

Swelling Characteristics of Temperature-Sensitive Polyelectrolyte Gels Based on N-Isopropylacrylamide: Role of Fixed Charges in the Swelling

Etsuo Kokufuta

Institute of Applied Biochemistry, University of Tsukuba,

Tsukuba, Ibaraki 305-8572, Japan.

Fax: 81-298-53-4605, e-mail:kokufuta@sakura.cc.tsukuba.ac.jp

The purpose of this paper is to discuss the role of ionic charges in the swelling of polyelectrolyte gels. For this there are two different models: Flory's model based on net osmotic pressure arising from mobile ions; and Katchalsky's model in which interactions between the small ions and the crosslinked polyions and between the fixed charges of the network are considered. We have thus attempted to experimentally study which is a reasonable model at the molecular level. Polyelectrolyte gels with different charge distributions were used, the preparation of which was made via copolymerization of N-isopropylacrylamide with both or either of acrylic acid and 1-vinylimidazole. Our gel samples ranged from the usual bulk gel to nano-sized particles in shape. The charge distribution within the gel phase was created by different ways: binding of ionic surfactants, physical entrapment of polyions; and immobilized enzyme reaction. Size measurements by microscopic observation for the bulk gels and by light scattering for the nanogels showed a marked effect of charge inhomogeneity on the swelling of polyelectrolyte gels. This result can be interpreted in the model of Katchalsky, but cannot be predicted from Flory's model. This is because in the latter model counterions to the ionized groups should move freely within the gel phase surrounded by the Donnan potential barrier, and thereby the swelling pressure would be independent of a distribution of the fixed charges. In case of polyampholyte gels, it is found that their swelling behavior strongly depends on interaction between the fixed charges with opposite sign.

Key words: Polyelectrolyte; Gel; Charge distribution; Swelling force, Flory's model, Katchalsky's model

1. INTRODUCTION

In studies on polyelectrolyte gels, we will often need to answer the most basic question "What is swelling forces in the gel system of subject?" Then, we must go back to two original models established by Flory [1] and Katchalsky [2] in the 1950s. In both models there is a big difference between the swelling forces arising from the fixed charges at the molecular level. Flory assumed that (i) the equilibrium between the swollen ionic gel and its surroundings closely resembles Donnan membrane equilibria, (ii) the polymer acts as its own membrane which prevents diffusion of the charged substituents inside the gel into the outer solution, and hence (iii) the swelling force resulting from the presence of the fixed charges may be identified with the swelling pressure, or net osmotic pressure, across the semipermeable membrane in a typical Donnan equilibrium. On the other hand, Katchalsky considered the electrostatic free energy ($\partial F_{el}/\partial V$) as the swelling force resulting from the presence of the fixed charges. Then, he assumed that $\partial F_{el}/\partial V$ is the sum of (i) the interaction between the small ions and the polyelectrolyte, the term of which favors deswelling, and (ii) the mechanochemical stretch due to the repulsive forces among the fixed charges on the polyelectrolyte network, the term of which favors the swelling of the gel.

Since Tanaka et al. [3] reported an abrupt volume collapse of gels, i.e., volume phase transition in gels, a

number of experimental and theoretical studies of neutral and polyelectrolyte gels have performed by assuming Flory model. A very few experiments have attempted to compare Flory and Katchalsky models; a good example is a study by Tong and Liu [4] who made a direct comparison of their experimental results with the calculations by Flory-Huggins (FH) equation and by Hasa-Ilavsky-Dusek (HID) equation [5] based on Katchalsky model. Then, they concluded that neither FH equation nor HID equation may provide a reasonable approach to the swelling equilibrium for the gels with strongly dissociating electrolytes as the fixed charge. As can be seen from this example, it is very difficult to judge experimentally which is a reasonable model for understanding the swelling of ionic gels at the molecular level.

Many of studies on hydrogels in 1990s employed N-isopropylacrylamide (NIPA) as the constitute monomer [6], often referring to as "thermo-sensitive monomer," or "amphipatic monomer." Usually considered in these previous studies was the fact that neutral hydrogels based on NIPA undergo a volume phase transition at temperature around 33 °C. Also considered was a rise of this temperature, i.e., volume-phase transition temperature (T_v), as ionic charges are introduced into the network by copolymerization of NIPA with suitable ionic monomers. Taking these into account, we may anticipate learning the role of the fixed charges in the

polyelectrolyte gel swelling from studies of NIPA-based ionic hydrogels as a function of temperature as well as of a factor affecting the charge density of gel networks. In particular, the study on the effect of charge inhomogeneity would provide a key to discuss the molecular mechanism of the swelling of polyelectrolyte networks. If the concept of osmotic pressure arising from mobile ions is correct, one would not observe any difference in the swelling curves between the two kinds of ionic gels into which the fixed charges were homogeneously and inhomogeneously introduced. This is because counterions to the ionized groups should move freely within the gel phase surrounded by the Donnan potential barrier and thereby increase the osmotic pressure acting to swell the gel.

The above idea prompted us to perform a systematic study on swelling behaviors of NIPA-based polyelectrolyte gels [7-18]. The purpose of the present paper is to provide a discussion about the nature of swelling force arising from the fixed charge of cross-linked polyion networks. Our gel samples ranged from the usual bulk gels to nanogel particles. Polymer samples were also used depending on the case. The network or the polymer has both or either of negative and positive sign.

2. EXPERIMENTAL SECTION

2.1 Monomers

NIPA was the main monomer usually employed through the whole experiment. Acrylic acid (AAc) and 1-vinylimidazole (VI) were used as an anionic and a cationic monomer, respectively. Also used as a cross-linker was *N,N'*-methylenebisacrylamide (Bis). All the monomers were obtained from commercial sources and purified by appropriate methods.

2.2 Preparation Methods

Bulk gels in cylindrical, cubic and other forms were prepared via gelation of a pregel solution containing the monomers required and Bis. The polymerization was initiated by a pair of ammonium persulfate (APS) and *N,N,N',N'*-tetramethylethylenediamin (TMED). The same redox system was also used in the preparation of nanogel particles which was carried out by stirring of a pregel solution in the presence of surfactant (sodium dodecylbenzene sulfonate; NaDBS) at temperatures above 55°C. More detailed information such as purification method has been described in our previous papers.

2.3 Measurements

Swelling ratio was determined upon the size measurements, regardless of bulk and nano-gel samples. The size of bulk gels usually in the form of a small cylinder was measured under a microscope. Dynamic light scattering (DLS) was employed in the size measurement of nanogel particles. Static light scattering (SLS) was also combined with DLS in case of need.

Potentiometric titration was performed to study the dissociation of protons from -COOH or -NH⁺ groups as a function of pH. Microscopic spectroscopy with UV

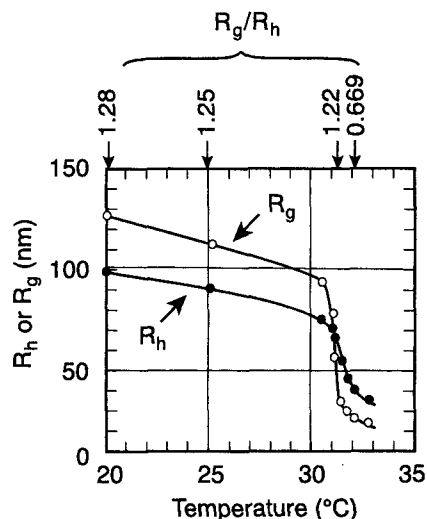


Fig. 1. Results of DLS and SLS for NIPA polymer in pure water. Weight-average molecular weight (M_w) of polymer = 8,400,000; Polymer concentration (C_p) = 10 mg/L.

light was employed in the study of local binding of NaDBS within the gel phase.

3. RESULTS AND DISCUSSION

3.1 Temperature-dependent Property Changes of NIPA Homopolymers and Gels

For our purpose, we must first learn how the conformation of NIPA polymer chain varies depending on temperature. Several of previous experimental studies using DLS and SLS have focused on this subject and reported abrupt changes of hydrodynamic radius (R_h) and radius gyration (R_g) of the NIPA chain at 31 ~ 32 °C with increasing or decreasing temperature. This experimental fact was confirmed in our experiments (Fig. 1) which were performed for the purpose of examining the accuracy of our laser light scattering apparatus.

Another important information obtained from DLS and SLS data is R_g/R_h ratio, the value of which becomes a key to learning polymer conformation in solutions. This is because hydrodynamic theory [19] shows that the R_g/R_h ratio changes from infinity to 0.775 when the polymer conformation changes from a long rod to a sphere, with values from 1.3 to 1.5 for random coils. It is thus found from Fig. 1 that the NIPA polymer undergoes an abrupt conformation change from a random coil ($R_g/R_h \sim 1.2$) to a globular shape ($R_g/R_h \sim 0.7$) at around 32 °C, the phenomenon of which often refers to as "coil-to-globule transition." Our thermal analysis with a differential scanning calorimeter (DSC) showed that the coil-to-globule transition upon heating is an endothermic process. Then we obtained $\Delta H \sim 6$ kJ/unit mol. Since this value is close to heat of fusion for ice, one might consider that the transition accompanies a decrease in the number of hydrogen-bonded water molecules in the aqueous polymer system. There is an assumption (without fearing the leap of logic) that transition takes place as a result of a decrease in the number of water

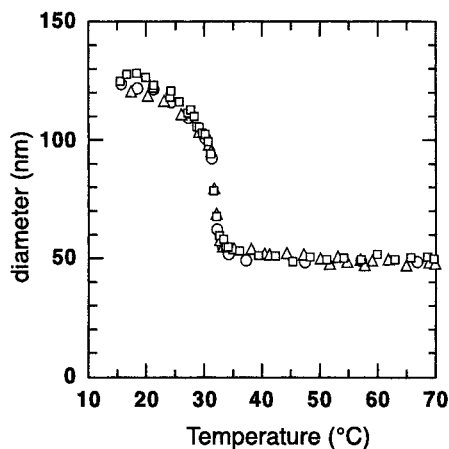


Fig. 2. Results of DLS for NIPA nanogel in pure water. M_w of the gel particle = 150,000,000 (from Zimm plots). $C_p = 1$ mg/mL. The polymer density (ρ) was 0.026 g/cm³, as estimated using a relation of $\rho = (ff_{\min})(3/4\pi)(M_w/N_A)(1/R_h)^3$, where f represents the actual frictional coefficient, f_{\min} is the minimum frictional coefficient for a hypothetical sphere, and N_A is Avogadro's number. Because our nanogels are spherical, it would be assumed that $ff_{\min} \sim 1$.

clusters per non-polar isopropyl group; that is, "hydrophobic interaction" among non-polar isopropyl groups.

In cases of bulk gels it is impossible to measure R_g by SLS; thus, the conformational change as mentioned above may not be demonstrated by temperature dependence of R_g/R_h . As can be seen from Fig. 2, however, DLS of aqueous dispersion of NIPA nanogel particles shows an abrupt change in R_h . In addition, we could perform SLS with the nanogel dispersion, from which R_g/R_h became ~ 0.7 at 25 °C. This strongly suggests that our nanogel is spherical in shape at temperatures at which the polymer adapts a random coil conformation. Thus, it is reasonable to consider that a spherical nanogel particle consisting of crosslinked random coils of the NIPA polymer undergoes a rapid collapse change at around 32 °C upon heating. In other words, we may assume that the molecular mechanism for thermal collapse of NIPA networks, regardless of bulk and nano-gels, is similar to that for the coil-to-globule transition of NIPA polymer in water.

With aqueous NIPA nanogel dispersions, we made thermal analysis from which $\Delta H \sim 4.8$ kJ/unit mol was obtained. Although it is not clear whether the difference in ΔH between the polymer and the nanogel is due to the introduction of sulfonate groups from the initiator to the chain end or of Bis to the network, the thermal analysis shows that the gel collapse upon heating is an endothermic process. This is another basis suggesting the above assumption.

3.2 Swelling Behavior of NIPA Gels Ionized by Binding of NaDBS

Fig. 3 shows the swelling curves of neutral NIPA gels in aqueous solutions containing different amounts of

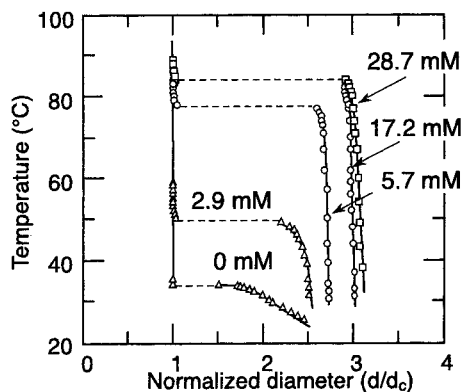


Fig. 3. Temperature dependence of equilibrium gel diameter as a function of NaDBS concentration. The surfactant concentrations in mM were shown in the figure. The diameters (d) were normalized by the fully collapsed diameter (d_c). All the data were originally obtained in [9]

NaDBS. It is found that T_v and the net volume change at T_v increased with increasing NaDBS concentrations. This finding can be interpreted by considering that non-ionic NIPA gels are effectively converted into an ionic gel through the binding of NaDBS to the polymer networks due to hydrophobic interaction, leading to a high transition temperature and a large volume jump [9]. Thus, we measured the uptake of NaDBS by gels, from which the "overall" charge density expressed in moles of bound NaDBS per one mole of monomer units in the gel was found to be 0.135 under the conditions used (initial NaDBS conc. = 28.7 mM; 35 °C). Such a NaDBS-bound ionic NIPA gel seems to correspond to a polyelectrolyte gel which can be prepared by substituting about 14 % of the NIPA monomers with ionic monomers such as sodium AAc. A copolymer gel consisting of NIPA (82 %) and sodium AAc (18 %) measured the T_v values to be 60 °C (shrinking process) and 50 °C (swelling process) in pure water. These T_v values are lower than that for the NaDBS-bound gel (82 °C), although the charge density of the copolymer gel was slightly larger than that of the NaDBS-bound gel. In contrast, the volume change at the T_v (60 °C) for the copolymer gel was much larger (372 times the fully collapsed volume) than that for the NaDBS-bound gel (27 times the fully collapsed volume at $T_v = 86$ °C).

Questions have been raised as to why the NaDBS-bound ionic NIPA gel exhibited a volume change smaller than that of the copolymer gel with a similar charge density, and why the T_v of the former was higher than that of the latter. The answer to these questions would help to clarify the nature of the surfactant-bound gels. To discuss this subject, we now assume that surfactant molecules bind only to the polymer networks within a layer (or part) of the gel near to the surface, but

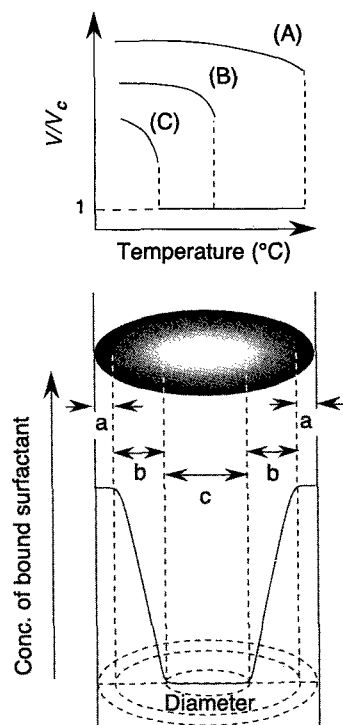


Fig. 4. Schematic representation for a cylindrical gel with inhomogeneously bound surfactant molecules. Swelling curve (A) corresponds to region (a) with a saturated level of bound surfactant; curve (B) represents a limited section of region (b) in which the surfactant concentration gradually decreases towards the center; curve (C) is for region (c) in which there is no bound surfactant (i.e., corresponding to neutral gel). This drawing was cited from [10] with a few rearrangements.

not to all of the networks in the body of the gel (see Fig. 4). This is because negative charges of the surfactant-bound layer seem to hinder the further diffusion into internal parts of the gel of the surfactant molecules with charges of the same sign. Under such an assumption, it is reasonable to expect that some part of the highly ionized polymer network in the NaDBS-bound gel has a net charge density much larger than the "overall" density, thereby showing a T_v value higher than that for the copolymer gel. However, the charge density of the internal part of the surfactant-bound gel is very low or close to zero, resulting in the volume collapse of this domain at temperatures $> T_v$ of pure NIPA gels in pure water. Therefore, the total change in the gel volume at T_v for the surfactant-bound gel was smaller than that for the copolymer gel.

The measurement of the spatial distribution of surfactant concentration within the gel phase should provide direct evidence for the local surfactant binding as assumed above. NaDBS is an appropriate surfactant for this purpose because it carries a phenyl group which exhibits an absorption band in the UV range. Fig. 5

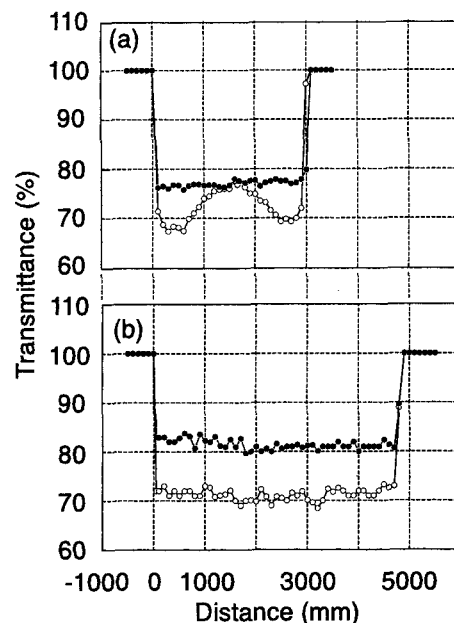


Fig. 5. Position dependence of transmittance (PDT) for cylindrical wet gel disks (a) with diameters (d_0) = 2 mm and for a cylindrical dry gel disk (b) with the same d_0 value. All the data were originally obtained in [10].

shows typical examples of the position dependence of transmittance (PDT) for the sample gel disks with bound NaDBS. The scanning was performed from the right-hand to the left-hand end of each gel disk. We used two wave-lengths, 261 nm and 400 nm, to measure the PDT. Since NaDBS has no absorption at 400 nm, the transmittance at this wave-length varied depending on the sample thickness. Therefore, the PDT at 400 nm should be used as a control. PDTs (a) and (b) were the results obtained using wet and dry gels with $d_0 = 2$ mm, respectively. The wet gel sample was fully swollen in pure water prior to contact with the NaDBS solution, whereas the dry gel was directly treated with the surfactant solution without swelling procedure.

In PDT(a), a rapid decrease in transmittance at both ends of each sample was observed when using the wave-length at 261 nm. However, the transmittance increased gradually and became constant when the scanning point approached the central core of the gel disk. On the other hand, the transmittance at 400 nm was almost constant, independent of the position. Therefore, it is evident that the surfactant molecules bound strongly only around the gel walls. This conclusion can be supported by PDT(b) for the dry gel in which we did not observe specific position-dependent changes in transmittance at 261 nm. In the case of the dry gel, the surfactant solution permeated throughout the gel phase allowing the surfactant molecules to bind to the network without distribution. This brought about a marked difference in the diameters of the surfactant-bound wet and dry gels; i.e., the distance between the right and left-hand ends which is larger for the dry gel than for the wet gel, although their diameters in the preparation were identical with each other.

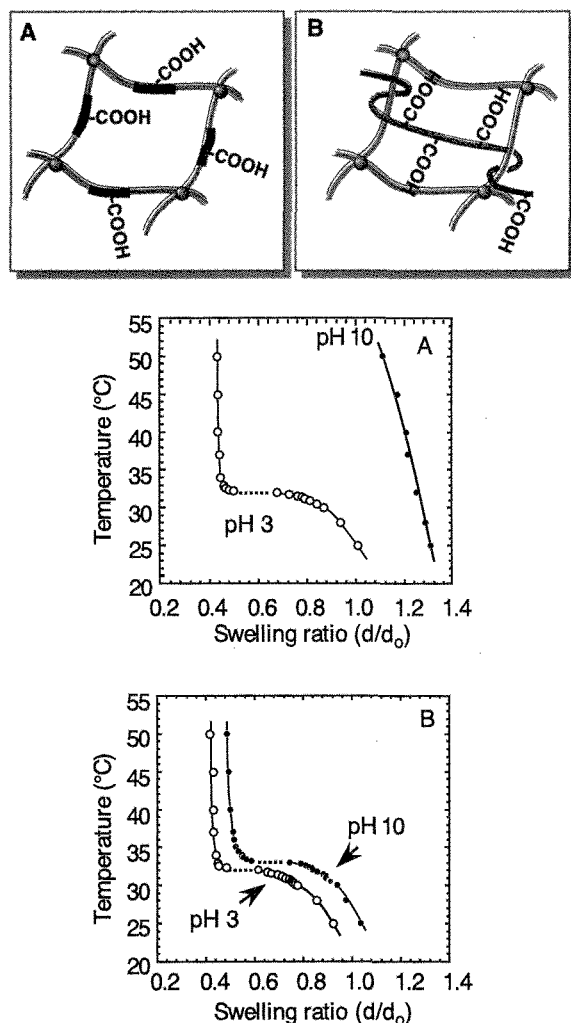


Fig. 6. Temperature dependence of normalized equilibrium diameters (d/d_0) at pHs 3 and 10 for Gels I (A) and II (B). PAAc with $M_w=450,000$ was used for the preparation of Gels II. This drawing was rearranged from Fig. 2 of our previous paper [12] with several modifications.

3.3 Effect of AAc Distribution in NIPA Networks

We have demonstrated that an inhomogeneous binding of surfactants brings about a different swelling behavior from that of the usual ionic gels prepared via random copolymerization of NIPA and AAc. It is thus interesting to examine the effect of the charge distribution (i.e., the distribution of AAc residues in the crosslinked NIPA network) on the swelling behavior of NIPA/AAc gels. For this purpose, we designed four ionic gels composed of NIPA and AAc residues (NIPA:AAc ratio of the feed $\sim 10:1$ by moles the monomers or repeating units) [12]: (i) for Gel I, the redox polymerization of an aqueous solution containing NIPA, AAc, and MBA which can be initiated by a pair of APS and TMED; (ii) for Gel II, the physical entrapment of poly(AAc), PAAc, by an MBA-crosslinked NIPA gel, the performance of which is based on the same method employed in (i) except for the use of PAAc instead of the AAc monomer; (iii) for Gel III, the

gelation of an aqueous solution containing PNIPA and PAAc by γ -rays from ^{60}Co under conditions where no complexation occurs between PNIPA and PAAc; (iv) for Gel IV, whose AAc distribution may be expected to be similar to that of Gel I, the γ -ray irradiation of an aqueous solution of a copolymer of NIPA and AAc, i.e., copoly(NIPA, AAc).

Fig 6 shows the temperature dependence of the normalized equilibrium diameters (d/d_0) at pHs 3 and 10 for Gels I and II as the example. At pH 10 at which the COOH groups bound to the AAc residues are ionized ($\text{COOH} \rightarrow \text{COO}^- + \text{H}^+$), there is a marked difference due to the AAc distribution; the localized COO^- ions are not effective in preventing the thermally induced gel collapse at temperatures above T_v . This clearly indicates an effect of the "charge distribution" in the network on the phase transition of ionic gels.

Since there is little disagreement between the transition temperatures for polymers and gels of NIPA, a similar molecular mechanism may be predicted in the phase separation and the volume transition. For Gel II composed of ca. 90 % (in unit mole base) of MBA-crosslinked "pure" NIPA chains, it is predictable that its phase transition behavior is not so different from those of NIPA polymers and gels, even at pH 10 where the incorporated PAAc chains (ca. 10 % in unit mole base) are ionized. Indeed, at pH 10 Gel II underwent a volume phase transition at temperatures near to the transition temperatures for NIPA polymers and gels.

The same result has been obtained by a comparison of Gels III and IV [12]. In addition, the study of changes in the swelling curves of Gel II at pHs 3 and 10 caused by the molecular weights of the entrapped PAAc chains showed the following results: (i) The increase in the molecular weight at pH 10 brought about an increase in the gel volume over the temperature range of 25 °C to 50 °C; and (ii) at pH 3 and at temperatures $< T_v$, the gel volume decreased with increasing molecular weight of the entrapped PAAc with the non-ionized COOH groups. Therefore, it is clear that the charge distribution has a marked effect on the swelling of polyelectrolyte gels.

3.4 Effect of Enzymatically Formed pH Gradients within Polyelectrolyte Gels on Their Swelling

To generalize the above conclusions, it is necessary to develop other techniques for establishing charge inhomogeneities in the gel. For this purpose, we studied an enzymatic approach for forming a pH gradient to establish an inhomogeneous distribution of charges within the gel phase [15,16]. Thermally responsive cationic NIPA/VI gels with immobilized urease, in the shape of a small cylinder with diameter 290 - 640 μm , were prepared via gelation of an aqueous monomer solution containing the enzyme. Diameters at different positions of the cylinder were microscopically measured in a cell through which substrate solution (pH 4; 35 °C) was passed at a constant flow rate; thus, both substrate concentration and pH at the gel surface were maintained at a constant level throughout the experimental period.

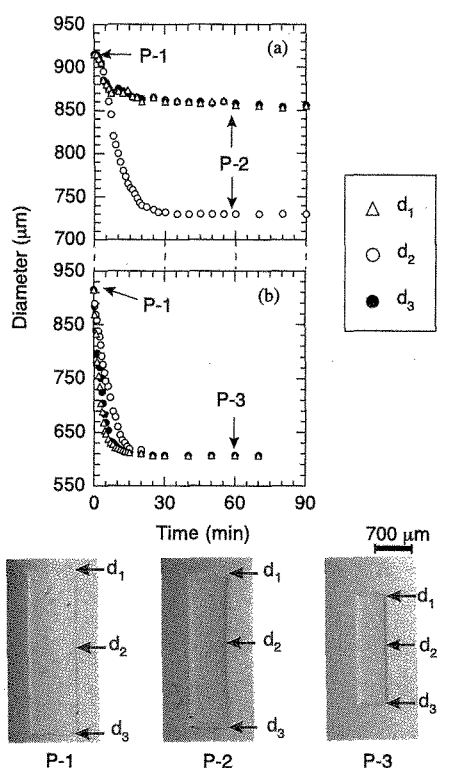


Fig. 7. Time-dependent changes in diameters at the top (d_1), center (d_2) and bottom (d_3) of cylindrical gel with immobilized urease: (a) Enzymatic shrinking which was made through quick replacement of the outer medium (5 mM maleate buffer not containing the substrate; pH 4) by the substrate solution (5 mM maleate buffer containing 1 mM urea as the substrate; pH 4); (b) Chemical shrinking made through quick replacement of the outer medium (5 mM maleate buffer, pH 4) by another medium (5 mM maleate buffer, pH 6). We used the same gel in measurements (a) and (b), so that P-1 denotes the gel before the replacements of the outer medium by the substrate solution or by the substrate-free buffer. P-2 is the gel in the substrate solution after 60 min, and P-3 the gel in the substrate-free medium at pH 6 after 60 min. The measurements were carried out at 35 °C in a flow (1 mL/min) of the outer solutions. All the data were originally obtained in [15]

Fig. 7 shows typical time courses of enzymatically and chemically induced diameter changes of a cylindrical gel with immobilized urease. The enzymatic and chemical means of shrinking the gel were respectively based on the use of a substrate-containing buffer (pH 4) and of a substrate-free buffer (pH 6 with NH_4OH). We measured diameters at the top (d_1), center (d_2) and bottom (d_3) of the cylindrical gel. It was observed that in the chemical gel collapse the diameters at these three positions are identical with one another, particularly in an equilibrium state at which the swelling ratio is independent of time. In the enzymatic process, there is no difference in the diameter at the top and at the bottom, but values at both positions are larger than

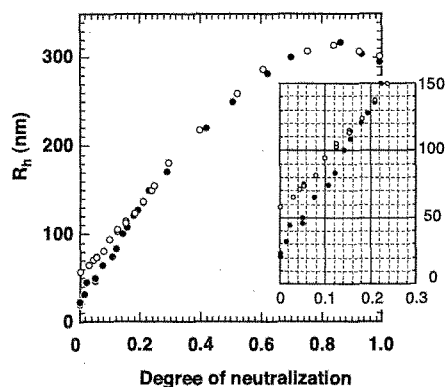


Fig. 8. Changes in R_h of the nanogel with the degree of neutralization in salt-free water at 25 °C (open circles) and 35 °C (closed circles). All the data were originally obtained in [14].

that at the center after the establishment of swelling equilibrium. Thus, the enzymatic shrinking allows the gel to change its shape of a “real” cylinder to a “distorted” cylinder with the top and bottom which are still in a swollen state. However, this shape change was not observed when the amount of the immobilized enzyme became very high, since the enzyme reaction takes place only at the liquid-gel interface.

The present cationic gels undergo a shrinking change when increasing pH, because the network charges are eliminated via the dissociation of protons from the imidazole ions. The immobilized enzyme reaction rises pH within the gel phase; therefore the gel shrinks. Such an enzymatic increase in pH occurs by diffusion of the substrate from the outer solution, but at the same time the reaction product diffuses into the outer solution. These permit to generate a pH gradient between the surface and the center of the gel. Such a pH gradient varies depending on time, but does not disappear even in a steady state. In contrast to the enzymatic process, the chemically induced shrinking of the gel takes place only through a pH difference between the gel (pH 4) and the outer medium (pH 6); thus, in an equilibrium state there is no pH gradient. Consequently, one may say that the position dependence of swelling ratio which has been observed in the enzymatic process should be due to a pH gradient within the gel phase. Then it is natural to conclude that the present results cannot be explained by considering osmotic pressure arising from mobile counterions within the gel phase surrounded by the Donnan potential barrier. This conclusion was supported by much more data through comparison of them with those obtained from mathematical simulations [15, 16].

3.5 Size Changes of NIPA/AAC Nanogels with Ionization Degree

Now we must learn how the swelling of NIPA/AAC gels varies depending on the ionization of COOH groups as well as on temperature. For this purpose, we studied R_h of NIPA/AAC nanogel as a function of the ionization degree (α_n) at 25 and 35 °C (Fig. 8). With ionizing

the COOH groups, the particle size linearly increased at $\alpha_n < 0.6$ and then leveled off at $\alpha_n > 0.6$. This aspect is quite analogous to the changes in the end-to-end extension of PAA ions in aqueous solutions. Kokufuta [20] has performed the viscometric and electrophoretic measurements of PAA as a function of pH, together with its potentiometric titration. The important conclusion obtained were: (i) The viscosity increases with increasing α_n at $\alpha_n < 0.6$ and levels off at $\alpha_n > 0.6$. (ii) The viscosity change corresponds to the mobility changes, because the mobility may be considered as an indication of the net charge density of a polyion when it behaves as a free draining coil in electrophoresis. Now we draw particular attention to the fact that the charge density scarcely increases at $\alpha_n > 0.6$. In general, this phenomenon is known as the "counterion binding effect," a strong experimental evidence for which has been reported by Wall et al. [21]. From their transference experiments using radioactive sodium (^{22}Na) in salt-free aqueous solutions containing PAA partially neutralized with NaOH, we may learn the following important two features: (a) The binding degree of Na^+ ions linearly increases at $\alpha_n < 0.6$ and levels off at $\alpha_n > 0.6$; and (b) the concentration of mobile Na^+ ions increases linearly at $\alpha_n < 0.2$, gradually at $0.3 < \alpha_n < 0.7$, and rapidly again at $\alpha_n > 0.8$. Thus, we may assume that at $\alpha_n > 0.6$ at which the gel little swells, the concentration of mobile Na^+ ions still increases. According to the Flory-Huggins theory for polyelectrolyte gels, a very slight increase in the concentration of mobile counterions within the gel phase brings about a dramatic increase in the swelling degree. Therefore, our results in Fig. 8 may not be understood by assuming that an increase in α_n rises osmotic pressure arising from mobile counterions within the "overall" gel phase. Otherwise, by considering that at $\alpha_n > 0.6$ the net charge density of the gel little increases but levels off due to the counterion binding, the dependence of the swelling degree upon α_n may favorably be accounted for. As a result, we may see the strong resemblance between the α_n changes in the swelling degree for the NIPA/AAC gel and in the end-to-end extension for PAA in solutions.

We examined the effect of temperature on the size of the nanogel in pure water at $\alpha_n < 0.3$ (see a window in Fig. 8). At $\alpha_n < 0.15$, the particle size at 35 °C was smaller than that at 25 °C because of $T_v \sim 33$ °C for neutral NIPA gels. However, this difference disappeared at $\alpha_n \sim 0.15$ at which the gel has 4.5 mol% "COONa" plus 25.5 mol% COOH. These mean that our nanogel undergoes "thermal" swelling transitions at $\alpha_n < 0.15$ when lowering temperature from 35 °C to 25 °C.

3.6 Swelling Behavior of Polyampholyte Gels

Polyampholytic hydrogels consisting of crosslinked polymer networks with positive and negative charges are interesting materials not only in polyelectrolyte studies, but also in polymer science and technology. Long-range Coulombic interactions between the opposite charges bound to the network are generally

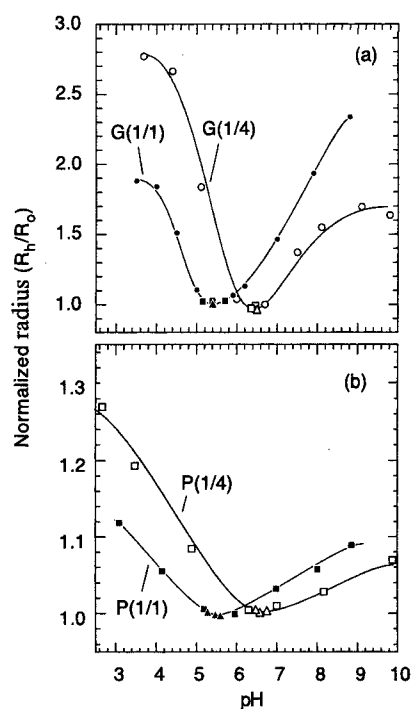


Fig. 9. Dependence of normalized hydrodynamic radius (R_h/R_0) on pH for nanogels (a) and terpolymers (b) in salt-free and KCl solutions at 25 °C. KCl conc. (mol/L): 0 (\circ, \bullet); 0.01 (\square, \blacksquare); and 0.1 ($\triangle, \blacktriangle$). Polym. conc.: 0.1 mg/mL for nanogels and 1 mg/mL for terpolymers. The normalization was made by each diameter (R_0) at KCl concentration = 0.1 M and at pH = pI. All the data were originally obtained in [17].

believed to be the chief factor which governs the swelling-shrinking behavior of polyampholyte gels [22]. For example, the gel volume minimizes at an isoelectric point (pI), defining as the pH at which the electrostatic attraction between the opposite charges becomes a maximum. The gel collapsed at pI however swells upon addition of salts such as NaCl in the outer solution. This behavior is a contrast to that of the usual polyelectrolyte gels, thus referring to as "anti-polyelectrolyte" behavior. To understand this behavior, weakening of the electrostatic *inter-chain* attraction in the gel network due to screening with counterions has been assumed. Thus, we must consider Katchalsky's model in the understanding of swelling behaviors of polyampholyte gels [17,18].

Taking the above into account, we studied the swelling characteristic of polyampholyte nanogels consisting of Bis-crosslinked terpolymers of NIPA, AAC and VI (Fig. 9). Potentiometric titration gave the following contents (in mol %) of anions (A) and cations (C) in the nanogels: A = 3 and C = 13 for nanogel G(1/4); and A = 14 and C = 12 for nanogel G(1/1). Both nanogels were characterized in detail by a combination of DLS, SLS, electrophoretic light scattering, and turbidity measurements. Note that G(1/1) is insoluble in pure water but soluble in KCl solutions over the salt concentrations

(C_S) > 0.01 M due to antipolyelectrolyte behavior. At pI at which the negative and positive charges are fully balanced, the electrophoretic mobilities became zero. From the light scattering of nanogels in 0.1 M KCl solution at pH = pI the following data were obtained: $M_w = 52,400,000$ for G(1/4) and 14,900,000 for G(1/1); $R_g = 107$ nm for G(1/4) and 81 nm for G(1/1); and $R_h = 132$ nm for G(1/4) and 87 nm for G(1/1). Thus, the R_h/R_g ratio was within 0.85 ± 0.05 , suggesting a spherical conformation of our nanogel particles.

As can be seen from Fig. 9, the pH dependence of the gel size exhibited a characteristic pattern, from which pI was observed: pH 6.5 for G(1/4) and pH 5.3 for G(1/1). A very similar size change was also observed in terpolymers P(1/1) and P(1/4) whose AAc and VI contents were the same as those of the nanogels. Therefore, it is reasonable to consider the same molecular mechanism for the swelling-shrinking characteristics of the nanogel and the terpolymer.

From the study of the effects of C_S and temperature the following characteristics were obtained: (i) R_h of G(1/4) varies little depending on KCl concentration, while G(1/1) shows a slight increase in R_h with C_S from 0.01 to 0.5 M and a marked decrease at $C_S \sim 2$ M without accompanying aggregation. (ii) G(1/1) undergoes a shape phase separation at $C_S \sim 0.008$ when decreasing C_S , whereas G(1/4) is dispersible both in pure water and in KCl solutions at $C_S < 1$ M, at the concentration of which aggregation takes place as observed in the pure NIPA nanogel system. (iii) Both G(1/4) and G(1/1) shrink up to 41 °C and 51 °C, respectively, and around these temperatures the gel suspensions undergo a shape phase separation. These phenomena caused by salt concentration and temperature were also observed in the terpolymer system. The results obtained suggest a similarity in the molecular mechanism between the stability of colloids and the solubility of polymer, both of which can be accounted for by considering hydrogen bonding and/or hydrophobic association, other than the usual electrostatic attraction.

4. CONCLUSIONS

The effect of charge inhomogeneity on the swelling of polyelectrolyte gels has been studied using NIPA-based hydrogels with AAc and/or VI, ranging from the usual bulk gel to nano-sized particles in shape. The charge distribution within the gel phase was created by binding of ionic surfactants, physical entrapment of polyions; and immobilized enzyme reaction. It has become apparent that there is a marked difference in the swelling ratio between the gels with a homogeneous and an inhomogeneous distribution of the fixed charges. To understand this difference at the molecular level, the interactions between the fixed charges of the network as well as between the fixed charges and small ions, as assumed in Katchalsky's model, should be considered. The consideration of these interactions allowed us to understand the counterion effect observed in NIPA-based polyelectrolyte nanogels with a random distribution of AAc and also the appearance of an isoelectric point in NIPA-based polyampholyte nanogels with AAc

and VI. The results obtained would provide a better understanding of our hypothetical balance model [23] in which we accounted for a volume phase transition in gels by considering a balance between the repulsion and attraction among functional groups attached to the crosslinked polymers which arise from a combination of four intermolecular forces: ionic, hydrophobic, van der Waals and hydrogen bonding.

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