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Studies of Gel Structure and Thermal Deswelling on Poly(*N*-isopropylacrylamide) Gel Treated by Freeze-Drying

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Fast-responsive deswelling of poly(*N*-isopropylacrylamide) gel after a freeze-dry (FD) treatment was investigated by means of SEM images and a kinetic method using a *N*-isopropylacrylamide (NIPAAm) monomer from the viewpoint of the mesoscopic structure comprising a partitioned polymer-network.

It was deduced from SEM images that an elastic frame comprising a partitioned polymer-network is formed by a hydrophobic interaction between polymer chains in the FD-treated gel. Fast-deswelling of the FD-treated gel results from the elasticity of a partitioned polymer-network caused water to release. The kinetic parameters on deswelling of both the conventional gel and the FD-treated gel were determined in the presence of an NIPAAm monomer. This monomer in solution is considered to play two directly-opposed roles in making a skin on the surface of the conventional gel: One is for disturbing the formation of hydrogen bonding between amide groups in the polymer; the other is for accelerating the separation of hydrated water from isopropyl groups in the polymer. Cracking the surface of a conventional gel was investigated in connection with the monomer.

Kinetic studies have been carried out in order to identify the rate-determining step in the deswelling of poly(*N*-isopropylacrylamide) gel, abbreviated as poly(NIPAAm) gel, which was treated with a freeze-dry (FD) and hydration process.[1—3] This FD-treated gel deswells approximately 10^1—10^3 times faster than an untreated gel (conventional gel). The FD treatment is a simple and prominent method for the gel to accelerate deswelling among other treatments, such as comb-type grafting and γ-ray irradiation.[4—8]

We have proposed the formation of macropores on the surface of the FD-treated gel.[1,2] The rate-determining step for deswelling was considered in relation to a hydrophobic skin layer formed on the surface of the conventional gel due to heating.[3,9]

In our previous paper,[3] it was concluded that the deswelling process for thermosensitive gels consists of three elementary processes: 1) dissociation of the hydrated water to the polymer (collapse of the "iceberg" as a distinctive structured water around the hydrophobic isopropyl groups), 2) a hydrophobic interaction between polymer chains, and 3) squeezing water out through the pores due to the deswelling pressure inside the gel. Processes 2 and 3 made the rate-determining steps for the FD-treated and the conventional gels, respectively.

However, a pending problem remained: Why the FD-treated gel could release water so rapidly during thermal deswelling. Aiming at a solution to this problem: (1) the structure of the macropore was examined based on SEM microphotographs of the FD-treated gels macroscopically, and (2) the structure of the polymer-network was examined based on kinetic studies of thermal deswelling of the FD-treated gels by using the monomer, NIPAAm, as a probe microscopically.

Up to now, we have considered the deswelling rate and its rate-determining step of the gel from the viewpoint of a hydrophobic interaction between polymer chains. It should also be considered that hydrophilic amide groups in the polymer could form hydrogen bonding between themselves, and that the polymer chains could aggregate near to each other to make a polymer network. It was assumed that the hydrophilic group of the polymer was surrounded by the hydrophobic polymer chains under the deswelling-state. The aggregation of polymer chains due to hydrogen bonding might be obstructed in the presence of a monomer. Because an additive monomer can be substituted for the hydrated water on the amide groups in the polymer.

A monomer containing the *N*-isopropyl amide group can form a hydrogen bond with amide groups in the polymer. In order to clarify the contribution of hydrogen-bond formation between polymer chains to the aggregation process, we investigate kinetically the deswelling process of FD-treated gels and conventional gels.

Experimental

Materials. *N*-Isopropylacrylamide was purchased from Wako Pure Chemical Ind., Ltd. All other chemicals were of guaranteed grade or the best commercially available.

Preparation of the Conventional Gel. Cylindrical conventional gels (2 mm in inner diameter of the mold) of poly(NIPAAm) crosslinked by *N*,*N*′-methylenediacrylamide (MDA) were prepared in water at 20 °C in the same way as described in our previous papers, except for the crosslinking ratio (R) [MDA/NIPAAm = 6/94 (mol/mol); R = 6].[1—3] The unreacted monomer was removed with repeated treatments of deswelling and swelling in water. The gel rods deswelled at 40 °C were re-swollen in 0—0.3 M NIPAAm monomer solutions (1 M = 1 mol dm^{-3}) at 22 °C.

Preparation of the FD-Treated Gel. The swollen conventional gel rods (22 °C) were frozen at −30 °C after washing in water, and then freeze-dried using FD-1 (Tokyo Rikakikai Co.).[1] The dried gel rods were re-swollen in 0—0.4 M NIPAAm monomer solutions at 22 °C.

Measurement of the Deswelling Rate. The deswelling rate of the gel was determined in the same manner as mentioned in the previous papers.[2,3] The temperature of the gel rod (rod length; L_o = 50—60 mm at 22 °C) immersed in solution was raised from 22 °C (T_1) to T_2 = 36—47 °C. The deswelling process of the gel rod was monitored with a CCD camera. The changes in the gel length (L) were measured from a picture recorded by video-tape. The deswelling rate, $-d(L/L_o)^3/dt$, was determined from the slope of the line obtained by plots of $(L/L_o)^3$ against time. The apparent activation energy (E_a) and the activation entropy change at 313 K (ΔS_{313}) were calculated by the Arrhenius equation.

SEM. Produced 6 and 10% crosslinked conventional gels were freeze-dried under the state of swelling. These freeze-dried gels were swollen at 22 °C and then deswollen at 40 °C. Finally, the deswollen gels were freeze-dried again. SEM microphotographs of gels freeze-dried under the states of swelling and deswelling were taken.

Results

SEM Images of Poly(NIPAAm) Gel. SEM microphotographs of the FD-treated gels are shown in Fig. 1.

Deswelling Profiles with and without the Skin. The volume change of the gels was measured in NIPAAm monomer solutions (0—0.4 M). The representative results are shown in Fig. 2. The FD-treated gel and the conventional gel were heated from 22 to 40 °C in a 0.3 M NIPAAm solution. The FD-treated gel deswelled rapidly in one-stage profile. On the other hand, two types of deswelling profiles were observed for the conventional gels: One had a time-lag between the first- and second-stage deswelling; the other had a one-stage profile of slow deswelling (0—100 min) without any time-lag. In the former case, the gel volume decreased drastically after the time-lag; this phenomenon had already been reported in a previous paper.[3] This catastrophe resulted from cracks of the skin layer under high pressure caused by the water release during the deswelling process. As monitored by a CCD camera, the gel rods cracked lengthwise (< 10 mm) in an NIPAAm solution. The cracks, which reached to the center of the cylindrical gel rod, appeared like a straight line drawn on the surface of the gel rod. Cracking occurs according to a certain probability. However, the cracks are irregular in size. The deswelling rate, $-d(L/L_o)^3/dt$, was obtained as the slope of the line in Fig. 2. The conventional gel after the time-lag deswelled as fast as the FD-treated gel.

Kinetic Parameters for the Conventional Gel. The deswelling rate, $-d(L/L_o)^3/dt$, should be equal to the deswelling rate constant (k), when the volume change of the gel is regarded as a zero-order reaction, as described in our previous report.[2,3] Accordingly, the kinetic parameters could be considered using the Arrhenius equation. Arrhenius plots for the deswelling of conventional gels with and without cracks are shown in Fig. 3. In the case of cracked gels, the plots fell on straight lines with almost the same slope in the region between 0—0.3 M NIPAAm. The rate constants for deswelling of the cracked gels were higher than those of non-cracked gels.

The E_a's and ΔS_{313}'s were obtained according to the Arrhenius equation with the slopes of the lines in Fig. 3. The E_a's and ΔS_{313}'s are plotted against the NIPAAm concentration (C) in Figs. 4A and 4B, respectively. The E_a's for deswelling of the cracked gels were around 90 kJ mol^{-1}, while the E_a's of non-cracked gels increased with increasing C in the region below 0.2 M. The cracking occurred too often to determine the E_a's of non-cracked gels above 0.2 M. The profile of ΔS_{313}'s–C shows a similar tendency in Fig. 4B.

Kinetic Parameters for the FD-Treated Gel. Arrhenius plots for the FD-treated gels are shown in Fig. 5. The E_a's and ΔS_{313}'s, calculated from the Arrhenius equation using the straight lines in Fig. 5 are given in Figs. 6A and 6B. Each maximum appeared on the profile of E_a–C and that of ΔS_{313}–C at around 0.1 M of C.

Probability of Cracking. The conventional gels (T_1 = 22 °C) were heated to 42.5 °C in a 0—0.3 M NIPAAm solution. The probability (P) of cracking on the skin surface of the gel was obtained from measurements with twelve gel rods, each at different concentrations of NIPAAm. The results are shown in Fig. 7. The addition of a monomer causeed P to increase. In particular, it was often observed that the gel rods split in two to three pieces in 0.3 M NIPAAm. On the other hand, the mm-sized cracks on the surface of the FD-treated gels were not monitored with a CCD camera.

E_a's and ΔS_{313}'s in Various Crosslinking Ratios. In the case of polymerization with a 6% crosslinking ratio, a small change in the polymerization temperature (T) brought about a different property of the gel, as shown in Fig. 8. Conventional gel rods were prepared at different temperatures. Five gel rods prepared at each temperature were heated from 22 to 50 °C in a 0.3 M NIPAAm solution. The lower was the polymerization temperature, the more did gel cracks appear. The gel, which was transparent at 17 °C, became slightly clouded at 20 °C, and more clouded at 22 °C, as the polymerization temperature.

Figures 9A and 9B show the relationship between E_a–R, and ΔS_{313}–R, respectively. The time lag was observed in the deswelling process of 2 and 4% crosslinked conventional gel to form a skin layer. No time lag was observed in the case of a 10% crosslinked gel. The data on 2, 4, and 10% of R were cited from our previous papers.[1—3] The E_a and ΔS_{313} of the conventional gel decreased, and reached to those of the FD-treated gel with increasing R.

Discussion

The Structure of Macropores. SEM microphotographs of the FD-treated gel are shown in Fig. 1. Figures 1-Ia and 1-IIa show macropores on a honeycombed surface of freeze-dried gels. The macropores (10—30 μm) appear as bottom-visible basins, which do not penetrate the gel. The surface of the macropores is an uneven plane, as shown in Figs. 1-Ib and 1-IIb. It was considered that water could be released

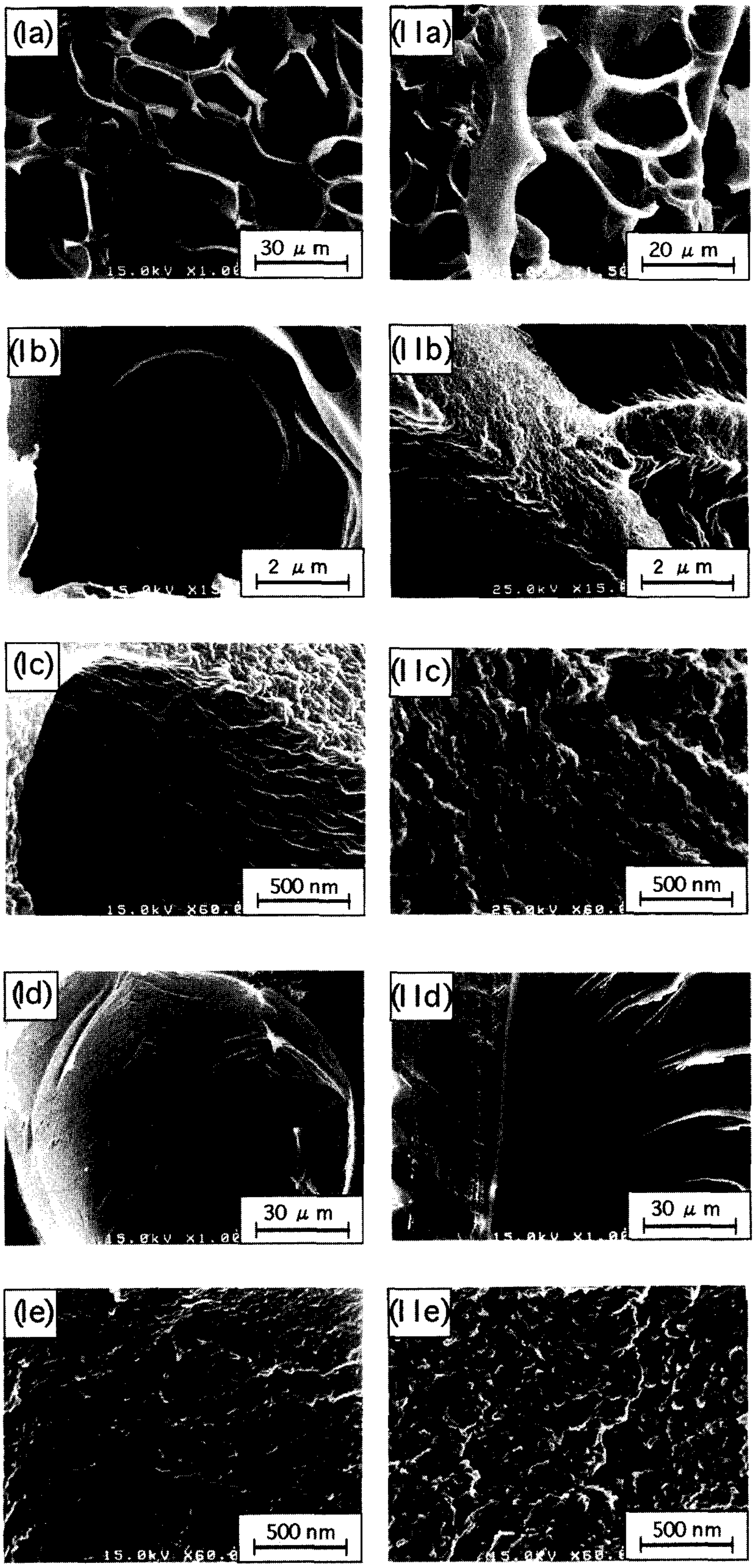


Fig. 1. SEM microphotographs of (I) 6%, and (II) 10% crosslinked gels. a—c: The gels freeze-dried from the swollen conventional gels. d—e: The gels freeze-dried from the gels of a—c, which were swollen at 22 °C and then deswollen at 40 °C.

from passing through the surface of the macoropores during deswelling of the FD-treated gel. We expected mesopores (2—50 nm) for the water releasing. However, mesopores can not be observed on the surface of macropores (Figs. 1-Ic and 1-IIc). The water-releasing pressure inside the gel may force the surface layer of the macropores to break, thus

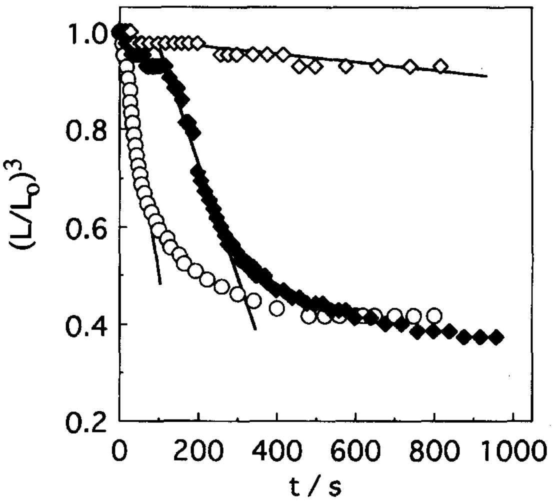


Fig. 2. Deswelling profiles of the conventional gel with (◆) and without cracks (◇), and the FD-treated gel (○). The gel rods equilibrated at 22 °C were transferred to the same solution at 40 °C in 0.3 M NIPAAm.

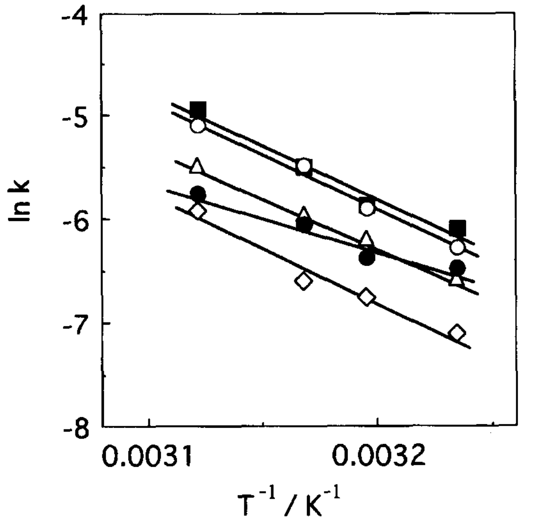


Fig. 3. Arrhenius plots on the conventional gels in water (○) and 0.3 M NIPAAm (■) with cracks, and without cracks in water (●), 0.05 M (△), and 0.1 M NIPAAm (◇).

excluding water from the gel through the macropores. On the other hand, the macropores disappeared from the surface of gels after the FD treatment under the state of deswelling (Figs. 1-Id and 1-IId), and the surface of the gels became flat. The surface of the gel freeze-dried under the state of deswelling (Fig. 1-IIe) was compared with that under the state of swelling (Fig. 1-IIc). The height of projections on the surface of the gel looks different. It seems that the surface is pressed down so as to lower the height of the projections in Fig. 1-IIe. The presence of mesopores could not be confirmed on the surfaces of gels in all SEM microphotographs.

Mesoscopic Structure of the Wall of Macropores on the FD-Treted Gel. The FD-treated gel had the property of fast-deswelling after a process of deswelling and then swelling. This result indicates the preservation of a distinctive polymer-network constructed on the wall of the macropores after

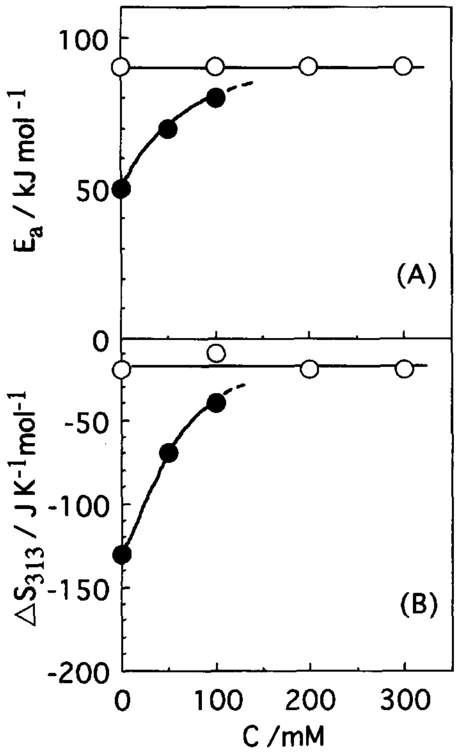


Fig. 4. (A) The monomer dependency of the apparent activation energy (E_a) for the deswelling on the conventional gel with (○) and without cracks (●). (B) The monomer dependency of the activation entropy change at 313 K (ΔS_{313}) for the deswelling on the conventional gel with (○) and without cracks (●).

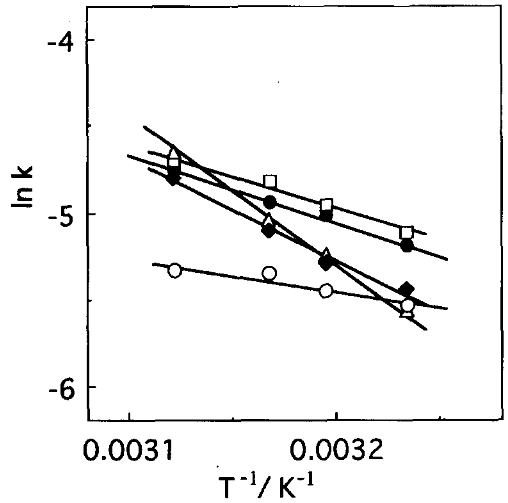


Fig. 5. Arrhenius plots on the FD-treated gels in water (○), 0.05 M (◆), 0.2 M (△), 0.3 M (□), and 0.4 M NIPAAm (●).

contracting and expanding the gel. It is plausible that the wall, which may be elastic and flexible, is restored to the former state after water release. If we suppose that an elastic frame comprising a partitioned polymer-network is formed by a hydrophobic interaction between polymer chains, the water squeezed out of the FD-treated gel must pass through the wall constructed by elastic frames into a macropore. Fig-

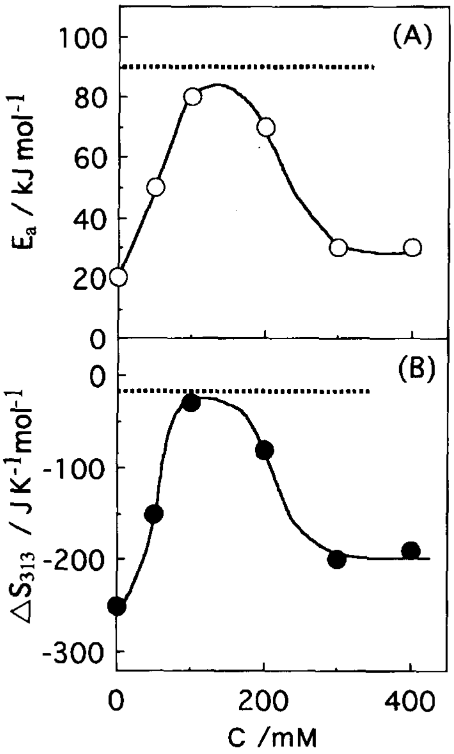


Fig. 6. (A) The monomer dependency of the apparent activation energy (E_a) for the deswelling on the FD-treated gel (○). (B) The monomer dependency of the activation entropy change at 313 K (ΔS_{313}) for the deswelling on the FD-treated gel (●). The dotted lines are cited from the data of cracked conventional gel in Fig. 4.

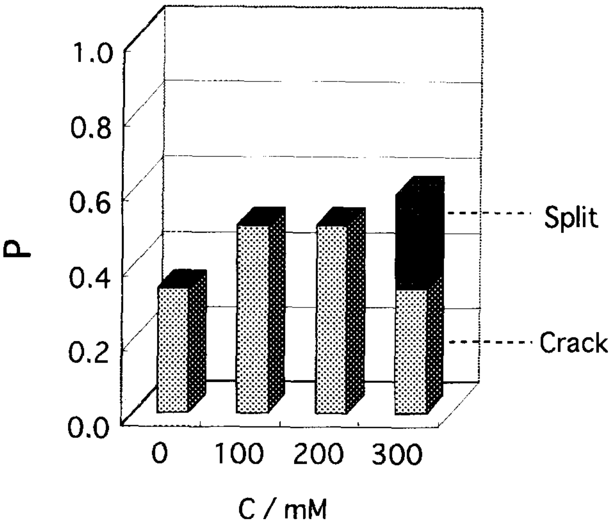


Fig. 7. The monomer dependency for the probability on cracking of the conventional gels. The cylindrical gels (L_0 = 60 mm at 22 °C) prepared within the silicone tubes (ϕ 2 mm) at 20 °C were heated from 22 to 42.5 °C.

ure 10 shows an illustration of the water-releasing process for the conventional gel with and without cracks, as well as the FD-treated gel. The skin was liable to crack when R was higher. This is because the elasticity of the polymer network became weak with increasing R.

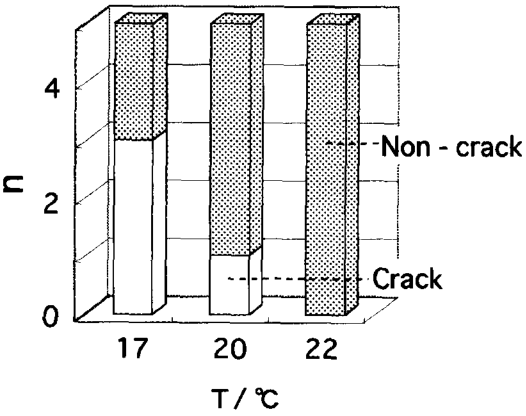


Fig. 8. The polymerization temperature and the occurrence of cracking in the conventional gels. The cylindrical gels (L_0 = 60 mm at 22 °C) prepared within the silicone tubes (ϕ 2 mm) at 17, 20, and 22 °C were heated from 22 to 50 °C in 0.3 M NIPAAm.

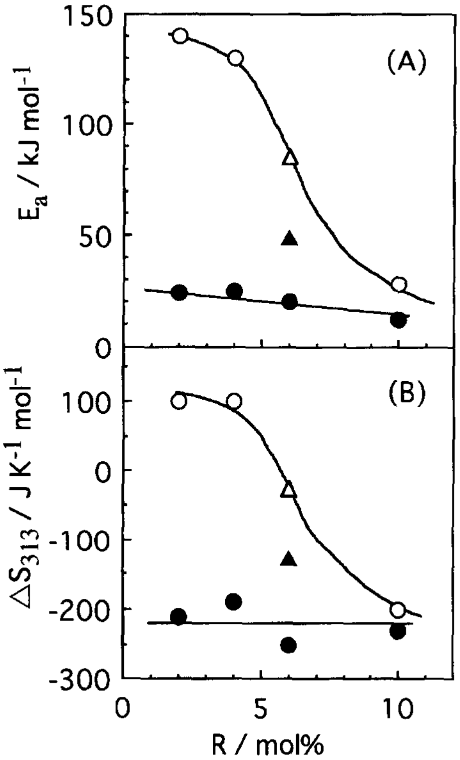
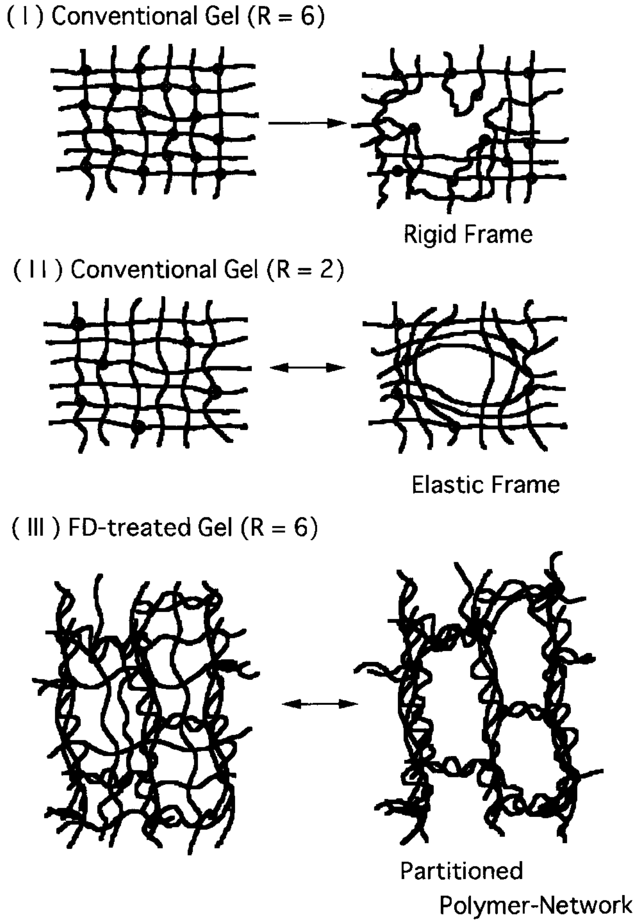


Fig. 9. (A) Relationship between R and E_a. (B) Relationship between R and ΔS_{313}. The E_a's and ΔS_{313}'s were plotted as the conventional (○) and the FD-treated gel (●). The conventional gels with (△) and without cracks (▲) respectively were given in the case of the 6% of R. The data for 2, 4, and 10% of R were cited from our previous report.[1—3]

Skin Layer of the Conventional Gel. It was reported in a previous paper that a time lag was observed before the skin layer split out in the deswelling process for the conventional gel.[3] The rate-determining step for deswelling was considered to change before and after the time-lag. The process for water release through the skin layer determines the rate-determining step for the non-cracked conventional gel before the time-lag. The skin layer is considered to be



(I) Conventional Gel (R = 6)

(II) Conventional Gel (R = 2)

(III) FD-treated Gel (R = 6)

Fig. 10. Schematic illustration of the polymer network for the conventional gel and the FD-treated gel. (I) The conventional gel (R = 6). The rigid frame of the polymer network cracks irreversibly due to the water-releasing pressure. Water can be released easily at the second-stage of the deswelling, because an elastic frame is appeared after cracking. (II) The conventional gel (R = 2). Water can be released through the elastic polymer-network due to the water-releasing pressure. (III) The FD-treated gel. During the freezing process, the gel was partitioned to form the elastic polymer network, of which frames were constructed from the bundle of polymer chains. The mesoscopic partitioned polymer-network become possible to exhaust water rapidly. The elastic frame may expand and contract to release water from inside to outside the gel.

constructed by rigid frames, as compared with elastic frames in the case of the FD-treated gel, because it is not observed to crack with the deswelling pressure. The water exhausts through the rigid frames of the skin layer.

Interaction of Monomer to Polymer of NIPAAm and to Water in the Gel. A miscible alcohol in water is known to make a hydrogen bond with poly(NIPAAm) in the gel as a hydrophilic additive.[10] A substance possessing the same functional group as that of the polymer is considered to interact easily with the polymer due to hydrogen bonding, rather than alcohol. In this work, the NIPAAm monomer was used as a hydrophilic additive. It should be mentioned that the monomer might play two directly opposing roles, as follows. The monomer can dissolve mutually in water. Since the monomer forms a hydrogen bond with amide groups, the skin formation may be disturbed under heating the conventional gel in the presence of a monomer. On the other hand, the monomer may act to break the iceberg due to hydrogen-bond formation between the monomer and the water molecules and, in turn, the monomer can separate the hydrated water from the isopropyl groups in the polymer. As a result, the monomer may act to accelerate bond formation between the polymer chains and the skin formation.

The Rate-Determining Step on the Deswelling of Gel. (1) Cracked Conventional Gel. The E_a's and ΔS_{313}'s are controlled by C in the case of the FD-treated gel, but not in the case of the conventional gel (Figs. 4 and 6). Judging from our results, more elastic frames appear in a crevice of the skin layer of the cracked conventional gel as compared with the FD-treated gel. The elasticity may influence the rate of water release. If the surface of the crevice is sufficiently elastic for a smooth release of water, the pressure of water release would determine the rate-determining step for the deswelling of the cracked conventional gel. Consequently, E_a's are considered to keep constant regardless of the monomer concentration (Fig. 4).

(2) FD-Treated Gel. Since the FD-treated gel has an elastic wall of macropores, the water is easily released under a low deswelling pressure. The E_a of the FD-treated gel (20 kJ mol^{-1}) was lower than that of the non-cracked conventional gel (50 kJ mol^{-1}) in water. The E_a's of the FD-treated gels increase with increasing C, and reach to the maximum at around 80 kJ mol^{-1} around 0.1 M NIPPAm (Fig. 6A). The profile for C–ΔS_{313} shows the same tendency as that of C–E_a. The profiles for C–E_a and C–ΔS_{313} in NaCl solution also had the maximum at around 0.1—0.2 M.[2] It was reported in our previous paper that there are two opposing effects to control E_a and ΔS_{313}. Similarly, two opposing effects should be considered for the rate-determining step in the presence of a monomer. Poly(*N*-vinylisobutyramide), of which the total hydrophobic and hydrophilic balance is exactly the same as that of poly(NIPAAm), has been compared with poly(NIPAAm) with respect to hydration of the CONH group in the polymer.[11,12] Therefore, it is worth considering the hydration of the amide groups in the polymer. Monomer NIPAAm below 0.1 M may obstruct the hydrogen-bond formation between the amide groups in the polymer, because the monomer may substitute the hydrated water on the amide groups in the polymer. At higher than 0.1 M, the monomer may act to dissociate the iceberg. It is thus advantageous to remove the water from the gel and to form hydrophobic bonding between the isopropyl groups in the polymer during the deswelling process. In the case of the FD-treated gel, the rate-determining step is concluded to be the elementary process 2 due to bond formation between the amide groups, and between the isopropyl groups in the polymer in order that the ΔS_{313}'s are negative.

(3) Effect of the Crosslinking Ratio. Since all data of the ΔS_{313}'s were negative for both the FD-treated and the conventional gels with 6% crosslinking, the rate-determining step of the deswelling was supposed to be the elementary process 2, due to bond formation between the polymer chains. ΔS_{313} was positive for 2—4% and negative for 10% crosslinking in the conventional gel (Fig. 9). Since a time lag was not observed in the deswelling process in the case of 10% crosslinking, a skin layer is supposed not to form under heating. Higher crosslinking is possible to bring about the formation of a partitioned polymer-network more easily inside the gel rather than skin formation on the gel surface. On the other hand, a skin layer, which exhibits more elastic property than that of 6% crosslinked gel, could be formed on the surface of a 2—4% crosslinked gel during the time lag in the deswelling process. R is considered to control the elasticity of the skin layer. Cracking in the case of a 2—4% crosslinked gel was not observed. Therefore, the rate-determining step of the non-cracked gel in the case of 2—4% crosslinking is different from the others. The release of water through the elastic skin layer may determine the rate-determining step without a cracking gel.

Conclusion

1. The elastic frames comprising the polymer network in the wall of macropores was deduced from the SEM images of poly(NIPAAm) gel.

2. Fast-deswelling of the FD-treated gel resulted from the elasticity of the partitioned polymer-network caused water to release.

3. Cracking of the surface of conventional gel occurred because the skin on the gel surface became fragile in the presence of a monomer.

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