Swelling Equilibria for Acrylamide-Based Polyampholyte Hydrogels

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ABSTRACT: Polyampholyte hydrogels were synthesized by copolymerizing acrylamide with the cationic monomer methacrylamidopropyl trimethylammonium chloride and the anionic monomer sodium styrene sulfonate. The total nominal charge density of the hydrogels was held constant at 4.7 ± 0.1 mol % (dry basis), while the molar ratio of anionic to cationic moieties within the hydrogels was varied. Swelling equilibria were measured in water and in aqueous sodium chloride solutions ranging in ionic strength from 10^{-5} to 1.0 M. The hydrogels showed increasing insensitivity to ionic strength as the molar ratio of anionic to cationic moieties in the hydrogel approached unity. Donnan membrane equilibria qualitatively explain the experimental results.

Introduction

In recent years, hydrogels have received attention for use as extraction solvents,[1] for soft contact lenses,[2] for medical therapeutics and diagnostics,[3] and for drug-delivery devices.[4,5] The medical and pharmaceutical applications of hydrogels have been extensively reviewed.[6]

This work with polyampholyte hydrogels is an extension of previous work with polyelectrolyte hydrogels. Confirming earlier work,[7] Hooper et al.[8] found that Donnan membrane equilibria satisfactorily described the swelling of acrylamide-based polyelectrolyte hydrogels in aqueous solution as a function of hydrogel charge density and solution ionic strength.

A hydrogel may be described as a polymeric material that can absorb a significant amount of water (>20% of its dry weight) while maintaining its structural integrity. For applications such as regenerable extraction solvents and soft contact lenses, it is important that the three-dimensional structure of the hydrogel be conserved. Our definition of a hydrogel excludes hydrophilic polymers that are added to solutions as binders or to increase viscosity. An elastic, not viscous, response to applied stress and the maintenance of mechanical integrity are essential characteristics of hydrogels. However, some previous work describes certain polyelectrolytes that form ionically bonded viscosity-enhancing network structures in aqueous solution.[9,10]

Little attention has been given previously to aqueous swelling of synthetic polyampholyte hydrogels. However, several studies have considered synthetic linear polyampholytes, i.e., polymers containing both cationic and anionic fixed charges.[11–16] Bekturov et al.,[16] recently reviewed the synthetic polyampholyte literature.

In this work, hydrogels were prepared with composition similar to that of linear polyampholytes studied by Peiffer and Lundberg,[13] viz. acrylamide (AAm) copolymerized with the cationic methacrylamidopropyl trimethylammonium chloride (MAPTAC) and the anionic sodium styrene sulfonate (SSS); we added a cross-linking agent, *N,N'*-methylenebis(acrylamide) (BIS), to form covalently bonded networks. Swelling equilibria for the polyampholyte hydrogels were measured as a function of ionic composition and solution ionic strength.

Experimental Methods

Materials. AAm, BIS, and APS were supplied by Eastman Kodak. MAPTAC (50% by weight in aqueous solution) and SSS were obtained from Aldrich, and sodium chloride was from Fisher. 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. Free-radical aqueous copolymerization of AAm, MAPTAC, and SSS was employed to prepare the hydrogels. BIS was used as the cross-linking agent. Polymerization was initiated by APS and occurred in 10- × 75-mm test tubes.

The composition of each hydrogel was determined by the nominal amounts of reagents present in the hydrogel-feed solution. Four parameters were used to define this composition:

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

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

$$\%\ \mathrm{MAPTAC} = \frac{\text{moles of MAPTAC in feed solution}}{\text{total moles of monomer in feed solution}} \times 100 \tag{3}$$

$$\%\ \mathrm{SSS} = \frac{\text{moles of SSS in feed solution}}{\text{total moles of monomer in feed solution}} \times 100 \tag{4}$$

Hydrogels with good mechanical properties were essential to the technique chosen in this work for measuring swelling equilibria (gravimetric measurement). The requirement of good mechanical properties, coupled with the desire to produce hydrogels that swelled appreciably (but not to the extent that the hydrogel cannot support its own mass), limited the acceptable ranges of the above parameters. Previous experience with polyelectrolyte hydrogels showed that a % T of 16 and a % C of 0.4 produce hydrogels with favorable mechanical properties.[8] The amount of charge polymerized into a hydrogel network is also limited. We have observed that acrylamide-based hydrogels are mechanically unstable if they contain a net charge density higher than 5%.

Seven hydrogels were prepared (I–VII). % T and % C were held constant (at 16% and 0.4%, respectively), while % MAPTAC and % SSS were varied. The total nominal charge density of the hydrogels was held nearly constant; the sum of % MAPTAC and % SSS was 4.7 ± 0.1%. Table I shows the composition parameters for the seven hydrogels.

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Table I
Composition Parameters for the Seven Hydrogels Prepared for This Work[a]

hydrogel	% MAPTAC	% SSS
I	4.2	0.6
II	3.6	1.1
III	3.0	1.7
IV	2.4	2.3
V	1.8	2.8
VI	1.2	3.4
VII	0.6	4.0

[a] The total nominal charge content of the hydrogels was held nearly constant; the sum of percent MAPTAC and percent SSS was 4.7 ± 0.1%. The hydrogels were 16% T and 0.4% C.

To illustrate the synthetic procedure, we give details for the preparation of hydrogel I (16% T, 0.4% C, 4.2% MAPTAC, 0.6% SSS). Added to 37.6 mL water were 6.684 g of AAm, 0.056 g of BIS, 1.83 mL of MAPTAC solution, and 0.816 g of SSS. The solution was stirred with a magnetic stirrer until well-mixed and then degassed under 27 in. of Hg. An initiator solution of 0.075 g of APS in 15 mL of water was degassed at the same time as the monomer solution. After 1 h, both solutions were transferred to a nitrogen atmosphere. Under nitrogen, 5 mL of the initiator solution was added to the monomer solution. The mixture was stirred until well-mixed and poured into 10- × 75-mm test tubes for reaction. The test tubes were placed in a thermostated bath at 50 °C. After 24 h, the hydrogels were removed from the test tubes and then sliced into disks approximately 5 mm thick. The hydrogel disks were soaked in water which was refreshed periodically to leach away the soluble fraction and initiator residues.

Swelling Studies. Hydrogels were swollen to equilibrium in water at 8 °C. Equilibrium was attained in 1 week; the approach to equilibrium was monitored by measurement of the mass of the swollen hydrogels. Once equilibrium was attained, the swelling capacity in water was determined for each hydrogel in the series. Equilibrated disks were weighed, dried at room conditions, and reweighed. The swelling capacity in water is defined as the mass ratio of swollen hydrogel to dry hydrogel.

Unlike hydrogels containing weakly ionizable groups, the hydrogels prepared for this work contained strongly ionizable groups, resulting in swelling equilibria insensitive to solution pH. Swelling measurements were performed at neutral pH in this work.

Aqueous solutions of NaCl were prepared ranging in concentration from 10^{-5} to 1.0 M. Hydrogel disks were transferred from water to each of the salt solutions and allowed to equilibrate. To compensate for possible solvent exchange between hydrogel and external solution, NaCl solutions bathing the hydrogels were changed every other day. Mass measurements of the hydrogels were taken to monitor attainment of equilibrium. After 2 weeks, mass measurements did not change; the swelling capacities were then determined by

$$\text{swelling capacity} = \frac{\text{mass of gel in water}}{\text{mass of dry gel}} \times \frac{\text{mass of gel in salt solutions}}{\text{mass of gel in water}} \qquad (5)$$

All swelling of studies were performed in triplicate. Table II provides mean values and deviations of the measured swelling behavior.

Results and Discussion

The overall nominal charge density of seven hydrogels was fixed at 4.7 ± 0.1 mol % (% MAPTAC + % SSS), while the cationic-to-anionic balance of the hydrogels was varied. Figure 1 shows swelling equilibria for seven hydrogels in water. A minimum in swelling capacity is observed with hydrogel IV (nearly equimolar amounts of SSS and MAPTAC). Swelling increases with rising prevalence of the MAPTAC comonomer (hydrogels I–III) or SSS comonomer (hydrogels V–VII).

A reasonable explanation for the swelling behavior observed in Figure 1 is that the number of osmotically active ions in the hydrogel phase increases as the molar ratio of MAPTAC to SSS diverges from unity. Conversely, the ability of a hydrogel to neutralize itself is enhanced as the molar ratio of MAPTAC to SSS approaches unity: when the hydrogels are swollen to equilibrium in water, excess free ions that are not needed to satisfy electroneutrality are effectively "dialyzed" from the hydrogel interior. The prevailing situation is analogous to the Donnan membrane equilibrium:[17] at equilibrium, there is an unequal distribution of osmotically active ions between the hydrogel interior and the external solution. Here, the external solution is deionized water and contains no added ions. The disparity in osmotically active ion concentration generates a net osmotic pressure between the hydrogel interior and the external solution, which causes water to enter the hydrogel. For swelling equilibria in water, the larger the number of osmotically active ions in the hydrogel phase, the larger the net osmotic pressure and the greater the swelling.

As can be seen from the comparison of hydrogels with similar amounts of "excess" charge in Figure 1, the hydrogel containing excess cationic character consistently swelled to greater capacity than the hydrogel containing excess anionic character. The "asymmetry" in swelling behavior is dramatic: hydrogel I (4.2% MAPTAC, 0.6% SSS) swelled 71% more in water than hydrogel VII (0.6% MAPTAC, 4.0% SSS); hydrogel II (3.6% MAPTAC, 1.1% SSS) swelled 77% more than hydrogel VI (1.2% MAPTAC, 3.4% SSS), and hydrogel III (3.0% MAPTAC, 1.7% SSS) swelled 112% more than hydrogel V (1.8% MAPTAC, 2.8% SSS).

Three mechanisms, possibly working in concert, may account for the asymmetry in swelling bracketing hydrogel IV:

(1) Differences in Cross-Link Density Caused by Different Rates of Copolymerization. Due to the difficulties associated with copolymerizing four monomers, the cross-linking reaction may be enhanced in the net anionic hydrogels, or it may be impeded in the net cationic hydrogels. This possible explanation could be tested by a thorough analysis of the copolymerization.

(2) Hydrophobicity Imparted to the Net Anionic Hydrogels by Styrenic Moieties. Hydrophobic interactions between the styrenic moieties of SSS may tend to reduce chain expansion inside the network, depressing the swelling of the hydrogel. The net anionic hydrogels should be less solvophilic than the net cationic hydrogels and should thus swell less.

(3) Differences in the Activities of the Counterions to the Charged Groups. Since a quaternary amine group is bulkier than a sulfonate group, the electric field near the interface between the quaternary amine group and water will be weaker than the corresponding field at the sulfonate–water interface. Because of the difference in electric field strength surrounding the two functional groups, the attraction between counterion and functional group will be weaker for MAPTAC than for SSS. Thus, the counterions for MAPTAC are more osmotically active than the counterions for SSS, resulting in higher swelling capacities for the net cationic hydrogels.

Figures 2 and 3 show swelling equilibria in aqueous NaCl solutions for the net cationic hydrogels (I–III) and for the net anionic hydrogels (V–VII), respectively. The same coordinate axes are used in both plots to facilitate qualitative comparisons. As observed in the swelling experiments in water, swelling of the net anionic hydro-

Table II
Swelling Capacity in NaCl Solutions for Ampholytic Hydrogels Prepared with Different Percent MAPTAC to Percent SSS Ratios[a]

	swelling capacity (g of swollen gel/g of dry gel) for specific NaCl concentration						
hydrogel	1.0 M	10^{-1} M	10^{-2} M	10^{-3} M	10^{-4} M	10^{-5} M	0 M[b]
I	16.6 (0.2)	15.1 (0.2)	28.1 (0.9)	67.8 (1.0)	95.4 (1.8)	100.2 (0.7)	100.0 (3.5)
II	16.4 (0.2)	14.1 (0.4)	21.3 (0.3)	47.9 (0.3)	64.9 (1.4)	68.6 (1.1)	68.1 (1.1)
III	16.2 (0.2)	13.4 (0.2)	15.4 (0.3)	28.3 (0.4)	36.0 (0.7)	37.4 (0.7)	37.5 (0.6)
IV	15.7 (0.4)	12.9 (0.2)	11.2 (0.2)	12.2 (0.1)	12.8 (0.6)	13.0 (0.2)	13.2 (0.2)
V	15.1 (0.2)	12.6 (0.4)	11.5 (0.7)	14.6 (0.1)	17.0 (0.5)	17.3 (0.2)	17.7 (0.2)
VI	14.8 (0.2)	12.6 (0.2)	15.0 (0.2)	27.4 (0.5)	36.4 (0.5)	37.9 (1.1)	38.4 (0.1)
VII	14.4 (0.2)	13.2 (0.2)	19.7 (0.2)	41.0 (0.1)	55.7 (0.2)	57.7 (0.6)	58.6 (1.9)

[a] Values in parentheses represent 95% confidence intervals. [b] Swelling equilibria in salt-free water.

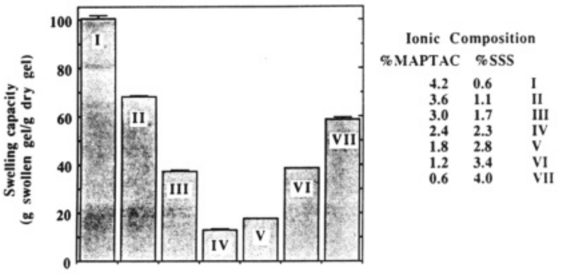

Figure 1. Swelling equilibria in water for ampholytic hydrogels with 16% T and 0.4% C. The amount of charged comonomer present in the hydrogel-feed solution was fixed at 4.7 ± 0.1% (molar basis). There is pronounced asymmetry in swelling behavior between the net anionic hydrogels and the net cationic hydrogels.

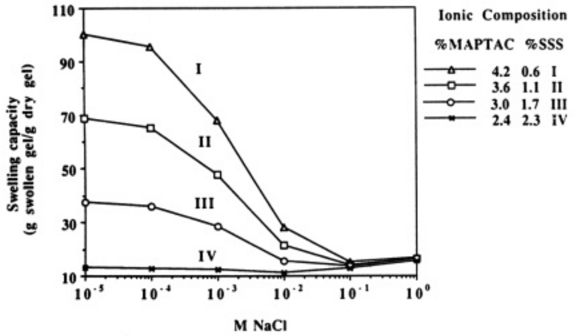

Figure 2. Swelling equilibria for net cationic ampholytic hydrogels. Swelling was measured as a function of NaCl concentration.

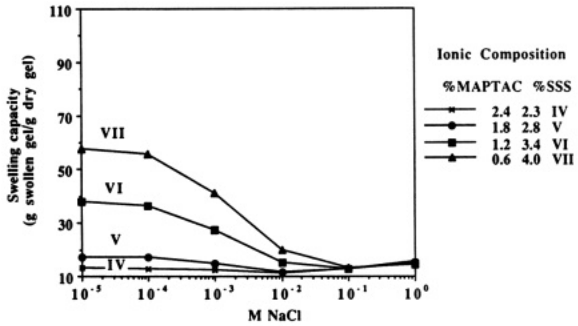

Figure 3. Swelling equilibria for net anionic ampholytic hydrogels. Swelling was measured as a function of NaCl concentration. Data are plotted on the same axes as those of Figure 2 to facilitate qualitative comparison.

gels was found to be depressed relative to that of the net cationic hydrogels.

In Figures 2 and 3, all hydrogels collapse as a function of rising NaCl concentrations up to moderate ionic strengths (10^{-5}–0.01 M). 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 due to the presence of the fixed charges, which require counterions for the maintenance of electroneutrality, but the difference in mobile ion concentration between the hydrogel and the external solution decreases as the ionic strength of the external solution rises. As the mobile ion concentrations become similar, the net osmotic pressure falls and swelling decreases.

An increase in swelling with rising NaCl concentration was observed for all three hydrogels at ionic strengths of 0.1 M or greater. Hooper et al.[8] observed similar behavior at high NaCl concentrations for AAm–MAPTAC polyelectrolyte hydrogels. Since charge effects are highly screened at appreciable ionic strength and since similar behavior has been observed at high ionic strength for both polyelectrolyte and polyampholyte acrylamide-based hydrogels, a possible explanation for this behavior may be salting-in of the polymer at appreciable NaCl concentration.

Conclusion

Acrylamide-based polyampholyte hydrogels were synthesized; their swelling properties were observed in water and in aqueous NaCl solutions. The hydrogels with excess cationic character (hydrogels I–III) consistently reached higher swelling capacities in aqueous media than those with similar amounts of excess anionic character (hydrogels V–VII). Methacrylamidopropyl trimethylammonium chloride (MAPTAC) and sodium styrene sulfonate (SSS) were, respectively, the cationic and anionic monomers chosen for this study. The structure of SSS appears to be more hydrophobic compared to that of MAPTAC; the hydrogels with excess anionic character may be relatively less solvophilic because of styrenic moieties within them. Structural differences between the two charged monomers, which may also lead to the observed asymmetric swelling behavior, may be responsible for differences in cross-link density and differences in counterion activity between the net anionic and net cationic hydrogels.

The hydrogels prepared for this study showed decreasing sensitivity to ionic strength as the molar ratio of anionic to cationic moieties in the hydrogel approached unity. The observed swelling phenomena were qualitatively explained by Donnan membrane equilibria. At ionic strengths of 0.1 M and above, all polyampholyte hydrogels showed an increase in swelling capacity with rising NaCl concentration, suggesting salting-in of the polymer at appreciable NaCl concentrations.

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References and Notes

(1) Freitas, R. F. S.; Cussler, E. L. *Chem. Eng. Sci.* **1987**, *42*, 97.

(2) Pedley, D. G.; Skelly, P. J.; Tighe, B. J. *Br. Polym. J.* **1980**, *12*, 99.

(3) Hoffman, A. S. *J. Controlled Release* **1987**, *6*, 297.

(4) Gehrke, S.; Lee, P. I. *Drugs Pharm. Sci.* **1990**, *41*, 333.

(5) Siegel, R. A.; Firestone, B. A. *J. Controlled Release* **1990**, *11*, 181.

(6) Peppas, N. A., Ed. *Hydrogels in Medicine and Pharmacy*; CRC Press: Boca Raton, FL, 1986.

(7) Ricka, J.; Tanaka, T. *Macromolecules* **1984**, *17*, 2916.

(8) Hooper, H. H.; Baker, J. P.; Blanch, H. W.; Prausnitz, J. M. *Macromolecules* **1990**, *23*, 1096.

(9) Michaels, A. S. *Ind. Eng. Chem.* **1965**, *57* (10), 32.

(10) Bekturov, E. A.; Bimendina, L. A. *Adv. Polym. Sci.* 1981, *41*, 99.

(11) Katchalsky, A.; Miller, I. R. *J. Polym. Sci.* **1954**, *13*, 57.

(12) Salamone, J. C.; Volksen, W.; Olson, A. P.; Israel, S. C. *Polymer* **1978**, *19*, 1157.

(13) Peiffer, D. G.; Lundberg, R. D. *Polymer* **1985**, *26*, 1058.

(14) McCormick, C. L.; Johnson, C. B. *Macromolecules* **1988**, *21*, 686.

(15) Higgs, P. G.; Joanny, J.-F. *J. Chem. Phys.* **1991**, *94*, 1543.

(16) Bekturov, E. A.; Kudaibergenov, S. E.; Rafikov, S. R. *J. Macromol. Sci. Rev. Macromol. Chem. Phys.* **1990**, *C30* (2), 233.

(17) Richards, E. G. *An Introduction to Physical Properties of Large Molecules in Solution*; Cambridge University Press: Cambridge, U.K., 1980.

Registry No. (AAm)(MAPTAC)(SSS)(BIS) (copolymer), 139100-78-0; NaCl, 7647-14-5.