

Swelling–Deswelling Kinetics of Ionic Poly(acrylamide) Hydrogels and Cryogels

Deniz Ceylan, M. Murat Ozmen, Oguz Okay

Department of Chemistry, Istanbul Technical University, Maslak, 34469 Istanbul, Turkey

Received 29 June 2004; accepted 19 May 2005

DOI 10.1002/app.22023

Published online in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: A series of ionic poly(acrylamide) (PAAm) gels was prepared by free-radical crosslinking copolymerization of acrylamide and *N,N'*-methylenebisacrylamide in aqueous solutions. The gels were prepared both below and above the bulk freezing temperature of the polymerization solvent water, which are called as the cryogels and the hydrogels, respectively. The deswelling behavior of swollen gels in acetone as well as the reswelling behavior of the collapsed gels in water were investigated. It was shown that the cryogels respond against the external stimuli much faster than the hydrogels. The interior morphology of the

cryogel networks exhibits a discontinuity and a two-phase structure, compared to the continuous morphology of the hydrogel networks. Introduction of the ionic units in the network chains further increased the response rate of the cryogels. In contrast to these advantages of cryogels, they exhibit lower swelling capacities than the conventional hydrogels. © 2005 Wiley Periodicals, Inc. *J Appl Polym Sci* 99: 319–325, 2006

Key words: hydrogels; cryogels; macroporous polymers; swelling; fast responsive hydrogels

INTRODUCTION

Hydrogels are useful materials for drug delivery systems, artificial organs, actuators, on–off switches, separation operations in biotechnology, and processing of agricultural products. In these applications, a fast response rate of the hydrogel to the external stimuli is needed. To increase the response rate of hydrogels, several techniques were proposed:

- (i) *Submicrometer-sized gel particles.*¹ Since the rate of response is inversely proportional to the square of size of the gel,² small gel particles respond to the external stimuli more quickly than bulk gels.
- (ii) *Gels having dangling chains.*^{3–5} Dangling chains in a gel easily collapse or expand upon an external stimulus because one side of the dangling chain is free.
- (iii) *Macroporous gels.*⁶ For a polymer network having an interconnected pore structure, absorption or desorption of water occurs through the pores by convection, which is much faster than the diffusion process that dominates the nonporous gels.

To obtain macroporous structures, a phase separation must occur during the course of the network

formation process so that the two-phase structure formed is fixed by the formation of additional crosslinks.^{6–8} The extent of phase separation during crosslinking and thus, the degree of macroporosity of the resulting networks depend on the gel synthesis parameters such as the temperature, the crosslinker, and the monomer concentrations as well as the amount and the type of the inert diluent (pore-forming agent) present during the network formation process. Several inert diluents were suggested for the preparation of macroporous hydrogels such as hydroxypropyl cellulose,⁹ acetone,¹⁰ 1,4-dioxane,¹¹ sucrose,¹² silica particles,¹³ inorganic salts,¹⁴ as well as poly(ethylene glycol) of various molecular weights.^{15–18} Zhang et al. showed increased degree of porosity in hydrogels on rising the crosslinker content.¹⁹ Recently, we have shown that a critical crosslinker concentration is necessary to produce a heterogeneous (macroporous) hydrogel network structure.^{20,21} Macroporous networks consist of spherical globules (called microspheres) of 1–2 μm in diameter, aggregated to large, unshaped, discrete clusters with dimensions of a few micrometers.^{6,20} At high crosslinker contents, the structure looks like cauliflowers, typical for a macroporous network. Changes from homogeneous to heterogeneous gelation results in the formation of fast responsive hydrogels.²⁰

Lozinsky and coworkers investigated the free-radical crosslinking copolymerization reactions carried out below the freezing point of the polymerization solvent, which is usually water.^{22–24} The essential feature of this reaction system is that the monomers and

Correspondence to: O. Okay (okayoo@itu.edu.tr).

the initiator are concentrated in the unfrozen microzones of the apparently frozen system. The polymerization reactions proceed in these unfrozen microzones and leads to the formation of a polymer network with continuous macroporous channels. Such materials are defined as cryogels. In these cryogelation systems, although there is no phase separation during the course of the network formation process, the frozen zones of the reaction system act as an inert diluent during gelation, which can easily be removed from the gel by thawing, leading to a porous structure.

In this study, we compared the swelling–deswelling kinetics of poly(acrylamide) (PAAm) gels formed at two different temperatures, namely 5°C and –18°C. The hydrogels were synthesized by free-radical crosslinking polymerization of acrylamide (AAM) and *N,N'*-methylenebisacrylamide (BAAM) at an initial monomer concentration of 3% w/v. 2-acrylamido-2-methylpropane sulfonic acid sodium salt (AMPS) was used as the ionic comonomer in the hydrogel preparation. As will be shown later, both the low polymerization temperature and the introduction of the ionic AMPS units in the network chains lead to the formation of fast responsive PAAm hydrogels with a two-phase morphology.

EXPERIMENTAL

Materials

Acrylamide (AAM, Aldrich), 2-acrylamido-2-methylpropane sulfonic acid sodium salt (AMPS, Merck), *N,N'*-methylenebisacrylamide (BAAM, Fluka), ammonium persulfate (APS, Merck), and *N,N,N',N'*-tetramethylethylenediamine (TEMED, Carlo Erba) were used as received. PAAm hydrogels were prepared by free-radical crosslinking copolymerization of AAM, AMPS, and BAAM at 5°C and –18°C. The polymerization reactions were initiated using 1.1 mM APS and 0.05% v/v TEMED. The polymerization time was set to 4 h. The initial monomer concentration was also fixed at 3% w/v. The experiments were carried out at 0, 1, and 5 mol % AMPS in the comonomer feed, while the crosslinker ratio *X* (molar ratio of the crosslinker BAAM to the monomers AAM and AMPS) was fixed at 1/30. To illustrate the synthetic procedure, we give details for the preparation of nonionic PAAm gels. AAM (0.84 g) and BAAM (0.06 g) were first dissolved in 30 mL of distilled water. The solution was purged with nitrogen gas at 0°C for 20 min. After addition of APS (7.5 mg) and TEMED (15 μ L), the reaction mixture was poured into a plastic 10-mL syringe with closed outlet at the bottom. The plastic syringe was kept at 5°C or at –18°C for 24 h and then, the gel matrix was taken out of the syringe and washed in distilled water.

Equilibrium swelling measurements

The equilibrium swelling measurements were carried out in distilled water at 25°C. To reach the equilibrium degree of swelling, the gels were immersed in water at 25°C for at least 2 weeks. The normalized volume of the equilibrium swollen hydrogels V_{eq} (volume of equilibrium swollen gel/volume of the gel just after preparation) was determined by measuring the diameter of the hydrogel samples by a calibrated digital compass (Mitutoyo Digimatic Caliper; Series 500; resolution, 0.01 mm). V_{eq} was calculated as

$$V_{eq} = (D/D_0)^3 \quad (1)$$

where D and D_0 are the diameter of hydrogels after equilibrium swelling in water and after synthesis, respectively.

Measurements of deswelling and reswelling kinetics

For the deswelling kinetics measurements, the hydrogels equilibrium swollen in water at 25°C were transferred into acetone at 25°C. The volume changes of gels were measured by measuring the diameter of the hydrogel at regular time intervals. For the measurement of the reswelling kinetics of gels, the equilibrium collapsed PAAm gel samples were transferred into water at 25°C. The volume changes of gels were also determined as described earlier. The water uptake or the water retention was calculated in terms of the relative gel volume V_{rel}

$$V_{rel} = \left(\frac{D_t}{D}\right)^3 \quad (2)$$

where D_t is the diameter of the gel sample at time t and D is its equilibrium swollen diameter in water.

Texture determination

Scanning electron microscopy studies were carried out at magnifications of 100 $\times$ and 300 $\times$ (Jeol 5600 LV).

RESULTS AND DISCUSSION

PAAm gels were prepared both at 5°C and –18°C, which were designated as the conventional hydrogels and the cryogels, respectively. They were first characterized by the equilibrium swelling tests in water. Figure 1 shows the equilibrium swelling ratio V_{eq} of the hydrogels and the cryogels plotted as functions of their AMPS contents. As expected, V_{eq} increases with increasing amount of AMPS present in the gel formation system. This is a consequence of the osmotic pressure exerted by the counterions (Na^+) of AMPS

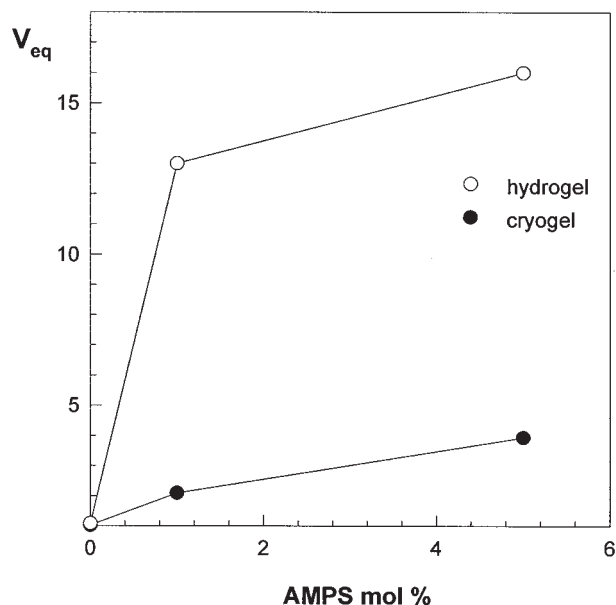


Figure 1 Equilibrium swelling ratio V_{eq} of PAAM hydrogels (○) and the cryogels (●) shown as a function of the AMPS content.

units in the network chains. This osmotic pressure increases as the concentration difference of the counterions between the inside and outside the gel phase increases. Another point shown in Figure 1 is that, the cryogels swell in water much less than the corresponding hydrogels. This behavior is due to the formation of the cryogels below the freezing point of water. Thus, the polymerization and crosslinking reactions at -18°C take place only in the unfrozen microzones of ice, which contain concentrated dissolved monomer and the crosslinker.^{23,24} As a result, although the initial monomer concentration in our experiments was set to 3% w/v, the actual monomer concentration in the reaction zones of cryogels is much higher. For example, assuming that the ice at -18°C contains 20% unfrozen water,²⁵ the actual monomer concentration is 15% w/v. Previous work shows that increasing monomer concentration causes the polymer chains to entangle so that the network formed in a concentrated solution can swell less than that formed in a dilute solution.²⁶ As a consequence, the equilibrium swelling capacities of the cryogels are much smaller than those of the corresponding hydrogels.

The hydrogels and the cryogels with 0, 1, and 5 mol % AMPS were subjected to the swelling and deswelling kinetics measurements. For this purpose, they were first swollen in water to their equilibrium state. Thereafter, the swollen gels were immersed in acetone and the deswelling process was monitored by recording the relative gel volume V_{rel} as a function of the time of deswelling. After attaining the equilibrium collapsed state, the gels were again immersed in water

and the reswelling behavior was monitored until the new equilibrium state is obtained. This deswelling–reswelling cycle was repeated two or three times to check the stability of the volume change.

Typical deswelling–reswelling cycles of the non-ionic hydrogel and the cryogel are shown in Figure 2A and 2B, respectively. The first cycles are shown by the filled symbols (●), while the following cycles are shown by the open symbols (△, ○). Several interesting features of both gels can be seen from the figures. First, the initial swollen hydrogel volume (i.e., $V_{rel} = 1$) cannot be recovered after collapsing the hydrogel in acetone (Fig. 2A). Experiments showed that even after 1 week of a swelling time in water, the collapsed hydrogel cannot attain to its initial volume. Second, both the deswelling and reswelling processes of the hydrogel require much longer times than those of the corresponding cryogel. For example, the hydrogel immersed in acetone cannot attain its equilibrium collapsed state within 250 min, whereas the cryogel reaches to the equilibrium state in acetone within about 30 min. Moreover, the reswelling process of the collapsed hydrogel occurs in two steps; a rapid reswelling step continuing for 50 min followed by a slow reswelling step, which required about 200 min to recover 50% of the initial gel volume (Fig. 2A). This two-step reswelling profile of the hydrogel can be explained with the formation of a two-phase structure during swelling of the hydrogels.²⁷ Thus, when a collapsed gel sample is immersed in water, the outer surface of the sample will first be in contact with water molecules so that the collapsed network chains at the gel surface will start to relax. Since the surface area of the collapsed gel is initially large, water absorption by the gel network occurs easily. However, as the gel swells, a two-phase structure will form: one containing solvated network chains at the gel surface and the other containing relatively unswollen network chains in the inner part of the gel sample. Since the surface area of the inner part of gel becomes smaller with increasing degree of swelling, the reswelling process slows down after the initial rapid-swelling period. In contrast to the hydrogel, however, the cryogel swells in water rapidly and reaches to its initial gel volume within 6 min along a single step process (Fig. 2B). This indicates the existence of solvent channels along the cryogel network, which provide unhindered diffusion of solvent molecules in and out of the gel phase. Another point shown in Figure 2 is that the relative volume V_{rel} of the hydrogel in the collapsed state is much smaller than that of the collapsed cryogel. This means that the total amount of losing water during deswelling is much larger for the hydrogels than the cryogels.

Figure 3A and 3B show the deswelling–reswelling cycles of the hydrogel and the cryogel, respectively,

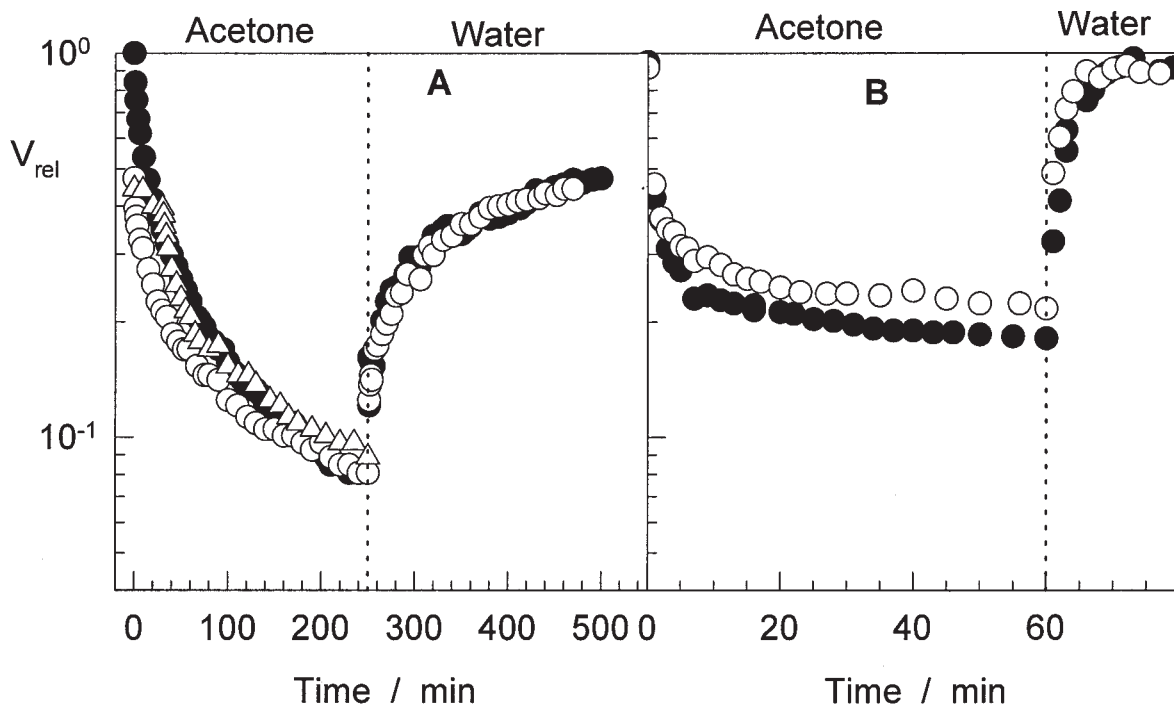


Figure 2 Deswelling–reswelling kinetics of nonionic PAAm hydrogels (A) and cryogels (B) shown as the variation of the relative gel volume V_{rel} with the time of swelling or deswelling. Number of runs = 1st (●), 2nd (△), and 3rd (○).

both with 1 mol % AMPS. The results shown here are similar to those obtained for the nonionic gels:

- (a) the first deswelling process of the hydrogel deviates from the following deswelling pro-

cesses while the cryogel shows the same behavior in each cycle

- (b) the deswelling processes in acetone occurs in 70 min and 15 min for the hydrogel and cryogel, respectively. Thus, the cryogel de-

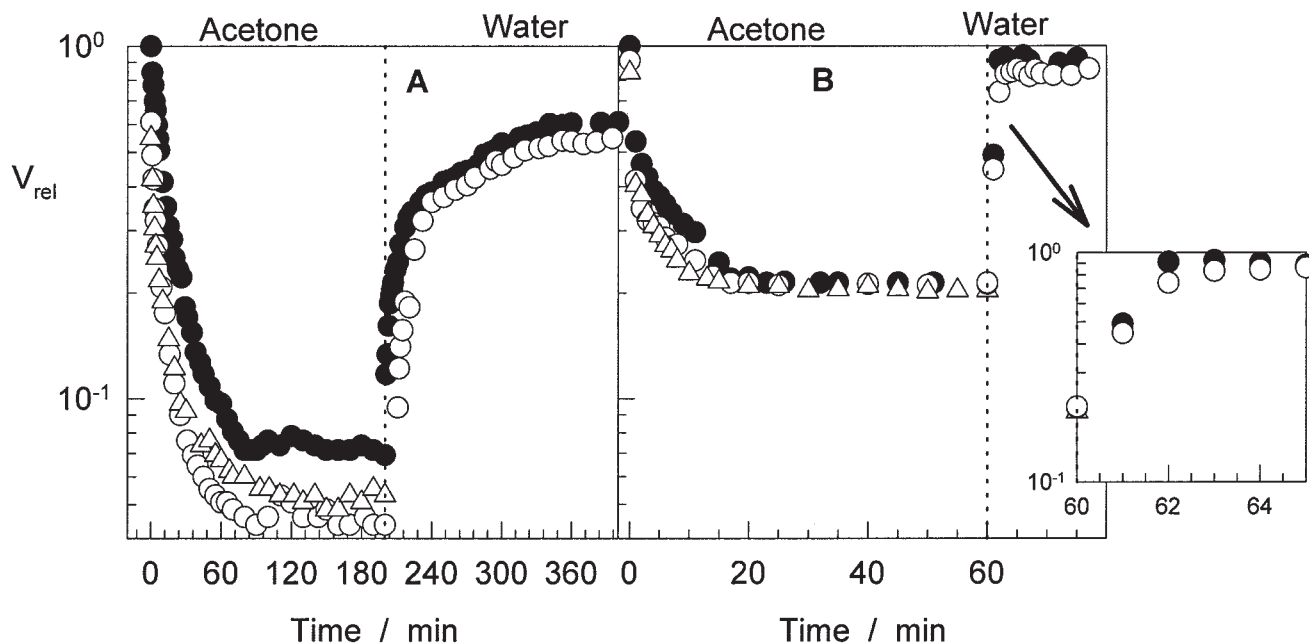


Figure 3 Deswelling–reswelling kinetics of PAAm hydrogels (A) and cryogels (B) with 1 mol % AMPS shown as the variation of the relative gel volume with the time of swelling or deswelling. Number of runs = 1st (●), 2nd (△), and 3rd (○). The inset to Figure 3B shows the initial reswelling profile of the cryogels.

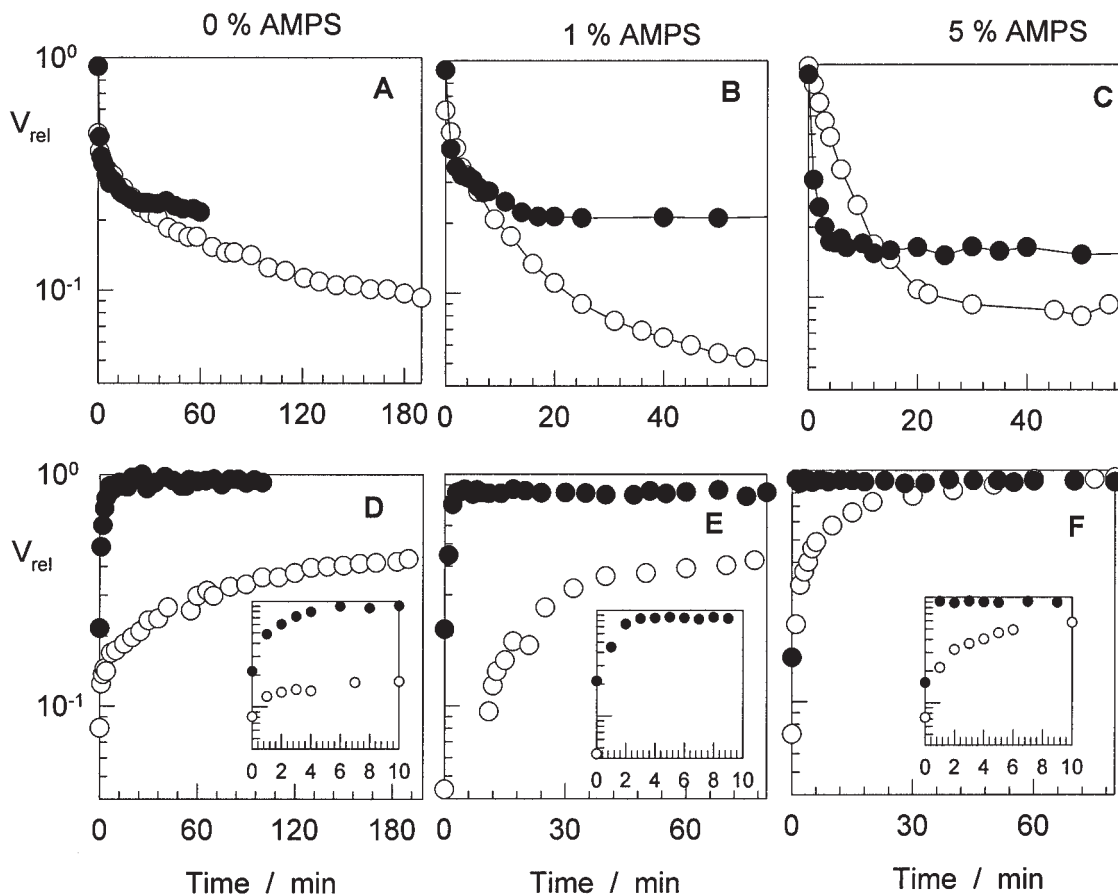


Figure 4 Deswelling-reswelling kinetics of PAAm hydrogels (○) and PAAm cryogels (●). AMPS contents are indicated in the figure. The insets show the reswelling behavior of gels in the first 10 min.

swells in acetone much more rapid than the hydrogel.

- (c) The reswelling of the collapsed hydrogel in water occurs in a two-step process and, the initial swollen gel volume cannot be recovered even after 200 min of swelling time, while the cryogel reswells in water within 2 min to its initial volume, as seen from the inset of Figure 3B.
- (d) The relative volume of the collapsed hydrogel is much smaller than the relative volume of the collapsed cryogel.

To compare the kinetic features of various gels, the second deswelling-reswelling cycles of the hydrogels and cryogels were compared. Figure 4 shows the deswelling and reswelling behavior of the hydrogels (○) and the cryogels (●) with 0, 1, and 5 mol % AMPS. The results clearly show the fast responsive behavior of the cryogels to the external stimuli when compared to the hydrogels at each AMPS content. Furthermore, increasing AMPS content from 0 to 5 mol % increases the deswelling and reswelling rates of both hydrogels and cryogels. The accelerated response rate of gels with increasing

AMPS content is more pronounced for the cryogels. As seen from the insets to Figures 4D–4E, the time required for attaining equilibrium swollen state decreases from 6 min to 1 min as the AMPS content is increased from 0 to 5 mol %.

Comparison of the swelling behavior of gels also shows that the deswelling of the cryogels stops at larger relative gel volumes V_{rel} compared to the hydrogels. This feature of the cryogels is a consequence of their low swelling capacities in water (Fig. 1), which result in a lesser amount of water release when immersed in acetone. However, this does not mean that the equilibrium collapsed cryogels are in a relatively swollen state. Assuming complete conversion of the monomers into the crosslinked polymer, one may estimate the polymer concentration in gels as c_{gel} (% w/v) = $c_0 / (V_{rel} V_{eq})$, where c_0 is the initial monomer concentration (3% w/v). Figure 5 shows the polymer concentration c_{gel} in the hydrogels (○) and in the cryogels (●) plotted against the time of deswelling in acetone. It is seen that the cryogels in acetone are in a more collapsed state than the hydrogels and the difference between the polymer concentration in both

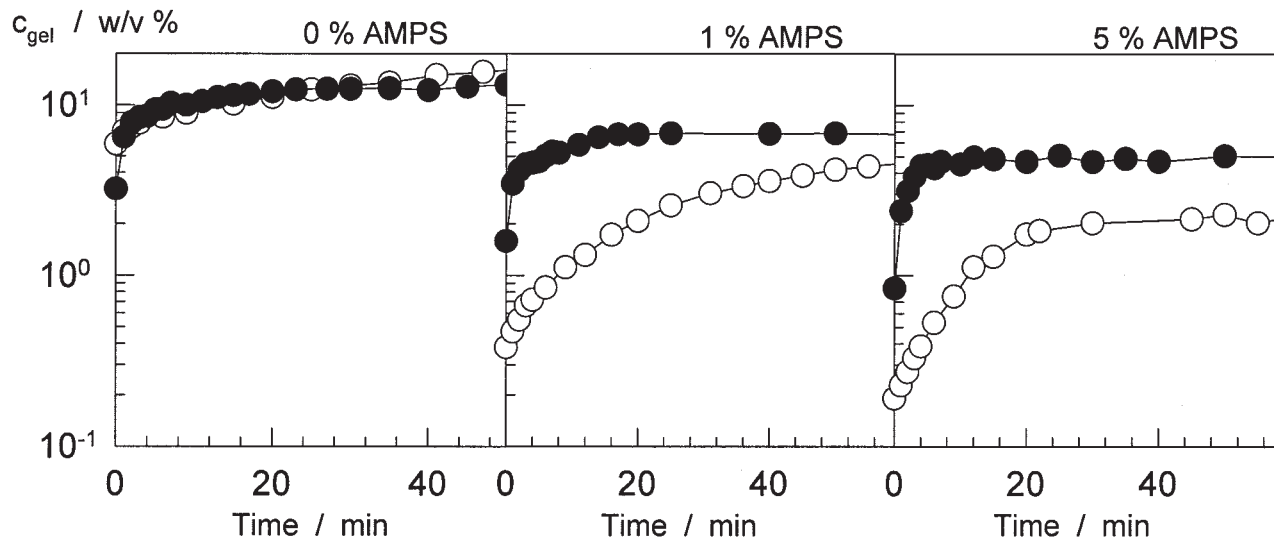


Figure 5 Deswelling kinetics of PAAm hydrogels (○) and PAAm cryogels (●) shown as the variation of the polymer concentration in gels (c_{gel}) with the time of deswelling. The second deswelling cycles are shown for comparison. AMPS contents are indicated in the figure.

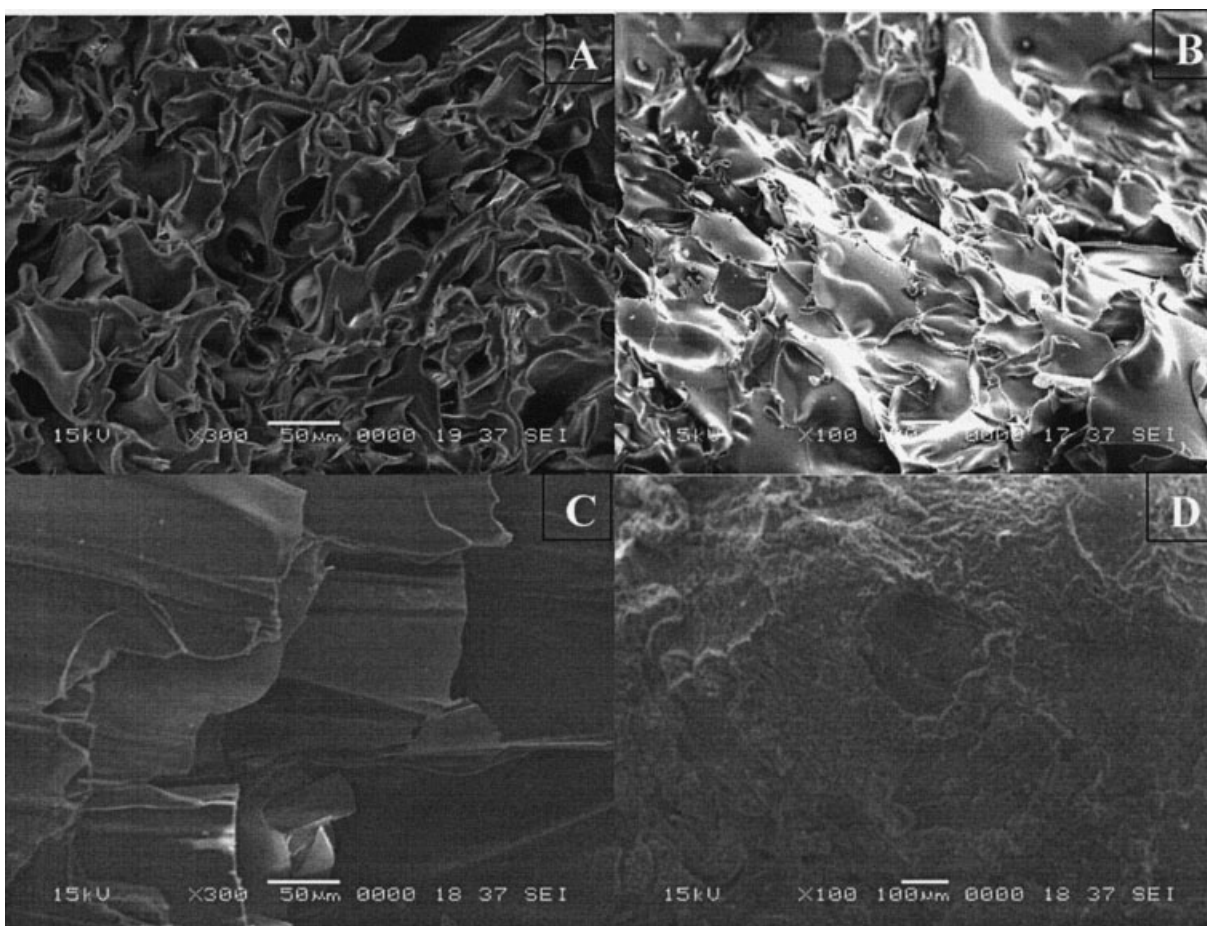


Figure 6 SEM of the cryogels (A,B) and the hydrogels (C,D). AMPS = 1 (A,C) and 5 mol % (B,D).

gels increases on rising the AMPS content. Thus, cryogels in collapsed state contain lesser amounts of water than the hydrogels.

The interior morphology of the gel samples was studied by using scanning electron micrographs (SEM). Figure 6 shows SEM of the cryogels (A and B) and the hydrogels (C and D) in their dried states, with 1 and 5 mol % AMPS, respectively. The hydrogel networks (C and D) consist of large polymer domains, while the cryogel networks (A and B) exhibit a discontinuous morphology with a two-phase structure, consisting of polymer phase separated by irregular shaped voids (pores). The porous structure of the cryogels is due to the action of ice crystals as a pore forming agent during gelation. Thus, during freezing of the monomer solution at -18°C , an unfrozen phase containing a high concentration of dissolved monomer and the crosslinker is formed as water is separated from the solution in the form of ice crystals. After gelation and thawing, the voids left from the ice crystals constitute the pore structure of cryogels. It should be noted that the SEM images of the cryogels largely deviate from those of the macroporous networks formed at large crosslinker contents,^{6,20} where the structure consists of aggregates of spherical polymer domains (microspheres) of $1\text{--}2\text{ }\mu\text{m}$ in diameter. This distinction can be explained with the collapse of the porous structure in the cryogels during drying, because of the relatively low density of crosslinking. The collapse of the pores in the cryogel networks can be ascribed to the cohesional forces when the solvated polymer chains approach each other because of the loss of water. As reported previously,⁶ the pores in polymer networks with a low crosslink density are unstable and thus, they collapse in the shrunken state of gel. As a result, the polymer domains in the microzones of the cryogel fuse together to larger, irregular aggregates of various sizes.

From the SEM images, one can identify the pores in the cryogel networks and the connectivity of the pores. The connectivity of the pores plays a crucial role in fast swelling and deswelling kinetics of the cryogels; water or acetone can enter or leave the cryogel through the interconnected pores by convection. In contrast to the cryogels, the swelling and deswelling kinetics of the hydrogels are controlled by the diffusion of solvent molecules through the gel network, which is a slow process.

CONCLUSIONS

In many gel applications, the swelling and shrinking kinetics are very important. In the present work, we

compared the swelling and deswelling kinetics of ionic PAAm gels prepared at 5°C and -18°C , which are called as hydrogels and cryogels, respectively. It was shown that the volume change of the cryogels in response to an external solvent composition change occurs much faster than that of the hydrogels prepared at the usual polymerization temperature. Introduction of the ionic AMPS units in the network chains further increases the response rate of the cryogels. In contrast to these advantages, cryogels exhibit lower swelling capacities and, they release a much smaller amount of water when compared to the hydrogels.

References

- Oh, K. S.; Oh, J. S.; Choi, H. S.; Bae, Y. C. *Macromolecules* 1998, 31, 7328.
- Tanaka, T.; Fillmore, D. J. *J Chem Phys* 1979, 70, 1214.
- Yoshida, R.; Uchida, K.; Kaneko, Y.; Sakai, K.; Kikuchi, A.; Sakurai, Y.; Okano, T. *Nature* 1995, 374, 240.
- Kaneko, Y.; Sakai, K.; Kikuchi, A.; Yoshida, R.; Sakurai, Y.; Okano, T. *Macromolecules* 1995, 28, 7717.
- Kaneko, Y.; Sakai, K.; Kikuchi, A.; Sakurai, Y.; Okano, T. *Macromol Symp* 1996, 109, 41.
- Okay, O. *Prog Polym Sci* 2000, 25, 711.
- Seidl, J.; Malinsky, J.; Dusek, K.; Heitz, W. *Adv Polym Sci* 1967, 5, 113.
- Dusek, K. In *Developments in Polymerization 3*; Haward, R. N., Ed.; Applied Science Publishers: London, 1982; p 143.
- Wu, X. S.; Hoffman, A. S.; Yager, P. *J Polym Sci Part A: Polym Chem* 1992, 30, 2121.
- Zhang, X.; Zhuo, R.; Yang, Y. *Biomaterials* 2002, 23, 1313.
- Zhang, J.; Huang, S.; Zhuo, R. *Macromol Chem Phys* 2004, 205, 107.
- Zhang, J.; Cheng, S.; Huang, S.; Zhuo, R. *Macromol Rapid Commun* 2003, 24, 447.
- Serizawa, T.; Wakita, K.; Akashi, M. *Macromolecules* 2002, 35, 10.
- Cheng, S.; Zhang, J.; Zhuo, R. *J Biomed Mater Res* 2003, 67A, 96103.
- Cicek, H.; Tuncel, A. *J Polym Sci Part A: Polym Chem* 1998, 36, 527.
- Zhang, X.; Zhuo, R. *Eur Polym J* 2000, 36, 2301.
- Zhuo, R.; Li, W. *J Polym Sci Part A: Polym Chem* 2003, 41, 152.
- Zhang, X.; Yang, Y.; Chung, T.; Ma, K. *Langmuir* 2001, 17, 6094.
- Zhang, X.; Wu, D.; Chu, C. *J Polym Sci Part B: Polym Phys* 2003, 41, 582.
- Sayil, C.; Okay, O. *Polymer* 2001, 42, 7639.
- Sayil, C.; Okay, O. *Polym Bull* 2002, 48, 499.
- Lozinsky, V. I. *Russ Chem Rev* 2002, 71, 489.
- Lozinsky, V. I.; Plieva, F. M.; Galaev, I. Y.; Mattiasson, B. *Bio-separation* 2002, 10, 163.
- Arvidsson, P.; Plieva, F. M.; Lozinsky, V. I.; Galaev, I. Y.; Mattiasson, B. *J Chromatogr* 2003, A986, 275.
- Okoroafor, E. U.; Newborough, M.; Highgate, D.; Augood, P. *J Phys Part D: Appl Phys* 1998, 31, 3120.
- Gundogan, N.; Okay, O.; Oppermann, W. *Macromol Chem Phys* 2004, 205, 814.
- Dogu, Y.; Okay, O. *J Appl Polym Sci*, to appear.