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Deuterium Substitution and Fluorescence Studies on Polymer Hydrogels and Complexes

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Summary: Deuterium isotope effects on swelling kinetics and volume phase transition in typical polymer hydrogels (poly(*N*-isopropylacrylamide) and polyacrylamide gels) are discussed. Deuterium substitutions affect on the swelling kinetics and volume phase transition of the polymer hydrogels. The slower swelling kinetics of hydrogels in D_2O than in H_2O arises mainly from the high viscosity of the medium. The deuterium isotope effect on the swelling-shrinking curve of hydrogels would come from the different polymer-solvent interaction. The microenvironments of hydrogels studied by solvatochromic fluorescence probe are compared with the bulk state. The zipper-type hydrogen-bonding inter-polymer complexes (poly(acrylic acid)-polyacrylamide and poly(acrylic acid)-poly(*N*-acryloylglycineamide)) are also investigated and show the huge isotope effect on the phase separation temperature.

1. Introduction

Phase transitions and critical phenomena in polymer gels have been paid great attentions by theoretical and experimental scientists and engineers. Volume phase transition of polymer gel was theoretically predicted by Dusek and Patterson in 1968.[1] They showed the possibility of a discontinuous volume change of polymer gels based on the analogy of the coil-globule transition of linear polymers in solution.[2] Tanaka experimentally discovered the discontinuous volume change of a partially ionized polyacrylamide (PAAM) gel against the continuous change of the solvent composition in a mixture of acetone and water in 1978.[3] After this discovery, the generality of volume phase transition in polymer gels has been well recognized and the study of this topic has become more extensive.[4,5]

This article is dedicated to the late Prof. Toyoichi Tanaka.

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The critical phenomenon (swelling-shrinking curve) of a polymer gel can be expressed by Flory-Rehner equation:[6-8]

$$\Pi = -\frac{k_B T}{V_s}[\phi + \ln(1-\phi) + \chi\phi^2] + \nu k_B T\left[\frac{1}{2}\left(\frac{\phi}{\phi_0}\right) - \left(\frac{\phi}{\phi_0}\right)^{\frac{1}{3}}\right] \tag{1}$$

where Π is the net osmotic pressure, k_B is the Boltzmann constant, T is the absolute temperature, V_s is the molar volume of the solvent, ν is the number of cross-links per unit volume, χ is the Flory's interaction parameter, and ϕ and ϕ_0 are the network volume fractions at the equilibrium and reference states, respectively. The first term of the right side denotes the mixing free energy and the second term of the right side denotes the elastic free energy. Although χ is very complex,[9-12] χ is often assumed to be linearly dependent on ϕ for the simplicity. [13-15]

$$\chi = \chi_1 + \phi\chi_2 \tag{2}$$

where

$$\chi_1 = \frac{\Delta H - T\Delta S}{k_B T} \tag{3}$$

and χ_2 is a constant. ΔH and ΔS are the mixing enthalpy and entropy of the polymer solution system. χ is a very important parameter, because polymer-polymer and polymer-solvent interactions are included in this factor.

The interactions in polymer solutions are comprised of the following four fundamental molecular interactions: (i) van der Waals interaction, (ii) hydrophobic interaction, (iii) electrostatic interaction, and (iv) hydrogen-bonding interaction. Here, we focus on the hydrogen-bonding interaction among these four fundamental molecular interactions. Although the bonding energy of a hydrogen bond is not large in comparison with that of a covalent bond, it plays a key role in many chemical and biological systems.[16-19] It would be expected that the hydrogen bonds have a great role in phase transitions of polymer gel and polymer solution, especially aqueous systems.

Deuterium substitution is a useful method to investigate both the static and dynamic features of condensed phases.[20] Because of the heavier mass of deuterium, the zero-point vibrational energy level of the deuterated hydrogen bond is lower than that of normal hydrogen bond. As the result, the hydrogen bond of deuterium is more stabilized than that of hydrogen, and the hydrogen-bonding network is more stiffened.[21] The differences between the properties of deuterated and undeuterated hydrogen bonding systems arise from the stabilized hydrogen-bonding interaction for deuterium in comparison with hydrogen. For example, the viscosity of D_2O is higher than that of H_2O and the melting and boiling points of D_2O are higher than those of H_2O.[22]

The deuterium isotope effects on the phase separation of nonaqueous polymer solutions have been well studied.[20] According to the extensive studies of the deuterium isotope effects of polystyrene solutions by Van Hook and co-workers, the region of the miscibility becomes large by the increase of the H/D ratio in the solvent and the decrease of the H/D ratio in the polymer.[23-25] In contrast to nonaqueous polymer systems, the deuterium isotope effects in polymer hydrogels have not been much extensively studied. As far as we know, the deuterium isotope effect of water on the volume phase transition temperature of a polymer hydrogel (poly(*N*-isopropylacrylamide) (PNIPAM) gel) was firstly observed by Shibayama et al. for the neutron scattering study.[26] However, the deuterium isotope effects on the whole swelling-shrinking state of hydrogels, the origin of the deuterium isotope effect in hydrogels, and the generality of the deuterium isotope effect in hydrogels were open questions.

On the other hand, fluorescence probe has been widely used to investigate the microscopic behavior of polymer systems. Especially, the dansyl group is well used to investigate the microscopic feature of the phase transition, phase separation, and conformational change in polymer systems, because its fluorescence shows the solvatochromism and it is relatively easy to synthesize the labeled polymer.[27-41] The microenvironment behavior on the phase transition of the polymer systems is not directly correlated with the bulk behavior in some cases.

In this review article, we focus on the deuterium isotope effects on the swelling kinetics[42] and volume phase transition[43-45] of typical polymer hydrogels, PNIPAM and PAAM gels, and the phase separation of the zipper-type hydrogen-bonding inter-polymer complexes, poly(acrylic acid) (PAA)-PAAM and PAA-poly(*N*-acryloylglycineamide) (PAG), in solution.[46] Since the deuterium substitutions change the hydrogen-bonding interactions in aqueous polymer systems, we can observe which state and process of polymer hydrogels and hydrogen-bonding inter-polymer complexes are strongly influenced by hydrogen bonds.

2. Swelling Kinetics of Polymer Hydrogel

To design polymer hydrogels as soft materials such as drug delivery systems, it is very important to understand the kinetics of swelling and shrinking processes. Tanaka and co-workers[47,48] and Peters and Candau[49,50] showed that the characteristic time of swelling process τ of spherical, cylindrical, and disk PAAM gels in water is proportional to the square of the size of the polymer gel:

$$\tau = \frac{[l(\infty)/(2\pi)]^2}{\alpha D} \qquad (4)$$

where $l(\infty)$ is the diameter of a spherical or a cylindrical gel or the thickness of a disk gel at the equilibrium state, D is the cooperative diffusion coefficient, and α is the shape factor. The values of α in a spherical gel, a long cylindrical gel, and a disk gel are 1, 2/3, and 1/3, respectively.[48] In this section, we discuss the deuterium isotope effect of the medium on the swelling kinetics of polymer hydrogels.[42]

Figure 1 shows the time dependence of the diameter, l, of (a) PNIPAM gel in H_2O and in D_2O and (b) PAAM gel in H_2O and in D_2O at 298 K. The exponential fit functions are also shown in Figure 1. The initial diameters of the sample hydrogels correspond to the as-prepared state at 289 K of each hydrogel. The swelling kinetics factors are summarized in Table 1. Since the shape of sample gels is short cylindrical, D is tentatively estimated by using eq. (4) with $\alpha = 1$.

The interesting points to be noted from Figure 1 and Table 1 are followings. (i) The characteristic time constant τ in swelling kinetics of the polymer hydrogels in D_2O is larger than that of the polymer hydrogels in H_2O, and the cooperative diffusion coefficient D of the polymer hydrogels in D_2O is smaller than that of the

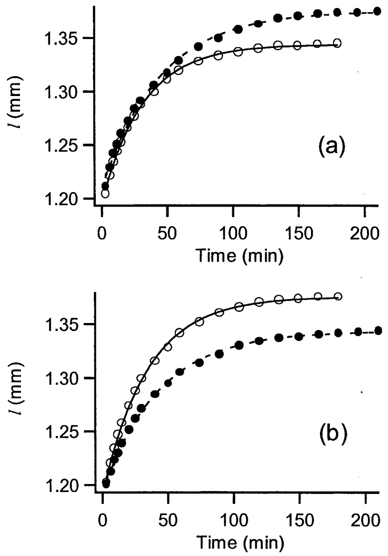

Figure 1. Comparison of the time dependence of the diameter l for (a) PNIPAM gel in H_2O (open circles) and D_2O (filled circles) and (b) PAAM gel in H_2O (open circles) and D_2O (filled circles). Exponential fit curves are also shown by solid line (H_2O) and broken line (D_2O).

Table 1. Characteristic times of swelling kinetics τ, diameters at the infinite time $l(\infty)$, and diffusion coefficient D of PNIPAM and PAAM gels in H_2O and D_2O.

Hydrogel	Solvent	τ (min)	τ_{D2O}/τ_{H2O}	$l(\infty)$ (mm)	$l_{D2O}(\infty)/l_{H2O}(\infty)$	D (cm^2/s)	D_{D2O}/D_{H2O}
PNIPAM	H_2O	32.0		1.344		2.38×10^{-7}	
	D_2O	44.8	1.40	1.375	1.023	1.78×10^{-7}	0.748
PAAM	H_2O	34.7		1.375		2.30×10^{-7}	
	D_2O	43.3	1.25	1.343	0.977	1.76×10^{-7}	0.765

polymer hydrogels in H_2O. (ii) The infinite-time (equilibrium state) diameter $l(\infty)$ of PNIPAM gel in D_2O is larger than that of PNIPAM gel in H_2O. In contrast to PNIPAM gel, the $l(\infty)$ of PAAM gel in D_2O is smaller than that of PAAM gel in H_2O. The cooperative diffusion coefficient D is expressed as,[51]

$$D = \frac{k_B T}{6\pi \eta \xi} \tag{5}$$

where k_B is the Boltzmann constant, T is the absolute temperature, η is the viscosity of the solvent, and ξ is the correlation length. As shown in eq. (5), D depends on the viscosity of the medium. The viscosities of H_2O and D_2O at 298 K are 0.890 mPa·s[22] and 1.095 mPa·s,[52] respectively. The inverse of the viscosity ratio between H_2O and D_2O ($(\eta_{D2O}/\eta_{H2O})^{-1}$) is, thus, 0.813. When the viscosity ratio is compared with the diffusion constant ratio, it would be clear that the slower swelling kinetics of hydrogels in H_2O than in D_2O arises mainly from the different viscosities between H_2O and D_2O. Since the polymer-solvent interaction is changeable by deuterium substitutions of the sources of hydrogel and solvent molecules, the residue of the deuterium isotope effect on the swelling kinetics can arise from the different microfrictions of deuterated and undeuterated systems.

Wang and Wu have studied the deuterium isotope effects of the average radius of gyration and the hydrodynamic radius of the coil-state linear PNIPAM in water using dynamic light scattering measurement.[53] Interestingly, both the average radius of gyration and the hydrodynamic radius of linear PNIPAM at about 298 K in D_2O are about 1.1 times larger than those in H_2O. This means that ξ of linear PNIPAM in D_2O is about 1.1 times longer than that in H_2O. If we include the deuterium isotope effects of η and ξ into eq. (5), the deuterium isotope effect on D of PNIPAM gel observed can be well reproduced. Kujawa and Winnik suggested that the hydration volume of PNIPAM in D_2O is larger than that of PNIPAM in H_2O from the pressure perturbation calorimetry study.[54] It would be possible that the deuterium isotope effect on the radiuses arises from the different interactions of PNIPAM and H_2O and PNIPAM and D_2O.

Another interesting point to be noted that the deuterium isotope effect on the diameter of hydrogels at the equilibrium state ($l(\infty)$). This deuterium isotope effect in PNIPAM gel shows the opposite feature to that in PAAM gel: Although the $l(\infty)$ of PNIPAM gel in D_2O is larger than that of PNIPAM gel in H_2O, the $l(\infty)$ of PAAM gel in D_2O is smaller than that of PAAM gel in H_2O.

PNIPAM in water has a lower critical solution temperature (LCST) and PAAM in water has an upper critical solution temperature (UCST) at near ambient temperature. A polymer solution system showing a UCST feature is characterized by positive values of ΔH and ΔS in a polymer-solvent interaction parameter, while one showing an LCST feature is characterized by negative values of these quantities (Table 2). In other words, the features of polymer-solvent interaction in PNIPAM and PAAM are different: PNIPAM dissolves into water enthalpically and PAAM dissolves into water entropically. The mixing free energy ΔG (= $\Delta H - T\Delta S$) is negative in the *swollen* polymer hydrogel. Deuterium isotopic substitutions give stabilization and structural effects on hydrogen-bonding systems.[21] In the hydrogen-bonding systems, the stabilization effect gives more negative ΔH, and the structural effect gives more negative ΔS by deuterium isotopic substitutions. The present result shows PNIPAM gel in D_2O is larger than in H_2O and PAAM gel in D_2O is smaller than in H_2O. Namely, the ΔG of PNIPAM in D_2O is more negative than that in H_2O and the ΔG of PAAM in D_2O is more positive than that in H_2O (Table 2). The dominant factor in the deuterium isotope effect on the swelling ratio of polymer hydrogel could thus be ΔH for LCST polymer and ΔS for UCST polymer for the driving force of mixing, though the deuterium isotopic substitutions should affect on both ΔS and ΔH of a polymer-solvent interaction parameter.

Table 2. Mixing parameters for UCST and LCST polymers and the isotope effects.

	ΔH (ΔH_D–ΔH_H)	ΔS (ΔS_D–ΔS_H)	ΔG (ΔG_D–ΔG_H)
LCST (H → D)	– (negative)	– (negative)	– (negative)
UCST (H → D)	+ (negative)	+ (negative)	– (positive)

3. Volume Phase Transition of Polymer Hydrogel

After Tanaka's discovery of the volume phase transition phenomenon of polymer gel,[3] the generality of volume phase transition in polymer gels was recognized not only by changing the composition of the solvent but also by temperature, ionic and pH changes, light irradiation, and electric field.[4,5] Here, we discuss the deuterium isotope effects of polymer hydrogel on the volume phase transition of polymer hydrogels triggered by temperature[43,44] and solvent composition.[45] Further, the bulk behavior of the volume phase transition of polymer hydrogel based on the size change are also compared with the microenvironment behavior observed by the fluorescence probe linked chemically with polymer hydrogels.[44,45]

3.1. Temperature Dependence

PNIPAM gel (and liner PNIPAM) in water is well known that this hydrogel shows the volume phase transition at about 307 K (the phase separation and coil-globule transition in the case of linear PNIPAM in water).[55-59] In D_2O, about 0.7 K increase of the transition temperature of PNIPAM gel in comparison with in H_2O have been observed.[26,43,44] The cloud point (or coil-globule transition temperature) of linear PNIPAM in D_2O is also about 1 K higher than that of liner PNIPAM in H_2O.[44,53,54,60-62]

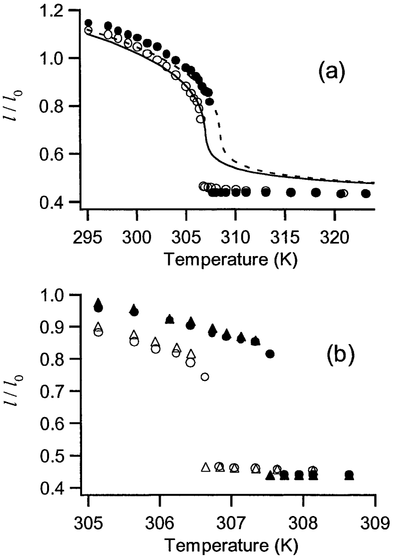

Figure 2. (a) Comparison of the swelling-shrinking curves of PNIPAM gel obtained by experiment (symbols) and prediction using the modified Flory-Rehner model (lines). Open circles and solid line show PNIPAM gel in H_2O, and filled circles and broken line show PNIPAM gel in D_2O. (b) Comparison between the heating (circles) and cooling (triangles) processes of the swelling-shrinking curves.

Figure 2 shows the swelling-shrinking curve of PNIPAM gel in H_2O and in D_2O against temperature. Besides the transition temperature, it becomes clear that (i) the swelling ratio at the swollen state of PNIPAM gel in D_2O is larger than that in H_2O, (ii) the swelling ratio at the shrunken state of PNIPAM gel in D_2O is equivalent to that in H_2O, and (iii) the magnitudes of the hysteresis of the transition temperatures (the difference between the transition temperatures in the heating process and the cooling process) are not affected by isotopic substitutions. These features have observed in PNIPAM gels with the several polymer concentrations.[44]

In order to understand the origin of the deuterium isotope effect on the volume phase transition of PNIPAM gel in water, we have examined the experimental result by a simple modified Flory-Rehner model proposed by Shibayama and co-workers.[15] The advantage of this model in comparison with the original Flory-Rehner model is that the swollen state is well reproducible, because the effect of the entanglements, which work as quasi-cross-links, is incorporated into the original Flory-Rehner model.[6-8,15] In this model, the number of cross-links per unit volume ν in eq. (1) is replaced by

$$\nu \frac{C_0}{C_{0,\mathrm{ref}}} \tag{6}$$

where $C_{0,\mathrm{ref}}$ is the lowest initial monomer concentration at which a uniform gel can be formed (0.3 M for PNIPAM).[14] As shown in Figure 2, the deuterium isotope effects of the swollen state and the transition temperature are qualitatively reproduced the experimental results. The parameters for PNIPAM gel in H_2O used were reported by Hirotsu,[14] and the three parameters, i.e., ΔH, ΔS, and χ_2, for PNIPAM gel in D_2O were determined by the fit to the experimental data.[43,44]

The different parameter between the simulation results of PNIPAM gels in H_2O and D_2O is only ΔH in χ, except for the molar volume of the solvent. The values of ΔH of PNIPAM gels in H_2O and D_2O are -1.246×10^{-20} J and -1.252×10^{-20} J, respectively. The change in the other possible parameters, χ_2 and ΔS, did not reproduce the experimental results.[43,44] We thus conclude that the deuterium isotope effect on the swelling-shrinking curve of PNIPAM gel would arise from ΔH in polymer-solvent interaction parameter χ. Namely, the solvent-polymer interaction in aqueous PNIPAM systems becomes stronger by deuterium substitutions because of the stabilized hydrogen-bonding interaction.

On the other hand, the deuterium isotope effects on the swelling ratio at the shrinking state have not been observed within experimental error. If the inter-polymer and/or intra-polymer hydrogen-bonding interaction is the dominant interaction to determine the shrinking state of the polymer hydrogel, the deuterium isotope effects on the swelling ratio of the polymer hydrogel at the shrinking state might be observable. Namely, the hydrophobic interaction is the dominant interaction to collapse PNIPAM gel. Maeda et al. also suggested that the globule state of linear PNIPAM is dehydrated around the hydrophobic groups of the polymer by IR experimental result.[60]

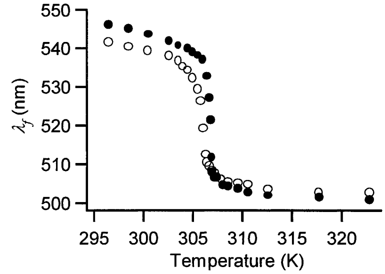

Figure 3. Temperature dependence of the fluorescence peak wavelength λ_f of the dansyl-group-labeled PNIPAM gel in H_2O (open circles) and D_2O (filled circles).

It may be interesting to compare the deuterium isotope effect of the swelling-shrinking curve of the bulk PNIPAM gel with that of the microscopic aspect of PNIPAM gel. Figure 3 shows the temperature dependence fluorescence peak wavelength λ_f of dansyl group chemically bonded with PNIPAM gel in H_2O and D_2O. Dansyl group shows a solvatochromism: λ_f becomes longer wavelength with higher polarity of the medium.[45] Therefore, it can observe the conformational change of polymer by using the fluorescence probe. The dramatic change of λ_f at about 310K, thus, indicates the microscopic (conformational) change of the polymer corresponds to the volume phase transition. It is clear from the comparison between Figures 2 and 3 that the overall features of the deuterium isotope effects in both macroscopic and microscopic observations are qualitatively similar. Aqueous linear PNIPAM solutions have been also shown the similar features.[44]

3.2. Solvent-Composition Dependence

The deuterium isotope effects on the swelling-shrinking curves of PNIPAM and PAAM gels against the solvent composition of the binary mixtures H_2O-acetone (and D_2O-acetone) and H_2O-methanol (and D_2O-CH_3OD) have been investigated.[45] Figure 4 shows the swelling-shrinking curves to the solvent composition of (a) PNIPAM gel and (b) PAAM gel in H_2O-methanol and D_2O-deuteriomethanol. Since PNIPAM gel has isopropyl groups in the side groups of the polymer, the selling-shrinking curve of the hydrogel in some aqueous binary mixtures shows a recurring feature to the solvent composition. The notable points from Figure 4 are followings. (i) The swelling ratio of PNIPAM gel in D_2O is larger than that in H_2O at the low organic solvent composition region. (ii) In contrast to PNIPAM gel, the swelling ratio of PAAM gel in D_2O is smaller than that in H_2O at the low organic solvent composition region. (iii) There is no isotope effect in the swelling ratio of both PNIPAM and PAAM gels at high organic solvent composition region. Acetone-water mixtures also show the similar deuterium isotope effect on the swelling-shrinking curve in both PNIPAM and PAAM gels.[45] The result in the low organic solvent composition region is similar to the results of the diameter at the swollen state of PNIPAM and PAAM gels in pure H_2O and D_2O discussed previously (*vide supra*).[42] The experimental result in the high organic solvent composition region indicates that the hydrophobic interaction (both polymer-polymer and polymer-solvent interactions) does not or very weakly affect on the swelling ratio (volume) of the polymer hydrogels by deuterium substitutions. (Note that the hydrogels for deuterated samples were rinsed and immersed in D_2O before put into the mixtures of organic solvent and D_2O. Therefore, hydrogens of amide groups of PNIPAM or PAAM gel exchange to deuteriums.) The swelling ratio of PNIPAM gel in pure water at the shrinking state in high temperature region (> 310 K) also showed no deuterium isotope effect on the swelling ratio of the hydrogel.[43,44]

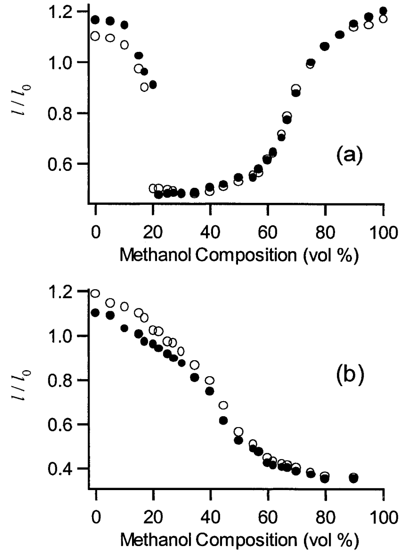

Figure 4. Methanol composition dependence of the swelling ratio l/l_0 for (a) PNIPAM gel and (b) PAAM gel in methanol-H_2O (open circles) and CH_3OD-D_2O (filled circles).

Figure 5 shows the fluorescence peak wavelength λ_f dependence of fluorescent-labeled (a) PNIPAM gel and (b) PAAM gel on the solvent composition of H_2O-methanol or D_2O-deuteriomethanol. The deuterium isotope effect in the microenvironment of the polymer hydrogels is also observed only in the low organic solvent composition region. However, the feature of the deuterium isotope effects of the swelling ratio and microenvironment of PAAM gel in the low organic solvent composition region is different from that in PNIPAM gel. λ_f of the fluorescent-labeled PNIPAM gel in D_2O is *longer* than that in H_2O and the swelling ratio of PNIPAM gel in D_2O is *larger* than that in H_2O. In contrast, the fluorescence peak of the fluorescent-labeled PNIPAM gel in D_2O is *longer* than that in H_2O, though the swelling ratio of PAAM gel in D_2O is *smaller* than that in H_2O.

The studies of aqueous PNIPAM or PAAM solutions and the polymer hydrogels by the molecular dynamics simulation and Raman and IR spectroscopies showed that the existence of the differently interacting water molecules.[60-70] Tamai et al. classified the water molecules of polymer solution in three categories: (i) around the hydrophilic group, (ii) around the hydrophobic group, and (iii) the bulk region.[63,64] Both the static and dynamic features of the hydrogen bonds in the three different regions were different from each other. It can be expected that the balance of the amplitudes of the three regions should determine the swelling ratio of the polymer hydrogel, because the solvent-polymer interaction parameter is related to the ensemble of the interaction strengths of solvent molecule and a part of polymer. In contrast to the macroscopic region, the information of the microscopic environment probed by fluorescent groups might come from one of the three categories in polymer solutions.

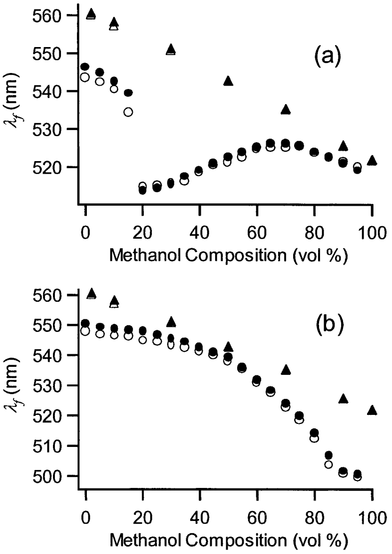

Figure 5. Methanol composition dependence of the fluorescence peak wavelength λ_f for dansyl-group-labeled (a) PNIPAM gel and (b) PAAM gel in methanol-H_2O (open circles) and CH_3OD-D_2O (filled circles). For the comparison, methanol composition dependence of λ_f for dansyl-group-labeled monomer in methanol-H_2O (open triangles) and CH_3OD-D_2O (filled triangles) are also shown.

4. Phase Separation of Inter-Polymer Complexes in Solution

Poly(acrylic acid) (PAA) forms cooperative inter-polymer hydrogen bonds with PAAM or the other polymers with amino groups as side groups only at low temperature, but dissociates at a certain temperature.[71-77] This phenomenon is so-called “zipper effect“. When an inter-polymer complex is formed due to cooperative inter-polymer hydrogen bonds, the binary polymer solution becomes turbid arising from the aggregations of the inter-polymer complexes due to the dehydration of the polymers. By utilizing the polymer-polymer interactions through the cooperative inter-polymer hydrogen bonds, a temperature-responsive polymer gel forming an interpenetrating polymer network has been prepared and studied by several groups.[77-81] We discuss the deuterium isotope effect on the phase separation of the zipper-type hydrogen-bonding inter-polymer complexes in solution in this section.[46]

Figure 6 shows the temperature dependence of the light transmittance at 500 nm of PAA-PAAM in H_2O and D_2O. For the reference, the temperature dependence of turbidity of PAA and PAAM in D_2O are also shown in Figure 6. Amazingly, the phase separation temperature of PAA-PAAM in D_2O is about 16 K higher than that of PAA-PAAM in H_2O. The other zipper-type hydrogen-bonding inter-polymer complex, PAA-poly(*N*-acryloylglycineamide) (PAG) complex, also shows the large deuterium isotope effect on the cloud point (about 5 K).[46]

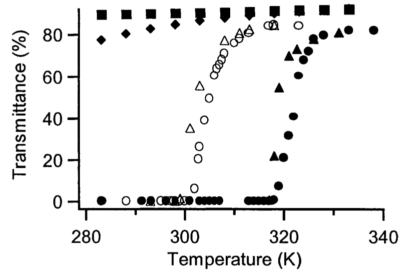

Figure 6. Temperature dependence of the light transmittance at 500 nm for PAA-PAAM in H_2O (open circles for heating process and open triangles for cooling process) and D_2O (filled circles for heating process and filled triangles for cooling process). Single component polymer solutions are also shown (filled squares denote PAA in D_2O and filled diamonds denote PAAM in D_2O).

These enormous deuterium isotope effects on the phase separation of the zipper-type hydrogen-bonding inter-polymer complex solutions have not been observed for other aqueous macromolecular solution systems, such as PNIPAM, cellulose, polypeptides, and proteins (about 1–2 K in these systems).[26,43,44,53,54,60,61,82-86] Since cooperative inter-polymer hydrogen bonds play a more significant role for the phase separation of the zipper-type polymer system than for the other simple aqueous polymer systems, it is possible to observe such huge isotope effects in the hydrogen-bonding inter-polymer systems. The smaller isotope effect on the phase separation temperature of PAA-PAG than PAA-PAAM could arise from the stronger hydration around PAG due to the extra hydrophilic groups present in PAG.

The interaction parameter χ in binary polymer solution systems is more complex than that in single polymer solutions. Although the phase state of single polymer solution can be expressed by one χ parameter, it is necessary to consider three interaction parameters in the case of polymer-polymer solutions: polymer(A)-solvent χ_{AS}, polymer(B)-solvent χ_{BS}, and so-called segregation factor χ_{AB} arising from polymer(A)-polymer(B) interaction.[8,51] From the estimation of the stabilization energies of formic acid dimer, formic amide dimer, and formic acid - formic amide dimer by MP2/6-31G(d,p)-level calculation, the molecular mechanics stabilization energy of formic acid - formic amide dimer is the largest among these three dimers.[87] We can easily imagine that since the inter-polymer hydrogen bonds has a great role to determine the phase state of hydrogen-bonding inter-polymer complex solution, the deuterium isotope effect on the phase separation of the hydrogen-bonding inter-polymer solution should mainly arise from the segregation factor. Although the polymer-solvent interaction factors can be changed by deuterium substitutions like in PNIPAM, PAAM, and other simple aqueous polymers, the contribution to the deuterium isotope effect of the polymer-solvent interactions on the phase separation of hydrogen-bonding inter-polymer complexes should be minor in comparison with the contribution of the polymer-polymer interaction.

5. Concluding Remarks

In this article, we have reviewed the deuterium isotope effects on the swelling kinetics and volume phase transition in the typical polymer hydrogels: PNIPAM and PAAM gels. The deuterium isotope effects of the phase separation of the hydrogen-bonding inter-polymer complexes have also discussed. Regarding the swelling kinetics of polymer hydrogels, the difference of the viscosities of H_2O and D_2O is the main origin of the isotope effect on the cooperative diffusion constant in the swelling process. The difference of the volume phase transition and phase separation of the polymer hydrogels in H_2O and D_2O arises from the different polymer-solvent interaction parameters. The deuterium isotope effect on the phase separation temperature in zipper-type hydrogen-bonding inter-polymer complex solution, PAA-PAAM in water, is as large as 16 K. In the case of zipper-type hydrogen-bonding inter-polymer complex, the polymer-polymer interaction could give large contribution to the phase separation rather than the polymer-solvent interactions. From the fluorescence studies, the microscopic features of the swelling-shrinking curves of polymer hydrogels have been observed. The deuterium isotope effects of the bulk and microenvironment in the polymer hydrogels are not always consistent. The difference between bulk and microenvironment of the polymer hydrogels may arise from the microheterogeneity of the polymer hydrogel systems.

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