

# Swelling properties of acrylamide-based ampholytic hydrogels: comparison of experiment with theory

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Ampholytic hydrogels were synthesized by copolymerizing acrylamide with specialty monomers. Two monomers, [(methacrylamido)propyl]trimethylammonium chloride (MAPTAC) and sodium styrene sulfonate (SSS), were copolymerized with acrylamide to form one ampholytic hydrogel. Also, the zwitterionic monomers *N*-(3-sulfopropyl)-*N*-methacrylamidopropyl-*N,N*-dimethylammonium betaine (SB1) and *N*-(3-sulfopropyl)-*N*-methacroyloxyethyl-*N,N*-dimethylammonium betaine (SB2) were both, in turn, copolymerized with acrylamide to form ampholytic hydrogels. Swelling equilibria were measured in water and in aqueous sodium chloride solutions ranging in concentration from  $10^{-5}$  to 5 M. Antipolyelectrolyte behaviour was observed for the ampholytic hydrogels prepared; hydrogel swelling increases as the sodium chloride concentration rises. To demonstrate theoretically antipolyelectrolyte behaviour for ampholytic hydrogels, we incorporate the Debye-Hückel theory of electrolyte solutions into a Flory-type swelling model to account for Coulombic interactions between fixed and mobile ions. Calculated swelling equilibria are in qualitative agreement with experiment.

(Keywords: ampholytic hydrogel; swelling model; polyacrylamide)

## INTRODUCTION

Polymeric ampholytes, materials containing cationic and anionic functional groups, have received much recent attention<sup>1–6</sup>. The properties of polymeric ampholyte materials include hydrophilicity, good biocompatibility, moderately high mechanical strength in the water-swollen state, and adjustable permeability to liquids depending on the type of fixed-charge groups present and the conditions of polymer preparation. The foremost practical use of ampholytic polymers is in the preparation of membranes with high water flux for biomedical applications<sup>7</sup>.

Linear ampholytic polymers with a balanced stoichiometry (equal numbers of negative and positive monomers) are known to be water-soluble only in the presence of low-molecular-weight salt; chain expansion increases in salt solutions of high concentration. This behaviour has been attributed to intra- and/or inter-macromolecular attractions between ionic groups and the screening of these attractions by the added salt<sup>4,8,9</sup>. Since linear polyelectrolytes may be characterized by a marked decrease in end-to-end distance in salt solutions, the behaviour of stoichiometrically balanced ampholytic polymers in aqueous salt solutions has been referred to as antipolyelectrolyte behaviour in the literature<sup>10</sup>.

Antipolyelectrolyte behaviour for ampholytic hydrogels is characterized by increasing water content in response to *rising* ionic strength in the external solution. Conversely, polyelectrolyte swelling behaviour for ionized hydrogels is characterized by increasing water content in response to *declining* ionic strength.

Swelling equilibria for covalently crosslinked ampholytic polymers have been reported in the literature<sup>10–26</sup>. Ampholytic hydrogels can be prepared by copolymerizing (in the presence of a divinyl crosslinking monomer) a monomer containing an anionic functional group with a monomer containing a cationic functional group<sup>17–26</sup>; alternatively, a zwitterionic monomer can be used, such as a sulfobetaine<sup>10–16</sup>. It has been shown that the swelling of ampholytic hydrogels made by the former method can be correlated by the stoichiometry of the material<sup>17,20,21,23</sup>; antipolyelectrolyte swelling behaviour has been observed near a net fixed-charge density of zero, while polyelectrolyte behaviour has been observed when the net fixed-charge density deviates from zero.

Below we present a simple Flory-type swelling model including Donnan equilibria to describe the swelling equilibria of acrylamide-based ampholytic hydrogels; we generalize the gel swelling theory presented by Flory<sup>27</sup> to the case where the gel contains both fixed cationic and fixed anionic charges (ampholytic gels). Calculated swelling equilibria are compared with the swelling data we have reported previously<sup>20</sup>.

In the present work, we also report results for swelling equilibria in aqueous salt solutions for acrylamide-based

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ampholytic hydrogels that have higher overall fixed-charge densities than those studied previously<sup>20</sup>; in the previous work the overall fixed-charge density of the hydrogels studied was 5 mol% whereas in the present work it is 20 mol%. The higher charge density is expected to show more pronounced antipolyelectrolyte swelling behaviour when the net charge on the hydrogel is near zero. Independent of ampholytic behaviour, enhanced swelling may also occur due to salting-in of the polymer. To control for such enhanced swelling at appreciable NaCl concentrations, an uncharged polyacrylamide hydrogel was also synthesized.

Flory-type hydrogel swelling models based on ideal Donnan theory cannot predict antipolyelectrolyte swelling behaviour because the electrostatic forces between ions are not considered directly. To account for Coulombic interactions between ions, fixed and mobile, we superimpose the Debye–Hückel theory of electrolyte solutions onto the swelling model. The Flory-type swelling model, including the Debye–Hückel theory, is capable of demonstrating antipolyelectrolyte behaviour: an increase in hydrogel swelling in response to rising solution ionic strength.

## EXPERIMENTAL SECTION

### Materials

Acrylamide (AAM) and *N,N'*-methylenebisacrylamide (BIS) were supplied by Eastman Kodak. [(Methacrylamido)propyl]trimethylammonium chloride (MAPTAC) (50% by weight in aqueous solution) and sodium styrene sulfonate (SSS) were obtained from Aldrich. Ammonium persulfate (APS) and sodium chloride (NaCl) were purchased from Fisher. The sulfobetaine monomers, *N*-(3-sulfopropyl)-*N*-methacrylamidopropyl-*N,N*-dimethylammonium betaine (SB1) and *N*-(3-sulfopropyl)-*N*-methacryloxyethyl-*N,N*-dimethylammonium betaine (SB2), were provided by Exxon. All reagents were used as received. All water used in synthesis and swelling measurements was distilled and then purified and filtered through a Barnstead Nanopure II system.

### Synthesis

Hydrogels were prepared by aqueous free-radical copolymerization. The composition of each hydrogel was determined by the nominal amounts of reagents present in the hydrogel feed solution. The following parameters were used to define this composition:

$$\%T = \frac{\text{mass of all monomers (g)}}{\text{volume of water (ml)}} \times 100 \quad (1)$$

$$\%C = \frac{\text{moles of BIS in feed solution}}{\text{total moles of monomer in feed solution}} \times 100 \quad (2)$$

$$\%CM = \frac{\text{moles of comonomer in feed solution}}{\text{total moles of monomer in feed solution}} \times 100 \quad (3)$$

Three acrylamide-based ampholytic hydrogels were prepared. By design, the three ampholytic hydrogels were nominally prepared with no net charge and with overall fixed-charge densities of 20% of all network structural

units (10% cationic structural units and 10% anionic structural units). One ampholytic hydrogel was prepared using the comonomers MAPTAC and SSS; this hydrogel, denoted AAm/MAPTAC/SSS, was 15%*T*, 0.2%*C*, 10%*MAPTAC* and 10%*SSS*. Two other ampholytic hydrogels were prepared using the zwitterionic sulfobetaine monomers SB1 and SB2; these hydrogels, denoted AAm/SB1 and AAm/SB2, were 15%*T*, 0.2%*C* and 10%*SB*. A fourth, uncharged polyacrylamide hydrogel was synthesized to serve as a control; this hydrogel, denoted AAm, was 15%*T* and 0.2%*C*. Note that %*T* and %*C* were held constant (at 15 and 0.2 respectively) in this work. The SB1 and SB2 monomers are sparingly soluble in pure water; to accommodate these two monomers, all syntheses were performed in 0.01 M NaCl.

To illustrate the synthetic procedure, we give details for the preparation of the AAm/MAPTAC/SSS hydrogel. Added to 48.3 ml gas-free aqueous NaCl (0.01 M) were 4.26 g AAm, 0.023 g BIS, 3.32 ml MAPTAC solution, 1.55 g SSS and 0.005 g APS. The solution was stirred with a magnetic spin bar until well mixed, then injected with a large-bore needle between silanized glass plates (10 cm<sup>2</sup>) separated by a 1.0 mm Teflon gasket. The plate assemblies were immersed in a water bath heated to 50°C. After 24 h, the hydrogel sheets were freed from the plates; discs were then punched from the sheets using a cork borer. The hydrogel discs were soaked in pure water, which was refreshed periodically to extract the NaCl, soluble fraction and initiator residues.

### Swelling studies

Hydrogels were swollen to equilibrium in an excess of water. Equilibrium was reached in one week; approach to equilibrium was monitored by mass measurement of the swollen hydrogels. Once equilibrium was attained, the swelling ratio in water was determined for each hydrogel. Equilibrated discs were weighed, dried at room temperature and reweighed. The swelling ratio in water is defined as the mass ratio of swollen hydrogel to dry hydrogel.

Aqueous solutions of NaCl were prepared ranging in concentration from 10<sup>-5</sup> to 5.0 M. Hydrogel discs were transferred from water to each of the salt solutions and were allowed to equilibrate. NaCl solutions bathing the hydrogels were changed every other day. Mass measurements of the hydrogels were taken to monitor for the attainment of equilibrium. After two weeks, mass measurements did not change. The swelling ratio in aqueous NaCl is obtained by dividing the equilibrium mass of the hydrogel by its dry mass.

All swelling studies were performed in triplicate. Table 1 gives mean swelling ratios in aqueous NaCl and corresponding standard deviations.

## SWELLING THEORY FOR ACRYLAMIDE-BASED AMPHOLYTIC HYDROGELS

### Flory-type swelling model

The model presented here is similar to that presented by Flory in his classic text<sup>27</sup>. Whereas Flory used the affine network theory to describe network elasticity, we use the phantom network theory<sup>28</sup>, which is more appropriate when considering highly swollen, acrylamide-based networks<sup>29</sup>. Also, we generalize Flory's gel swelling

**Table 1** Swelling ratios (g swollen gel/g dry gel) for 15%T, 0.2% C hydrogels in aqueous sodium chloride solutions. Values in parentheses are standard errors

NaCl (M)	Uncharged	SB1 <sup>a</sup>	SB2 <sup>b</sup>	MAPTAC/SSS <sup>c</sup>
0.000010	19.3(0.8)	24.6(0.1)	21.5(0.6)	369.3(34.6)
0.00010	19.3(0.8)	23.8(0.1)	21.9(0.3)	255.5(10.9)
0.0010	–	23.2(0.5)	21.7(0.4)	28.7(0.4)
0.010	19.6(0.7)	23.5(0.4)	22.0(0.5)	23.9(2.5)
0.10	20.1(0.2)	25.7(0.4)	23.7(0.3)	20.4(2.6)
1.0	23.5(1.0)	30.0(4.0)	33.4(4.0)	61.3(4.5)
5.0	31.9(1.8)	45.4(0.2)	42.9(2.7)	75.1(7.1)

<sup>a</sup> Ampholytic hydrogel prepared with 10% zwitterionic sulfobetaine monomer SB1

<sup>b</sup> Ampholytic hydrogel prepared with 10% zwitterionic sulfobetaine monomer SB2

<sup>c</sup> Ampholytic hydrogel prepared with 10% cationic monomer (MAPTAC) and 10% anionic monomer (SSS)

theory to the case where the gel contains both fixed cationic and fixed anionic charges (ampholytic gels).

In principle, calculation of swelling equilibria for a hydrogel equilibrium swollen in an aqueous solution containing a single salt requires solution of two equations with two unknowns. The two equations arise from setting the chemical potential of the salt equal in both gel and bath, and setting the chemical potential of water equal in both gel and bath. The chemical potential of water is expressed in this work through the (osmotic) swelling pressure.

When a hydrogel (phase  $\alpha$ ) is in equilibrium with its surroundings (phase  $\beta$ ):

$$\mu_i^\alpha = \mu_i^\beta \quad (4)$$

where  $\mu_i^\alpha$  is the chemical potential of  $i$  in the hydrogel and  $\mu_i^\beta$  is the chemical potential of  $i$  in the external solution. Equation (4) holds for all diffusible components, including ions, that exist both in the hydrogel and in the external solution. For an ion,  $\mu_i$  represents the electrochemical potential. When  $i$  represents the solvent (water, component 1), equation (4) is commonly recast in the form:

$$\Delta\Pi_{\text{swelling}} = -\frac{\mu_1^{\text{gel}} - \mu_1^{\text{bath}}}{V_1} = 0 \quad (5)$$

where  $\Delta\Pi_{\text{swelling}}$  is the osmotic-pressure difference between the hydrogel and the external solution (also called the swelling pressure) and  $V_1$  is the solvent molar volume. The osmotic swelling pressure  $\Delta\Pi_{\text{swelling}}$  is zero at equilibrium. Assuming that  $\Delta\Pi_{\text{swelling}}$  is the sum of three independent contributions<sup>27</sup>, we write:

$$\Delta\Pi_{\text{swelling}} = \Delta\Pi_{\text{mixing}} + \Delta\Pi_{\text{elastic}} + \Delta\Pi_{\text{ion}} = 0 \quad (6)$$

where  $\Delta\Pi_{\text{mixing}}$  is the contribution from polymer-solvent mixing,  $\Delta\Pi_{\text{elastic}}$  is the elastic contribution from deforming the hydrogel network and  $\Delta\Pi_{\text{ion}}$  represents the contribution from mobile and bound ions.

**Polymer-solvent mixing.** For  $\Delta\Pi_{\text{mixing}}$ , we need a model for a non-crosslinked polymer-solvent system. For the present work, we choose the simple Flory-Huggins theory:

$$\Delta\Pi_{\text{mixing}} = \frac{RT}{V_1} [\ln(1 - \phi_2) + \phi_2 + \chi\phi_2^2] \quad (7)$$

Here,  $R$  is the gas constant,  $T$  is temperature,  $\phi_2$  is the volume fraction of polymer in the hydrogel and  $\chi$  is the Flory parameter that characterizes the polymer-solvent interaction energy.

**Network elastic contribution.** For isotropic swelling of a perfect tetrafunctional network, the phantom network theory gives:

$$\Delta\Pi_{\text{elastic}} = -C_c RT \left( \frac{\phi_2}{\phi_{2c}} \right)^{1/3} \quad (8)$$

where  $C_c$  is the concentration of crosslinks in the reference state, i.e. at hydrogel preparation, and  $\phi_{2c}$  is the volume fraction of hydrogel in the reference state.

**Ionic contribution.** The presence of fixed charges on the polymer network, plus the requirement of bulk electroneutrality, mandate that an unequal distribution of mobile ions exists between hydrogel and external solution; this produces an additional contribution  $\Delta\Pi_{\text{ion}}$  to the swelling pressure  $\Delta\Pi_{\text{swelling}}$ . Ideal Donnan equilibria have been used to characterize this contribution to the swelling pressure for acrylamide-based hydrogels<sup>30,31</sup>. A complete description of the effect of fixed and mobile ions on hydrogel swelling would require expressions for ion-ion, ion-solvent and ion-polymer interactions; these interactions are neglected in ideal Donnan equilibria, which give the expression:

$$\Delta\Pi_{\text{ion}} = RT \sum_i (C_i^{\text{gel}} - C_i^{\text{bath}}) \quad (9)$$

where  $C_i^{\text{gel}}$  and  $C_i^{\text{bath}}$  represent, respectively, mobile-ion concentrations within the hydrogel and in the bath (external solution). Equation (9) assumes that ion concentrations are small and that the solvent osmotic coefficient is unity.

The concentration of salt in the external solution is fixed by experimental conditions. The concentration of mobile ions within the hydrogel is calculated according to Donnan equilibria: first, the chemical potential of an ionic species in the hydrogel phase must be equal to its chemical potential in the external solution, and secondly, the constraint of electroneutrality is placed on all charged species, fixed and mobile, in the hydrogel phase. For a hydrogel in solution containing a single 1:1 salt we have:

$$(C_+^{\text{gel}})(C_-^{\text{gel}}) = (C_s^{\text{bath}})^2 \quad (10)$$

where  $C_+^{\text{gel}}$  and  $C_-^{\text{gel}}$  refer, respectively, to the concentration of cations and anions in the hydrogel and  $C_s^{\text{bath}}$  refers to the concentration of 1:1 electrolyte in the external solution. Equation (10) assumes that the mean ionic activity coefficient of the diffusible salt in the hydrogel phase is equal to that in the bath. To maintain electroneutrality, the number of positive ions must equal the number of negative ions in the hydrogel phase. We write for univalent electrolytes:

$$C_+^{\text{gel}} + IC_{\text{mc}} \frac{\phi_2}{\phi_{2c}} = C_-^{\text{gel}} + JC_{\text{mc}} \frac{\phi_2}{\phi_{2c}} \quad (11)$$

where  $I$  and  $J$  represent, respectively, the fraction of monomer units in the hydrogel that contain bound positive and negative charges, and  $C_{\text{mc}}$  is the concentration of monomer at network formation. At swelling equilibrium, the second term on the left-hand side of

equation (11) gives the concentration of fixed positive charges in the hydrogel phase, while the second term on the right-hand side gives the concentration of fixed negative charges in the hydrogel phase.

**Calculation of swelling equilibria.** In principle, the elastic and ionic terms in equation (6) contain no adjustable parameters:  $C_c$  is a function of the nominal crosslink density (%C),  $\phi_{2c}$  is calculated from %T,  $I$  and  $J$  are determined from the nominal amounts of comonomers present during hydrogel synthesis,  $V_1$  is  $18 \text{ cm}^3 \text{ mol}^{-1}$  and  $C_s^{\text{bath}}$  is fixed by experimental conditions. The mixing contribution contains the Flory  $\chi$  parameter that was fitted to swelling data for *uncharged* polyacrylamide hydrogels reported by Hooper *et al.*<sup>31</sup>; for this fitting, the ionic contribution of equation (6) was set to zero, leaving only the mixing and elastic terms. The optimal  $\chi$  was 0.48, a physically reasonable value. The  $\chi$  parameter was held constant in the calculations described below.

For given hydrogel and solution conditions, equilibrium swelling is determined by substituting equations (7), (8) and (9) into equation (6), and substituting for  $C_+^{\text{gel}}$  in equation (10) by using equation (11). These steps leave two equations with two unknowns,  $\phi_2$  and  $C_-^{\text{gel}}$ . An iterative procedure using a generalized Newton–Raphson routine (Universal Technical Systems Inc., Rockford, IL) was used to solve the equations.

#### Debye–Hückel theory for ampholytic hydrogels

The expression for the hydrogel swelling pressure  $\Delta\P_{\text{swelling}}$  (equation (6)) is a balance of forces. The mixing term  $\Delta\P_{\text{mixing}}$  is positive and favours hydrogel swelling, while the elastic term  $\Delta\P_{\text{elastic}}$  is negative and opposes it. In the model presented earlier, the ion term  $\Delta\P_{\text{ion}}$  is always positive and favours hydrogel swelling, except for ampholytic hydrogels whose charges are exactly balanced (net zero charge); in this case,  $\Delta\P_{\text{ion}}$  is zero. A swelling model that demonstrates antipolyelectrolyte behaviour for ampholytic hydrogels should contain an expression for  $\Delta\P_{\text{ion}}$  that may be negative and oppose hydrogel swelling under certain situations including when a hydrogel has a balanced charge complement.

To account for antipolyelectrolyte behaviour for hydrogels, we superimpose the Debye–Hückel theory of electrolyte solutions onto the swelling model. Under some conditions, addition of this theory allows us to calculate negative values for  $\Delta\P_{\text{ion}}$  that oppose hydrogel swelling. Higgs and Joanny<sup>2</sup> have developed a similar theoretical description for the dimensions (swelling) of linear polyampholyte chains in salt solutions. Khokhlov and coworkers<sup>25,32</sup> have developed a similar description for swelling of ampholytic hydrogels.

We insert mean ionic activity coefficients  $\gamma_{\pm}$  into equation (10):

$$(C_+^{\text{gel}})(C_-^{\text{gel}})(\gamma_{\pm}^{\text{gel}})^2 = (C_s^{\text{bath}})^2(\gamma_{\pm}^{\text{bath}})^2 \quad (10a)$$

Extended Debye–Hückel theory is used to calculate the activity coefficients<sup>33</sup>:

$$\ln \gamma_{\pm} = - \left( \frac{|z_+ z_-| F^2}{8 \pi \epsilon_0 \epsilon N_A R T} \right) \left( \frac{\kappa}{1 + \kappa a} \right) \quad (12)$$

where  $\kappa$  is the inverse screening length

$$\kappa^2 = \frac{F^2}{\epsilon_0 \epsilon R T} \sum_i C_i z_i^2 \quad (13)$$

and where  $N_A$  is Avogadro's number,  $a$  is the ion radius,  $F$  is the Faraday constant,  $C_i$  is the anion or cation concentration,  $z_i$  is the anion or cation valence,  $\epsilon_0$  is the permittivity of vacuum and  $\epsilon$  is the dielectric constant of water. For 1:1 electrolytes,  $a$  is of the order of 3 or 4 Å<sup>34</sup>. We set  $a$  equal to 3.04 Å for this work. This value of  $a$  has been used by others so that, for an aqueous solution of 1:1 electrolyte at 25°C,  $\gamma_{\pm}$  is a function of the square root of the salt concentration, expressed in moles per litre<sup>35</sup>. We set  $\epsilon$  equal to 78.3 (the dielectric constant of pure water).

Equation (9) for  $\Delta\P_{\text{ion}}$  is rewritten to include terms that arise from the Debye–Hückel theory:

$$\Delta\P_{\text{ion}} = (\Pi_{\text{ion,gel}} - \Pi_{\text{ion,bath}}) \quad (9a)$$

In equation (9a), for the external solution,  $\Pi_{\text{ion,bath}}$  is given by<sup>35</sup>:

$$\Pi_{\text{ion,bath}} = RT \sum_i C_i^{\text{bath}} - \frac{RT}{N_A} \frac{\kappa_{\text{bath}}^3}{24\pi} \sigma(\kappa_{\text{bath}} a) \quad (14)$$

where

$$\sigma(\kappa a) = \frac{3}{(\kappa a)^3} \left( 1 + \kappa a - \frac{1}{1 + \kappa a} - 2 \ln(1 + \kappa a) \right) \quad (15)$$

$\Pi_{\text{ion,bath}}$  contains two terms: the ideal ' $\Pi = CRT$ ' term and the Debye–Hückel correction term. The ideal, entropically derived osmotic pressure is diminished by electrostatic interactions between ions. This Debye–Hückel term appears in equation (14) when equation (10a) is used to derive the chemical potential of water in an electrolyte solution through integration of the Gibbs–Duhem equation<sup>35</sup>. When  $\kappa a$  is much less than 1 (dilute limit),  $\sigma$  approaches unity, recovering the familiar term (proportional to  $\kappa^3/24\pi$ ) from the Debye–Hückel limiting law<sup>34</sup>. The mobile-ion concentrations in the bath, shown in the summation in equation (14), are implicitly used to calculate the inverse screening length,  $\kappa_{\text{bath}}$ .

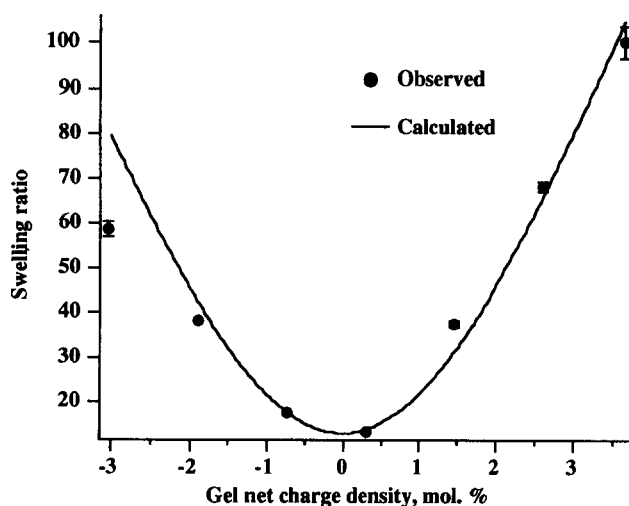
The situation is somewhat different for  $\Pi_{\text{ion,gel}}$  because of the presence of fixed charges in the hydrogel phase. We use equation (14) to calculate  $\Pi_{\text{ion,gel}}$ , but we include the fixed charges on the gel network along with the mobile ions when calculating the inverse screening length  $\kappa_{\text{gel}}$ . We include only the mobile ionic species in the hydrogel phase in the summation for the entropically derived ideal term  $\Pi = CRT$ .

## RESULTS AND DISCUSSION

### Comparison of experiment with theory for lightly charged ampholytic hydrogels

First, we demonstrate that the simple swelling model without a Debye–Hückel contribution qualitatively describes the swelling equilibria of lightly charged acrylamide-based ampholytic hydrogels. This model is based on ideal Donnan theory.

Figure 1 shows calculated and measured swelling equilibria in water for seven acrylamide-based ampholytic hydrogels. The experimental data are from Baker *et al.*<sup>20</sup>. The hydrogels prepared by Baker *et al.* were identical, except that the net fixed-charge density (%MPTAC – %SSS) in the hydrogels varied from +3.6% to –3.0%; the overall fixed-charge density (%MPTAC + %SSS) was held constant at 4.5%. Although not shown here, calculated swelling equilibria



**Figure 1** Observed and calculated swelling ratios (g swollen gel/g dry gel) in pure water for amphotytic hydrogels. The net charge density (per cent cationic structural units – per cent anionic structural units) of the hydrogels varied from  $-3.0$  to  $+3.6\%$ , while the amount of charged structural units in the hydrogels was fixed at  $4.5\%$ . The hydrogels were  $16\%T$  and  $0.2\%C$ . Experimental data from Baker *et al.*<sup>20</sup>

are in qualitative agreement with experiment when the calculations use the nominal hydrogel preparation parameters (initial total monomer concentration  $\%T$ , mole per cent crosslinking monomer  $\%C$ , mole per cent cationic monomer  $\%MAPTAC$ , mole per cent anionic monomer  $\%SSS$ ) reported by Baker *et al.*; the semi-quantitative agreement shown here was obtained by adjusting the mole per cent crosslinker ( $\%C$ ) from  $0.4$  reported by Baker *et al.* to  $0.6$ . We give our rationale for adjusting this parameter below.

In Figure 1, the measured swelling ratios are not symmetric with respect to the hydrogel isoelectric point; at the same absolute value of fixed-charge density the hydrogels containing net cationic character consistently swell to a greater extent than the hydrogels containing net anionic character. The asymmetry in the observed swelling behaviour is related to physicochemical differences in the charged monomers chosen for the study<sup>20</sup>. In contrast, the calculated swelling ratios are symmetric with respect to the hydrogel isoelectric point; the specific properties of the charged comonomers used by Baker *et al.*<sup>20</sup> are not considered by the simple theory. Similar asymmetric swelling behaviour in water was observed by Katayama *et al.*<sup>17</sup> for a series of acrylamide-based hydrogels prepared with various amounts of the cationic monomer trimethyl(*N*-acryloyl-3-aminopropyl)-ammonium chloride and the anionic monomer sodium acrylate.

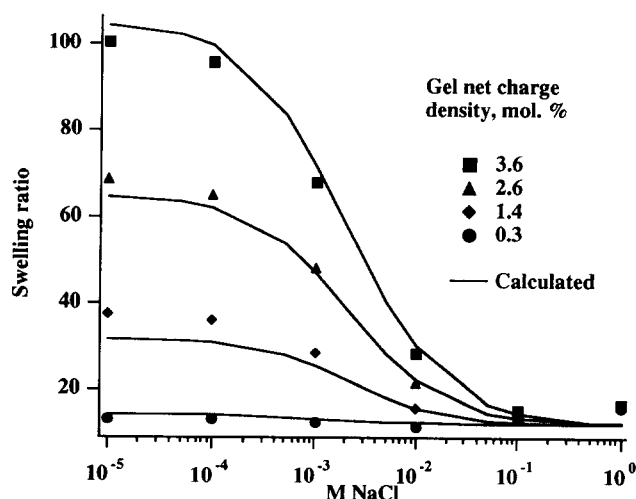
Figure 2 shows calculated and measured swelling equilibria in aqueous NaCl solutions for net cationic acrylamide-based amphotytic hydrogels; the net fixed-charge density of the hydrogels varied from  $+0.3\%$  to  $+3.6\%$  ( $\%MAPTAC - \%SSS$ ). The experimental data are from Baker *et al.*<sup>20</sup>. Qualitative agreement between theory and experiment was obtained using the nominal hydrogel preparation parameters ( $\%T$ ,  $\%C$ ,  $\%MAPTAC$ ,  $\%SSS$ ) reported by Baker *et al.*; semi-quantitative agreement was obtained by adjusting the crosslink density ( $\%C$ ) from  $0.4$  reported by Baker *et al.* to  $0.6$ . Baker *et al.* prepared their hydrogels with the same nominal crosslink density; the same value for  $\%C$ ,  $0.6$ ,

was used for the generation of all curves shown in Figure 2. The effective crosslink density ( $0.6$ ) is larger than the nominal crosslink density ( $0.4$ ) because, perhaps, the fixed positive and negative charges interact with each other inside the hydrogel to form effective crosslinks. These interacting ion pairs would provide additional crosslinking over and above the covalent crosslinks characterized by the  $C_c$  parameter of equation (8). Because we do not consider the formation of inter-chain charge complexes in the simple theoretical treatment, the presence of these effective crosslinks may be taken into account by increasing the value of  $C_c$ .

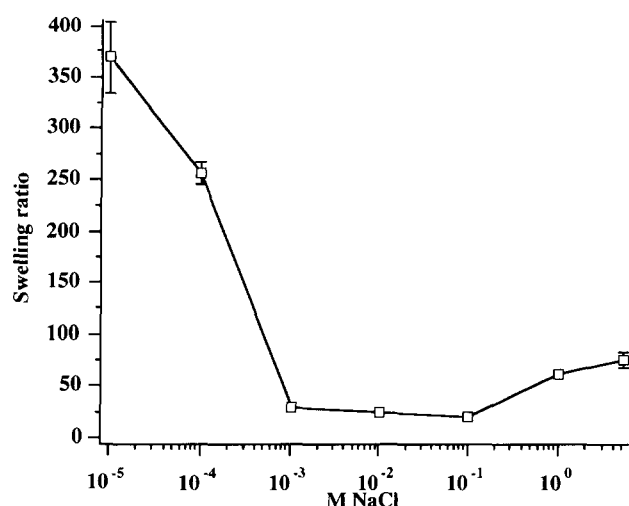
The swelling behaviour observed in Figure 2 may be understood by noting that the number of osmotically active (mobile) ions in the hydrogel phase increases as the molar ratio of fixed cationic charges to fixed anionic charges diverges from unity. Conversely, the ability of an amphotytic hydrogel to neutralize itself is enhanced as the molar ratio of fixed cationic charges to fixed anionic charges approaches unity; when the hydrogels are swollen to equilibrium in low-ionic-strength media (or in salt-free water), excess free ions that are not needed to satisfy electroneutrality are effectively dialysed from the hydrogel interior. In low-ionic-strength media (or in salt-free water), as the ability of an amphotytic hydrogel to self-neutralize falls, the greater is the number of osmotically active counterions inside the hydrogel. It is the presence of these osmotically active counterions that drives hydrogel swelling in low-ionic-strength media.

In Figure 2, all hydrogels collapse as the NaCl concentration rises. Free exchange of mobile ions and solvent occurs between the hydrogel and the external solution. The concentration of osmotically active, mobile ions is greater inside the hydrogel owing to the presence of fixed charges, but the difference in mobile-ion concentration between the hydrogel and the external solution decreases as the ionic strength of the external solution rises.

These simple arguments provide good agreement between calculated and observed swelling equilibria. The Donnan equilibria-based calculations correctly predict that an amphotytic hydrogel with balanced cationic and anionic charges (net zero charge) is not sensitive to



**Figure 2** Observed and calculated swelling equilibria in aqueous NaCl for net cationic amphotytic hydrogels. Experimental data from Baker *et al.*<sup>20</sup>. The calculated points are connected by straight lines



**Figure 3** Observed swelling equilibria in aqueous NaCl for the AAm/MAPTAC/SSS hydrogel. This hydrogel was nominally prepared with 15%T, 0.2%C, 10%MAPTAC and 10%SSS

changes in ionic strength of the swelling medium. Conversely, these calculations correctly predict swelling behaviour in salt solutions characteristic of polyelectrolyte hydrogels as the molar ratio of cationic charge to anionic charge in the hydrogel diverges from unity.

#### Experimental results for moderately charged ampholytic hydrogels

We have obtained experimental results for acrylamide-based ampholytic hydrogels that have higher overall fixed-charge densities (per cent cationic structural units plus per cent anionic structural units) than those in the hydrogels studied earlier<sup>20</sup>. The fixed-charge densities in the new studies are 20% versus 4.5% in the previous research.

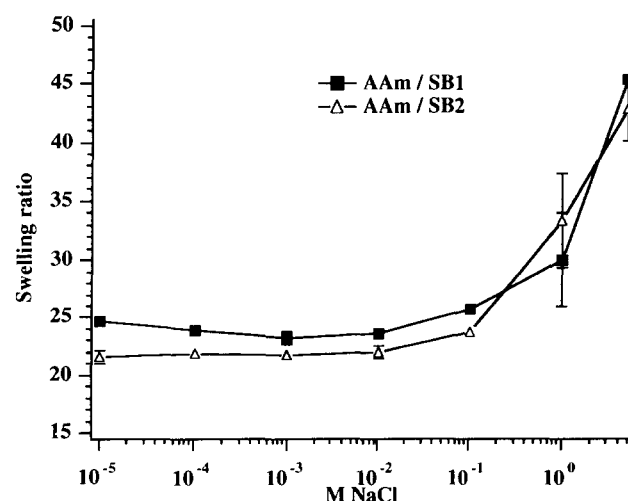
Figure 3 shows measured swelling equilibria in aqueous NaCl solutions for the AAm/MAPTAC/SSS hydrogel, which achieved a swelling ratio of over 350 in  $10^{-5}$  M NaCl; swelling declines with rising NaCl concentration up to 0.1 M NaCl. This hydrogel was nominally prepared with 10 mol% cationic monomer (MAPTAC) and 10 mol% anionic monomer (SSS). Because of the balanced reaction stoichiometry, we expected that this hydrogel would not demonstrate polyelectrolyte behaviour and be relatively unswollen in low-ionic-strength media; however, as shown in Figure 3, significant polyelectrolyte behaviour was observed.

As shown in Figure 3, the AAm/MAPTAC/SSS hydrogel demonstrated antipolyelectrolyte swelling behaviour in that it reswelled with rising NaCl concentration above 0.1 M NaCl. This reswelling gives the swelling curve in Figure 3 an overall U-shape in which the hydrogel is least soluble in aqueous NaCl at intermediate NaCl concentrations. Corpart and Candau<sup>4</sup> synthesized a series of linear ampholytic copolymers from the cationic monomer [2-(methacryloyloxy)ethyl]trimethylammonium chloride (MADQUAT) and the anionic monomer sodium 2-acrylamido-2-methylpropanesulfonate (NaAMPS). The ratio of cationic monomer to anionic monomer was varied in the syntheses, and the solution properties of the resulting copolymers were studied. Corpart and Candau observed that a net charged ampholytic copolymer

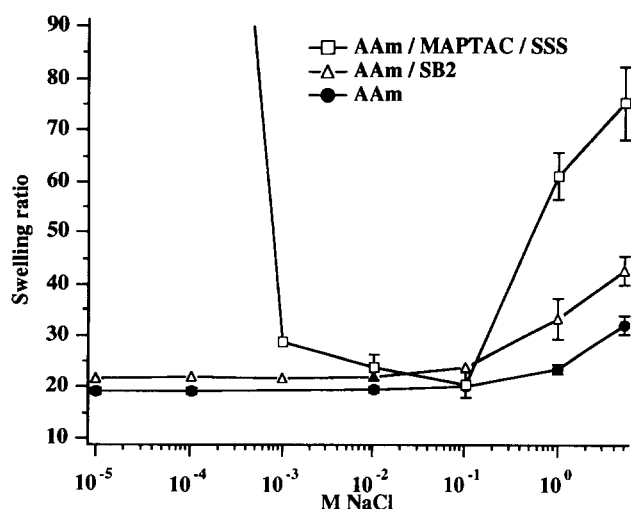
containing 68% MADQUAT and 32% NaAMPS was soluble in pure water and in aqueous NaCl solution up to about 0.01 M, was insoluble at intermediate NaCl concentrations, and was soluble at NaCl concentrations above 1 M. A plot of optical transmission versus NaCl concentration is U-shaped for an aqueous solution of this linear copolymer, indicating that a phase boundary is crossed at about 0.01 M NaCl and again at about 1 M. Corpart and Candau<sup>4</sup> suggest that the addition of a small amount of salt to an aqueous solution of the copolymer screens the electrostatic repulsions between charges of like signs, allowing the chains to contract and precipitate; upon further addition of salt, resolubilization occurs by the screening of attractive interactions between charges of opposite signs. Analogous behaviour is seen for the AAm/MAPTAC/SSS hydrogel in Figure 3: Below 0.001 M NaCl, the effect of osmotically active counterions on swelling is reduced and electrostatic repulsions between fixed charges of the same signs are screened with rising NaCl concentration, causing the hydrogel to collapse. In the intermediate concentration range 0.001 to 0.1 M the hydrogel is least solvophilic. Above 0.1 M NaCl electrostatic attractions between fixed charges of opposite signs are screened and the hydrogel reswells.

The results shown in Figure 3 indicate that it is difficult to produce a net-zero-charge ampholytic hydrogel (with a moderate overall fixed-charge density) from an AAm/MAPTAC/SSS/BIS copolymerization. In subsequent syntheses, we replaced the cationic MAPTAC and the anionic SSS with zwitterionic sulfobetaine monomers (SB1, SB2). Using a zwitterionic monomer provides a relatively simple way to produce an ampholytic hydrogel with net zero charge. On the other hand, because of the close proximity of the cationic and anionic charges in the zwitterionic monomers, intra-group associations are possible; only inter-group associations of fixed charges are possible between fixed charges in the AAm/MAPTAC/SSS hydrogel. Thus, qualitative differences in swelling behaviour are expected between the sulfobetaine-containing hydrogels and the AAm/MAPTAC/SSS hydrogel.

Figure 4 shows swelling equilibria in aqueous NaCl solutions for the AAm/SB1 and AAm/SB2 hydrogels. The



**Figure 4** Observed swelling equilibria in aqueous NaCl for the AAm/SB1 and AAm/SB2 hydrogels. These hydrogels were nominally prepared with 15%T, 0.2%C and 10%SB



**Figure 5** Comparison of swelling equilibria in aqueous NaCl solutions for the AAm/MAPTAC/SSS, AAm/SB2 and AAm hydrogels. The AAm hydrogel was nominally prepared with 15%T and 0.2%C

swelling of these hydrogels is relatively insensitive to rising NaCl concentration from  $10^{-5}$  to 0.01 M as expected because they have essentially net zero charge. A slight decrease in swelling with rising NaCl concentration was observed for the AAm/SB1 hydrogel, suggesting a non-zero charge density that produces polyelectrolyte behaviour. Osmotically active counterions principally drive the swelling of charged hydrogels; the AAm/SB2 hydrogel appears to be self-neutralized, and thus free of osmotically active counterions. Figure 4 shows that the AAm/SB1 and AAm/SB2 hydrogels began to swell with rising NaCl concentration once the NaCl concentration reached a threshold value of 0.01 M. Screening of electrostatic attractions between fixed charges of opposite signs may result in the observed antipolyelectrolyte swelling behaviour; overall, the swelling ratios of both sulfobetaine-containing hydrogels increase by a factor of 2 when transferred from  $10^{-5}$  M NaCl to 5 M NaCl.

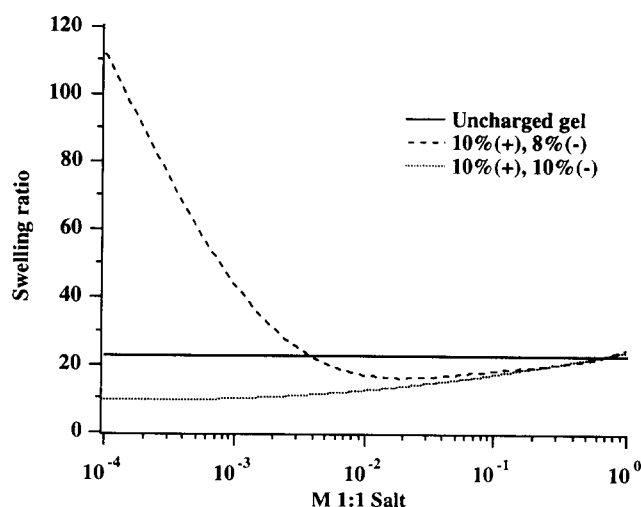
Figure 5 shows a comparison of swelling equilibria in aqueous NaCl solutions for two acrylamide-based ampholytic hydrogels (AAm/MAPTAC/SSS and AAm/SB2) plus an uncharged acrylamide-based hydrogel (AAm); some of the swelling data shown in Figures 3 and 4 are replotted in Figure 5. All three hydrogels were prepared with the same %T and %C (15 and 0.2, respectively) to ensure similarity in their physical networks. Both AAm/MAPTAC/SSS and AAm/SB2 hydrogels exhibit antipolyelectrolyte swelling behaviour; interestingly, the screening of electrostatic attractions between fixed charges allows the AAm/SB2 hydrogel to reach a swelling ratio that is only 57% of that for the AAm/MAPTAC/SSS hydrogel. This discrepancy in swelling may be related to the positioning of the fixed charge groups with these two hydrogels. The addition of NaCl breaks up the ionic associations and frees the charged functionalities for aqueous solubilization of the polymer. In the AAm/SB2 hydrogel, the presence of residual intra-group associations may impair the water solubilizing effect of the ionic functionalities and render the AAm/SB2 hydrogel less hydrophilic than the AAm/MAPTAC/SSS hydrogel.

The uncharged AAm hydrogel was synthesized to serve as a control; its swelling was found to increase with

rising salt concentration (Figure 5). In our experience, virtually all acrylamide-based hydrogels we have studied exhibit an increase in swelling as the external salt concentration rises from 0.1 to 1.0 M NaCl<sup>20,31</sup>. This increase in swelling occurs at moderate salt concentrations where specific ion-solvent and ion-polymer interactions may be important<sup>36</sup>. We have not observed a similar salting-in effect in our studies of relatively hydrophobic *N*-isopropylacrylamide-based hydrogels in aqueous electrolyte solutions<sup>37,38</sup>. Therefore, some of the antipolyelectrolyte behaviour we have observed in the present study may actually be a consequence of specific interactions between NaCl and the acrylamide-based polymer networks.

#### Results of Debye-Hückel calculations

Figure 6 shows calculated swelling equilibria for three hydrogels in a 1:1 electrolyte solution. The three hydrogels are an uncharged hydrogel, a net-zero-charge hydrogel containing 10% cationic structural units and 10% anionic structural units, and a net cationic hydrogel containing 10% cationic structural units and 8% anionic structural units. The calculations were performed by inserting the Debye-Hückel theory into the swelling model presented earlier. All three hydrogels are *structurally equivalent* in that for the calculated results shown in Figure 6 the polymer-solvent interaction parameter  $\chi$  was fixed at 0.48; also, %T and %C were fixed at 15 and 0.2, respectively. The calculations were performed for 1:1 electrolyte concentrations ranging from  $10^{-5}$  to 1.0 M; the form of the Debye-Hückel theory used in this work is accurate to a concentration of 0.1 M; calculated swelling ratios at an electrolyte concentration of 1.0 M are extrapolations. The error in this extrapolation is not large because the calculated swelling ratios for the two ampholytic hydrogels at 1.0 M are very close to that for the uncharged gel, as expected. As explained below, we expect the hydrogels to attain similar degrees of swelling once all electrostatic interactions between fixed charges have been effectively screened by added 1:1 electrolyte.



**Figure 6** Calculated swelling equilibria in aqueous 1:1 electrolyte solutions for three 15%T, 0.2%C hydrogels. One hydrogel had a net zero charge and contained 10% cationic structural units and 10% anionic structural units; another had a net positive charge and contained 10% cationic structural units and 8% anionic structural units; the third hydrogel contained no charged structural units

Figure 6 compares the calculated swelling ratios for the uncharged hydrogel with those for the net-zero-charge ampholytic hydrogel. As expected, swelling for the uncharged hydrogel is insensitive to the electrolyte concentration in the bath (external solution). However, for the net-zero-charge ampholytic hydrogel, antipolyelectrolyte behaviour is seen; swelling is an increasing function of the 1:1 electrolyte concentration. The swelling of the net-zero-charge ampholytic hydrogel falls below that of the uncharged hydrogel at all ionic strengths except 1.0 M, where their swelling ratios are essentially the same. For a net-zero-charge ampholytic hydrogel, the net electrostatic forces are attractive; therefore, its swelling is less than that of the *structurally equivalent* uncharged hydrogel. The origin of the attractive force is the screening effect present in ionic solutions. In pure solvent, each fixed charge attracts an atmosphere of fixed charges of opposite sign, leading to a net decrease in electrostatic energy and to deswelling of the hydrogel. The addition of salt screens the electrostatic interactions between fixed charges, tending to swell the net-zero-charge ampholytic hydrogel to the dimensions of the uncharged hydrogel.

Figure 6 also shows calculated swelling equilibria for a net cationic ampholytic hydrogel (10% cationic, 8% anionic). Both polyelectrolyte and polyampholyte behaviour is seen. Swelling decreases as ionic strength rises to 0.01 M; above 0.01 M, swelling increases with rising ionic strength.

The hydrogel structural parameters (fixed-charge content, %T, %C,  $\chi$  parameter) used to generate the calculated curves in Figure 6 were chosen so that qualitative comparison could be made with the experimental results shown in Figure 5. Figure 6 shows that the swelling (in aqueous electrolyte solution) of a net-zero-charge ampholytic hydrogel is less than the swelling of the *structurally equivalent* uncharged hydrogel. However, Figure 5 shows experimental results for ampholytic hydrogels and the nominally structurally equivalent uncharged hydrogel; not once in Figure 5 does a swelling ratio of an ampholytic hydrogel fall below that for the uncharged hydrogel. A possible explanation of this discrepancy between calculated and observed results follows from polymer-solvent interactions. The calculations assume that placing fixed charges on a polymer network has no influence on polymer-solvent interactions; in the calculations, we assumed  $\chi$  to be independent of the charge density of the network. Placing fixed charges onto a polymer network renders the network more hydrophilic, thereby decreasing the effective  $\chi$  parameter for the network. In the experimental results shown in Figure 5, the increase in network hydrophilicity for the ampholytic hydrogels is large enough to counteract the effect of electrostatic attractions between charged groups of opposite signs, so that swelling below that for the structurally equivalent uncharged hydrogel is not observed.

As shown in Figure 6, a U-shaped swelling curve may be calculated if it is assumed that an ampholytic hydrogel contains 10% cationic structural units and 8% anionic structural units. The calculated results suggest that of the order of 1 or 2 mol% of the anionic comonomer was not incorporated into the AAM/MAPTAC/SSS hydrogel. The osmotic activity of the counterions (present in an ampholytic hydrogel with a net charge) is primarily

responsible for the high swelling ratios reached at the low values of ionic strength ( $\leq 0.001$  M).

## CONCLUSIONS

Hydrogel swelling that increases with external salt concentration is called antipolyelectrolyte behaviour for hydrogels. Such behaviour is obtained in ampholytic hydrogels when electrostatic attractions between fixed charges opposite in sign are screened by the addition of salt.

Ideal Donnan theory describes qualitatively the swelling of lightly charged acrylamide-based ampholytic hydrogels in water and in aqueous NaCl. Swelling calculations based on ideal Donnan theory are compared with experimental data reported by Baker *et al.*<sup>20</sup>. Ideal Donnan theory is not capable of describing antipolyelectrolyte behaviour for ampholytic hydrogels, but no significant antipolyelectrolyte behaviour was observed by Baker *et al.* for lightly charged ampholytic hydrogels.

However, hydrogel behaviour changes when the overall fixed-charge density increases from 4.5 to 20 mol%. Antipolyelectrolyte behaviour is observed for one hydrogel prepared by copolymerizing acrylamide with an anionic monomer and a cationic monomer and also for two hydrogels prepared by copolymerizing acrylamide with zwitterionic monomers. Differences in solution behaviour for the two different types of ampholytic hydrogels prepared for this work can be explained by considering how the fixed charges are distributed within the hydrogels. Some of the increase in swelling at appreciable NaCl concentrations ( $> 0.1$  M) for the ampholytic hydrogels may be attributed to salting-in of the acrylamide-based polymer.

Antipolyelectrolyte swelling behaviour for ampholytic hydrogels can be demonstrated theoretically by extending the swelling model based on ideal Donnan theory through inclusion of the Debye-Hückel theory of electrolyte solutions to account for electrostatic interactions between charges, fixed and mobile. Although the calculations are only semi-quantitative, it is possible to calculate a swelling curve for a net-zero-charge ampholytic hydrogel that is an increasing function of ionic strength.

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## REFERENCES

- 1 Bekturov, E. A., Kudaibergenov, S. E. and Rafikov, S. R. *J. Macromol. Sci.-Rev. Macromol. Chem. Phys. (C)* 1990, **30**(2), 233
- 2 Higgs, P. G. and Joanny, J.-F. *J. Chem. Phys.* 1991, **94**(2), 1543
- 3 McCormick, C. L. and Johnson, C. B. *J. Macromol. Sci. Chem. (A)* 1990, **27**(5), 539

- 4 Corpart, J.-M. and Candau, F. *Macromolecules* 1993, **26**, 1333
- 5 Corpart, J. M., Selb, J. and Candau, F. *Polymer* 1993, **34**(18), 3873
- 6 Knoesel, R., Ehrmann, M. and Galin, J. C. *Polymer* 1993, **34**(9), 1925
- 7 Philipp, B., Kötz, J., Linow, K.-J. and Dautzenberg, H. *Polym. News* 1991, **16**, 106
- 8 Michaels, A. S. *Ind. Eng. Chem.* 1965, **57**(10), 32
- 9 Peiffer, D. G. and Lundberg, R. D. *Polymer* 1985, **26**, 1058
- 10 Huglin, M. B. and Rego, J. M. *Macromolecules* 1991, **24**, 2556
- 11 Salamone, J. C., Volksen, W., Israel, S. C. and Raia, D. C. *Polym. Prepr.* 1974, **15**(2), 291
- 12 Salamone, J. C., Volksen, W., Israel, S. C., Olson, A. P. and Raia, D. C. *Polymer* 1977, **18**, 1058
- 13 Itoh, Y., Abe, K. and Senoh, S. *Makromol. Chem.* 1986, **187**, 1691
- 14 Huglin, M. B. and Rego, J. M. *Polymer* 1991, **32**(18), 3354
- 15 Rego, J. M. and Huglin, M. B. *Polym. J.* 1991, **23**(12), 1425
- 16 Huglin, M. B. and Rego, J. M. *Colloid Polym. Sci.* 1992, **270**, 234
- 17 Katayama, S., Myoga, A. and Akahori, Y. *J. Phys. Chem.* 1992, **96**, 4698
- 18 Katayama, S., Myoga, A. and Akahori, Y. *Polym. Bull.* 1992, **28**, 227
- 19 Kang, S. K. and Jhon, M. S. *Macromolecules* 1993, **26**, 171
- 20 Baker, J. P., Stephens, D. R., Blanch, H. W. and Prausnitz, J. M. *Macromolecules* 1992, **25**, 1958
- 21 Wen, S. and Stevenson, W. T. K. *Colloid Polym. Sci.* 1993, **271**, 38
- 22 Yu, H. and Grainger, D. W. *J. Appl. Polym. Sci.* 1993, **49**, 1553
- 23 Wada, N., Yagi, Y., Inomata, H. and Saito, S. *J. Polym. Sci. (A) Polym. Chem.* 1993, **31**, 2647
- 24 Annaka, M. and Tanaka, T. *Nature* 1992, **355**, 430
- 25 Khokhlov, A. R., Stardubtzev, S. G. and Vasilevskaya, V. V. *Adv. Polym. Sci.* 1993, **109**, 123
- 26 Stardubtzev, S. G. and Ryabina, V. R. *Polym. Sci. USSR (A)* 1987, **29**, 2281
- 27 Flory, P. J. 'Principles of Polymer Chemistry', Cornell University Press, Ithaca, NY, 1953, Ch. XIII
- 28 James, H. M. and Guth, E. *J. Chem. Phys.* 1947, **15**, 669
- 29 Mark, J. E. and Erman, B. 'Rubberlike Elasticity—A Molecular Primer', Wiley, New York, 1988, Ch. 7
- 30 Ricka, J. and Tanaka, T. *Macromolecules* 1984, **17**, 2916
- 31 Hooper, H. H., Baker, J. P., Blanch, H. W. and Prausnitz, J. M. *Macromolecules* 1990, **23**, 1096
- 32 Vasilevskaya, V. V. and Khokhlov, A. R. *Polym. Sci. USSR (A)* 1986, **28**, 316
- 33 Castellan, G. W. 'Physical Chemistry', Addison-Wesley, Reading, MA, 1983, Ch. 16
- 34 Hill, T. L. 'An Introduction to Statistical Thermodynamics', Addison-Wesley, Reading, MA, 1960, Ch. 18
- 35 McQuarrie, D. A. 'Statistical Mechanics', Harper and Row, New York, 1976, Ch. 15
- 36 Saito, S. *J. Polym. Sci. (A-1)* 1969, **7**, 1789
- 37 Beltran, S., Hooper, H. H., Blanch, H. W. and Prausnitz, J. M. *J. Chem. Phys.* 1990, **92**(3), 2061
- 38 Baker, J. P., Stephens, D. R., Blanch, H. W. and Prausnitz, J. M. 'Swelling Equilibria for Temperature-Sensitive Ampholytic Hydrogels', Report No. 32956, Lawrence Berkeley Laboratory, Berkeley, CA, 1992