Discontinuous Binding of Surfactants to a Polymer Gel Resulting from a Volume Phase Transition

Yasuyuki Murase,[†] Tomohiro Onda,[‡] Kaoru Tsujii,*[,†] and Toyoichi Tanaka[§]

Tokyo Research Center, Kao Corporation, 2-1-3 Bunka, Sumida-ku, Tokyo 131-8501, Japan; Mechanical Processing Technology Research Laboratories, Kao Corporation, 2606 Akabane, Ichikai-machi, Haga-gun, Tochigi 321-3498, Japan; and Department of Physics, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139

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ABSTRACT: Binding isotherms of surfactants onto a polymer gel, poly(*N*-isopropyl acrylamide) (NIPA), have been measured to understand the interaction between them and found to change reversibly and discontinuously at the phase-transition point of the gel. This result indicates that the affinity of the surfactants to the gel is cooperatively altered by a conformational change of the polymer chains. The discontinuous change of the surfactant binding mentioned above can be regarded as an artificial mimic of the protein functions such as enzymatic reactions and oxygen uptake of hemoglobin by the polymer gel. In the discontinuous binding isotherms, a hysteresis with respect to the surfactant concentration is first observed. It is interestingly found that the increment of the phase-transition temperature of the NIPA gel on addition of a surfactant is linearly related to the jump in the amount of the surfactant binding at the phase-transition point.

Introduction

Polymer gels undergo volume phase transition in response to a change of surrounding solution conditions.[1−5] They are used as drug delivery systems[6] and actuators or chemo-mechanical devices.[7−9] In particular, controlled release of small molecules from a gel attracts much attention and has been extensively studied.[10] Most of such studies, however, were done to utilize the mesh-size change of gel networks accompanied by their volume phase transition. In this study, we have succeeded in switching the adsorption−desorption property of surfactants by utilizing the coupling effect of the affinity of the agents with the phase transition of the gel.

NIPA gel is well-known as a thermoresponsive gel[11] and shows a phase transition at about 34 °C. This phase-transition temperature increases dramatically on addition of small amount of some ionic surfactants.[12−17] It is interesting to note that the change of the transition temperature of the above depends highly upon the chemical structure of the surfactants, i.e., hydrophobic chain length and hydrophilic headgroup.[16,17] Similarly to the interaction between surfactants and water-soluble linear polymers,[18−20] the effectiveness of the hydrophilic group on the elevation of phase-transition temperature is roughly in the order of anionics > cationics > nonionics. Even among the anionic surfactants, however, sulfate-type surfactant elevates more than 60 °C, whereas phosphate-type surfactant only elevates by 2−3 °C.[17] Elevation of transition temperature on addition of ionic surfactants is supposed to result from the ionization of the polymer chains of NIPA gel by adsorption of ionic surfactant molecules.[3,16,17] However, such a simple model cannot explain the large difference of transition temperature by a small difference of chemical structure of hydrophilic groups.

Then, this work has been done for two purposes: one is to make clear the reason small differences in chemical structure of the surfactants change greatly the phase-transition temperature of NIPA gel, and the other is to make a control system of discontinuous adsorption−desorption of surfactants in polymer hydro-gels. Binding isotherm measurements of surfactants onto the NIPA gel has been mainly made to achieve the above two purposes.

Experimental Section

Materials. Monomers and a reaction accelerator for preparation of gel samples were *N*-isopropylacrylamide (Eastman Kodak Co.), *N*,*N*-methylenebis(acrylamide) (a cross-linker; Wako Pure Chemical Industries Ltd.), and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (an accelerator of polymerization reaction; Wako Pure Chemical Industries Ltd.). Surfactants used in this work were sodium dodecyl sulfate (abbreviated as $R_{12}SO_4Na$; Sigma Chemical Co.), sodium dodecyl sulfonate ($R_{12}SO_3Na$; Tokyo Chemical Industry Co., Ltd.), triethanolammonium mono-dodecyl phosphate ($R_{12}PO_4$·TEA; Kao Corp.), dodecylamine hydrochloride ($R_{12}NH_3Cl$; Tokyo Chemical Industry Co., Ltd.), dodecyltrimethylammonium chloride (R_{12}-TAC; Tokyo Chemical Industry Co., Ltd.), and polyoxyethylene ($p = 10$) nonylphenyl ether ($R_9\phi(EO)_{10}$; Kao Corp.). The counterion of mono-dodecyl phosphate is an organic one to depress its Krafft point, because no effect of counterion is known on the phase-transition temperature of the NIPA gel.[17] Polyoxyethylene chain length of the nonionic surfactant is not monodispersed or in a certain distribution. All the samples were used without further purification. Deionized and distilled water was purchased from Wako Pure Chemicals Industries and used to prepare the gel samples.

Sample Preparations. Poly(*N*-isopropylacrylamide) (NIPA) gel was prepared by radical polymerization. A mixture of 39.6 g (700 mM) of NIPA monomer, 0.65 g of *N*,*N*-methylenebis-(acrylamide), and 1.2 mL of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine was dissolved in pure water to make 500 mL of aqueous solution. For at least 30 min before polymerization, nitrogen gas was bubbled into the above solution to purge oxygen. An aqueous solution of ammonium persulfate (4 wt

* Present address: Japan Marine Science and Technology Center, 2-15 Natsushima-cho, Yokosuka 237-0061, Japan.
† Tokyo Research Center.
‡ Mechanical Processing Technology Research Laboratories.
§ Massachusetts Institute of Technology.

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%) was bubbled by N_2 gas, and a part of it (5 mL) was added to the above monomer solution. Polymerization reaction was performed under N_2 gas atmosphere in a thin capillary (inner diameter of 140 or 800 μm) or in a beaker dipped in an ice/water mixture. Gel samples thus obtained were washed thoroughly with pure water. The cylindrical gel of 140 μm diameter was employed for the phase-transition measurements. The bulk gel prepared in a beaker was cut to be about 1 mm diameter by pushing out through a mesh with an injector. These cut gels and the cylindrical gels of 800 μm diameter were used for determination of binding isotherms.

Measurements of Volume Phase Transition. Volume phase transition of NIPA gel was observed by measuring the diameter of the cylindrical gel (140 μm). The apparatus and the procedures of the phase-transition measurements were described elsewhere.[17] Gel diameter was measured with a micrometer equipped with a charge-coupled device (CCD) camera. Phase-transition experiments with respect to temperature were performed in both temperature-increasing and -decreasing processes.

Binding Isotherms. Several tens of gel samples ($\sim 1 \times 1 \times 5$ mm^3) were put in a surfactant solution-containing glass tube with a screw seal. Many such tubes with different surfactant concentrations were allowed to stand at 25, 35, 40, 50, and 60 °C (±1 °C) for 1 week. Equilibrium was attained for 1 week because no change in binding amount was observed for longer equilibration times. The amount of surfactant binding onto NIPA gel was calculated by determining the surfactant concentration change in the solution outside the gel as follows:

$$A = \frac{W_0 C_0 - C_1(W_0 + W_W)}{W_P/M_w} \quad (1)$$

where A is the binding amount expressed as the number of surfactant molecules per one monomer unit of NIPA; C_0 and C_1 are the surfactant concentrations (mole/kg) of the solution outside the gel at initial and final (equilibrated) state, respectively; W_0, W_W, and W_P are the mass (g) of surfactant solution, of water in the gel, and of polymer in the gel at initial state (before immersion in the surfactant solution), respectively; and M_w is the molecular weight of NIPA monomer. In eq 1, the surfactant concentration in the aqueous phase inside the gel is assumed to be equal to that of the solution outside the gel. The surfactant concentration of the solutions was determined by the high-performance liquid chromatography (HPLC) technique. An RI (refractive index) detector was employed for most of the surfactants, and a UV (275 nm) detector was used for $R_9\phi(EO)_{10}$.

Special care was taken to obtain the hysteresis near the phase-transition point in the binding isotherms. The cylindrical gel samples (3−5 g) of 800 μm diameter were put in a glass tube with a screw seal and equilibrated in the surfactant solution (130 mL) for 2 days. This time, 2 days, was enough for equilibration in this case because the gel samples were thin. The binding amount was determined by the same fashion as above. Then, 4 mL of pure water was added to the same tube when the gel was in the swollen state, and the binding amount was determined again after 2 days. This procedure was repeated until the gel turned to the collapsed state. Furthermore, 4 mL of a concentrated surfactant solution was added stepwise similarly to the above procedure when we started from the collapsed gel samples. If we used the samples of heterogeneous size, swollen and collapsed gels coexisted in a single tube and good hysteresis data could not be obtained.

Electric Conductivity. Electric conductivity of ionic surfactant solutions was measured to estimate the dissociation degree of counterions. Experiments were carried out with an electric conductivity meter (TOA Dempa Industry Ltd.; type CM-20S) at constant temperature (±1 °C).

Measurements of Sodium Ion Concentration. The degree of dissociation of counterions was estimated also by the sodium ion concentration of the surfactant solutions. A sodium ion electrode (ORION Co.; type 86−11) and an ion meter (ORION Co.; type EA920) were employed at room temperature of about 25 °C for the measurements of electromotive force.

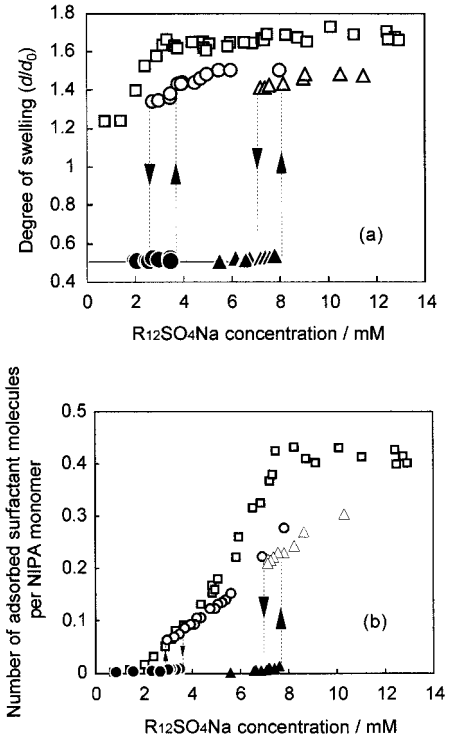

Figure 1. Degree of swelling of a NIPA gel (d/d_0) as a function of $R_{12}SO_4Na$ concentration (a) and isotherms of $R_{12}SO_4Na$ binding onto the gel (b) at 25 (□), 40 (○ and ●), and 60 °C (△ and ▲). Open and filled symbols denote the swollen and the collapsed state of the gel, respectively.

Results

Volume Phase Transition and Binding Isotherms. Figure 1a shows the volume phase transition (degree of swelling) of a NIPA gel as a function of $R_{12}SO_4Na$ concentration at 25, 40, and 60 °C. Diameter of a cylindrical gel normalized by the original (as synthesized) diameter (140 μm) is plotted as the ordinate of the figure. The gel is always in the swollen state at 25 °C but shows a phase transition at 40 and 60 °C. The collapsed state of the gel at 40 or 60 °C transformed discontinuously to a swollen state with increasing concentration of $R_{12}SO_4Na$. When the surfactant concentration was decreased, the gel changed again discontinuously to the collapsed state. One can see clear hysteresis in these phase-transition behaviors. The hysteresis of the phase transition of the NIPA gel with respect to the surfactant concentration is first observed in this work, although many cases have been known in the transition with respect to temperature.[11,17]

It is clearly seen from Figure 1b that the phase transition and the swelling behavior of the gel are governed by the adsorption of the surfactant. The binding isotherms at 40 and 60 °C exhibit discontinuous jumps at 3.4 (40 °C) and 7.8 mM (60 °C) of the surfactant with increasing concentration of the agent and sudden drops at 2.8 and 7.2 mM with decreasing concentration. The surfactant concentrations at which these discontinuous changes take place coincide quite well with those of the phase transition in Figure 1a. These results indicate that the phase transition of the NIPA gel originates the discontinuous adsorption−desorption cycle of the surfactant. The binding isotherm

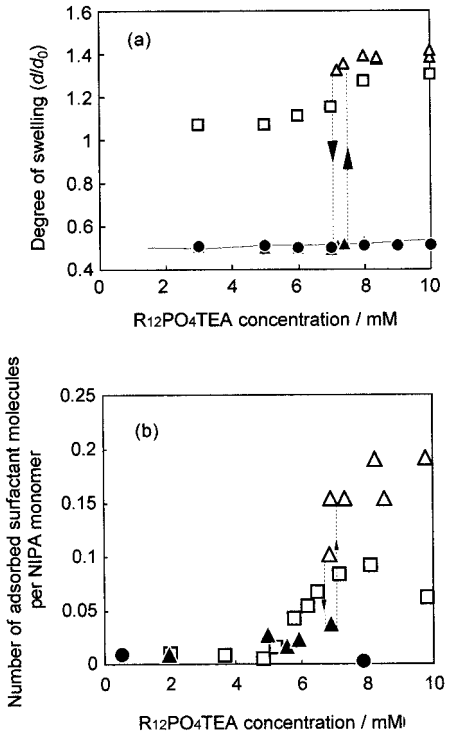

Figure 2. Degree of swelling of a NIPA gel (d/d_0) as a function of $R_{12}PO_4$·TEA concentration (a) and isotherms of $R_{12}PO_4$·TEA binding onto the gel (b) at 25 (□), 35 (△ and ▲), and 40 °C (●). Open and filled symbols denote the swollen and the collapsed state of the gel, respectively.

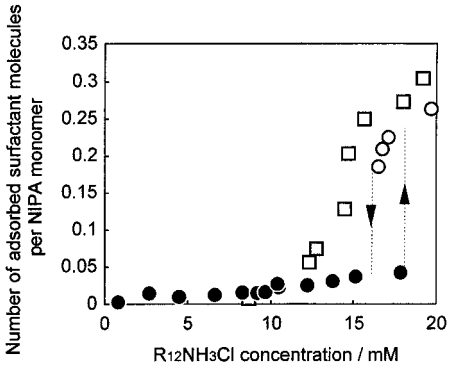

Figure 3. Isotherms of $R_{12}NH_3Cl$ binding onto the NIPA gel at 25 (□) and 40 °C (○ and ●). Open and filled symbols denote the swollen and the collapsed state of the gel, respectively.

of $R_{12}SO_4Na$ at 25 °C is continuous and in sigmoidal shape with respect to the surfactant concentration, corresponding to the continued swollen state of the gel in the whole range of the surfactant concentration.

A similar relationship between the phase transition and the binding isotherm was observed also in the R_{12}-PO_4·TEA solution (Figure 2). Figure 3 shows the continuous (at 25 °C) and discontinuous binding isotherm (at 40 °C) of a cationic surfactant, $R_{12}NH_3Cl$. The binding behaviors are essentially the same as those of anionic agents. These results mean that the phase transition caused by the surfactant adsorption is a general phenomenon in the systems of NIPA gel and ionic surfactants. Figure 4 shows the degree of swelling of NIPA gel in nonionic surfactant, $R_9\phi(EO)_{10}$, solutions (a) and the binding isotherms of the agent (b). In this case, no effect of the surfactant on the swelling behavior of the NIPA gel is observed.

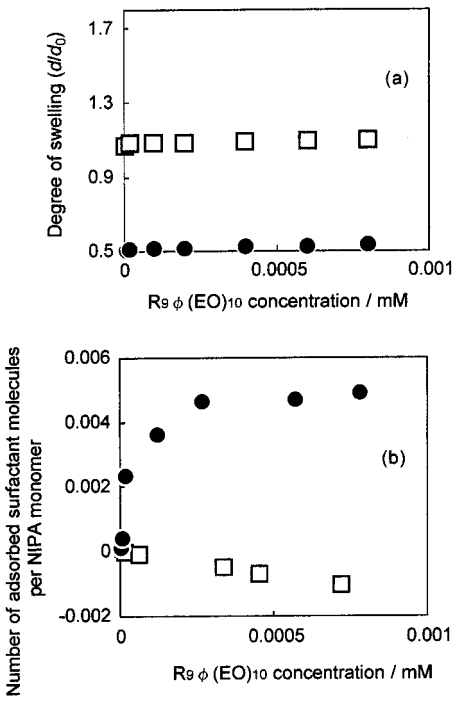

Figure 4. Degree of swelling of a NIPA gel (d/d_0) as a function of $R_9\phi(EO)_{10}$ concentration (a) and isotherms of $R_9\phi(EO)_{10}$ binding onto the gel (b) at 25 (□) and 40 °C (●). Open and filled symbols denote the swollen and the collapsed state of the gel, respectively.

The saturation amount of surfactant binding is very much in variety highly dependent on the surfactant. The amount of $R_{12}SO_4Na$ binding is much greater than that of $R_{12}PO_4$·TEA, and further, that of $R_9\phi(EO)_{10}$ is even 2 orders of magnitude smaller than that of the ionic surfactants. It is worth noting that the effectiveness of the agents on the elevation of the phase-transition temperature of the gel follows the same tendency as the binding amount. One more interesting phenomenon should be pointed out. One can see from Figures 1b−3 that the amount of ionic surfactants binding is quite small in the collapsed state of the gel and suddenly increases at the phase-transition point to the swollen state. On the contrary, the amount of the nonionic surfactant, $R_9\phi(EO)_{10}$, binding to the collapsed state is greater than that to the swollen one. The tendency of the binding to the swollen and collapsed state is completely opposite to that of the ionic surfactants. The negative adsorption of the nonionic surfactant appearing in Figure 4b is an artifact due to the concentration of the agent inside the gel being different from that of the bulk solution.[21]

A three-dimensional representation for the phase-transition behavior of NIPA gel in the presence of various concentrations of $R_{12}SO_4Na$ is shown in Figure 5. One can see the clear discontinuous changes in both surfactant-binding (a) and gel-swelling (b) behaviors at the same region of temperature and surfactant concentration. The jump in the binding amount at the phase-transition point seems linearly related to the transition temperature itself.

Electric Conductivity. Figure 6 shows electric conductivity data for aqueous solutions of $R_{12}SO_4Na$ and $R_{12}SO_3Na$ at 25, 40, and 60 °C. The inflection point in each curve indicates the critical micelle concentration (cmc) that agrees well with the published data.[22,23] Below the cmc, data for both $R_{12}SO_4Na$ and $R_{12}SO_3Na$

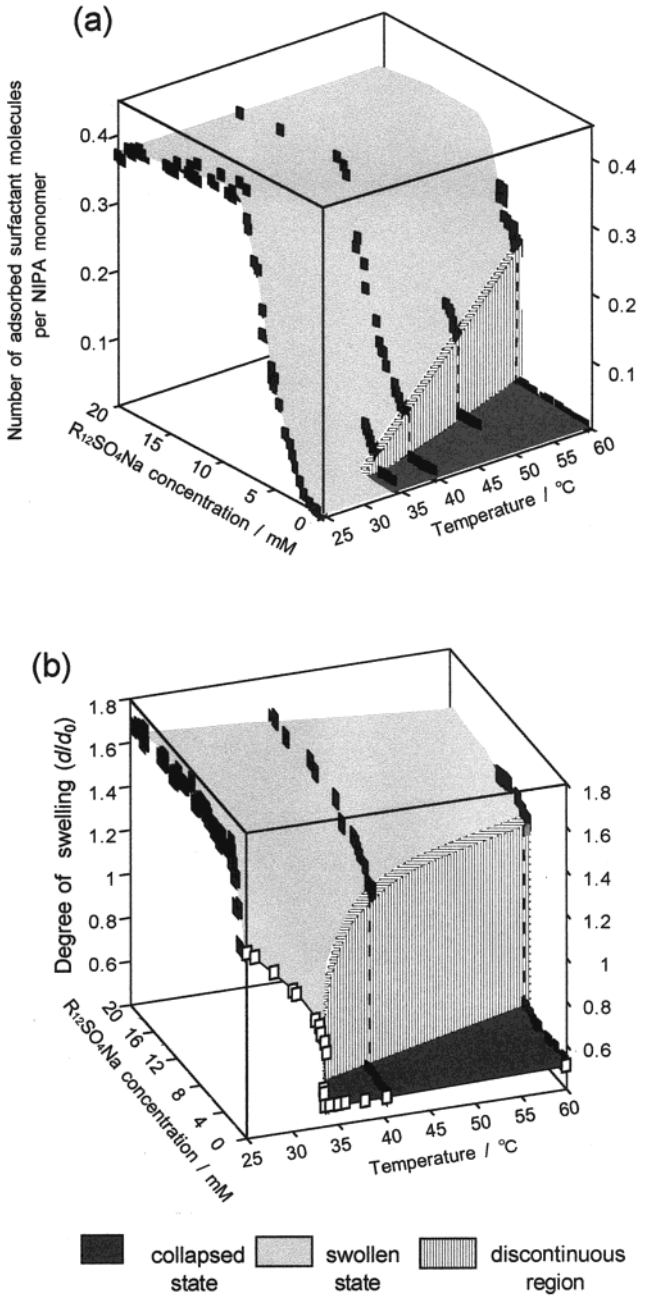

Figure 5. Three-dimensional representations of the phase-transition behavior of NIPA gel as functions of temperature and $R_{12}SO_4Na$ concentration. Binding of the surfactant (a) and the swelling behavior of the gel (b).

are identical. Furthermore, both curves for $R_{12}SO_4Na$ and $R_{12}SO_3Na$ above the cmc show the same slope at each observation temperature. These results indicate that the degree of dissociation of the above two surfactants is the same in both monomer and micellar forms.

Sodium Ion Concentration. The electromotive force of sodium ions for the samples of $R_{12}SO_4Na$ and $R_{12}SO_3Na$ is shown in Figure 7. The data are quite similar to those of the electric conductivity (Figure 6). The results indicate again that the degrees of dissociation of monomer and micelle of both surfactants are the same.

Discussion

Effects of Surfactants on the Phase-Transition Behavior of NIPA Gel. As mentioned previously, the

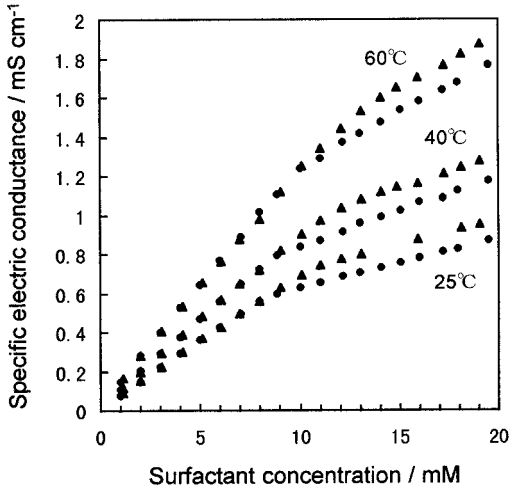

Figure 6. Specific electric conductance of $R_{12}SO_4Na$ (●) and $R_{12}SO_3Na$ (▲) plotted against their concentrations. Temperatures are at 60, 40, and 25 °C from top to bottom curves.

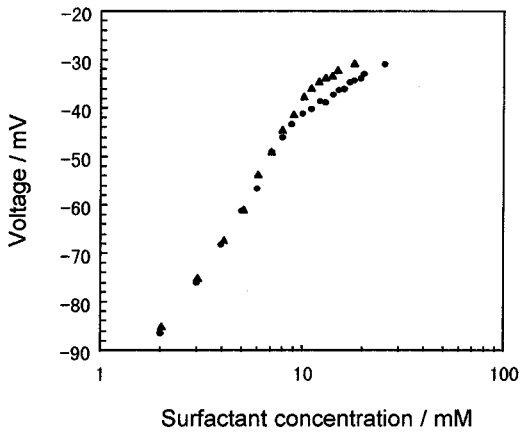

Figure 7. Electromotive force (sodium ion concentration) in aqueous solutions of $R_{12}SO_4Na$ (●) and $R_{12}SO_3Na$ (▲) plotted against their concentrations at 25 °C.

phase-transition temperature of NIPA gel changes dramatically with the addition of some ionic surfactants. The increment of the transition temperature is highly dependent on the chemical structure of the surfactants. The most straightforward way to solve this problem may be to attribute to the difference in binding amount of each surfactant. Then, we measure the binding isotherms of the surfactants onto the polymer chains of NIPA gel.

Qualitatively speaking, the surfactant that binds more in amount affects more significantly the change of the phase-transition temperature of the NIPA gel. $R_{12}SO_4Na$ elevates the transition temperature of the gel by more than 60 °C and $R_{12}PO_4$·TEA only does by 2−3 °C.[17] By comparing these results with the binding data shown in Figures 1b and 2b, one can see a qualitative relationship between the binding ability of surfactant and its effect on the transition-temperature change of the gel. However, to examine the above relationship quantitatively, we should plot the transition-temperature change as a function of the discontinuous jump in binding amount at the transition point as shown in Figure 5a for $R_{12}SO_4Na$. Because this jump is the exact amount of adsorption just at the phase transition. The increments of the transition temperature of the gel are plotted against the jump amount of surfactant binding for several kinds of surfactant in Figure 8. It can be

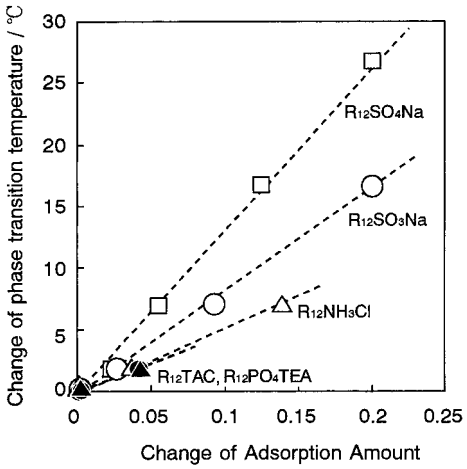

Figure 8. Increments of phase-transition temperature of the NIPA gel on addition of surfactant plotted against the discontinuous jump in the amount of the surfactants binding at the transition point. Data for $R_{12}SO_4Na$ (□), $R_{12}SO_3Na$ (○), $R_{12}PO_4$·TEA (●), $R_{12}NH_3Cl$ (△), and $R_{12}TAC$ (▲).

concluded from the figure that the phase-transition temperature change of the NIPA gel is caused by and even linearly related to the binding amount of the surfactant.

We have obtained a beautiful linear relationship between the increment of transition temperature and the jump in surfactant amount at the transition point. However, we have still two questions. Why do we have a linear relationship, and why does the slope of this straight line depend on surfactant? We have no idea for the first question. For the second question, one possible mechanism comes from the degree of dissociation of ionic surfactant. The charges attached to a polymer chain are different from surfactant to surfactant in such a case even if the same amount of the surfactant molecules is adsorbed. The degree of dissociation was checked by electric conductivity and sodium ion concentration measurements for all of the surfactants used. Unfortunately, however, we could not obtain the different dissociation behavior among the sample surfactants as shown in Figures 6 and 7 as typical examples. We may only say that the surfactant molecules bound to a polymer chain change the interaction between the polymer chains and the polymer chain−solvent interactions.

Finally, it is interesting to note that the amounts of surfactant binding onto the swollen and the collapsed state of the NIPA gel show completely opposite tendencies in ionic and nonionic surfactants. In the case of ionic surfactants, the amount binding onto the swollen state is much greater than that to the collapsed one. For nonionic surfactant, on the other hand, the binding on the collapsed state of the gel is greater than that on the swollen one, although the amount itself is smaller by 2 orders of magnitude than that of ionic surfactants (see Figure 4b). This clear difference in the ionic and the nonionic surfactant may suggest different binding mechanisms for both kinds of surfactants.

Discontinuous Binding Control of Surfactant via Phase Transition of NIPA Gel. There are many kinds of adsorbing agent such as active carbons and silica gels. They are strong adsorbents but cannot be easily reactivated. In addition, the adsorbate molecules once adsorbed onto such adsorbing agents are not readily recovered. In biological systems, on the other hand, adsorption and desorption occur reversibly, and adsorbates molecules are recovered to make some physiological functions. For instance, hemoglobin adsorbs oxygen molecules cooperatively through its conformational change and releases them in completely reversible fashion. Adsorption of substrate onto enzyme molecule and desorption of product molecule from it are also one more example of the reversible cycle of the above.

To mimic such smart biological systems, hydro-gels have been utilized as controlled-release devices. Most of such studies, however, have been done to achieve the controlled release just through the mesh-size change of gel networks accompanied by their volume phase transition.[6,10] Switching in affinity of small molecules by conformational change of a macromolecule should be the true mimic of the biological function. The discontinuous change of surfactant binding at the phase-transition point of the NIPA gel has been found in this work. These results indicate that the binding affinity of the surfactant is coupled with the conformational change of the gel. Furthermore, the binding transition is first-order, as seen from the hysteresis, which means that the cooperativity here is even higher than that of hemoglobin. Then, we have succeeded in making a system to control the adsorption−desorption property reversibly, cooperatively, and discontinuously with response to the environmental stimuli.

The affinity-switching gel through its conformational change is not just a biological mimic but an interesting material for practical applications. Ionic surfactants could be concentrated by cycling the adsorption−desorption process with temperature. The surfactant may be recovered very easily without any chemical damage. In addition, this system gives a guiding principle to make an ideal drug delivery systems (DDS).

Conclusions

It is first found that the amount of surfactant binding onto the NIPA gel changes reversibly and discontinuously through the volume phase transition of the gel. The hysteresis in the binding isotherm is also first observed. These results mean that the affinity of the surfactant to the polymer chain alters by the conformational change of the polymer just like the functions of hemoglobin, enzyme, and so on. The increase of the phase-transition temperature of the NIPA gel with the addition of the ionic surfactants has been quantitatively explained by the amount of the agents binding at the transition point.

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