its predictions are presented in Sec. V. The latter section also provides some technical details of our Monte Carlo simulations. Section VI describes the behavior of unconstrained randomly charged PA's. At high temperatures T the electrostatic interactions only slightly perturb the behavior of the polymer

and some insights can be gained by performing $1/T$ expansions of R_g^2 . These results are presented in Sec. VII. Finally, in Sec. VIII we discuss some possibilities for further progress, and point out several unresolved issues.

II. POLYELECTROLYTES

Polymers carrying easily ionizable groups are quite common [15]. In a solvent, a (counter) ion becomes disconnected from the polymer, moving away and leaving behind a charged group on the chain. The remaining charged polymer is called a *polyelectrolyte*. Usually the counterions remain in the vicinity of the polyelectrolyte, screening the interactions of charges on the polymer. However, at strong dilution they gain entropy by moving around the entire available volume, leaving the homogeneously charged polymer in an almost neutral environment. In such a case, the fixed charges on the polymer chain are subject to unscreened Coulomb interactions. The inhomogeneous groups on *polyampholyte* chains result in a sequence of positive and negative charges. The distribution of these charges is not necessarily symmetric about zero: the average value is controlled by pH and other properties of the solvent, but can be tuned to zero at the so-called isoelectric point. As long as there is a nonzero average, the polymer behaves asymptotically like the uniformly charged polyelectrolyte described in this section, but with a reduced monomeric charge. It is the point of exact compensation which is of greatest interest to us, and the subject of succeeding sections. We shall restrict our treatment only to the case of unscreened interactions.

The minimal statistical-mechanical description of such polymers must include the entropic elasticity originating from connectivity, as well as terms representing short-range (steric) and long-range (electrostatic) interactions. It is also convenient to 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. The Hamiltonian for the polymer now takes the form

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

The first term is the entropic elasticity of the polymer with a force constant K . This term enforces the connectivity of the chain, and $1/K$ is approximately equal to the mean-squared distance a^2 between neighboring monomers on a flexible chain. The remaining terms in Eq. (1) represent the two-body interactions composed of a long-ranged electrostatic component and a short-ranged steric repulsion. The strength ν of the latter is of order of a^d in athermal solvents. The linear charge density $q(x)$ is assumed to be fixed (quenched) for a given chain. Many other terms can in principle be added to Eq. (1), such as a monopole-dipole interaction,

$$\frac{\mathcal{H}_{\text{md}}}{k_B T} = \int_0^L \int_0^L dx dx' \frac{q(x)p(x') \cdot [\mathbf{r}(x) - \mathbf{r}(x')]}{k_B T |\mathbf{r}(x) - \mathbf{r}(x')|^d}, \quad (2)$$

where $p(x')$ is the linear dipole density. Dipole-dipole and higher-order interactions may also be generated under the RG procedure. However, dipoles and higher multipoles are not independent variables, as they are all produced by the same charge distribution.

Homogeneously charged polymers (polyelectrolytes) are described by a constant $q(x) = q_0$. This case provides a rare example in that certain aspects of its critical behavior can be calculated exactly [16]. We first note

that, under the rescalings of the internal coordinate, $x \rightarrow \lambda x$, and the external coordinate, $\mathbf{r} \rightarrow \lambda^\nu \mathbf{r}$, the coefficient of the entropic (first) term, electrostatic term, and steric term in (1) are scaled by factors of λ^{y_K} , λ^{y_q} , and λ^{y_v} , respectively, where:

$$y_K = 2\nu - 1, \quad (3)$$

$$y_q = 2 - (d-2)\nu, \quad (4)$$

$$y_v = 2 - d\nu. \quad (5)$$

Now for $d > d_u = 6$, one can set $y_K = 0$ by choosing $\nu = \nu_0 = \frac{1}{2}$. Such a choice of ν leaves the entropic term in Eq. (1) unchanged under rescaling, while the remaining terms decay ($y_q < 0$ and $y_v < 0$) to zero. Thus neither excluded volume interactions nor electrostatic ones are relevant above six space dimensions. For $d < d_u$, the electrostatic terms are the most relevant, and we set y_q to zero by choosing $\nu = \nu_h \equiv 2/(d-2)$. The exponent ν_h is unity for $d=4$, and below this dimension the polymer is fully stretched. In fact, by a full RG treatment, Pfeuty, Velasco, and de Gennes [16] proved that the above result from dimensional analysis is in fact exact. This is a consequence of the trivial renormalization of charge: When the chain is rescaled by λ , the charge of each new segment is precisely increased by λ due to charge conservation. This exact result can also be obtained by noting that the electrostatic energy of a polymer is of the order of $q_0^2 L^2 / R_g^{d-2}$, where R_g is the radius of gyration. Equating this term to $k_B T$ gives $R_g \propto L^\nu$ with $\nu = \nu_h$. Such arguments are easily extended to arbitrary D -dimensional manifolds, e.g., two-dimensional membranes, embedded in d -dimensional space [17].

Although the Coulomb interaction itself does not renormalize under RG, it does modify the shorter-range interactions. Fortunately, all higher-order multipole interactions are irrelevant, and do not change the final result. For example, the monopole-monopole term in Eq. (2) has a bare scaling dimension of $y_{md} = 2 - (d-1)\nu$, which is negative for $\nu = \nu_h$. It is interesting to note that the exact behavior of the monopole-dipole term depends on the details of the RG transformation, since the value of a dipolar moment in a non-neutral system is dependent upon the choice of the reference point for its measurement. If we choose the centers of mass of subchains of λ monomers as new coordinates, and integrate out the remaining $\lambda-1$ degrees of freedom, then the dipoles remain identically zero. Thus both monopole-dipole and dipole-dipole interactions are completely absent from the rescaled Hamiltonian, and are absorbed into the rescaled monopole-monopole energy.

There is also an approximate Flory-type approach to the problem of homogeneously charged polymers, developed by de Gennes *et al.* [18] slightly before the RG analysis. In the spirit of the Flory approximation [5], this approach equates the free energy of a noninteracting polymer, $K R_g^2 / L$, with a mean-field estimate of its electrostatic energy, $q_0^2 L^2 / R_g^{d-2}$. In terms of the rescaling exponents defined in Eqs. (3) and (4), this corresponds to setting $y_K = y_q$, leading to a Flory estimate, $\nu = \nu_{FH} \equiv 3/d$. This expression reproduces the correct upper critical di-

mension of $d=6$, where $\nu = \frac{1}{2}$. However, it predicts a nontrivial value of ν down to $d=3$, where it becomes unity. These results are clearly distinct from the predictions of RG. Early Monte Carlo simulations of charged polymers appeared to support the Flory approximation [19], but more recent simulations [20] have confirmed the validity of the RG analysis. The failure of the earlier simulation [19] to recover the RG result can probably be attributed to extremely slow crossover caused by long-range forces: approach to the asymptotic behavior depends on the ratio of the two energies $k_B T$ and q_0^2 / a . If the temperature is too high, short polyelectrolytes resemble uncharged polymers. The effective value of the exponent ν is smaller than ν_h , and slowly increases with increasing L . While we do not know in advance what ratio of energies ensures the fastest approach to the asymptotic value of ν , it is reasonable to set it to unity.

III. POLYAMPHOLYTES

In a polyampholyte (PA), both positive and negative charged groups exist on the chain backbone. They can still be described by the Hamiltonian in Eq. (1), but unlike the case of the uniform polyelectrolyte, $q(x)$ is not a constant. In the simplest model the charges along the chain are uncorrelated, in which case in the continuum limit, $\{q(x)q(x')\} = q_0^2 \delta(x-x')$, where $\{\dots\}$ denotes the average over quenched configurations of charges. [We concentrate on chains at the isoelectric point, where $\{q(x)\} = 0$.] In this section we shall describe some analytical properties of this model, and also introduce a numerical model used to simulate the problem.

We first apply scaling arguments similar to those of the previous section to randomly charged polymers [7]. Due to the averaging of independent charges, the random product $q(x)q(x')$ in Eq. (1) contributes an additional factor of λ^{-1} to the rescaling of the electrostatic term. (The sum of λ random charges increases as $\sqrt{\lambda}$ rather than λ for uniform charges.) This changes the dimension of the electrostatic term in Eq. (4) to

$$y'_q = 1 - (d-2)\nu. \quad (6)$$

Applying arguments similar to those used for homogeneous polymers, either by setting y'_q to zero, or by estimating the total charge of the polymer as $q_0 \sqrt{L}$ and equating the resulting electrostatic energy $q_0^2 L / R_g^{d-2}$ to $k_B T$, we find the exponent

$$\nu = \nu_r \equiv 1/(d-2). \quad (7)$$

This result should be valid for $3 < d < 4$. For $d \leq 3$ the polymer is stretched ($\nu=1$). Note that the scaling analysis shows that the electrostatic interactions are irrelevant for $d > 4$. We should add that the latter conclusion is valid only within the subspace of configurations which do not differ significantly from a Gaussian chain. It does not exclude the possibility of a phase transition to equilibrium configurations to a very different nature. As in the case of polyelectrolytes, Flory-type arguments are not expected to produce a reliable estimate of ν . Nevertheless, for completeness we note that equating y'_q to y_K

leads to an exponent $\nu = \nu_{Fr} \equiv 2/d$, for dimensions $2 \leq d \leq 4$.

However, closer examination suggests that the shape of the polymer is quite sensitive to the actual distribution of randomness. The swelling exponent obtained by setting Eq. (6) to zero relies on the independence of charges, and the resulting net charge of a typical realization. On the other hand, if the net charge of the chain is zero it is likely to contract [11]. (If we mentally divide a neutral PA into two halves, they will have opposite total charges and attract each other, resulting in a contraction in size.) We may consider more general charge distributions in which the random charges are correlated such that their sum Q increases faster (or slower) than \sqrt{L} , i.e.,

$$\{Q^2\} = \int_0^L \int_0^L dx dx' \{q(x)q(x')\} \approx AL^\mu. \quad (8)$$

The exponent $\mu = 1$ corresponds to uncorrelated charges, while $\mu = 2$ describes homogeneously charged polymers. Such a dependence of the total charge can be achieved if for large separations $|x - x'|$ the quenched average behaves as

$$\{q(x)q(x')\} \approx \frac{\mu(\mu-1)}{2} A |x - x'|^{\mu-2}. \quad (9)$$

[This is true only for $\mu > 1$. For $\mu < 1$, the integral in Eq. (8) depends on the behavior of $\{q(x)q(x')\}$ at short separations. The condition $\mu = 0$ for neutral PA's is achieved by making $\{q(x)q(x')\}$ dependent on L .] Such long-ranged correlations have indeed been observed in the nucleotide sequences of DNA [21]. The dimensional argument is now modified since under rescaling of x by λ , the product $q(x)q(x')$ contributes a factor $\lambda^{\mu-2}$. Consequently, the electrostatic interaction term is rescaled with exponent $\nu_q'' = \mu - (d-2)\nu$, leading to the value of

$$\nu = \nu_{\mu r} \equiv \mu / (d-2). \quad (10)$$

This result should be valid for $\mu + 2 < d < 2\mu + 2$. For $1 \leq \mu \leq 2$, it interpolates between the exponents for uncorrelated PA's and homogeneously charged polyelectrolytes. For $\mu < 1$, the explicit dependence of $\{q(x)q(x')\}$ on L casts doubts on the validity of Eq. (10). Also, excluded-volume interactions will become relevant for sufficiently small μ . The $\mu = 0$ case of a neutral PA is discussed in more detail in the next section.

IV. DEBYE-HÜCKEL THEORY

It was noted by Edwards, King, and Pincus [9] that a polymer confined to a volume much smaller than its natural radius, so as to have a uniform density, can be approximately treated as a liquid. In particular, they suggested that a PA behaves as a regular (micro)electrolyte. Elaborating those arguments, Higgs and Joanny [11] assume 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. The typical size is found by minimizing a Debye-Hückel (DH) approximation to the free energy of a PA. The final result indeed corresponds to a collapsed state, and hence the treatment is internally consistent.

The collapse is assumed to result from an attractive in-

teraction due to the screening of the long-range electrostatic forces. The screening length r_e in a liquid or gas with two types of charges (electrolyte) is related to their density c . This scale can be found by equating the typical electrostatic interaction energy within a volume r_e^d to the thermal energy $k_B T$, i.e., $(cr_e^d)q_0^2/r_e^{d-2} \approx k_B T$, leading to $r_e \approx \sqrt{k_B T / cq_0^2}$. At shorter length scales the charges do not rearrange, since the possible gain in electrostatic energy is outweighed by the loss of entropy. However, at length scales of order r_e groups of atoms can rearrange their positions in such a way that positively charged regions are surrounded mainly by negatively charged ones, and vice versa. The magnitude of the resulting attractive free energy is then estimated from the Debye-Hückel theory [22] of electrolytic solutions as

$$F_e \approx -k_B T \frac{V}{r_e^d} \approx -q_0^d L^{d/2} R_g^{d(2-d)/2} (k_B T)^{1-d/2}. \quad (11)$$

The second equality is obtained using a monomer of density $c \approx L/V$, and a polymer volume of $V \approx R_g^d$. (Here, and in other expressions, we omit dimensionless constants of order unity.)

It is important to note that the strict neutrality condition is an essential ingredient of DH theory. The formal derivation begins with the free energy of the uncharged gas, and attempts to evaluate the corrections caused by the Coulomb energy. It is assumed that the mere introduction of charges without the change of positions of particles does not change the energy. This is true only if the gas is completely neutral. The gain described by Eq. (11) is a consequence of adjustments to positions of particles, which also lead to screening. This attraction reduces the polymer size until the pressure from excluded-volume interactions prevents further collapse.

The excluded-volume contribution to the free energy can be estimated [11] as follows. The osmotic pressure Π of a single polymer embedded in an arbitrary volume V has the scaling form [23] $\Pi = (k_B T c / L) f(c/c^*)$, where c is the number density of monomers, while f is a scaling function. (This is essentially the ideal gas law, i.e., the pressure is proportional to $k_B T$ multiplied by the density of molecules c/L .) The critical concentration c^* is such that the polymer occupies the entire volume V , i.e., $c^* \approx L / (a^d L^{d\nu_0})$, where the exponent ν_0 applies to a regular self-avoiding polymer without any additional interactions. At small concentrations ($c \ll c^*$) f is a constant, reproducing the ideal gas law. At large concentrations the pressure must be a function of c only, independent of L . This is achieved by $f(x) \sim x^m$, with $m = 1/(d\nu_0 - 1)$, leading to $\Pi = k_B T c^{d\nu_0/(d\nu_0 - 1)}$. From this expression for Π we can immediately evaluate the free energy as

$$F_r \approx k_B T a^{d/(d\nu_0 - 1)} L^{d\nu_0/(d\nu_0 - 1)} R_g^{-d/(d\nu_0 - 1)}. \quad (12)$$

This result can also be obtained by the "blob" picture suggested by de Gennes [5]. A polymer confined to a restricted volume forms L_r -monomer "blobs", each behaving as an unconfined self-avoiding polymer. The "blobs" are then packed compactly in a homogeneous structure.

The number of the monomers, l_r , in each blob is therefore determined from $R_g^d \approx (al_r^{\nu_0})^d (L/l_r)$. By attributing $k_B T$ of free energy to each blob, we recover the result in Eq. (12).

Minimization of the total free energy $F_e + F_r$ with respect to R_g leads to the radius of gyration,

$$R_g \approx aL^{1/d} \left[\frac{k_B T a^{d-2}}{q_0^2} \right]^\alpha, \quad (13)$$

with

$$\alpha = \frac{d\nu_0 - 1}{d[1 - (d-2)\nu_0]} \quad (14)$$

The exponent $1/d$ confirms that the polymer is indeed compact. However, the term "compact" refers to a homogeneous density, and does not imply a densely packed configuration. Indeed, Eq. (13) shows that the maximum monomeric density is only achieved at a temperature of $k_B T \approx q_0^2/a^{d-2}$, below which Eq. (13) is no longer valid. The density decreases as the polymer expands at higher temperatures, until the DH approximation fails. An upper bound to this temperature is obtained by setting R_g in Eq. (13) to the size of the uncharged chain. Equation (13) was obtained for general space dimensions d . However, the exponent α for the T dependence of R_g diverges at $d=4$ and is negative for $d > 4$. This happens because for $d > 4$ the electrostatic interactions of remote parts of a swollen polymer become negligible and the entire picture of a gradually contracting polymer is no longer valid. However, this does not imply that a collapsed state of the polymer does not exist: at very low temperatures there may be a folded state resembling a random ionic crystal. As temperature is increased the "crystal" can "melt" into a configuration resembling the uncharged polymer. Thus the gradual crossover is replaced by a first-order phase transition. Obviously, the above calculations are not applicable to such a situation.

For future reference we rederive 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, as the interaction between two halves of the chain each having a nonbalanced total charge of order of $q_0 \sqrt{L}$, while typical distances are of the order of R_g . At 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 $d=3$, $\nu_0 \approx 0.588$. Electrostatic interactions become important when $q_0^2 L / R_g \approx k_B T$, i.e., at a temperature $T_0 = q_0^2 L / (k_B R_g) \approx [q_0^2 L / (ak_B)] L^{-\nu_0}$. The temperature variations of R_g should depend on the dimensionless variable $z \equiv T/T_0$. We can thus set $R_g = aL^{\nu_0} G(z)$, with

$$G(z) \approx \begin{cases} \text{const,} & \text{for } z \gg 1; \\ z^\alpha, & \text{for } z \ll 1. \end{cases} \quad (15)$$

The exponent α depends on the state of the PA at low temperatures. The assumption that at low temperatures

the polymer is compact [11], i.e., $R_g \propto L^{1/3}$ in $d=3$, then implies $\alpha = (\nu_0 - \frac{1}{3}) / (1 - \nu_0)$. The same argument can be repeated in general space dimensions d leading to the value of α given by Eq. (14). While this derivation seems to be more "robust" than the results obtained from minimization of the total free energy, we should keep in mind that both approaches essentially use the scaling (or the "blob") picture for estimates of the free energy.

V. NUMERICAL RESULTS

Since analytical results for the behavior of PA's are inconclusive, we rely heavily on the Monte Carlo (MC) simulations discussed in this section. We use a relatively simple numerical scheme, and confine our analysis to chains of $L=4, 8, 16, 32$, and 64 monomers. The monomer positions are discretized to a cubic lattice ($d=3$), and the polymer connectivity 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 [24] and discrete simulations of linear polymers [25]. The excluded-volume interaction is implemented by not allowing two monomers to come any closer than $\sqrt{2}$ lattice constants. The electrostatic interaction $\mathcal{U} = \sum_{\langle i,j \rangle} U_{ij}(|\mathbf{r}_i - \mathbf{r}_j|)$ is included by assigning energy $U_{ij}(r) = c' q_i q_j / \sqrt{c + r^2}$ to every pair $\langle i,j \rangle$ 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 future discussions of numerical results the lattice constant is used as the unit of length, while the choice of the electrostatic energy $U(r)$ sets the energy and temperature scales. All the reported results refer to such dimensionless quantities. We shall discuss neutral and randomly charged PA's separately.

A. Neutral polyampholytes

Random PA's with zero total charge were constructed by randomly assigning a charge of $+1$ to half of the monomers and -1 to the rest. The use of relatively short chains enabled us to achieve good equilibration, although we partially sacrificed accurate quantitative knowledge of the asymptotic behavior. A single MC time step is defined as the simulation time during which an attempt is made to move every monomer by a single lattice spacing in a randomly chosen direction, and the resulting configuration accepted or rejected according to its Boltzmann weight. It should be noted that due to the long-range nature of the interaction, an attempt to move a single atom involves recalculation of its interactions with all the surrounding atoms, and therefore the CPU time per single MC time step increases as L^2 . For each quenched configuration of $\{q_i\}$ the PA is equilibrated first at a temperature $T \gg T_0$, and then cooled through a sequence of lower temperatures, by reducing T by a factor of 2 each time, over a range of three decades. At each T , $2500 \times L$ MC time steps are performed. The high-temperature equilibration time τ can be estimated as the time it takes the polymer 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. This sequence is repeated for different quenches (twenty quenches for $L=4,8,16$, ten quenches for $L=32$, and five quenches for the longest chain). All the following results were obtained by averaging over the quenches.

Figure 1 depicts the geometrical shape of a 64-monomer polymer at five different temperatures. The estimated crossover temperature for a polymer of this length is $T_0 \approx 2.7$. Indeed, for $T > T_0$ the shapes are indistinguishable from regular self-avoiding polymers, while at $T=2.5$ we see the beginning of a contraction. At $T \approx 0.05$ the density of monomers reaches its maximal value and further decrease in T freezes the system. These pictures qualitatively confirm the predictions of the previous section.

The temperature and L dependence of the electrostatic energy of a PA can be calculated by substituting the value of R_g given by Eq. (13) into Eq. (11). (Up to a numerical prefactor, the electrostatic part of the energy is equal to the free energy.) Alternatively, we note that in the scaling regime $T_0 \gg T \gg T_m \equiv q_0^2 / (k_B a^{d-2})$, the electrostatic energy behaves as $E_e \propto -k_B T (T_0/T)^w$. At the upper limit the energy becomes equal to $k_B T$, while at the lower temperature the monomer density reaches its maximal possible value; the screening length becomes equal to intermonomer separation, and $E_e \sim -k_B T L$. To ensure such behavior we must choose $w = 1/[1-(d-2)\nu]$. The electrostatic energy per mono-

mer is independent of both T and L for $T < T_m$. It remains independent of L for $T_m < T < T_0$, but decays with temperature as $T^{-(w-1)}$ (as $T^{-1.4}$ in $d=3$). Actually, the size of the scaling region $T_0/T_m = L^{1-(d-2)\nu}$ is smaller than a single decade even for the longest polymers in our simulations. Figure 2 is a semilogarithmic plot of the electrostatic energy as a function of T for different values of L . There appears to be a partial collapse of data for intermediate temperatures within a somewhat larger range (up to two decades for $L=64$) than expected. At $T < T_m$, all graphs asymptotically approach the same energy of $\approx -0.5k_B T_m$, consistent with the definition of T_m . However, the absolute values of energies in the high-temperature limit are larger than expected, and consequently the behavior in the intermediate range is not a simple power law.

The temperature dependences of R_g for different values of L are presented in Fig. 3. In accordance with the expected data collapse we have employed a scaling form $R_g/L^\nu = G(T^\alpha/L^{\beta/2})$, using the exponents ν and α as fitting parameters [$\beta = 2\alpha(1-\nu)$]. 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. 3 that the neutral PA indeed collapses at low temperatures as predicted by Higgs and Joanny [11]. While the data collapse is quite reasonable, we note several deviations from the expected behavior: ν is smaller than its known value of about 0.588. 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. At the low-temperature extreme, the exponent $\alpha=0.40$ corresponds to a "collapsed" state in which $R_g \sim L^{0.37}$. It is again quite likely that the exponent of 0.37 (instead of $\frac{1}{3}$) is also a result of crossover. This deviation is consistent with the very slight dependence of the energy per atom on L mentioned in the previous paragraph.

B. Randomly charged polyampholytes

The overall neutrality of a PA is an important condition for the validity of the DH approximation, and conse-

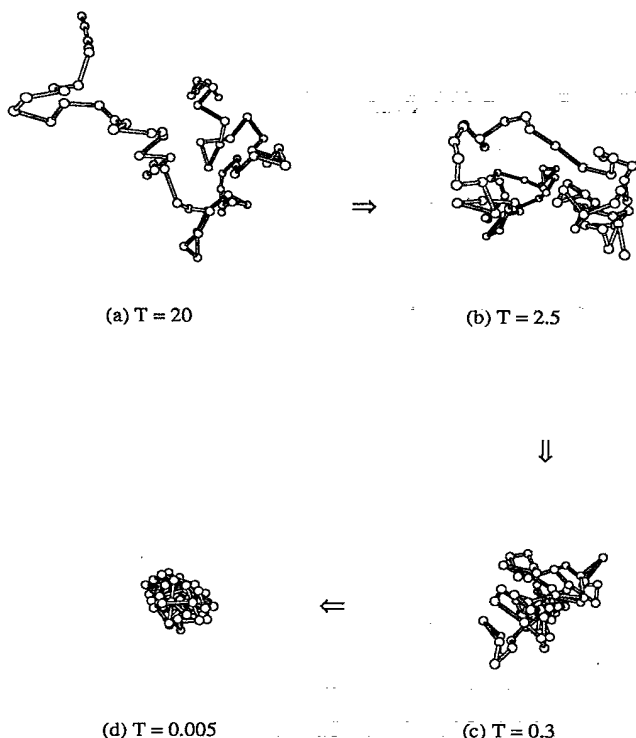


FIG. 1. Neutral 64-monomer polyampholyte at (a) $T=20$, (b) $T=2.5$, (c) $T=0.3$, and (d) $T=0.005$.

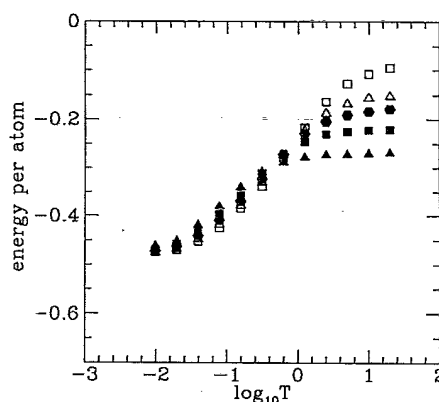


FIG. 2. Semilogarithmic plot of the electrostatic energy per atom versus temperature (in dimensionless units, see text). \square , \triangle , \bullet , \blacksquare , and \blacktriangle correspond to $L=64, 32, 16, 8$, and 4 respectively.

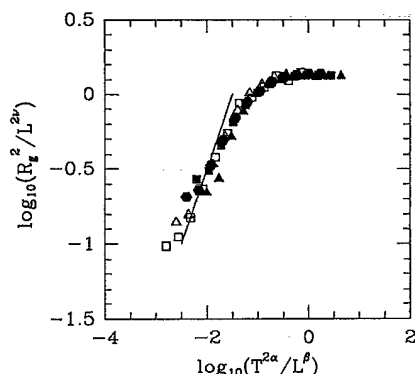


FIG. 3. Scaled R_g^2 is plotted against scaled temperature T for polymers that are overall neutral. Distances are measured in lattice constants while the temperature is in units of electrostatic energy divided by k_B . (The symbols have the same meaning as in Fig. 2.) The straight line indicates the expected slope for compact conformations.

quently for its low-temperature collapse. In the absence of such a constraint, the dimensional analysis of Sec. III predicts the PA to be swollen with $\nu = \nu_r = 1$ in $d = 3$. Here we present numerical evidence supporting such behavior. The model and MC procedure are identical to those described above. The only difference is in the choice of quenched configurations: each monomer is randomly assigned a charge of $+1$ or -1 independently of other monomers. Thus, typical quenches for $L = 64$ result in total charges in the range of 5 to 10 (of either sign).

Figure 4 depicts the spatial configurations of such a

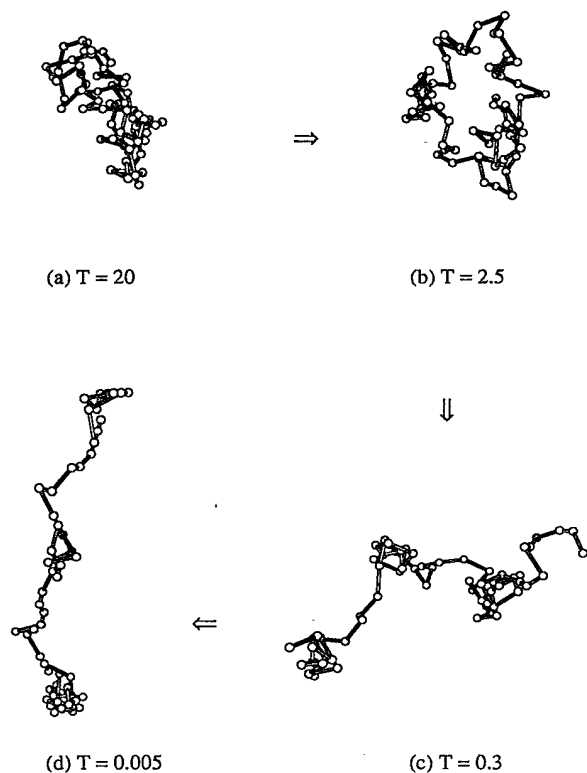


FIG. 4. Same as Fig. 1, but for polyampholytes without the constraint of overall charge neutrality.

64-monomer PA. The Coulomb interactions become important at the same value of T_0 as for the neutral PA in Fig. 1. The high-temperature configurations are again indistinguishable from self-avoiding polymers. As the temperature is decreased towards T_0 the polymer slightly contracts, and then expands upon further decrease of T . It reaches its final state at $T = T_m$ and "freezes" into a particular configuration. Several comments should be made regarding the shape of low-temperature configurations: (a) These configurations are by no means straight lines, although they are "stretched." They have some segments folded into double lines in which monomers of opposite charges form permanent pairs. We have also observed low-temperature configurations that are branched. In some cases we see almost straight lines containing small "globules" of many monomers forming almost compact structures. (A menagerie of these configurations is included in Fig. 5.) (b) A particular quench of charges seems to have many low-energy states with almost identical energies: repeated heating and cooling sometimes results in quite different "ground states." Since for $T < T_m$ the system freezes, there is no practical way to find the true ground state. The glassy behavior of many nearly degenerate ground states is naturally a problem if such random chains are to be regarded as model proteins.

Figure 6 depicts the temperature dependence of R_g on a logarithmic scale. We attempted to apply the same method of data collapse used in Fig. 3. However, we could not collapse the curves over the whole temperature interval. Only the exponent ν has been used to collapse

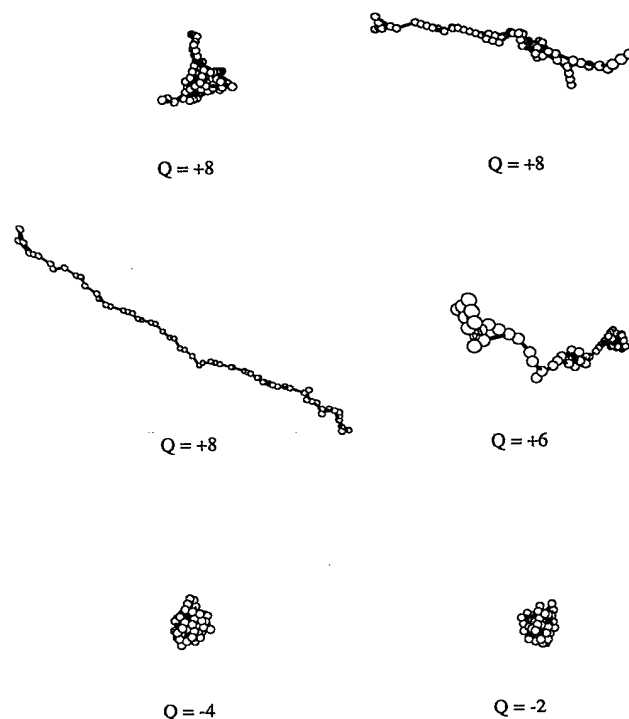


FIG. 5. Some low-temperature configurations obtained for randomly charged polymers of $L = 64$. The net charge of each configuration is indicated by Q .

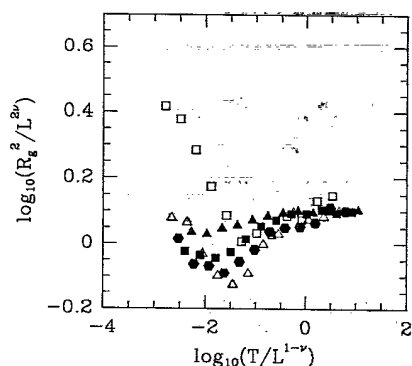


FIG. 6. Same as Fig. 3, for randomly charged polyampholytes without the overall neutrality constraint.

the high-temperature data, and the best fit is obtained for $\nu=0.57$. As temperature decreases below T_0 the radii first contract and then expand again. Actual pictures of polymer configurations indicate the following process. At T somewhat smaller than T_0 , positive and negative charges start to pair up, thereby reducing the chain size. At lower temperatures the "excess charges" can only reduce their energy by stretching the entire chain. Thus at the lowest temperatures the chain "unfolds" as depicted in Fig. 4.

Although the low-temperature configurations are "stretched," the absolute values of R_g at $T < T_m$ in Fig. 5 are rather small due to branching, globules, and double strands. For $L \leq 16$ the low-temperature values of R_g are seven smaller than their values at $T > T_0$. Only for the $L=64$ chain do we see a significant increase in R_g . On average, at very low temperatures R_g indeed becomes proportional to L as predicted earlier [7]. Figure 7 depicts the L dependence of R_g at very low temperatures. The results are consistent with the exponent $\nu=1$, which corresponds to the stretched case. A visually compelling illustration of the importance of neutrality is presented in Fig. 8 which depicts the compact configuration of a neu-

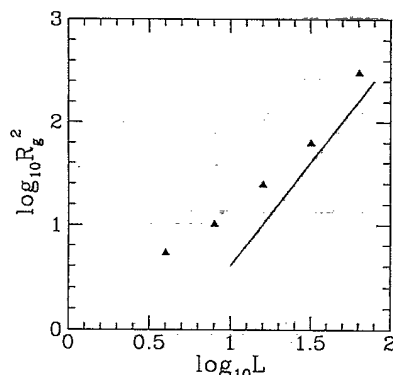


FIG. 7. Logarithmic plot of R_g^2 at $T \ll T_m$ as a function of L for unconstrained polyampholytes. The straight line indicates the expected slope for stretched configurations with $\nu=1$.

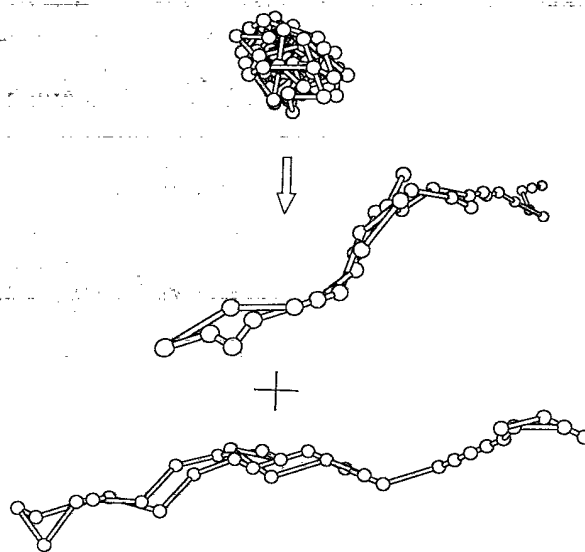


FIG. 8. The low-temperature configurations of a neutral PA, and its two halves.

tral polyampholyte, and the stretched conformations obtained by breaking the same polymer in half (the two halves typically have opposite nonvanishing charges).

VI. HIGH-TEMPERATURE PROPERTIES OF POLYAMPHOLYTES

In the previous section we demonstrated the extreme differences between randomly charged and neutral PA's at low temperatures. It is possible to carry out a perturbative analysis that is valid at high temperatures. We shall see that there are differences between the two types of PA even in this limit. The difference in this case originates from the charge-charge correlation function. Since the number of charges grows as L , the naive expectation is that imposing the one constraint of neutrality should not affect the asymptotic behavior of these correlations. Indeed, if we randomly scatter exactly $L/2$ charges $-q_0$ and $L/2$ charges q_0 on L monomers, we expect $\{q_i q_j\} = q_0^2 (L \delta_{ij} - 1)/(L-1)$, where i and j are the discrete indices for monomers. The additional correlations due to the neutrality constraint decay as $1/L$. They are, however, sufficiently important to modify the high-temperature behavior.

We start with the Hamiltonian in Eq. (1) with $\nu=0$, treating the first integral (denoted $\mathcal{H}_0/k_B T$) as the unperturbed Hamiltonian, and the electrostatic interactions (denoted $\mathcal{V}/k_B T$) as a perturbation. Only the electrostatic part of the Hamiltonian includes the effects of randomness, and, therefore, expansion in this term permits direct calculation of thermal $\langle \dots \rangle$ and quenched $\{ \dots \}$ averages. The lowest-order terms in the expansion of the averaged end-to-end distance $R(L)^2 = \langle |r(L) - r(0)|^2 \rangle$ have the following form

$$\begin{aligned} \langle \{R(L)^2\} \rangle = & \left\{ \frac{\text{Tr} R^2 e^{-\mathcal{H}}}{\text{Tr} e^{-\mathcal{H}}} \right\} = \langle \{R^2\}_0 \rangle - \frac{1}{k_B T} \{ (\langle R^2 \mathcal{V} \rangle_0 - \langle R^2 \rangle_0 \langle \mathcal{V} \rangle_0) \} \\ & + \left[\frac{1}{k_B T} \right]^2 \left\{ \frac{1}{2} (\langle R^2 \mathcal{V}^2 \rangle_0 - \langle R^2 \rangle_0 \langle \mathcal{V}^2 \rangle_0) + (\langle R^2 \rangle_0 \langle \mathcal{V} \rangle_0^2 - \langle R^2 \mathcal{V} \rangle_0 \langle \mathcal{V} \rangle_0) \right\} + \dots, \end{aligned} \quad (16)$$

where $\langle \dots \rangle_0$ represents a thermal average with the unperturbed Hamiltonian \mathcal{H}_0 . Note that the terms in this expansion are organized in powers of $1/T$. The result in three dimensions to order of $1/T$ is

$$\begin{aligned} \langle R(L)^2 \rangle = & \frac{3L}{K} \left[1 + \sqrt{K/2\pi} \frac{1}{3L} \int_0^L \int_0^L dx dx' |x-x'|^{1/2} \right. \\ & \left. \times \frac{\{q(x)q(x')\}}{k_B T} \right]. \end{aligned} \quad (17)$$

Note that the corrections to the size of the polymer at this order are most sensitive to the charge correlations along the chain at short distances. As long as the charges are positively correlated the net effect is a repulsion. For example, correlations such as Eq. (9) ($\mu > 1$) give

$$\langle R(L)^2 \rangle = \frac{3L}{K} \left[1 + \sqrt{K/2\pi} \frac{\mu(\mu-1)}{(\mu^2 - \frac{1}{4})} \frac{AL^{\mu-3/2}}{3k_B T} \right]. \quad (18)$$

Some anticorrelation is necessary to achieve a net charge that scales with $\mu < 1$. For example, if the polymer is constrained to be neutral, $\{q(x)q(x')\} = -q_0^2/L$ for $x \neq x'$. Such anticorrelations lead to a reduction in size, and for the neutral PA

$$\langle R(L)^2 \rangle_{\text{neutral}} = \frac{3L}{K} \left[1 - \frac{8\sqrt{3}}{45\sqrt{2\pi}} \frac{T_0}{T} \right], \quad (19)$$

where $T_0^2 = LKq_0^4/3k_B^2$. This result is consistent with the observed collapse of neutral PA's, although the mechanism is distinct from DH.

For uncorrelated random charges there is no first-order correction to the end-to-end distance, and a second-order calculation is necessary to find any effect. We performed such a calculation, and obtained the result

$$\langle R(L)^2 \rangle_{\text{random}} = \frac{3L}{K} \left[1 - \left[\frac{1}{2} - \frac{1}{\pi} \right] \left[\frac{T_0}{T} \right]^2 \right]. \quad (20)$$

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 the higher-order terms in the latter case must be of opposite sign and 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 a RG has been attempted for the case where the interactions due to random charges are short ranged [26].

VII. DISCUSSION

Finally we point out the delicate role played by the choice of ensemble in this problem. Higgs and Joanny [11] examine the behavior of unconstrained PA's in an annealed approximation, and again find collapsed states. In most cases the annealed approximation gives results that are qualitatively, if not quantitatively, similar to the quenched system. However, in this case the quenched polymers are stretched while the annealed ensemble yields compact states. This is because the annealing procedure automatically selects out neutral polymers due to 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 environment the monomers would tend to form neutral PA's, while in an ionic solvent the screening of charges favors PA's with a typical excess charge. These results will hopefully be tested by ongoing experiments [13].

Naturally in experiments it is hard to tune to precisely the isoelectric point. We can imagine that as pH or other solution property is changed the averaged charge on the monomer changes sign. The size of a particular PA will change with this parameter and is a minimum at the point when its net charge is zero. For a solution of neutral PA's the transition point is sharp and all polymers in the solution have roughly the same size. On the other hand, for a solution of randomly charged PA's the neutrality condition is reached at different points for different polymers. In the vicinity of the isoelectric point the size distribution of polymers is wide. The width of the transition region scales as $L^{-1/2}$ and vanishes as $L \rightarrow \infty$.

Due to the limited number of quenched configurations, we cannot make detailed studies of the distribution of R_g^2 in low-temperature configurations in the case of unconstrained randomness. The complete ensemble of all quenches contains also neutral and almost neutral configurations which are, presumably, collapsed. These configurations, however, have a negligible probability for large L . Even for unconstrained PA's the nature of the probability distribution for R_g^2 is not obvious. If the width of the distribution is significantly narrower than its mean, then almost all configurations are stretched. Alternatively, the distribution may be broad, and centered on

small values of R_g^2 , in which case the exponent ν is unity only because the sample contains a finite portion of stretched configuration. The latter scenario is more likely in $d=3$ which is a "borderline" dimension above which $\nu < 1$. A quantitative answer to this question requires simulations of a few thousand realizations of chains at least as long as those considered here.

Our study was restricted to the behavior of an isolated PA, and therefore applies to the experimental case of very dilute solutions. Interesting effects may be observed as the concentration of the solution increases. While a single PA can have an unconstrained charge distribution, and therefore prefer to be stretched, in solution it is likely to pair with another PA of opposite charge, thus reducing energy, while losing translational entropy. At sufficiently high concentrations such pairings may lead to phase separation into a collapsed state.

The arguments in this paper rely heavily on the long-range nature of the interactions. However, problems of this type are also present with only short-range interac-

tions. Recently we repeated the simulations of polymers in $d=1$ with random contact interactions [7], with the constraint of overall neutrality, and obtained strong deviations from the previously published results for unconstrained polymers. It is not yet clear whether this is a finite-size effect, or whether global constraints can indeed modify the behavior of polymers with short-range interactions. Recent results on a directed version of the problem also observe a dependence on net charge for short-range interaction [27], favoring the latter possibility.

ACKNOWLEDGMENTS

We would like to thank T. Tanaka and X.-H. Yu for useful discussions. Y.K. acknowledges the support of the Basic Research Foundation of the Israel Academy of Sciences. The work at MIT was supported by the NSF Grant No. DMR-87-19217 through the Center for Materials Science and Engineering, and the PYI program (M.K.).

- [1] See, e.g., T. E. Creighton, *Proteins: Their Structure and Molecular Properties* (Freeman, San Francisco, 1984).
- [2] D. L. Stein, Proc. Natl. Acad. Sci. U.S.A. **82**, 3670 (1985); J. D. Bryngelson and P. G. Wolynes, *ibid.* **84**, 7524 (1987).
- [3] T. Garel and H. Orland, Europhys. Lett. **6**, 307 (1988).
- [4] E. I. Shakhnovich and A. M. Gutin, Europhys. Lett. **8**, 327 (1989).
- [5] P. G. de Gennes, *Scaling Concepts in Polymer Physics* (Cornell University, Ithaca, 1979).
- [6] C. Tanford, *Physical Chemistry of Macromolecules* (Wiley, New York, 1961).
- [7] Y. Kantor and M. Kardar, Europhys. Lett. **14**, 421 (1991).
- [8] A more recent confirmation of this result is by D. P. Foster, C. Vanderzande, and J. Yeomans, J. Stat. Phys. **69**, 857 (1992).
- [9] S. F. Edwards, P. R. King, and P. Pincus, Ferroelectrics **30**, 3 (1980).
- [10] C. Qian and A. Kholodenko, J. Chem. Phys. **89**, 5273 (1988).
- [11] P. G. Higgs and J.-F. Joanny, J. Chem. Phys. **94**, 1543 (1991).
- [12] M. Annaka and T. Tanaka, Nature **355**, 430 (1992).
- [13] T. Tanaka and X.-H. Yu (private communications).
- [14] Y. Kantor, H. Li, and M. Kardar, Phys. Rev. Lett. **69**, 61 (1992).
- [15] F. Oosawa, *Polyelectrolytes* (Marcel Dekker, New York, 1971).
- [16] P. Pfeuty, R. M. Velasco, and P. G. de Gennes, J. Phys. (Paris) **38**, L5 (1977).
- [17] Y. Kantor and M. Kardar, Europhys. Lett. **9**, 53 (1989).
- [18] P. G. de Gennes, P. Pincus, R. M. Velasco, and F. Brochard, J. Phys. (Paris) **37**, 1461 (1977).
- [19] A. Baumgärtner, J. Phys. (Paris) Lett. **45**, L515 (1984).
- [20] Y. Kantor, Phys. Rev. A **42**, 2486 (1990).
- [21] C.-K. Peng, S. V. Buldyrev, A. L. Goldberger, S. Havlin, F. Sciortino, M. Simons, and H. E. Stanley, Nature **356**, 168 (1992).
- [22] L. D. Landau and E. M. Lifshitz, *Statistical Physics* (Pergamon, New York, 1981), Part 1.
- [23] J. des Cloizeaux, J. Phys. (Paris) **36**, 281 (1975).
- [24] Y. Kantor, M. Kardar, and D. R. Nelson, Phys. Rev. Lett. **57**, 791 (1986).
- [25] I. Carmesin and K. Kremer, Macromolecules **21**, 2819 (1988).
- [26] S. Stepanow, M. Schulz, and J.-U. Sommer, Europhys. Lett. **19**, 273 (1992).
- [27] B. Derrida, R. B. Griffiths, and P. G. Higgs, Europhys. Lett. **18**, 361 (1992).