Fast pH-Thermo-Responsive Copolymer Hydrogels with Micro-Porous Structures

R. Kishi,[1] T. Miura,[1] H. Kihara,[1] T. Asano,[2] M. Shibata,[2] R. Yosomiya[2]

[1]*Research Center of Macromolecular Technology, National Institute of Advanced Industrial Science and Technology, 1-1-1 Higashi, Tsukuba, Ibaraki 305-8565, Japan*
[2]*Department of Industrial Chemistry, Chiba Institute of Technology, 2-17-1, Tsudanuma, Narashino, Chiba 275-0016, Japan*

Received 2 April 2002; accepted 22 July 2002

ABSTRACT: Micro-porous copolymer hydrogels were prepared by γ-ray irradiation of mixed solutions of *N*-isopropylacrylamide (NIPAAm) and acrylic acid (AAc) above the lower critical solution temperature (LCST). From Cryo-SEM observations, the gels were found to consist of three-dimensional fibrous micro-gels and micro-pores. The copolymer gels swelled at temperatures below the LCST and shrunk at temperatures above it, and they showed rapid volume transitions on a time scale on the order of a minute when experiencing temperature changes between 10 and 40°C. The transition times for thermal shrinking were almost the same regardless of AAc composition, but the transition times for thermal swelling were increased with increasing AAc contents. The copolymer gels also showed rapid volume transitions with time constants on the order of an hour on experiencing pH changes between 2 and 12. The transition times for pH volume change at 10°C were within one hour, except for the gels containing only small amounts of AAc. On the other hand, the transition times for pH-dependent volume change at 40°C were increased with increasing AAc content. The lower responsiveness of the transition results from an increase in hydrophobicity arising from the formation of inter- and intra-molecular hydrogen bonds between the non-ionized carboxylic acid groups and the amide groups. © 2003 Wiley Periodicals, Inc. J Appl Polym Sci 89: 75–84, 2003

Key words: copolymerization; crosslinking; hydrogels; phase separation; radiation

INTRODUCTION

Polymer gels have recently attracted great interest in the field of functional polymers. These materials have properties intermediate between solids and liquids, since they consist of a three-dimensional network of crosslinked polymers and solvent. Some polymer gels can change their volume reversibly, depending on factors such as temperature, solvent composition, ionic strength, pH, electric field, and light.[1,2] This effect can be widely applied in a variety of fields such as chemical engineering, medicine and pharmacy, life sciences, food, and agriculture. An important factor governing their application is the response time of their volume changes. It is well known that the characteristic time of volume change is proportional to the square of the linear size of the gel.[3] Therefore, gels of small size such as microspheres, fine fibers and thin films were synthesized with the intention of improving their responsiveness. However, these small gels present some handling problems.

Correspondence to: R. Kishi (r-kishi@aist.go.jp).

Journal of Applied Polymer Science, Vol. 89, 75–84 (2003)

In order to improve the response time without simultaneously decreasing the gel size, our research group successfully synthesized micro-porous poly(methyl vinyl ether) (PVME) hydrogels by γ-ray crosslinking of PVME above the lower critical solution temperature (LCST).[4,5] The aqueous solution of PVME shows phase separation at the LCST of 34°C,[6] and is easily crosslinked into hydrogels by high energy radiation. The structure of the resulting hydrogels is dependent upon the γ-ray intensity and the irradiation temperature.[5]

When the radiation intensity is lower than 1.5 kGy/h, the PVME solution was kept at room temperature during irradiation. Under these conditions, PVME was crosslinked below the LCST, and a transparent gel with a homogeneous and dense structure was formed. On the other hand, close to the ^{60}Co source, the PVME solution temperature increased by the radioactive heating induced by the high intensity radiation (>9 kGy/h). At this position, PVME was crosslinked during a temperature rise from 25 to 45°C.[7] Phase separation occurred, and an opaque gel with a micro-porous structure was formed. The micro-porous gel showed a rapid volume transition on alteration of its temperature. This effect is derived from its structure of continuous reticulated fibrous gels and

TABLE I
Feed Compositions Used in Preparation of Copolymers and Properties of Copolymers

Sample code	Feed composition (mmol)		Fraction in polymer[a] (mol %)		Molecular weight[b]		Cloud point (°C)
	NIPAAm	AAc	NIPAAm	AAc	Mw × 10^{-5} (g/mol)	Mw/Mn	
PNA-0 (PNIPAAm)	25	0	100	0	3.8	4.39	32.7
PNA-10	22.5	2.5	92.36	7.64	3.4	4.21	31.7
PNA-20	20	5	82.65	17.35	3.5	4.42	30.8
PNA-30	17.5	7.5	74.48	25.52	2.5	3.94	29.2
PNA-50	12.5	12.5	59.29	40.71	0.94	2.42	25.8

[a] Determined by titration.
[b] Molecular weight (Mw) and Mw/Mn measured by GPC.

pores, which can behave as water channels when the gel undergoes volume transitions.

γ-ray irradiation appears to be an effective and reproducible method for the preparation of other micro-porous hydrogels. In the previous paper, we reported the preparation and properties of fast responsive, micro-porous poly(*N*-isopropylacrylamide) (PNIPAAm) hydrogels prepared by γ-ray polymerization of *N*-isopropylacrylamide (NIPAAm) aqueous solution above the LCST.[8] Close to the radiation source, PNIPAAm micro-porous hydrogels were formed reproducibly. The gels showed a fast and reversible volume transition, similar to the PVME micro-porous gels described above, following a change in temperature.

The micro-porous PNIPAAm gels can be synthesized by radical polymerization. Gehrke et al. synthesized fast response, temperature-sensitive PNIPAAm hydrogel by the copolymerization of NIPAAm with crosslinker at room temperature for nine minutes with subsequent maintenance of temperature (37.9°C) above the LCST for 24h.[9] The volume change of their hydrogel was much faster than a homogeneous PNIPAAm gel prepared below the LCST. Hoffman et al. also reported the preparation of micro-porous PNIPAAm hydrogels by radical copolymerisation of NIPAAm with crosslinker above the LCST in the presence of hydroxypropyl cellulose as a pore-forming agent.[10] Furthermore, Sakohara et al. synthesized fast responsive PNIPAAm and poly(*N*,*N*-diethylacrylamide) (PDEAAm) hydrogels by radical polymerization above the LCST.[11] They investigated the relationship between the gels' synthetic conditions, their porous structure and their swelling or shrinking kinetics. However, all of these methods appear to generate difficulties in making reproducible gels. In the past studies, the micro-porous gels consisted of single components such as PVME, PNIPAAm and PDEAAm. However, the study of the micro-porous copolymer gels has not yet been explored. The micro-porous copolymer gels consist of a thermo-responsive unit and other functional units which are expected to respond not only to temperature change but also to other stimuli.

For the present work, we chose acrylic acid (AAc) as a co-monomer and attempted to prepare micro-porous copolymer gels by γ-ray irradiation. The responsive properties of micro-porous poly(NIPAAm-*co*-AAc) hydrogels obtained are investigated as a function of polymer condition and external condition. It was found that the micro-porous copolymer gels show fast volume transitions on both temperature and pH change.

EXPERIMENTAL

Materials

NIPAAm (ACROS Organics, Geel, Belgium) was recrystallized from a hexane / benzene mixture. AAc and tert-butyl alcohol (Wako Pure Chemical Industries, Osaka, Japan) were distilled before use. Hydrochloric acid (0.01*M*) and sodium hydroxide (0.01*M*) solutions were purchased from Wako Pure Chemical Industries. All other materials were used as received.

Synthesis and characteristics of linear PNIPAAm and poly(NIPAAm-*co*-AAc)

The LCST of copolymers is a decisive factor in the phase separation process, which plays an important role in forming the micro-porous structures of gels. Hence, it is necessary to examine the LCST of the linear copolymers in aqueous solution. The homopolymer [PNA-0 (PNIPAAm)] and the random copolymers (PNA-10, 20, 30, 50) were synthesized using the feed compositions shown in Table I. The feed compositions of NIPAAm and AAc were varied, but their sum was fixed at 25 mmol. NIPAAm, AAc and α,α′-azobisisobutyronitrile (0.25 mmol) were dissolved in tert-butyl alcohol (30 mL). After nitrogen gas was introduced into the monomer solution at room temperature for 30 min, the polymerization was carried out at 60°C for 8 h. After completion of the polymerization, the solvent was evaporated and the remaining solid dissolved in deionized water. PNIPAAm and copolymers were purified by dialysis using Spectra / Por Membrane (Spectrum Laborato-

TABLE II
Feed Compositions and Swelling Properties of Micro-Porous Copolymer Gels

Sample code	Feed composition (mmol)		Fraction in gel[a] (mol %)		Degree of swelling in water, L/Lo			LCST[b] (°C)
	NIPAAm	AAc	NIPAAm	AAc	10°C	25°C	40°C	
PGNA-0 (PNIPAAm gel)	30	0	100	0	1.79	1.57	0.99	33.3
PGNA-10	27	3	91.1	8.9	1.94	1.64	1.03	32.9
PGNA-20	24	6	84.3	15.7	1.9	1.57	1.03	31.9
PGNA-30	21	9	76.9	23.1	1.99	1.49	1.02	30.1
PGNA-50	15	15	59.1	40.9	1.62	1.06	0.99	26.9

[a] Determined by elemental analysis using freeze-dried samples.
[b] Determined by swelling measurement in deionized water. Temperature was raised stepwise from 5 to 50°C.

ries, MWCO: 3,500) in deionized water at 5°C for over one week and then freeze-dried.

The molecular weights (Mw) of the polymers were determined by gel permeation chromatography (column: TOSOH TSK-GEL α-M, eluent: MeOH with 10 *mM* LiBr) calibrated with standard polyethyleneoxide and polyethleneglycol. The fraction of AAc in the copolymers was determined by the titration method reported by Feil et al.[12] The cloud point of 1 wt % aqueous polymer solutions was determined from the 50% transparency at 500 nm at different temperatures. The rate of heating of the samples was adjusted to 1°C/min.

Preparation of micro-porous gels

In this system, it is not necessary to add the crosslinker to the monomer solution, because the polymers produced by irradiation can be crosslinked by exposure to the radiation. The details of the reaction processes under the irradiation have been reported in the literature.[13] NIPAAm and AAc were dissolved in deionized water (16 mL), and purged with nitrogen gas. Deionized water without additives was used as the solvent in order to avoid the formation of by-products under irradiation. The feed composition of NIPAAm and AAc were varied, but their sum was fixed to be 30 mmol (Table II). These solutions were then transferred into several disposable polystyrene cells (10 x 10 x 45 mm). The gels were prepared by γ-ray irradiation in the vicinity of a ^{60}Co source (110.5 TBq). The intensity and time of radiation were 9.21 kGy/h and 14 h, respectively. The temperature change during irradiation was monitored by thermocouple.

Measurements

The gels, prepared in disposable cells, were cut into slices (thickness: 5 mm) and washed several times with a large amount of water at 5°C. Size and shape changes of the gel were recorded on a Hi-8 videocassette recorder (SONY, EVO-9650) equipped with a CCD camera. The size of the gel was measured under various conditions using an image analysis system (Kenko, Measure unit MC-50). The degree of swelling in length, L/L_0 was calculated from the size of the gel under various conditions (L) and the inner size of the disposable cells (L_0; 10 mm) used in their preparation. The infrared spectra of freeze-dried gels in KBr disks were recorded on a JASCO, FTIR-620. The content of AAc units in the copolymer gels was determined by elemental analysis of the freeze-dried gels. The internal structures of the gels were observed by Cryo-SEM to prevent structural change during the drying process.[14] The field emission scanning electron microscope (TOPCON, DS-720) equipped with a cryo unit (VG Microtech, Polarprep 2000 cryo system) was used for the structural observations. The cryo-SEM images were obtained by the method reported by Suzuki et al.[15] Gels swelled at room temperature were used for the preparation of Cryo-SEM samples. The structure of the shrunk gels at 40°C was also observed.

RESULT AND DISCUSSION

LCST of linear PNIPAAm and poly(NIPAA-co-AAc) in water

The LCST of PNIPAAm and copolymers prepared by radical polymerization were examined in distilled water prior to the synthesis of the gels. The LCST values for the polymers are shown in Table I. Aqueous solutions of PNIPAAm underwent phase separation at approximately 33°C. On the other hand, the LCST of poly(NIPAAm-*co*-AAc) was lower than that of the NIPAAm homopolymer and decreased with increasing AAc content in the copolymers. Thermal phase transition phenomena of poly(NIPAAm-*co*-AAc) in various pH solutions have previously been reported. Chen and Hoffman studied the effect of AAc content on the LCST of random copolymers of over a limited pH range from 4.0 to 7.4.[16,17] The LCST of random copolymers increased rapidly with increasing AAc content. Especially at a pH of 7.4, phase separation

was not observed for copolymers without low AAc content, owing to electrostatic repulsion produced by the complete ionization of carboxylic acid groups. Jones investigated the thermal properties of poly-(NIPAAm-*co*-AAc) under acidic conditions.[18] In the pH range of 1.5 to 3.5, the LCST of a copolymer containing 32 mol % AAc units was lower than that of the PNIPAAm homopolymer and decreased with decreasing pH values. Below the pK_a, the carboxylic acid groups of the AAc unit changed to the undissociated non-ionized state. Jones considered that the lowering of the LCST in the low pH range resulted from the hindrance of the water-NIPAAm interactions and from an increase in the hydrophobicity owing to the formation of inter- and intra-molecular hydrogen bonds between the unionized carboxylic acid groups of AAc and the amide groups of NIPAAm. From cloud-point determinations, Yoo et al. estimated the pK_a value of a copolymer containing 20 mol % AAc units to be 4.2.[19] The dissociation constant of the carboxylic acid groups of the copolymer in pure water is estimated to be below 10^{-4} from the pK_a value. In pure water, carboxylic acid groups in the copolymers are almost completely undissociated and can form inter- and intra-molecular hydrogen bonds with amide groups in NIPAAm units. Therefore, the lower LCST in pure water (Table I) results from the hindrance of the water-NIPAAm interactions and the increase in hydrophobicity resulting from hydrogen bonding.

It is expected that the LCST of γ-ray formed copolymers will be almost the same as that of the copolymers prepared by radical copolymerization shown in Table I, which are lower than that of PNIPAAm. Therefore, the micro-porous copolymer gels may be obtained by the same radiation method used to prepare the micro-porous PNIPAAm gel.[8]

Formation of micro-porous (poly(NIPAAm-*co*-AAc)) gels

At all monomer compositions employed, opaque and heterogeneous poly(NIPAAm-*co*-AAc) gels were formed by γ-ray irradiation. Figure 1 shows the temperature changes of water and an aqueous solution of NIPAAm-AAc (molar ratio of monomer; NIPAAm : AAc of 9 : 1) during irradiation. The temperature of the water was gradually increased by the radioactive heating and after 6 h was held constant at 45°C. In contrast, in the case of the monomer solution, the exothermic peak caused by the radiation-induced polymerization was observed immediately after commencing irradiation. After the exothermic reaction, the temperature of the monomer solution increased gradually to that of the water reference sample. Other solutions having different monomer fractions showed similar temperature profiles. We suggest that the formation of phase-separated gel is caused by polymerization and crosslinking reactions at temperatures above the LCST of copolymers.

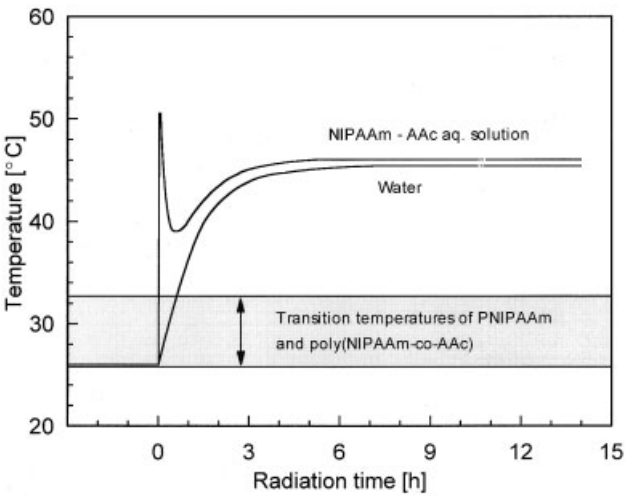

Figure 1 Temperature changes of water and aqueous solution of NIPAAm-AAc (molar ratio of monomers NIPAAm : AAc of 9 : 1) during irradiation. Intensity of radiation: 9.21 kGy/h. LCST of PNIPAAm and copolymers are also shown in this figure.

Except for PGNA-50 (Table II), the micro-porous gels (PGNA-0, 10, 20, 30) swelled approximately 1.5 times by length in deionized water at room temperature. PGNA-50 hardly swelled under the same conditions, but swelled approximately 1.6 times by length in water at 10°C. At 40°C, all gels shrank completely. The LCST values of copolymer gels are also shown in Table II. The LCST of the gels lowered with increasing AAc content in the copolymer gels. The degree of swelling of the gel likely decreases as a result of the increase in hydrophobicity arising from the hydrogen bond formation between AAc units and NIPAAm units similar to linear copolymers of NIPAAm and AAc.

In order to obtain information about their interiors, FTIR spectra were recorded on freeze-dried gels. Figure 2 shows the infrared spectra of the homopolymer gel (PGNA-0) and copolymer gels (PGNA-30, 50). The infrared spectrum of homopolymer gel shows amide I and amide II peaks at 1640 and 1550 cm^{-1}, respectively. In addition to these peaks, the carbonyl stretching bond attributed to the carboxylic acid group of AAc units is observed at 1715–1725 cm^{-1} in copolymer gels (PGNA-30, 50). Aoki et al. observed the hydrogen-bonded carbonyl peak at 1613 cm^{-1} originating from inter-polymer associations between poly(*N, N*-dimethylacryamide) and poly(acrylic acid) (PAAc).[20] It is well known that poly(acrylamide) derivatives and PAAc form inter-polymer complexes in solution through nearly one-to-one hydrogen bonding between amide groups and carboxylic acid groups.[21] Therefore, the hydrogen-bonded carbonyl peak is easily detected by IR measurement. On the other hand, it is difficult to

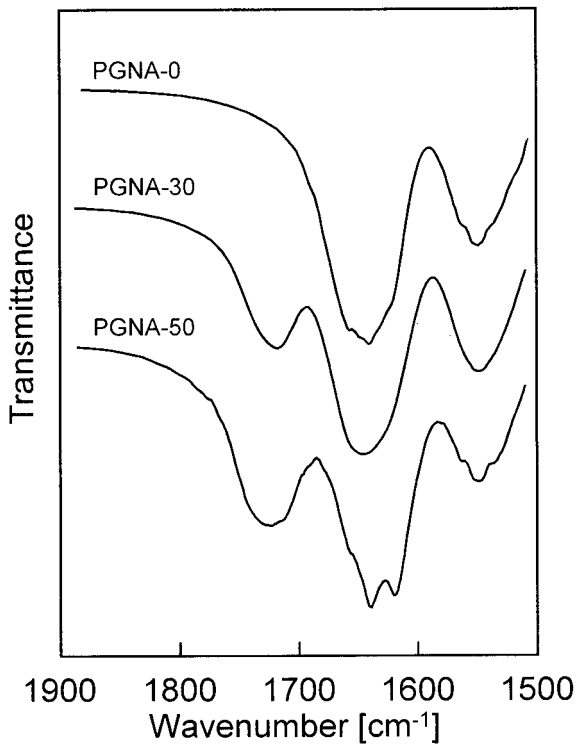

Figure 2 Infrared spectra of the freeze-dried homopolymer gel (PGNA-0) and copolymers gels (PGNA-30, 50).

form one-to-one hydrogen bonds between amide groups and carboxylic acid groups if the gels consist of random copolymers of NIPAAm and AAc. The hydrogen bonding in copolymer gels seems to be partial, and the amount of hydrogen bonding is much lower than that of the inter-polymer complex. Therefore, detection of the hydrogen bonding in the copolymer gels is difficult compared to the inter-polymer complex. In our work, an absorption peak originating from a hydrogen-bonded AAc carbonyl group was observed at 1619 cm^{-1} only for the PGNA-50. The amount of hydrogen bonding in the gels decreases with decreasing numbers of AAc units in the gel. Hence, except for PGNA-50, the peak indicating hydrogen bonding seemed to be covered by the large peak of amide I, and therefore it could not be detected by IR measurement.

Structural observation of micro-porous [poly(NIPAAm-*co*-AAc)] gels

The Cryo-SEM images of the inside of the micro-porous gels are shown in Figure 3. Porous structures consisting of a fine fibrous network are observed in all gels. PGNA-0 (PNIPAAm homopolymer gel) was composed of fine fibers of diameter <2 μm and fine particles of diameter approx. 3-5 μm [Fig. 3(a)]. In the case of copolymer gels, PGNA-10, 30, the size of fibers, particles and pores were larger than those of homopolymer gel [Fig. 3(b) and (c)], but the fibrous structure was almost the same as the homopolymer gel. For example, the fibrous network of PGNA-10 consisted of fibers with diameters of 2–5 μm and particles with diameters of 4–7 μm [Fig. 3(b)]. The Cryo-SEM image of PGNA-10 shrunk in water (40°C) is shown in Figure 3(e). The micro-porous structure at room temperature [Fig. 3(b)] was changed to an aggregated structure consisting of shrunken fibrous gels assembled in close contact. Above the LCST, shrinkage of the gel may be generated by contraction and aggregation of each fibrous gel and subsequent water release from the inside pores to the outside of the gel. On the other hand, the fibers and particles of PGNA-50 [Fig. 3(d)] were much smaller than those of the other copolymer gels. Moreover, the morphorgy of PGNA-50 was different from not only the other copolymer gels but also the homopolymer gel. PGNA-50 almost shrank in water (25°C) rather than swelling, shown in Table II. However, the Cryo-SEM image of PGNA-50 [Fig. 3(d)] was completely different from the image of PGNA-10 shrunk in water at 40°C [Fig. 3(e)].

These fibrous networks are considered to be fibrous gels produced by the phase separation of polymers, since the temperature during radiation is much higher than the LCSTs of polymers (Fig. 1). The lowering of the LCST with increasing hydrogen bonding between NIPAAm and AAc has already been described above. The change in the hydrophobicity associated with hydrogen bond formation affects the phase separation process, which in turn plays an important role in forming the micro-porous structures of gels. In addition, the rates of copolymerization and crosslinking reactions are also considered important factors in the formation of micro-porous structures. The differences in the structure of PGNA-50 seem to result from these factors. It is not easy to clarify the mechanism of porous structure formation, because observation of samples is impossible during γ-ray irradiation. Apparently these factors interact in a complex fashion during the gelation process, resulting in the different micro-porous structures formed by γ-ray irradiation.

Thermal volume changes of micro-porous gels in water

The thermal shrinking and swelling behaviors of the micro-porous hydrogels were studied in deionized water. Figure 4 shows the time profile of the volume change of these gels. They underwent thermal contraction when, after swelling to equilibrium at 10°C, they were immersed in water at 40°C. The time required for the gels to shrink to their equilibrium state was remarkably short, approximately 3 min. The micro-porous gels completely recovered their original size and shape when the shrunk gels were immersed in water

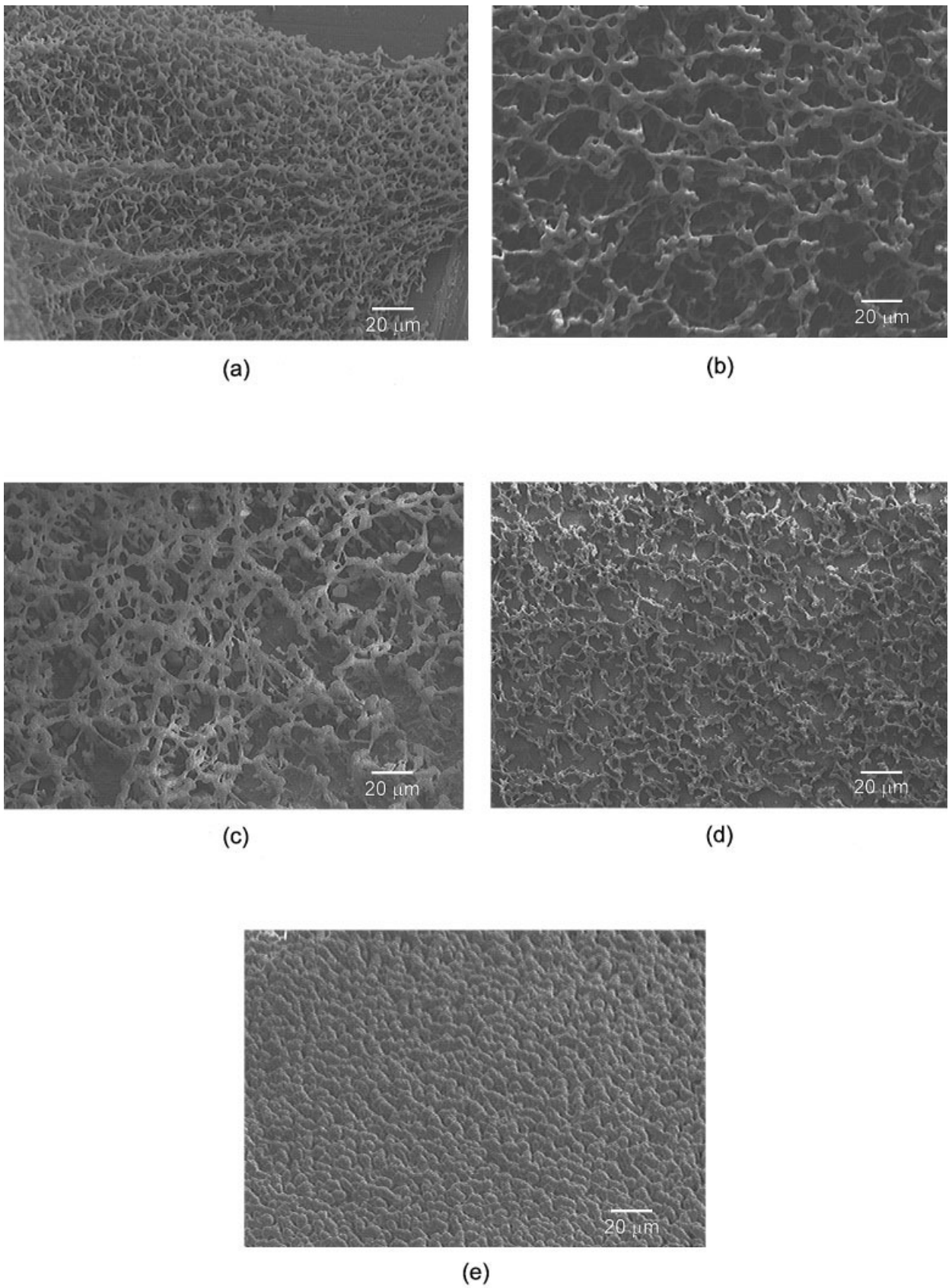

Figure 3 Cryo-SEM images of the interior of the micro-porous copolymer gels: (a) PGNA-0; (b) PGNA-10; (c) PGNA-30; (d) PGNA-50; and the inside of shrinking PGNA-10 (e). For the structural observation of the shrinking gels, PGNA-10 was immersed in water at 40°C for 10 min, and then transferred to the Cryo unit. The Cryo-SEM image of shrinking gel was obtained by the same method used for swelling gel.

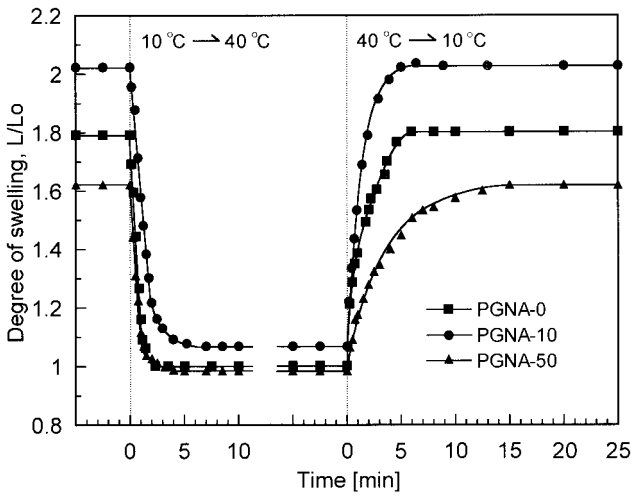

Figure 4 Time profiles of the shrinking and the swelling of the micro-porous gels (PGNA-0, 10, 50) by temperature change. Swelling ratio L/L_0, was calculated from the size of the gel at each time (L) and the inner size of the disposable cells (L_0 = 10 mm). The solid line is provided to aid the viewer.

at 10°C. The thermal volume change could be repeated many times while cycling the temperature change between 10 and 40°C. In the previous paper, the thermal properties of the micro-porous PNIPAAm gel prepared by γ-ray radiation above the LCST were compared to those of the transparent and homogeneous PNIPAAm gel prepared by radical polymerization below the LCST.[8] The response time of the micro-porous gel is much shorter than that of the homogeneous PNIPAAm gel, which showed no shrinking in the time scale shown in Figure 4.

The effect of the copolymerization on the response time of the volume change was investigated with the shrinking and swelling data shown in Figure 4. The time required for shrinking and swelling to the equilibrium state is plotted against the AAc fraction in copolymer gels in Figure 5. The transition times for thermal shrinking were 2-4 min, which are almost the same for all polymers. On the other hand, the thermal transition for swelling shows different behavior from the transition for shrinking. The copolymer gels containing fewer AAc units, such as PGNA-0, 10, 20, recovered their original size and shape within about 5 min, but the AAc rich gels such as PGNA-30, 50 took a longer time for swelling, and the transition times were increased with increasing AAc content. In the shrinking state at 40°C, the hydrophobicity of the gel increased with the increase in hydrogen bonding between AAc units and NIPAAm units. Accordingly, it was suggested that the hydrophobic interaction markedly retarded the swelling of AAc rich gels below the LCST.

Shrinking and swelling of micro-porous gels by pH change

The shrinking and swelling behaviors of the micro-porous hydrogels were studied in HCl (0.01*M*; pH 2) and NaOH (0.01*M*; pH 12) aqueous solutions at constant temperatures above (40°C) and below (10°C) the LCST. In the NaOH solutions at 10°C, the micro-porous gels, except for PGNA-0 (PNIPAAm gel), swelled greatly in comparison with the water. This is ascribed to the electrostatic repulsion produced by complete ionization of the carboxylic acid groups (Table III). Tanaka et al. reported that the degree of swelling of transparent and homogenous poly(NIPAAm-*co*-sodium acrylate) gels was drastically increased on increasing the electrolytic components at a constant temperature below the LCST.[22] These homogenous gels consist of continuous three-dimensional networks so that they show the largest swelling towards their exteriors by electrostatic repulsion of ionized groups. However, the degrees of swelling (L/L_0) of our micro-porous copolymer gels were approximately 2.6– 3.1, and did not depend on the fraction of AAc present (Table III). The swelling properties of the micro-porous copolymer gels can be explained as follows. The micro-porous gels consist of fibrous gels and pores filled with water. The fibrous gels can be swollen by ionization of carboxylic acid groups, but their swelling may also occur in the direction of the pores. Therefore, the degree of swelling of the gels appears to be independent of the ionized units.

The time profiles of the volume changes of homopolymer gel (PGNA-0), copolymer gels containing

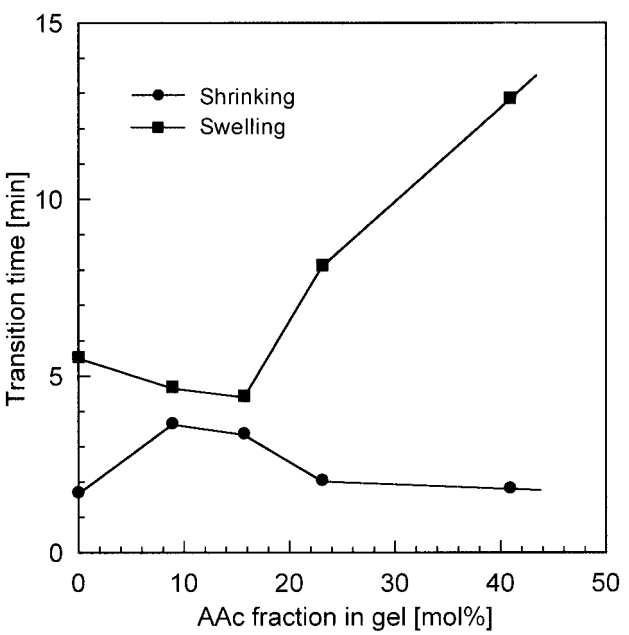

Figure 5 The dependence of time required for the thermal shrinking and swelling to equilibrium state on the AAc fraction in copolymer gels.

TABLE III
Degree of Swelling of Gels in Various Conditions

Sample code	Degree of swelling, L/Lo					
	HCl solution (pH 2)			NaOH solution (pH 12)		
	10°C	25°C	40°C	10°C	25°C	40°C
PGNA-0 (PNIPAAm gel)	1.79	1.57	0.99	1.79	1.58	1
PGNA-10	1.86	1.65	1	2.63	2.55	2.54
PGNA-20	1.78	1.47	1.03	2.58	2.58	2.55
PGNA-30	1.84	1.36	0.97	3.12	3.1	3.06
PGNA-50	1.49	1.02	0.96	2.92	2.9	2.85

fewer AAc units (PGNA-10), and larger amount of AAc (PGNA-50) are shown in Figure 6 (40°C) and Figure 7 (10°C). In the solutions at 40°C, homopolymer gel (PGNA-0) completely shrunk and showed no volume change with changes in pH (Fig. 6). On the other hand, PGNA-10 swelled about two-and-a-half times by length in a solution of pH 12 at 40°C. PGNA-10 was shrunk completely within one hour in HCl solution, and it returned to its original size and shape within two hours in NaOH solution (Fig. 6).

The volume changes induced by pH changes of the copolymer gels occurred more slowly than those induced by thermal change, because solvent diffusion to the interior of the gels is slower than thermal diffusion. However, the time required for the pH shrinking and swelling of PGNA-10 was much shorter than that of the disk-like homogenous poly(NIPAAm-*co*-AAc) gel whose size was considerably smaller than the PGNA-10 used in this study.[23] PGNA-50 also showed shrinkage in acidic solution; however, the shrinkage speed was reduced after 1 h. PGNA-50 recovered its original size and shape in basic solution, but the time required for swelling was over 10 h.

The time required for the pH induced shrinking and swelling to reach equilibrium is plotted against the AAc fraction present in the copolymer gels in Figure 8(a). At 40°C, the transition times for the pH induced shrinking were within one hour except for that of PGNA-50. In the case of PGNA-50, two hours were required to reach the full extent of shrinkage. It is well known that the thermo-responsive, homogeneous poly(NIPAAm-*co*-butyl methacrylate) gel forms the collapsed dense skin layer on the surface of the gel during the thermal shrinking process.[24] The collapsed skin layer prevents the release of water molecules from the inside of the gel to the outside, thereby reducing the shrinking speed of the gel at the initial stage of thermal shrinkage. However, the surface skin layer was not observed in our micro-porous gels during the pH induced shrinkage process, and slowing down occurred in the later period of shrinking. In the case of the micro-porous gels, the mechanism of the lowering of the shrinking rate is not related to skin

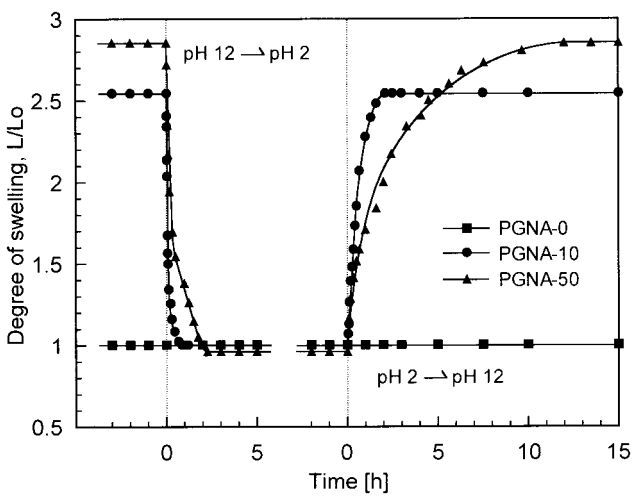

Figure 6 Time profiles of the shrinking and the swelling of the micro-porous gels (PGNA-0, 10, 50) by pH change at 40°C. Swelling ratio L/L_0, was calculated from the size of the gel at each time (L) and the inner size of the disposable cells (L_0: 10 mm). The solid line is provided to aid the viewer.

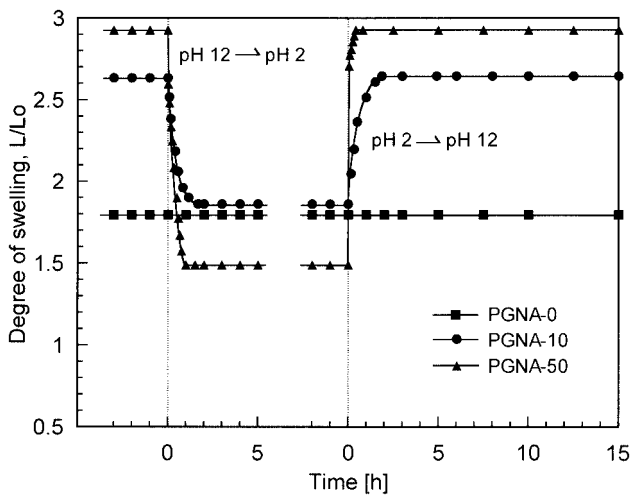

Figure 7 Time profiles of the shrinking and the swelling of the micro-porous gels (PGNA-0, 10, 50) by pH change at 10°C. Swelling ratio L/L_0, was calculated from the size of the gel at each time (L) and the inner size of the disposable cells (L_0: 10 mm). The solid line is provided as a visual aid.

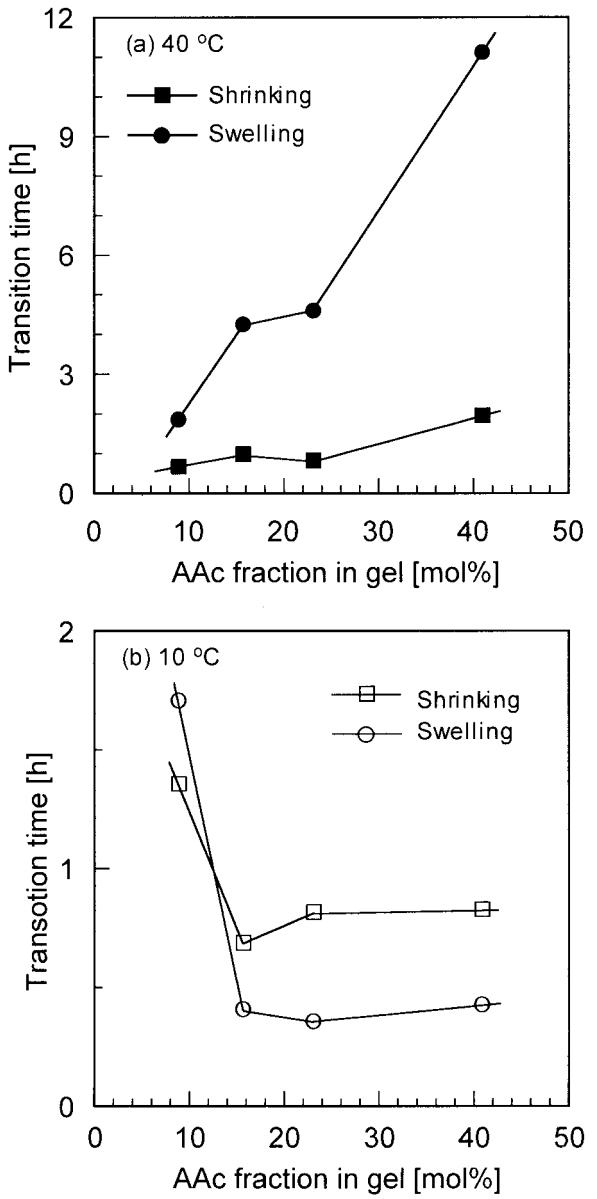

Figure 8 The dependence of the time required for the pH shrinking and swelling to equilibrium state on the AAc fraction in copolymer gels [(a) 40°C; (b) 10°C].

layer formation. Under acidic conditions, the fibrous gels shrank and aggregated with each other because of the disappearance of electrostatic repulsion and the generation of hydrophobic interactions owing to hydrogen bond formation between undissociated carboxylic acid groups and amide groups. Notably, the hydrophobic aggregation of the fibrous gels composing PGNA-50 is much stronger than that of other fibrous gels because it contains equivalent molar NIPAAm and AAc units. Consequently, the strong aggregation of the fibrous gels seems to prevent the transfer of water from the inside of the gel outwards during the shrinking process. Thus the shrinking speed is reduced.

The pH induced swelling patterns of copolymer gels at 40°C were, compared to the shrinking behavior, significantly influenced by the AAc fraction. The transition times for swelling were sharply increased with increasing AAc units [Fig. 8(a)]. It appears that the hydrophobic aggregation of the fibrous gels inhibits the swelling of the micro-porous gels in basic solution as compared to the shrinking in acidic solution.

On the other hand, the volume transition at 10°C showed different behavior from that at 40°C. The micro-porous copolymer gels showed rapid shrinkage at 10°C, when the swollen gels in NaOH solution were immersed in HCl solution (Fig. 7). The shrunken copolymer gels completely recovered their original sizes and shapes within two hours of immersion in NaOH solution. However, homopolymer gel (PGNA-0) retained a constant volume on pH change. The time required to reach equilibrium for the pH shrinking and swelling is plotted against the AAc fraction in copolymer gels in Figure 8(b). The transition time of PGNA-10 for pH shrinking and swelling at 10°C was approximately 1.5 hours. A reduction of the transition time for volume change was not observed relative to the volume change at 40°C. On the contrary, the times required for the pH shrinking and swelling of PGNA-20, 30, 50 were each shorter than that of PGNA-10. In the solutions at 10°C, it seems that the micro-porous gels were not affected by the hydrophobic interaction and changed their volume only by electrostatic repulsion. However, we did not investigate the differences in the time required for volume change of the PGNA-20, 30, 50 materials in this work.

CONCLUSION

Fast responsive and pH-thermo-responsive copolymer hydrogels were prepared by γ-ray irradiation of mixed solutions of NIPAAm and AAc above the LCST of poly(NIPAAm-*co*-AAc). Irradiation of samples close to the radiation source resulted in the formation of opaque and milky white copolymer gels. From Cryo-SEM observations of the gels, micro-porous structures consisting of three-dimensional fibrous micro-gels and micro-pores were recorded. The micro-porous gels immersed in deionized water swelled below and shrunk above the LCST. The LCST of the copolymer gels lowered with increasing AAc contents, due to hydrogen bond formation between AAc units and NIPAAm units, which is similar to the phenomenon in linear copolymers of NIPAAm and AAc. Actually, an absorption band characteristic of a hydrogen-bonded AAc carbonyl group was observed by FTIR in the freeze-dried copolymer gel containing a large amount of AAc (PGNA-50). The micro-porous gels showed rapid volume transition with times on the order of minute in response to temperature changes between 10 and 40°C. The transition times for thermal

shrinking were almost the same irrespective of AAc composition, but the transition times for thermal swelling were increased with increasing AAc content. The micro-porous gels also showed rapid volume transition with a time on the order of one hour at constant temperatures (10, 40°C) in response to changes in pH between 2 and 12. The transition times for pH shrinking and swelling at 10°C were slightly decreased with increasing AAc content in the gels. On the other hand, the transition times for pH shrinking and swelling at 40°C were increased with increasing AAc content. Particularly for pH swelling at 40°C, the transition time was greatly influenced by the amount of AAc in the gels. The reduced response of the thermal and pH swelling processes resulted from the increase in hydrophobicity following the formation of inter- and intra-molecular hydrogen bonding between the non-ionized carboxylic acid groups of AAc and the amide groups of NIPAAm. According to the experimental results, it became clear that the micro-porous copolymer gels containing small amounts of AAc (PGNA-10, 20) showed good responsiveness not only with changes in temperature but also with changes in pH in comparison with gels containing more AAc units (PGNA-30, 50).

The authors wish to thank Dr. Kiyoshi Yase and Dr. Yuji Okada of the National Institute of Advanced Industrial Science and Technology for the Cryo-SEM observation measurements. And furthermore, we acknowledge Miss Hanako Kogure of the Chiba Institute of Technology for her provision of the FTIR data.

References

1. Osada, Y. Adv Polym Sci 1987, 82, 1.
2. Tanaka, T. Scientific American 1981, 110, 244.
3. Tanaka, T.; Fillmore, D. J. J Chem Phys 1979, 70, 1214.
4. Hirasa, O. Koubunshi 1986, 35, 1100.
5. Suzuki, M.; Hirasa, O. Adv Polym Sci 1993, 110, 241.
6. Horne, R. A.; Almeida, J. P.; Day, A. F.; Yu, N. J. Colloid Interface Sci 1971, 35, 77.
7. Miura, T.; Kishi, R.; Ichijo, H. Polym J 1999, 31, 447.
8. Kishi, R.; Hirasa, O.; Ichijo, H. Polym Gels Networks 1997, 5, 145.
9. Kabra, B. G.; Gehrke, S. H. Polymer Communications 1991, 32, 322.
10. Wu, X. S.; Hoffman, A. S.; Yager, P. J Polym Sci Part A 1992, 30, 2121.
11. Gotoh, T.; Nakatani, Y.; Sakohara, S. J Appl Polym Sci 1998, 69, 895.
12. Feil, H.; Bae, Y. H.; Fiejen, J.; Kim, S. W. Macromolecules 1993, 26, 2496.
13. Spinks, J. W. T.; Woods, R. J. An Introduction to Radiation Chemistry; John Wiley & Sons, Inc., New York, 1964, Chapter 11.
14. Fujikawa, S. Electron Microsc Rev 1988, 1, 113.
15. Suzuki, M.; Tateishi, T.; Matsuzawa, M.; Saito, M. Macromol Symp 1996, 109, 55.
16. Chen, G.; Hoffman, A. S. Macromol Rapid Commun 1995, 16, 175.
17. Chen, G.; Hoffman, A. S. Nature 1995, 373, 49.
18. Jones, M. S. Eur Polym J 1999, 35, 795.
19. Yoo, M. K.; Sung, Y. K.; Cho, C. S.; Lee, Y. M. Polymer 1997, 38, 2759.
20. Aoki, T.; Kawashima, M.; Katono, H.; Sanui, K.; Ogata, N.; Okano, T.; Sakurai, Y. Macromolecules 1994, 27, 947.
21. Eustace, D. J.; Siano, D. B.; Drake, E. N. J Appl Polym Sci 1988, 35, 707.
22. Hirotsu, S.; Hirokawa, Y.; Tanaka, T. J Chem Soc 1987, 87, 1392.
23. Lee, W. F.; Shieh, C. H. J Polym Res 1999, 6, 41.
24. Kaneko, Y.; Yoshida, R.; Sakai, K.; Sakurai, Y.; Okano, T. J Memb Sci 1995, 101, 13.