Conformational Phase Transition of a Polyampholyte in a Low Dielectric Solvent

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Abstract. – The Debye-Hückel theory augmented by Bjerrum's ideas of dipole formation and Flory's affine network theory of rubber elasticity is applied to the study of neutral polyampholytes (PAs), polymers that in addition to neutral monomers contain charged groups. It is shown that, in the low-temperature state, a PA with N monomers resembles an affine network, or a microgel, and has a radius of gyration which scales as N^ν, with $\nu = 2/5$. As the temperature is raised, a PA undergoes a first-order collapse transition into a dilute globular state in which $\nu = 1/3$. The value of the transition temperature is calculated numerically as a function of polymer size. It is argued that this transition should be observable in a low dielectric solvent.

Interest in the conformational properties of long molecules goes more than 40 years back to the pioneering work of Flory[1]. Over the last two decades this topic has gotten a renewed attention due to the fact that a transition from an extended coil to a compact globular state is directly connected with the chemical activity of many biologically important molecules. This transition is also interesting from a purely theoretical standpoint since, as was argued by de Gennes, it can be related to a tricritical point in magnetic materials[2].

Most of the theoretical effort so far has been directed towards the study of polymers that do not contain any charged groups. Polyampholytes (PAs), which are copolymers containing both charged and neutral monomers, have received much less attention. The reason for this is partially due to the practical difficulty of treating a long-range Coulomb force, and to the fact that, in many cases, the Coulomb force can be neglected due to the counterion condensation. However, since proteins are a special case of PAs, it is important to get a deeper insight into the role that the Coulombic interaction plays in protein folding.

The first attempt at a description of the coil-globule transition in a PA at infinite dilution came from Edwards *et al.* They argued, on the basis of the Debye-Hückel *limiting law*, that a *neutral* PA will collapse into a *dilute* globular state (microelectrolyte) with a density significantly smaller than that of close-packed monomers characteristic of the collapsed state of a polymer whose groups interact through a short-range potential[3]. The analysis was

further modified and extended by Higgs and Joanny who concluded that a *sufficiently long neutral* PA *will always* collapse into a *dilute* globular state[4]. This conclusion was questioned by Victor and Imbert[5] who, on the basis of Monte Carlo (MC) simulation, found that an *alternating* PA, in which oppositely charged monomers are periodically spaced along the chain, undergoes a coil-globule transition as the temperature is decreased, and that this transition exhibits all of the characteristics of the usual θ-point. Wittmer *et al.* then argued, on the basis of random phase approximation, that the Debye-Hückel theory is inapplicable to an *alternating* PA and that it behaves as a dielectric[6].

If the PA is only *statistically neutral*, when averaged over charge distribution, a swelling of the chain is observed in the MC simulations. This can be attributed to the presence of a net charge of the order $\pm q \sqrt{N}$, where $\pm q$ is a monomer charge and N is the length of the PA. This will then produce domains on a PA which will have the same net charge, and will tend to repel each other. It is this repulsion that causes a statistically neutral PA to swell[7].

As it stands, the situation remains quite unclear. Does a *neutral non-alternating* PA undergo a coil-globule transition, or does it exist in a collapsed dilute globule state for any temperature? In this letter we shall address these questions on the basis of the *full* Debye-Hückel theory (DH)[8] augmented by Bjerrum's idea of ion association[9] and Flory's affine network theory[10]. We shall demonstrate that in the low-temperature state a PA resembles an affine network (or a microgel)[11]. If the temperature is raised PA undergoes a first-order collapse transition into a dilute globular state. This behaviour is very different from that of a polymer whose monomers interact through a short-ranged potential.

Before proceeding any further, however, it is instructive to go back and review the results for a phase separation in a *restricted primitive model* (RPM). This model consists of $N = \varrho V$ hard spheres of diameter a, $(1/2) N$ carrying charge $+q$ and the rest $-q$, inside a medium of dielectric constant D. It has long been believed that this model should exhibit a liquid-gas phase separation between a high- and a low-density phases[12]. After twenty years of trying, Monte Carlo simulations have finally converged to the values for the critical parameters which are now believed to be within (3–6)% of reality[13]. It is natural to ask if DH theory can account for the observed phase separation. In fact it can easily be shown that the DH *limiting law* for the electrostatic *free-energy density*, $\beta f^{\mathrm{LL}} = -\kappa^3/12$, where $\beta = 1/k_{\mathrm{B}} T$ and $\kappa = \sqrt{4\pi\varrho/D k_{\mathrm{B}} T}$ is the inverse screening length, predicts critical parameters $(T_{\mathrm{c}}, \varrho_{\mathrm{c}})$ which are in complete *disagreement* with the MC simulations, both being too large by a factor of 9 to 10[12,14]. On the other hand, the *full* Debye-Hückel theory, which takes into account the excluded volume due to the presence of hardcores, predicts a critical temperature that is only 10% higher than the MC estimate[14,15]. Furthermore, accounting for the non-linearity omitted in the process of linearization[16] of the Poisson-Boltzmann equation, through Bjerrum's concept of dipole formation[9], brings the coexistence curve into a close agreement with MC[14,15]. This calculation can easily be extended to general dimension d, in particular, reproducing the Kosterlitz-Thouless[17] result of an infinite-order line of metal-insulator transitions in $2d$, with an additional prediction that this line terminates in a tricritrical point[18]. It is now natural to ask if this approach can help shed any more light on a conformational phase transition in a PA.

We consider an isolated polymer chain that has a total of N constitutional units of three different types, each spherical in shape with a diameter a, neutral monomers, as well as positive and negative monomers which can associate into dipole pairs producing intramolecular bridges. Let $N_1 = N_+ + N_-$ be the number of free (unassociated) charged monomers, N_2 the number of associated charged monomers (dipoles). Then the number of neutral monomers is $N_0 = N - N_1 - 2N_2$. The whole polymer can be viewed as a network of segments connected by crosslinks of functionality 4. The total free energy for the chain is then $F = F^{\mathrm{EL}} + F^{\mathrm{IN}}$, where F^{EL} is the elastic energy due to the elongation and contraction of

active strands of the network, and F^{IN} is the contribution to the free energy due to the interaction and mixing of monomers. (Note that in the text F will be used to indicate free energy, while $f = F/V$ is the free-energy density.) The goal of the theory is to take a proper account of these two contributions.

According to Flory's affine network theory of rubber elasticity, the elastic free energy of the network is [1, 10, 19]

$$\beta F^{EL} = \frac{\nu}{2}(\lambda_x^2 + \lambda_y^2 + \lambda_z^2) - \mu_J \ln(V/V_0), \tag{1}$$

where ν is the number of elastically active strands in the network, μ_J the number of junctions, $\lambda_x, \lambda_y, \lambda_z$ are the principal extension ratios measured with respect to the non-interacting Gaussian state of volume $V_0 = (4\pi/3)R_0^3$, with $R_0 \approx lN^{1/2}$ and l the average separation between the monomers, while V is the total volume spanned by the network. In our case we assume a uniform expansion so that $\lambda_x = \lambda_y = \lambda_z = \alpha$ and $V/V_0 = \alpha^3$. From geometrical considerations, $\nu = 2N_2 + 1$, $\mu_J = N_2 + 1$, and the elastic free energy then takes the form [19]

$$\beta F^{EL} = 3\left(\frac{\alpha^2 - 1}{2} - \ln(\alpha)\right) + 3N_2(\alpha^2 - 1 - \ln(\alpha)). \tag{2}$$

Following Flory [1], the excluded-volume interaction can be accounted for at a second virial level by

$$\beta F^{HC} = \frac{N}{2}\varrho W_1, \tag{3}$$

here $\varrho = \varrho_0 + \varrho_1 + 2\varrho_2 = N/V$ and W_1 is the excluded-volume coefficient. The electrostatic interaction between charged monomers leads to DH contribution to the free energy [8]

$$\beta F^{DH} = \frac{N_1}{T^*(\kappa a)^2}\left((\kappa a) - \frac{(\kappa a)^2}{2} - \ln(\kappa a + 1)\right), \tag{4}$$

where $(\kappa a)^2 = 4\pi\varrho_1^*/T^*$ while reduced density and temperature are $\varrho^* = \varrho a^3$, $T^* = k_B T D a/q^2$. The full expression for the DH free energy is used since it is this form that proved so successful in the study of Coulombic criticality. However, an important distinction between the RPM and the PA must be remembered. While in the RPM ions are free to move independently of each other, in the PA monomers are constrained by the bonds that maintain the integrity of the polymer. Thus, the basic theory of the RPM would, in addition to the interaction terms discussed above, require an ideal-gas contribution.

No such term is necessary for a PA. Nevertheless, even in the case of a PA it is necessary to account for an increase in the total free energy due to the entropy of mixing [19, 20]. If the bonds were cut and the chain were separated into a mixture of N_2 dipoles, N_1 monopoles, and N_0 neutral particles, the ideal-gas contribution to the free energy would be $\beta F^{id} = \sum_j N_j \ln(\varrho_j \Lambda_j^{3k_j}/\xi_j) - N_j$, where $\Lambda_j(T)$ is the mean thermal wavelength, $\Lambda_j(T) = h/\sqrt{2\pi \overline{m}_j k_B T}$, $\overline{m}_j$ is the geometric mean mass for a cluster of k_j atoms and $\xi_j(T)$ is the molecular partition function. In our case $k_0 = k_1 = 1$, $k_2 = 2$, and without loss of generality, $\overline{m}_0 = \overline{m}_+ = \overline{m}_- = \overline{m}_2$. In reality, of course, all the monomers are connected by bonds. To obtain the correct increase in the free energy it is then necessary to subtract from the

expression above the ideal free energy for a gas of free monomers [19]. We then find

$$\beta F^{\mathrm{MIX}} = \sum_j \left(N_j \ln (\varrho_j \Lambda_j^{3k_j} / \xi_j) - N_j \right) - \left(N \ln (\varrho \Lambda^3 / \xi) - N \right). \tag{5}$$

Furthermore, since it was assumed that all the monomers are spheres with no internal structure, $\xi = \xi_0 = \xi_1 = 1$, while

$$\xi_2(T) = 4\pi \int\limits_a^c \exp\left[a/T^* r\right] r^2 \, \mathrm{d}r \equiv K(T) \tag{6}$$

defines $K(T)$ as an association constant for the formation of bound dipole pairs (inter-molecular bridges). For a cut-off, c, we adopt Bjerrum's choice, $a/2T^*$ [9], which corresponds to the inflection point of the integral as a function of c, and is the length scale most naturally arising in the problem. Ebeling's careful analysis [21] showed that this value is consistent with the cluster expansion, in particular producing the exact asymptotic low-temperature behaviour. For an extensive discussion of the equilibrium constant see ref. [15]. It should also be mentioned that the dielectric constant appearing in eq. (6) can, in principle, differ from its bare value D, being strongly affected by the hydration forces. For the present, however, we shall neglect this effect. The total free energy is then $F = F^{\mathrm{EL}} + F^{\mathrm{DH}} + F^{\mathrm{HC}} + F^{\mathrm{MIX}}$.

In order to find the equilibrium configuration of the chain, this free energy must be minimized with respect to α under the constraint of chemical equilibrium between dipoles and monopoles, $\mu_+ + \mu_- = \mu_2$. The minimization condition is equivalent to the requirement that both the pressure and the chemical potential of the solvent are the same inside and outside the region occupied by the polymer. The chemical potential for the species j is $\mu_j = \partial F / \partial N_j$. Details of the calculations will be presented elsewhere [22]. In order to demonstrate our results it is convenient to define the following number fractions. Let f be the fraction of charged monomers in the polymer chain, while x the fraction of the charged monomers that form dipoles. It is then possible to express all the densities in terms of the total density ϱ, $\varrho_0 = (1-f)\varrho$, $\varrho_1 = (1-2x)f\varrho$, $\varrho_2 = xf\varrho$. The results of minimization are shown in fig. 1, with $W_1 = 4\pi a^3 / 3$, the value corresponding to the second virial coefficient for the gas of hard spheres, $N = 100$ and $f = 1$. For a range of temperatures, α is not a single-valued function, indicating that the first-order transition must take place. The transition occurs when the two locally stable branches of the free energy become equal. This temperature is indicated by a vertical line. If the fraction of charged monomers is lowered the transition temperature increases. In the low-temperature state, $x \approx 1/2$ and the radius of gyration scales as $R \sim l N^\nu$, with $\nu = 2/5$ (compare to the usual Flory exponent of $\nu = 3/5$). For higher temperatures, the polymer will collapse into a dilute globular state with $\nu = 1/3$. It is interesting to note the reversal in the behaviour from that of a polymer whose monomers interact through a *short*-range potential. In that case, it is the collapsed state that occurs at low temperature with the extended state being confined to the temperatures $T > \theta$. The reversal in behaviour is not hard to understand. The collapse in a PA is driven by a charge density fluctuation that induces around each charged monomer a distribution of charges of opposite sign. Within DH theory this net attraction is already evident at the level of the DH *limiting law* for the free-energy *density*, $\beta f^{\mathrm{LL}} \propto -\varrho^{3/2} / T^{3/2}$. This must be compared with an effective repulsive interaction expressed through the second virial contribution to the free-energy *density*, $\beta f^{\mathrm{HC}} = (W_1 / 2) \varrho^2$. It is evident that, for low densities, the DH contribution to the free energy will always dominate the hardcore repulsion, causing the PA to collapse. This, however, does not take into account the tendency of oppositely charged monomers to come together and to form intermolecular bridges. At low temperature this tendency is overwhelming, causing most of the charged monomers to pair up. Once the
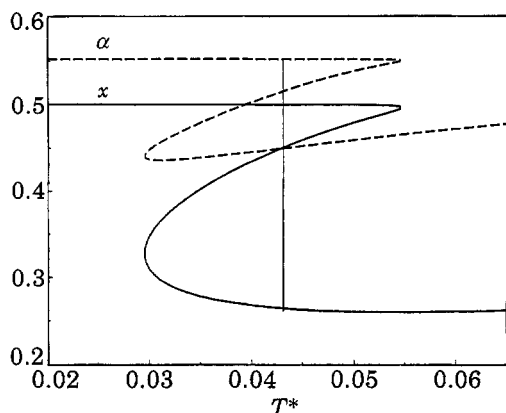
Fig. 1.

Fig. 2.

Fig. 1. – Behaviour of x and α as a function of temperature for $N = 100$, $f = 1$, and $W_1 = 4\pi a^3/3$ corresponding to the second virial coefficient for the gas of hard spheres. The non-single-valued dependence of α on the temperature indicates the presence of the first-order phase transition. The transition occurs at the temperature for which two locally stable branches of the free energy become equal and is indicated by the vertical line.
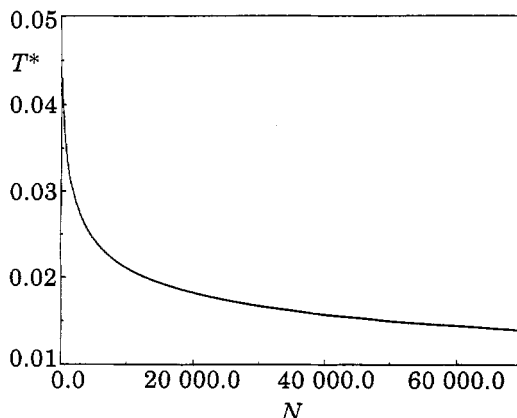
Fig. 2. – Dependence of the transition temperature on the length of the polyampholyte for $f = 1$ and $W_1 = 4\pi a^3/3$. For large N the decay is *close* to algebraic.

bridges are formed and the polymer resembles an affine network, there are not enough unpaired charged monomers left to produce any significant screening, diminishing the DH contribution all the way down to zero. The polymer then does not collapse but will, nevertheless, have an extension significantly lower than if the charged monomers were absent.

In fig. 2 we present the dependence of the transition temperature on the size of the polymer. From the graph it is evident that the transition temperature decreases as the length of the polymer grows. This is a manifestation of an increase in entropy for a longer PA, which favours a break-up of the intermolecular bridging. From the numerical analysis it appears that the decay of the transition temperature with the size of polymer is *close* to algebraic with $T_t \sim 1/N^\gamma$, however, the exponet γ is non-universal and depends on the value of W_1. If the quality of solvent is decreased, W_1 will decrease as well. At the θ line, $W_1 = 0$, and it is necessary to add an additional third virial contribution to the free energy $\beta F^{3V} = (1/2) W_2 N \varrho^2$. We then find that the size of the affine network scales with $\nu_\theta = 3/8$. When W_1 becomes negative the network collapses. The full three-dimensional phase diagram as well as the influence of the dipole-ion interactions on the phase transition will be presented in a subsequent publication[22].

Can this transition be observed under the normal laboratory conditions? An aqueous system around 300 K has a dielectric constant of $80\varepsilon_0$, ε_0 is the permittivity of vacuum, and is strongly dependent on the temperature. For the polymer with $N = 100$, this yields T_c around 100 K, and the transition into the microgel state cannot be realized in water under the normal laboratory conditions. The polymer will always exist in a dilute globule state. However, there are many organic solvents which have dielectric constants of around $20\varepsilon_0$ at 300 K. For these solvents the transition into the microgel phase should occur around the room temperature. In his experiments on ionic criticality Pitzer used as a solvent diphenyl ether which has a dielectric constant of around $4\varepsilon_0$; furthermore by mixing one-dodecanol with 1,4-butanediol he was able to vary the dielectric constant between $5\varepsilon_0$ and $30\varepsilon_0$[23]. We, thus, expect that

there should not be too much difficulty in finding an appropriate solvent for the experiments.

From our arguments it is evident that the absolute minimum of the free energy for the PA corresponds to a microgel. However, we expect that the full free energy for this complex system will have a large number of metastable minima. It is then possible that, as the temperature is lowered, PA will get trapped inside one of these states. Possibility of the glass transition will then have to be considered.

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