Angewandte
Chemie

Polymer–Surfactant Gels

Rapid Swelling/Collapsing Behavior of Thermoresponsive Poly(*N*-isopropylacrylamide) Gel Containing Poly(2-(methacryloyloxy)decyl phosphate) Surfactant**

Hu Yan, Hideki Fujiwara, Keiji Sasaki, and Kaoru Tsujii**

Poly(*N*-isopropylacrylamide) (PNIPA) gel has attracted considerable attention, from both the academic and technological viewpoints.[1–6] PNIPA gel undergoes an abrupt volume change at the phase-transition temperature (ca. 34 °C),[1] which can be utilized in several promising applications such as drug delivery systems and actuators.[4,5] For better performance of these applications, several strategies have been reported to exploit the rapid volume change of PNIPA gels.[7–9] However, PNIPA gel also exhibits salt-tolerant water absorbency through the incorporation of surfactants such as sodium dodecyl sulfate (SDS).[2] The behavior of the PNIPA gel in surfactant solutions has been extensively studied,[10] but little research has been reported on PNIPA gels containing polymeric surfactants. In our studies, poly(2-(methacryloyloxy)decyl phosphate) (PMDP) was chosen as the polymeric surfactant, which was expected to afford a superabsorbent PMDP-containing PNIPA (PNIPA–PMDP) gel in the presence of salts. The PNIPA–PMDP gel did not exhibit superabsorbency in sodium chloride solutions, but interestingly showed a rapid volume change above its phase transition temperature when compared to conventional PNIPA gels. Herein, we report the rapid volume change of PNIPA–PMDP gels as a function of temperature as well as by laser-beam irradiation. Our results clearly demonstrate the PMDP-induced enhancement of the response dynamics for the polymeric network of PNIPA gels.

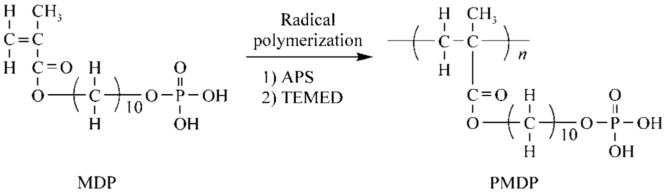
The PNIPA gels were synthesized by free-radical polymerization under the reaction conditions shown in Table 1 (see Experimental Section). PMDP was readily prepared from 2-(methacryloyloxy)decyl phosphate by free-radical polymerization at about 25 °C (Scheme 1). To determine the phase-transition temperature of the gels, the value of V/V_c was measured, in which V and V_c are the gel volumes at the target and at the highest temperatures of the measurements, respectively. Notably, V_c does not represent the volume of the completely collapsed structure, especially for the PNIPA gel,

---

[*] Dr. H. Yan, Dr. H. Fujiwara, Prof. Dr. K. Sasaki, Prof. Dr. K. Tsujii
Research Institute for Electronic Science (RIES)
Hokkaido University, Sapporo 001-0021 (Japan)
Fax: (+81) 11-706-9357
E-mail: yanhu@es.hokudai.ac.jp
tsujik@es.hokudai.ac.jp

[**] H.Y. acknowledges fellowship support from the 21st century COE program “Center of Excellence for Advanced Life Science on the Base of Bioscience and Nanotechnology” of Hokkaido University, Japan. The authors thank Prof. T. Akutagawa of RIES, Hokkaido University, for assistance with the infrared spectroscopic measurements.

DOI: 10.1002/ange.200462288



Scheme 1. Synthesis of PMDP. APS = ammonium persulfate, TEMED = tetramethylethylenediamine.

since V and V_c were measured at intervals of 1 h and the gel samples were not in the perfect equilibrated state. This situation, however, had little influence on the determination of the transition temperature. The shrinking kinetics of the gels was determined by measuring $\Delta V\%$ at 43 °C as a function of time, in which $\Delta V\% = (V_i - V_t)/V_i \times 100\%$ (V_i and V_t are the volumes at the initial and the target time, respectively).

As shown in Figure 1, the water absorbencies (V/V_c) of the PNIPA–PMDP gels were five- and fourfold greater than those of PNIPA in pure water (Figure 1a) and in 0.15 M NaCl solution (Figure 1b), respectively, within the investigated time (1 h). The salt-tolerant superabsorbency behavior, which was observed in the PNIPA–SDS system,[2] was not observed for PNIPA–PMDP gels; in fact, completely different behaviors were observed for PNIPA–PMDP gels as compared to those of the PNIPA–SDS gel. Interestingly, the phase-transition temperature of the PNIPA–PMDP gel was comparable, within experimental error, to that of the conventional PNIPA gel, both in pure water and in 0.15 M NaCl solution, whereas the transition temperature of PNIPA–SDS gel increased to 90 °C in 0.15 M NaCl solution.[2] It is important to note that the PNIPA gel has been extensively studied as a tool of drug delivery systems as its transition temperature is approximately 34 °C, which is comparable to body temperatures.[4]

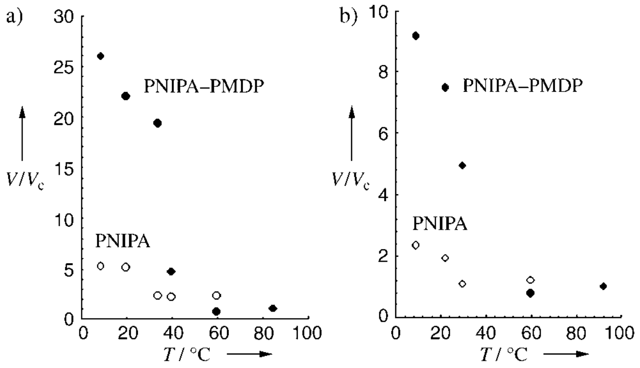


Figure 1. Temperature dependences of normalized gel volumes in pure water (a) and in 0.15 M NaCl solution (b). V_c denotes the gel volume in the collapsed state (but not in a completely collapsed state). Values for V/V_c did not have any significant effect on the estimation of phase-transition temperatures.

The time-dependent volume changes ($\Delta V\%$) of PNIPA–PMDP and PNIPA gels at 43 °C are shown in Figure 2. The PNIPA–PMDP gel showed a significantly greater volume change than that of the PNIPA gel (Figure 2a). The PNIPA–PMDP gel had a ΔV value of 88% within 30 min, and subsequently collapsed within 120 min; in contrast, the PNIPA gel showed a ΔV value of only 24% within 30 min, and did not attain the completely collapsed state within the experimental time. Figure 2b shows that the $\Delta V\%$ values of the PNIPA–PMDP gel are both reproducible and reversible. The PNIPA–PMDP gel contracted to 88% at 43 °C in 30 min, and swelled back to the initial volume at 20 °C within 30 min. The reversible volume change was repeated at least six times. No escape of PMDP molecules from the PNIPA–PMDP gel system was observed even after repeated reversible volume changes, which was confirmed by ultraviolet absorption spectra. The volume changes of PNIPA–PMDP and PNIPA gels at 43 °C can be visually observed in Figure 3. For the PNIPA–PMDP gel, significant changes in the diameter and the length were observed within 30 min. Specifically, a sample with dimensions of 1.7 × 9.2 mm (diameter × length) contracted to 0.8 × 3.4 mm; in contrast, a PNIPA sample with initial dimensions of 1.6 × 9.6 mm contracted to 1.4 × 8.8 mm.

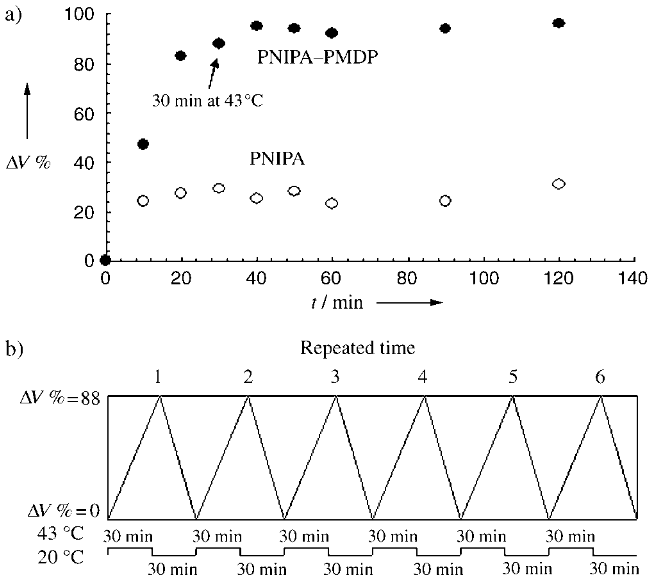


Figure 2. a) Degree of volume change (shrinkage) of PNIPA and PNIPA–PMDP gels at 43 °C after specific times. b) Reproducibility and reversibility of the volume change between 20 and 43 °C. Initial sizes of the gels were 1.7 × 9.2 mm (diameter × length) for PNIPA–PMDP gel and 1.6 × 9.6 mm for PNIPA gel.

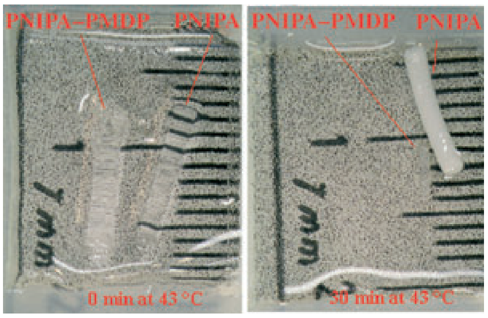


Figure 3. The hydrogels before (left) and after (right) the volume phase-transition under the conditions described.

Furthermore, the PNIPA–PMDP gel remained almost transparent, even after a large volume change in a short time, whereas the PNIPA gel turned completely turbid. Unlike the conventional PNIPA gel, no skin formed on the surface of the PNIPA–PMDP gel, which could accelerate the phase transition in the PNIPA–PMDP system.

To verify the effects of polymeric surfactant PMDP on the prevention of skin formation and the acceleration of the phase transition of the PNIPA gel, a cylindrical sample of PNIPA gel with a PMDP concentration gradient was utilized for the phase-transition experiments. Images of the PMDP-gradient PNIPA gel below (at 9 °C) and above (at 60 °C) the phase transition temperature are shown in Figure 4. Half of the PMDP-gradient PNIPA gel was transparent, whereas the other half was turbid. In such gels, the negatively charged PMDP molecules migrated from the turbid to the transparent region by electrophoretic action, thus forming a half-and-half PNIPA–PMDP-like and PNIPA-like gel. Both regions consist of a structurally identical PNIPA polymer network with the same degree of cross-linkage, and differ only in the amounts of PMDP. Therefore, the observed phase transition for the PMDP-gradient PNIPA gel unambiguously demonstrated that the polymeric surfactant PMDP prevents the formation of a skin structure and accelerates the volume change of PNIPA gel above the phase-transition temperature. The PNIPA–PMDP gel solubilized an oil-soluble dye, Yellow AB, which comprises hydrophobic crystals and is insoluble in water. The results indicate that PMDP forms micelles within the PNIPA gel network. It is, however, unclear at this stage how the micelles of PMDP prevent skin formation.

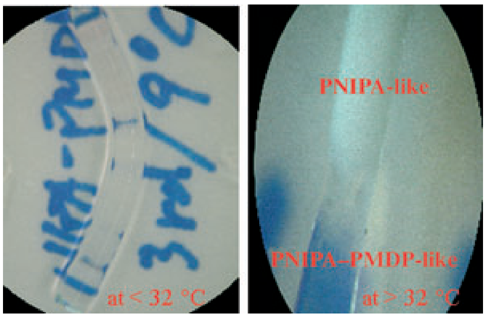


Figure 4. The PMDP-gradient PNIPA gel below (left, at 9 °C) and above (right, at 60 °C) the volume phase-transition temperature.

The PNIPA–PMDP gel also responded significantly quickly to the stimulus of a laser beam (Nd:YAG; wavelength, 1064 nm; power, ca. 100 mW) compared with conventional PNIPA gels. Interestingly, upon laser-beam irradiation, the rapid volume change of the PNIPA–PMDP gel resulted in a jet stream of water from the gel (Figure 5). A small block of PNIPA–PMDP gel (0.2 mm diameter, 0.2 mm length) in a glass capillary was used in the laser-irradiation experiments. No water droplets were observed on either side of the gel in the capillary before irradiation by the laser beam. Irradiation for 1 min resulted in the formation of numerous water droplets on the inside wall of the glass tube. The observation of some water droplets relatively far away from the gel on both sides indicated that the abrupt contraction or rapid volume change of the swollen PNIPA–PMDP gel by the stimulus of the laser beam caused a jet stream of water. Juodkazis and co-workers recently reported that PNIPA gels undergo laser-induced volume phase transition under well-controlled conditions, in which D_2O was used as the solvent to avoid any temperature rise as a result of light absorption (wavelength, 1064 nm).[11] However, when laser beams with a power less than 700 mW were used, the PNIPA gel did not exhibit any volume changes.[11] In contrast, the present PNIPA–PMDP gel clearly showed a volume change using a laser beam with a power as weak as ≈100 mW. In a comparison experiment in which D_2O was used instead of H_2O solvent, no such rapid volume change was observed. Therefore, it is considered that the volume phase transition was triggered by rising temperatures inside the gel through absorption of near-infrared light (1064 nm) by water.

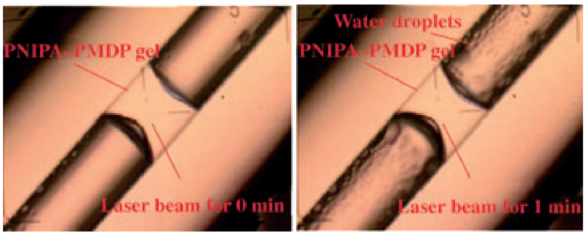


Figure 5. The PNIPA–PMDP gel before (left) and after (right) laser irradiation (Nd^{3+}:YAG; wavelength, 1064 nm; power, 100 mW).

In conclusion, a PNIPA gel containing the polymeric surfactant PMDP (PNIPA-PMDP gel) has been synthesized and found to show a rapid volume change above its phase-transition temperature (ca. 34 °C). Interestingly, the phase-transition temperature of the PNIPA–PMDP gel is equal to that of the PNIPA gel. A concentration gradient of PMDP within the PNIPA gel can be obtained by applying an electric field to the gel, similar to the gel electrophoresis technique. The PMDP-gradient PNIPA gel clearly demonstrates the prevention of skin formation and acceleration of the phase transition of the PNIPA gel by PMDP, which forms micelles and does not escape from the gel system. Upon laser-beam irradiation (wavelength, 1064 nm; power, 100 mW), which is possibly converted to thermal energy, the PNIPA–PMDP gel undergoes rapid volume change, which can result in expulsion of a stream of water from the gel. Accordingly, this PNIPA–PMDP gel system could be extended to drug delivery systems[4] in which the target drug is exclusively released by laser stimuli on a diseased part, or to microvalves that can finely control fluids in the microchannels of a micro/miniaturized total analysis system (μTAS).[12]

Experimental Section

Sample preparation: PMDP was synthesized from MDP, which was prepared according to a previous report,[13] as follows: MDP (9.2 g) and ammonium persulfate (APS; 0.2 g) were dissolved in deionized water (397 g) at 25 °C. The solution was degassed by N_2 gas bubbling and polymerized for 1 h after addition of tetramethylethylenediamine (TEMED; 240 μL). The resulting precipitate (PMDP) was isolated by filtration, washed with pure water, and dried overnight under vacuum at 60 °C. Infrared spectra revealed that the characteristic peaks of the methylene groups at 3034 and 1637 cm^{-1} diminished, whereas those of the alkyl groups at around 2900 cm^{-1} increased after the reaction, which indicated the polymerization of MDP. PMDP showed a strong ultraviolet absorption at 205 nm. No such absorption was observed in the UV spectra of water in which the PNIPA–PMDP gel repeatedly underwent volume phase transition, which indicated that the PMDP did not escape from the gel network, probably because of entanglement of the polymeric surfactant with the network. Attempts to determine the molecular weight (M_w or M_n) of PMDP by gel-permeation chromatography were unsuccessful, probably because the polymeric surfactant forms micelles or aggregated structures in organic solvents. Some experimental and instrumental problems remain, but further investigations to determine the molecular weight of the polymers are currently underway. The PMDP dissolved well in water and its solubility increased with increasing temperature.

The PNIPA-based gels were synthesized by free-radical polymerization as follows (see Table 1): PMDP (0.044 g), PNIPA (0.87 g), *N*,*N'*-methylenebisacrylamide (MBA; 0.014 g), and APS (0.013 g) were dissolved in deionized water (8.5 g). The solution was adjusted to pH 6 with NaOH solution (0.1 M, 0.93 g), then degassed and polymerized at 4 °C by the addition of TEMED (24 μL). Polymerizations were carried out in 1.3-mm capillaries (for measurements of phase-transition temperature, time dependence of volume change at 43 °C, and response to stimulus of laser beam) or in 0.2-mm capillaries (for observations of jet streams of water from the gels upon laser-beam irradiation). The resulting PNIPA–PMDP gels were repeatedly washed by immersion in pure water for several days. The PNIPA gels were similarly synthesized but without PMDP. In addition, a concentration gradient of PMDP inside the PNIPA gel was created by applying a 10-V electric field for 2 h between both ends of the cylinder-shaped PNIPA–PMDP gel within a glass capillary.

Table 1: Preparation of PNIPA and PNIPA–PMDP gels.[a]

PNIPA-based gel	Concentration [wt%]			Appearance
	PNIPA	MBA	polymeric surfactant	
PNIPA gel	8.6	0.12	–	colorless
PNIPA–PMDP gel[b]	8.2	0.12	0.42	colorless

[a] APS and TEMED as an initiator and accelerator, respectively, at 4 °C. [b] PMDP was neutralized by an aqueous solution of NaOH before addition of TEMED.

Measurements: PNIPA–PMDP and PNIPA gels with initial sizes (diameter × length) of 1.7 × 9.2 and 1.6 × 9.6 mm, respectively, were used for measurements of volume phase transition. The experiments were performed in a temperature-controllable water bath filled with deionized water. The sizes of the gels were measured by optical microscopic observation. The measurements were carried out twice, and the data were in good agreement within a standard deviation of 1%.

The optical stimulus was obtained by introducing a Nd^{3+}:YAG laser (cw mode; wavelength, 1064 nm; power, 100 mW) into an optical microscope (IX-70 Olympus, 10 ×) and focusing on the gel sample at about 25 °C. Changes in the shape and the occurrence of water jet streams were monitored with a charge-coupled device camera and recorded as moving images. Pictures of the jet streams of water from the PNIPA–PMDP gel were transformed from the moving images.

Received: October 13, 2004

Keywords: gels · phase transitions · polymers · surfactants

[1] Y. Hirokawa, T. Tanaka, *J. Chem. Phys.* **1984**, *81*, 6379–6380.
[2] Y. Zhang, T. Tanaka, M. Shibayama, *Nature* **1992**, *360*, 142–144.
[3] H. G. Schild, *Prog. Polym. Sci.* **1992**, *17*, 163–249.
[4] L. E. Bromberg, E. S. Ron, *Adv. Drug Delivery Rev.* **1998**, *31*, 197–221.
[5] R. Yoshida, K. Uchida, Y. Kaneko, K. Sakai, A. Kikuchi, Y. Sakurai, T. Okano, *Nature* **1995**, *374*, 240–242.
[6] T. Okajima, I. Harada, K. Nishio, S. Hirotsu, *J. Chem. Phys.* **2002**, *116*, 9068–9077.
[7] X. Zhang, R. Zhuo, Y. Yang, *Biomaterials* **2002**, *23*, 1313–1318.
[8] W. Xue, I. W. Hamley, M. B. Huglin, *Polymer* **2002**, *43*, 5181–5186.
[9] T. Matsuura, M. Sugiyama, M. Annaka, Y. Hara, T. Okano, *Polymer* **2003**, *44*, 4405–4409.
[10] Y. Murase, K. Tsujii, T. Tanaka, *Langmuir* **2000**, *16*, 6385–6390.
[11] S. Juodkazis, N. Mukai, R. Wakaki, A. Yamaguchi, S. Matsuo, H. Misawa, *Nature* **2000**, *408*, 178–181.
[12] A. Manz, N. Graber, H. M. Widmer, *Sens. Actuators B* **1990**, *1*, 244–248.
[13] T. Koudate, Y. Nakano, JP patent P2000-26481A, **2000**.