

Polymer and solution ion shielding in polyampholytic hydrogels

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This study has examined balanced and unbalanced polyampholyte hydrogel swelling transitions as a function of total polymer ion and bath salt concentration. The total polymer ion concentration ranged from 0 to 1.4 M and the bath salt concentration from 1 μ M to 1 M. Polyampholyte swelling transitions were studied experimentally using hydrogels with varying proportions of acryl-amido methyl propylsulfonic acid (AMPS-H), methacryl-amido propyl trimethyl ammonium chloride (MAPTA-Cl), and dimethyl acrylamide (DMAAm). The equilibrium swelling has been treated analytically using a modified Flory–Huggins model with ionic corrections which incorporate ion excluded volume effects. We have obtained qualitative agreement between our theory and experimental results and have discussed the limitations of our model. © 1998 Elsevier Science Ltd. All rights reserved.

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INTRODUCTION

Polyampholytic hydrogels are cross-linked polymer networks consisting of acidic, basic, and even neutral monomers. The physical properties of these materials depend on an intricate balance between attractive and repulsive ionic interactions, solvent mediated effects, and the network elasticity. In addition, ion dissociation and the presence of other small ions can create a very sensitive physical state dependence on the surrounding bath composition. Understanding the competing interactions within polyampholytes and their dependence on external control variables is crucial to the successful application of these materials in many technologies. In addition, the physical properties of these materials are also relevant to the study of protein folding, spin glass transitions, and other soft condensed matter phase transitions.

The relative monomeric composition of acidic, basic, and undissociable neutral groups plays a particularly important role in determining the physical properties of polyampholytes. The specific role of charge asymmetry on the conformation of random polyampholyte polymers has received much attention. Higgs and Joanny concluded that a charge offset of $|(f_B^+ - f_A^-)| > u(f_A^- + f_B^+)^{3/2}$ is required to produce a swelling transition in polyampholytes, where f_B^+ and f_A^- represent the fraction of completely dissociated basic and acidic monomers, respectively, and u is the ratio of the Bjerrum length to the monomer size¹. Based on renormalization group arguments and extensive Monte Carlo simulations Kantor and Kardar concluded that polyampholytes with N monomers, where e is the unit charge, require a

charge offset of $eN^{1/2}$ to produce a swelling transition^{2,3}. A study by Dobrynin and Rubinstein concluded that polyampholytes with $N_+ = f_B^+N$ positive monomers and $N_- = f_A^-N$ negative monomers having a charge asymmetry of $|N_+ - N_-| > u(N_+ + N_-)^{1/2}$ are dominated by solvent, repulsive electrostatic, and finally attractive electrostatic effects as the temperature decreases⁴.

Compared to polyampholyte polymers in dilute solution, the effects of polymer ion charge concentration and charge offset in macroscopic polyampholytic hydrogels can behave quite differently. The effects of counter and co-ions in aqueous solutions cannot be ignored at very low ionic strengths. Even in the absence of added salt, hydrogen and hydroxide ions are always present in aqueous solutions. In a macroscopic hydrogel any form of polymer charge imbalance will be accompanied by counter-ions on a Debye length scale. In addition, the charge density and offset can create a much different internal mobile ion concentrations than that present in the surrounding bath^{5,6}.

Many theories which incorporate solution and polymer ion screening have their foundations based on classic ionic solution theory^{7,8}. In particular, the use of the lowest order correction to the Mayer virial expansion, or the Debye–Hückel limiting law (DHLL), has been the most popular^{4,9,10}. For polymer ion and bath salt concentrations exceeding 10 mM, however, the DHLL gives unphysically large negative osmotic pressures^{6,11}. Higher order approximations in a Mayer virial expansion, such as the Debye–Hückel limiting law + second virial coefficient (DHLL + B₂) and hypernetted chain (HNC) approximations, are necessary to include the excluded volume effects needed to avoid diverging osmotic pressure contributions^{12,13}.

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Using neutral monomeric spacers in polyampholytes with different charge offsets it should, in principle, be possible to examine the different screening effects from polymer ions and the mobile counter- and co-ions. This study, therefore, examines the swelling transitions of balanced and unbalanced polyampholyte hydrogels as a function of polymer charge density and bath salt concentration. Copolymer hydrogel swelling transitions with varying proportions of acryl-amido methyl propylsulfonic acid (AMPS-H), methacryl-amido propyl trimethyl ammonium chloride (MAPTA-Cl), and dimethyl acrylamide (DMAAm) are studied experimentally. Using varying concentrations of neutral monomers and by examining the swelling behaviour as a function of bath salt concentration, the competing effects of ion dissociation, polyelectrolyte repulsion, polyampholyte attraction, and solvent interactions are illustrated. The equilibrium swelling is studied analytically using a modified Flory–Huggins model with ionic corrections suitable for ion concentrations up to 1 M.

EXPERIMENTAL

To examine the specific role the polymer ion density has on the equilibrium properties of balanced and unbalanced polyampholytes, copolymer hydrogels with varying proportions of acryl-amido methyl propylsulfonic acid (AMPS-H), methacryl-amido propyl trimethyl ammonium chloride (MAPTA-Cl), and dimethyl acrylamide (DMAAm) were synthesized. The monomer charge balance point in a stock solution of AMPS-MATPA was estimated using a counterion precipitation technique and the silver salt of AMPS-H. A 1.0 M AMPS-Ag solution was prepared by reacting an aqueous solution of AMPS-H at approximately 4°C with Ag₂CO₃. The AMPS-Ag solution was centrifuged at 3000 rpm and filtered with a 0.2 μm filter. A 1.0 M solution of AMPS-MAPTA was then made by adding MAPTA-Cl and filtering out the AgCl precipitate with a 0.2 μm filter. Small aliquots of the AMPS-MAPTA stock solution were tested with MAPTA-Cl and AMPS-Ag to ensure the solution had an approximately equal concentration of AMPS and MAPTA monomers.

In all cases the hydrogels were cross-linked using 8.6 mM *N,N'*-methylene-bis-acrylamide (BIS), polymerization was initiated using 1.76 mM ammonium persulfate (APS), and the gelation temperature was 60°C. Hydrogel samples with a net charge offset were made by adding MAPTA-Cl while keeping the total monomer concentration at 1.4 M. The hydrogels were formed in 500 μm inner diameter micropipettes and all samples were washed continuously and in parallel for several days to ensure equilibrium had been obtained.

THEORETICAL BACKGROUND

The model system we consider in this study consists of a hydrogel and bath phase. Dissociable acidic and basic monomeric groups and undissociable neutral monomers are restricted to the hydrogel phase. Mobile ions are free to distribute themselves between the bath and hydrogel phases according to the chemical potential set by the bath ion concentrations. As described in previous studies^{5,6,14} the condition for thermodynamic equilibrium arises when the free energy becomes an extremum or equivalently the chemical potential of the solvent and mobile ion components balance in each phase.

Balance of solvent chemical potentials is equivalent to

osmotic pressure balance, that is,

$$-\frac{1}{\nu_{\text{site}}}[\ln(1 - \phi) + \phi + \chi\phi^2] + \frac{\phi_0}{N_x \nu_{\text{site}}} \left[\frac{1}{2} \left(\frac{\phi}{\phi_0} \right) - \left(\frac{\phi}{\phi_0} \right)^{\frac{1}{3}} \right] + \left(\sum_{i=0}^{\sigma} c_i^{\text{H}} + \frac{\pi_{\text{ex}}^{\text{H}}}{k_{\text{B}}T} \right) - \left(\sum_{i=0}^{\sigma} c_i^{\text{B}} + \frac{\pi_{\text{ex}}^{\text{B}}}{k_{\text{B}}T} \right) = 0, \quad (1)$$

where ν_{site} represents the molar lattice site volume, ϕ the volume fraction, ϕ_0 the reference state volume fraction, c the solvent interaction parameter, N_x the number of monomers between cross-links, k_{B} is the Boltzmann constant, T the absolute temperature, and c_i the number concentration of the i th ion. The first and second terms of equation (1) represent osmotic pressure contributions arising from the solvent and network elasticity. The remaining terms represent the difference in the osmotic pressures between the hydrogel and the bath. Each of these terms contains an ideal and excess osmotic pressure, π_{ex} , correction. The superscripts H and B refer to the hydrogel and bath phases, respectively, and σ to the total number of ion species.

In the DHLL + B₂ approximation the excess osmotic pressure is

$$\left(\frac{\pi_{\text{ex}}}{k_{\text{B}}T} \right)_{\text{DHLL} + \text{B}_2} = -\frac{5\kappa^3}{192\pi} - \sum_{i=1}^{\sigma} \sum_{j=1}^{\sigma} c_i c_j S_{ij}(\kappa) - \frac{\kappa}{8\pi\epsilon\epsilon_0 k_{\text{B}}T} \sum_{i=1}^{\sigma} \sum_{j=1}^{\sigma} c_i c_j S'_{ij}(\kappa), \quad (2)$$

where ϵ is the dielectric constant of the medium and ϵ_0 the permittivity of free space. The term κ represents the inverse Debye length and is defined as

$$\kappa = \sqrt{\frac{\sum_{i=1}^{\sigma} c_i z_i^2 e^2}{\epsilon\epsilon_0 k_{\text{B}}T}} \quad (3)$$

where z_i is the i th ion valence. The terms S_{ij} and S'_{ij} are defined as

$$S_{ij}(\kappa) = 2\pi \int_0^{\infty} \left\{ \exp\left[-\frac{u_{ij}^*(r)}{k_{\text{B}}T}\right] \times \exp(q_{ij}) - 1 \right\} r^2 dr \quad (4)$$

and

$$S'_{ij}(\kappa) = 2\pi \int_0^{\infty} \left\{ \exp\left[-\frac{u_{ij}^*(r)}{k_{\text{B}}T}\right] \times \exp(q_{ij}) - 1 \right\} \times \exp(-\kappa r) r^2 dr \quad (5)$$

where u_{ij}^* is the hard core Coulombic interaction between ions i and j and

$$q_{ij}(r) = -\left(\frac{z_i z_j e^2}{4\pi\epsilon\epsilon_0 k_{\text{B}}Tr} \right) \exp(-\kappa r) \quad (6)$$

The excess osmotic pressure can also be calculated from integral equation methods that give the pair correlation function using the pressure equation modified to include more than one component

$$\left(\frac{\pi_{\text{ex}}}{k_{\text{B}}T} \right)_{\text{DHLL} + \text{B}_2} = -\frac{1}{6} \sum_{i=1}^{\sigma} \sum_{j=1}^{\sigma} c_i c_j \int_0^{\infty} r \frac{\partial u_{ij}}{\partial r} g_{ij}(r) 4\pi r^2 dr \quad (7)$$

where g_{ij} is the pair correlation function.

The chemical potential of the i th ionic species in the hydrogel phase is given by the relation

$$\mu_i^0 + k_B T \ln c_i^H + z_i e \phi^H + k_B T \ln \gamma_i^H = \mu_i^0 + k_B T \ln c_i^B + z_i e \phi^B + k_B T \ln \gamma_i^B \quad (8)$$

where μ_i^0 is the standard state chemical potential of the i th ion and j the uniform contribution to the potential created by the hydrogel boundary double layers, and γ_i is the activity coefficient of the i th ion. This leads to relations between ions i and j of the form

$$\left(\frac{C_i^H \gamma_i^H}{C_i^B \gamma_i^B} \right)^{\frac{1}{z_i}} = \left(\frac{C_j^H \gamma_j^H}{C_j^B \gamma_j^B} \right)^{\frac{1}{z_j}} \quad (9)$$

where we use capital letters to represent molar quantities.

Equality of chemical potentials between unbound and bound hydrogen ion states can be expressed as

$$\begin{aligned} \mu_{A^-}^0 + k_B T \ln c_{A^-}^H + z_{A^-} e \phi^H + k_B T \ln \gamma_{A^-}^H + \mu_{H^+}^0 \\ + k_B T \ln c_{H^+}^H + z_{H^+} e \phi^H + k_B T \ln \gamma_{H^+}^H = \mu_{AH}^0 \\ + k_B T \ln c_{AH}^B + k_B T \ln \gamma_{AH}^B \end{aligned} \quad (10)$$

where subscripts A^- , H^+ , and AH are associated with the dissociated, free hydrogen ion, and bound states, respectively. A similar relation can be written for base dissociation. In terms of the acid and base dissociation constants this is equivalent to the relations

$$K_a = \frac{\gamma_{A^-} C_{A^-} \gamma_{H^+} C_{H^+}}{\gamma_{AH} C_{AH}} \quad (11)$$

and

$$K_b = \frac{\gamma_{BOH} C_{BOH} \gamma_{H^+} C_{H^+}}{\gamma_{B^+} C_{B^+}} \quad (12)$$

Solutions to the above equations have been described in previous studies¹¹.

RESULTS AND DISCUSSION

Figure 1 shows the swelling of cationic polyampholytes equilibrated in a 0.1 mM NaCl bath that results with increasing proportions of charged monomers. A 0.1 mM NaCl bath was used to minimize the effects of ion

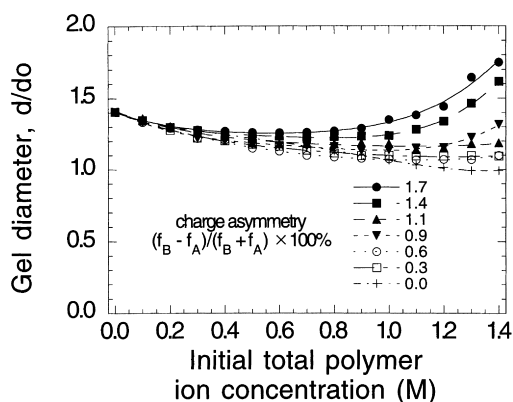


Figure 1 Swelling of cationic polyampholytes equilibrated in a 0.1 mM NaCl bath with increasing proportions of charged monomers normalized to the original casting diameter d_o . With increasing proportions of charged monomers an initial collapse transition results when there is a large background of balanced positive and negative monomers. Increasing charge asymmetry leads to polyelectrolyte repulsive effects which dominate the swelling response at higher polymer charge densities.

dissociation. Over the observed polymer charge concentration range balanced polyampholytes show a de-swelling transition with increasing relative proportions of positive and negative monomers. Unbalanced polyampholytes exhibit an initial de-swelling transition followed by a swelling transition at higher charge concentrations. Although the total monomeric concentration at preparation remains the same in all cases, changing the monomeric composition can alter the polymer reference state volume fraction, the effective solvent interaction, and even the elasticity. A great deal of intuition, however, can still be obtained by examining the swelling contributions predicted from ionic solution theory.

Figure 2 shows that in the DHLL + B_2 approximation the osmotic pressure initially becomes increasingly more negative as the charged monomer concentration increases. With further increases in polymer ion density, however, the osmotic pressure eventually rises. Increasing charge offsets result in increasing polyelectrolyte or osmotic pressure effects. In comparison with the experimental results of Figure 1 it also appears that at high ionic strengths the assumption of freely mobile monomeric ions is not entirely correct. The excluded volume effects in the DHLL + B_2 approximation give rise to marked increases in swelling even in unbalanced polyampholytes.

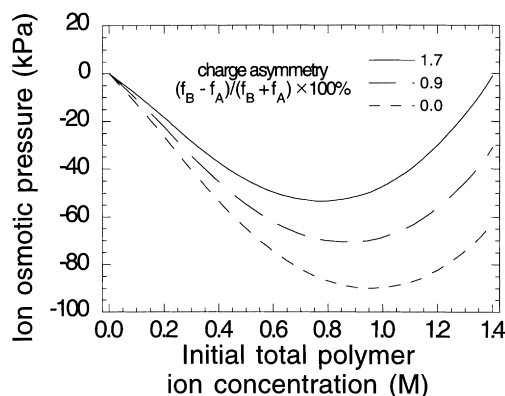


Figure 2 The two phase DHLL + B_2 approximation predicts an initial decrease and then an increase in ion osmotic pressure with increasing polymer ion concentration. The initial decrease in osmotic pressure is the result of the large background of balanced positive and negative polymer ions. At high monomer and bath ion concentrations the excluded volume and polyelectrolyte effect make a positive contribution to the ion osmotic pressure.

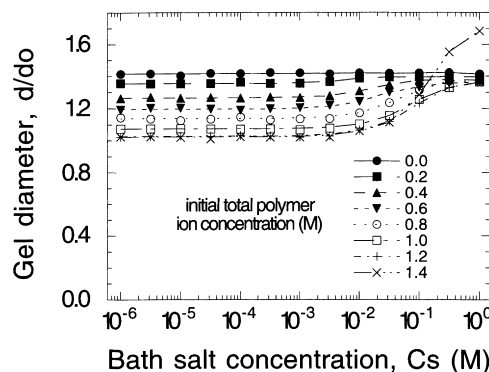


Figure 3 Equilibrium swelling of balanced polyampholytes with different proportions of neutral monomers versus bath salt concentration. Neutral DMAAm hydrogels do not respond to changes in bath salt concentration. Hydrogels with a balanced concentration of positive and negative monomers, however, give rise to swelling transitions when the bath salt concentration is increased.

Figure 3 shows the equilibrium swelling pattern of balanced polyampholytes that results when the bath salt concentration is varied. At low bath ionic strengths increasing the background of positive and negative charges causes a de-swelling transition. Hydrogels consisting entirely of neutral DMAAm monomers do not respond to changes in bath salt concentration. Hydrogels with increasing concentrations of balanced positive and negative charges, however, show progressively greater swelling transitions with increasing bath salt concentration.

Figure 4 shows the equilibrium swelling of balanced polyampholytes predicted by the DHLL + B₂ approximation with fixed elastic and solvent components. At low bath ionic strengths increasing the monomer ion concentration up to 1 M gives progressively greater negative osmotic pressures. As indicated in Figure 2, however, increasing the monomer ion concentration beyond 1 M results in a greater osmotic pressure from the excluded volume effect. Increasing the surrounding bath concentration gives rise to swelling transitions from both the polyampholyte screening and the hard core effects. Despite the fact that changing the monomeric composition will change the solvent quality and possibly the elasticity, the predicted swelling shown in Figure 4 is in qualitative agreement with the experimental data shown in Figure 3.

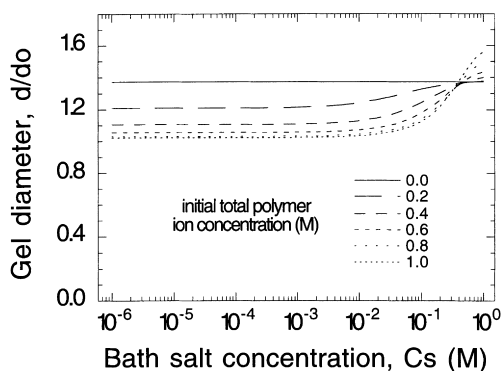


Figure 4 Equilibrium swelling predicted by the two phase DHLL + B₂ approximation with fixed elastic and solvent contributions. In the DHLL + B₂ approximation the ionic contribution to the osmotic pressure in balanced polyampholytes monotonically increases with bath salt concentration. Up to a total monomer ion concentration of 1 M the osmotic pressure becomes more negative at low bath ionic strengths.

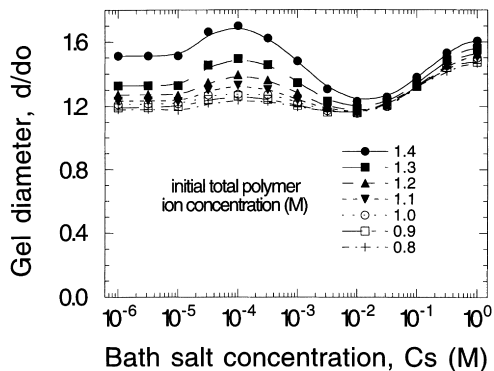


Figure 5 Equilibrium swelling of unbalanced polyampholytes with initial total polymer ion concentrations ranging from 0.8 to 1.4 M versus bath salt concentration normalized to the original casting diameter d_0 . The charged monomer component had a 1.43% asymmetry during preparation in all cases. With a large proportion of charged monomers the competing polyelectrolyte and polyampholyte effects are evident.

Figures 5 and 6 show the effect of washing polyampholytes with different bath salt concentrations where the dissociable monomeric component has a 1.4% basic monomer offset. As expected, neutral hydrogels consisting of only DMAAm show no swelling response to changes in bath salt concentration. By gradually increasing the relative proportion of acidic and basic monomers the competing dissociation, polyampholyte, and polyelectrolyte effects become evident. At low ion strengths base dissociation of the MAPTA monomers results in a small de-swelling transition. With increasing bath salt concentrations hydroxide ions are exchanged for chloride ions. Further increases in bath salt concentration show the characteristic effects of polyelectrolyte de-swelling and finally polyampholyte swelling.

A direct comparison of our experimental results with current theories of polyampholyte swelling transitions is problematic for a number of reasons. Attempting to incorporate polyampholyte effects using only the Debye-Hückel correction failed at the ion concentrations of interest in this study. As a result, it has been necessary to include higher order ionic solutions theory correction. The DHLL + B₂ approximation used in this study, however, requires greater charge offsets to agree with our data. This appears to be a limitation of considering the polyampholyte network as a freely mobile plasma. The elongation of the individual polyampholyte polymers with increasing charge offset and the effects of interacting double layers should be considered in future studies.

CONCLUSIONS

At low polymer and bath ion concentrations an increasing background of balanced positive and negative monomers results in an increasingly negative contribution to the osmotic pressure. Balanced polyampholytes exhibit swelling transitions with increasing bath salt concentration. Both a two phase ionic solution theory and experimental results give balanced polyampholyte swelling transitions that occur between 10 mM and 1 M.

Unbalanced polyampholytes with a relatively large background of positive and negative charges show ion dissociation effects at bath ion concentrations below 0.1 mM. Polyelectrolyte screening occurred at lower salt concentrations than polyampholyte screening. The application of classic ionic solution theories to polymer ion

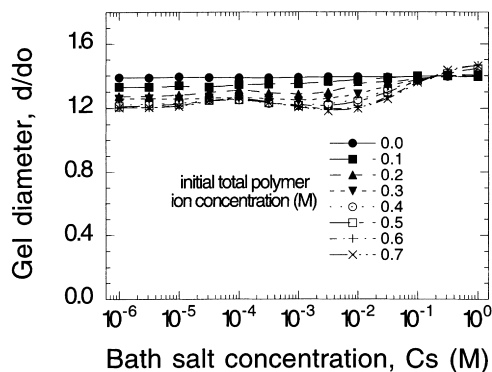


Figure 6 Equilibrium swelling of unbalanced polyampholytes with initial total polymer ion concentrations ranging from 0 to 0.7 M versus bath salt concentration normalized to the original casting diameter d_0 . With increasing proportions of neutral monomers the electrostatic contributions to the swelling response are diminished.

screening appear to break down at polymer ion concentrations on the order of 1 M. In future, we would expect that osmotic pressure expansions which simultaneously include the constrained polymer interactions and higher order ionic interactions will be necessary to capture the equilibrium and non-equilibrium behaviour of polyampholytic hydrogels.

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