Stimuli-Response of Microsphere Having Poly(N-isopropylacrylamide) Shell

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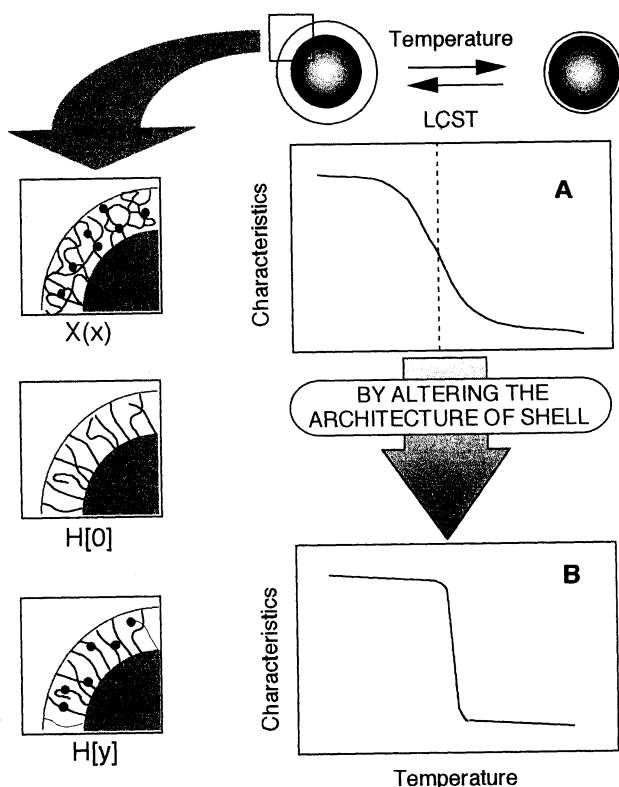*Keio University, Yokohama 223-8522, Japan*

ABSTRACT: Several kinds of submicron-sized microspheres having environment-sensitive shells were prepared and the effect of shell structure on the properties of microspheres was studied. The shell was composed of crosslinked or hairy poly(N-isopropyl acrylamide) (PNIPAM) whose lower critical solution temperature was about 32°C but depended on the architecture of the shell. The resposivity of the shell to the change in environmental condition was sluggish when the shell was crosslinked. The decrease in the crosslink density of the shell was slightly effective in sharpening the response. But even non-crosslinked, hairy PNIPAM shell did not exhibit discontinuous transition at the critical condition. The response of hairy PNIPAM shell to environmental change was drastically sharpened by incorporating a slight amount of acrylic acid (AAc) in the hair.
    KEY WORDS   Core Shell Particle / Thermosensitive Polymer / Poly(N-isopropylacrylamide) / Volume Phase Transition / Hairy Layer / Cosolvency

We have prepared unique core-shell particles whose shell is composed of poly(N-isopropylacrylamide) (PNIPAM) gel.[1-5] Because PNIPAM has the lower critical solution temperature (LCST) at 32°C and exhibits volume phase transition at the temperature, the above-mentioned core-shell particles swell below 32°C and shrink above 32°C in the aqueous dispersion. In addition to the hydrodynamic size, some other characteristics such as electrophoretic mobility, hydrophilicity, dispersion stability, etc. also

Figure 1. The objective of this study on response control of PNIPAM shell-carrying particles with different architectures. X: crosslinked shell-carrying particle, H: hairy shell-carrying particle, x: wt% of MB in shell polymer, y: wt% of AAc in hair polymer.

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change through 32°C. But the transition and changes were not sharp as shown in Figure 1A.

We intended to make the transition sharp at the critical temperature (Figure 1B) to produce an intelligent device which exhibits on-off response in the narrow temperature range or with some small changes of environmental conditions. First, the effect of the crosslink density in the PNIPAM shell of particles X(x) (Figure 1) on the response was examined. As the uncrosslinked linear polymer layer is the ultimate structure of the least crosslinked gels, the particles carrying hairy PNIPAM shell (H[0] in Figure 1) are expected to exhibit sharp on-off response. A new method was developed for the preparation of particles carrying hairy PNIPAM shell and the sharpness of response was examined as a function of the content of ionic groups in PNIPAM hair (H[y] in Figure 1).

EXPERIMENTAL

The X(x) series particles were prepared soap-free emulsion copolymerization of styrene (St, 9.09 g) and NIPAM (0.91 g), followed by second shot polymerization of NIPAM (6.0 (100 - x) / 100 g) and methylenebis-acrylamide (MBAAm, 6.0 x / 100), using potassium persulfate (KPS) as an initiator at 70°C. The x was changed from 5.0 to 1.75. The diameter of dried particle was measured by electron microscopy. The hydrodynamic diameter of particles in water was measured, as a function of temperature in the range from 20°C to 50°C, by photon correlation spectroscopy (PCS) using an LPA3100/3000 (Ohtsuka Electric Co.).

The preparative procedure for H[y] series particles included two steps shown below;
(1) soap-free emulsion polymerization to form core particle with the following recipe: St / glycidyl methacrylate(GMA) / divinylbenzene / KPS / water = 1.2 / (1.8 (1st shot) + 2.0 (2nd shot)) / 0.04 / 0.06 / 120 (g) at 70°C, and
(2) graft polymerization on core particle with the following recipe: core particle / NIPAM / Ce(NH3)2(NO3)6 / acetic buffer (pH 3.4) = 0.50 / 3.75 / 0.075 / 80 (g) at 25°C.

The molecular weight of grafted PNIPAM was determined by size exclusion chromatography (SEC) after

detaching the grafted PNIPAM from the core particle by hydrolysis of methacryl ester units on the core particle surface. The hydrolysis was carried out by incubating the microspheres at pH 1.0 with HCl at room temperature for 3 days and then neutralized with NaOH. The PNIPAM sample was dialyzed and dissolved in a 0.2 M phosphate buffer solution. The solution was shot into a column of TSK GEL G-2000 (TOSOH) and the elusion buffer was flew at 0.5 ml/min. The molecular weight was obtained by calibrating the elusion volumes with those of polyacrylamide standards.

RESULTS AND DISCUSSION

Response of Crosslinked PNIPAM Shell-Carrying Particle

X(x) series of particles were prepared by two step soap-free emulsion copolymerization at 70°C under nitrogen. The NIPAM in the first shot was effective in inviting the second shot NIPAM to the core particle surface and building up the thick crosslinked PNIPAM shell layer on the core particle. The resulting particles had a diameter around 450 nm and were monodisperse as confirmed by the polydispersity (the ratio of the weight average diameter to the number average diameter) less than 1.01. A very small amount of nano-particles, whose diameter was less than one tenth of core-shell particles, were formed but they were easily separated from the core-shell particles by centrifugation.

The state of the crosslinked PNIPAM shell was assessed by measuring the hydrodynamic size (HD), electrophoretic mobility, permeability of water-soluble solute through the shell, and emission of fluorescence as a function of temperature. One example is shown in Figure 2 which presents the temperature dependence of HD[6]. Measurement of HD of soft particles or highly solvated particles by PCS is a matter of argument and therefore, in this study, the values were compared as relative ones. As shown in the figure, the change in the hydrodynamic size around 32°C is not sharp but rather sluggish.
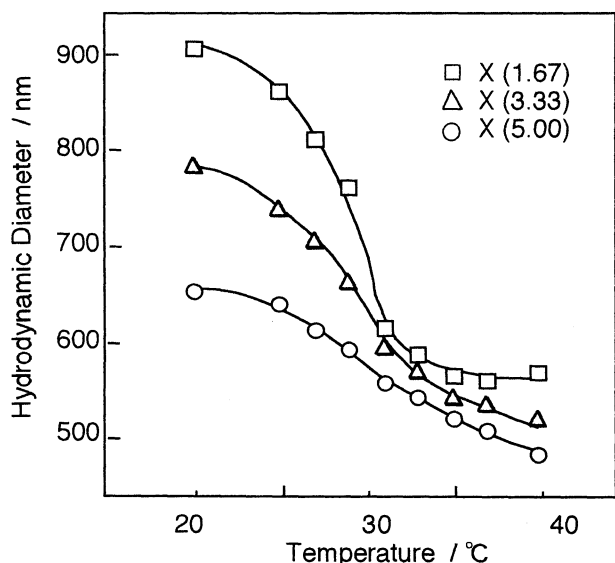
The swollen-shrunk state of shell could be assessed with

electrophoretic mobility of particles by Ohshima's method which was applied to soft particles to give two parameters, that is, the softness of shell and ionic group density in the shell[4]. The electrophoretic mobility of X(x) particles changed gradually around 32°C. The softness and ionic group density changed with temperature in the manner such that we could estimate from the temperture-dependent hydrodynamic thickness of the shell.

Three curves in Figure 2 show that the HD of crosslinked PNIPAM shell-carrying particles increased with decreasing x (percent of MB in shell polymer). The change of HD around LCST seems to become more conspicuous with decreasing degree of crosslinking although Crowther and Vincent argued the opposite trend in terms of the effect of crosslink density on the sharpness of response[7]. Anyway the control of crosslink density can not be effective to make the change of microsphere's properties discontinuous at the transition temperature. This would be attributed to restricted response caused by heterogeneous network structure.

Thermosensitivity of Hairy PNIPAM Shell-Carrying Microspheres

We expected that the volume of PNIPAM shell changes sharply at the transition temperature if the shell is not crosslinked and composed of hairy polymer. There are two methods to give hairs on the surface of existing microspheres. One is to bind polymer chains onto the microsphere at the chain ends. The other is to grow up polymer hair from the surface of microspheres. We took the latter way in this study. That is, NIPAM was graft-polymerized on the existing particles. The core particles were prepared by soap-free emulsion copolymerization of St and glycidyl methacrylate (GMA) followed by second shot polymerization of GMA at 70°C for 24 h. The diameter of core particle was 310 nm and the dispersity (ratio of weight average- to number average-diameters) was less than 1.01. The epoxy groups of GMA units were automatically converted to glycol groups during the soap-free emulsion polymerization. Therefore, Ceric ion-glycol redox reaction was used for the initiation of graft polymerization because it formed radicals of carbon adjacent to hydroxy group on the core particles at room temperature as shown in Figure 3. The polymerization of PNIPAM at room temperature was
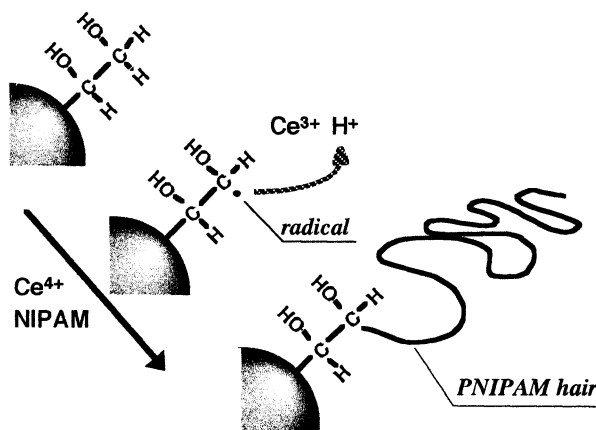

Figure 2. Temperature dependence of crosslinked PNIPAM shell-carrying particles with different crosslink densities.

Figure 3. Schematic representation of graft polymerization by redox initiation.

1140

Polym. J., Vol. 31, No. 11-2, 1999

expected to form PNIPAM having a unique texture different from the PNIPAM prepared at a temperature higher than the LCST (32°C) of PNIPAM.

The polymerization was carried out at 25°C for 8 h. The conversion was about 97 % and the resulting microspheres were referred to as H[0] where 0 indicates that no ionic comonomer was used in graft polymerization. Differing from the polymerization to form crosslinked shell-carrying microspheres at 70°C, no new ultrafine particles were detected in this redox-initiated polymerization.

The molecular weight of PNIPAM hair of H[0] was measured by gel permeation chromatography and found to be about 500,000 which corresponded to the degree of polymerization (DP) 4,500. The root-mean-square end-to-end distance of polymer chain of DP 4,500 is calculated to be about 15 nm. The thickness of swollen PNIPAM shell of H[0] was about 50 nm as shown in Figure 4. These values suggest that the PNIPAM chains were loosely coiled when swollen in water.

The monodispersity of resulting particles enabled us to measure HD by PCS and the the HD of H[0] is shown as a function of temperature in Figure 4. First, we have to point out from the comparison with above-mentioned X(x) system that the temperature dependence of HD for the particle H[0] is very small. This was attributed to the absence of ionic groups in the shell layer of H[0]. Figure 4 clearly shows that state of nonionic hair is not affected by pH. It would be worth mentioning that the shell of X(x) includes a significant amount of ionic end groups brought from initiator. The sharpness of the response of H[0] at the transition temperature was also poor. Therefore the temperature-responsiveness of H[0] was different from what we expected. Gradual but not discontinuous change in the size of H[0] around the LCST was considered to be attributed to physical crosslinking or entanglement of coiled PNIPAM hairs.

Another cause for the sluggish response was suggested by Zhu and Napper[8]. The shape of HD vs. temperature curve for H[0] resembled that in Zhu and Napper's papers which reported the thickness of adsorbed PNIPAM layer on latex particles. The thickness, in their case, started to decrease gradually at 20°C and suddenly at 32°C. The authors attributed the gradual shrinkage below LCST to many-body
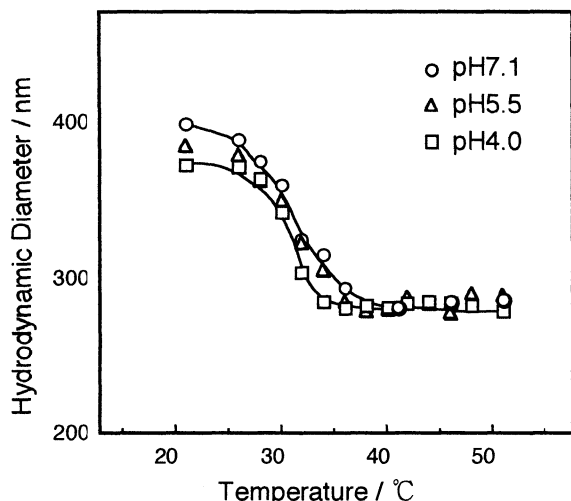
interactions, i.e. n-clustering and the sharp shrinkage at LCST was to transition of PNIPAM. The gradual temperature dependence of the size of H[0] in the temperature range from 20°C to 32°C probably resulted from the n-clustering.

Effect of Incorporation of Ionic Groups on Thermosensitivity of PNIPAM Hair Grafted on Microsphere

According to Hirotsu et al, incorporation of acrylic acid (AAc) in PNIPAM gel is effective in sharpening the response at the transition temperature[9]. To examine the effect of AAc incorporation on temperature responsive property of particles, AAc was mixed by 0.02, 0.1 and 1.0 wt% of NIPAM in the graft polymerization onto core particles using ceric ion at 25°C. The resulting hairy microspheres were referred to as H[y] (y's are 1.0, 0.1 or 0.02 which are the percentage of AAc in monomer) .

The HD of H[y] series was measured in the temperature range of 20 to 50°C. The results on H[1.0] are shown in Figure 5. The large change in HD with changing temperature from room temperature to 40°C is not unreasonable because the PNIPAM hair (the degree of polymerization: 4,500) can be as long as 1 μm if it is fully extended. The surface density of hair was calculated from the conversion and the degree of polymerization of PNIPAM. It was 2.7 chains / 10 nm^2 core surface, or 2.2 x 10^5 chains / particle. These data suggested us that the H[1.0] has a brush-like surface below the LCST.

The HD of H[1.0], whose AAc content was the highest among the H[y] series microspheres, changed discontinuously at pH 4.0 although the change itself was not so quite large. On the contrary, the diameter changed gradually, or rather in step-wise at pH 5 and 7. At these two pHs the hydrodynamic size started to decrease gradually at 28 - 32°C and then decreased rapidly at about 40 - 42°C.

There are two possible reasons for these size changes. One is based on the mechanism for shrinkage. The shrinkage in the lower temperature range (28 - 32°C) and higher temperature range (around 40°C) would be attributed to n-
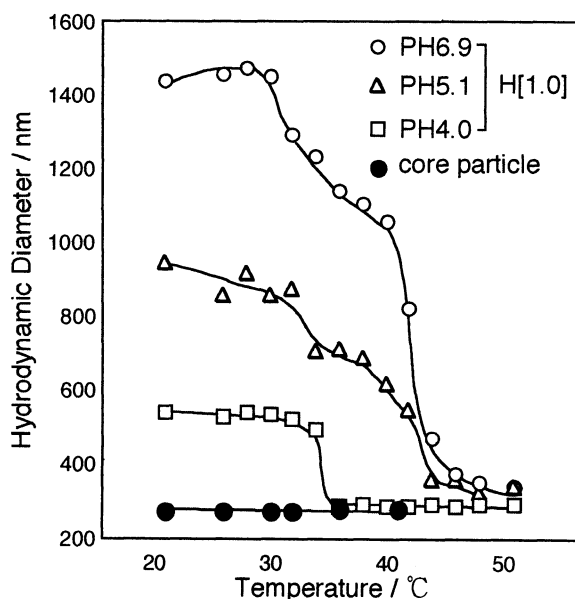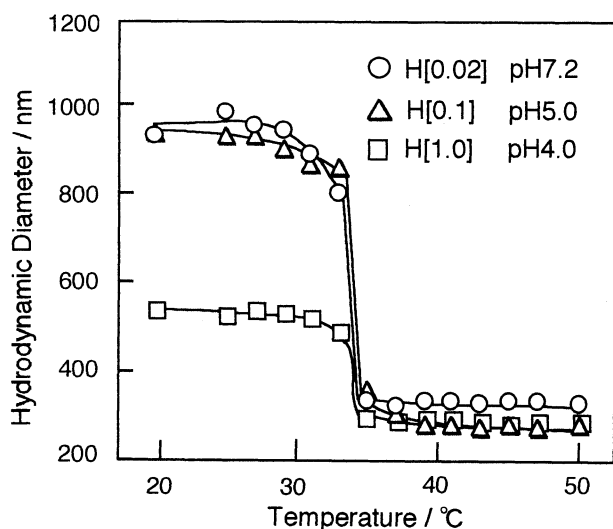

Figure 4. Hydrodynamic diameter of H[0] particles in water as a function of temperature.

Figure 5. Temperature and pH dependence of hydrodynamic size of particles with ionized hairy PNIPAM shell.

Polym. J., Vol. 31, No. 11-2, 1999

1141

clustering and volume-phase transition, respectively. An increase in pH promotes dissociation of AAc in NIPAM-AAc copolymer hair of H[1.0] and, consequently, the microsphere swells highly and the LCST rises at high pH. Both of n-clustering and transition temperatures were elevated by incorporation of AAc in PNIPAM. In H[1.0] system, the transition temperature seems to increase more than the n-clustering temperature and, as a result, the interval between n-clustering and transition temperatures might be spread to give a stepwise curve as in Figure 5.

The other explanation is based on the existence of two kinds of hairs having different transition temperatures. The PNIPAM hair formed in the early stage of polymerization is believed to contain more AAc units because of the preferential polymerizability of AAc to NIPAM. After AAc is used up, almost pure PNIPAM seems to form. The former is supposed to have a higher transition temperature and the latter has it around 32°C. If this is the case, we expect to be able to prepare the microspheres having uniform poly(NIPAM-co-AAc) hairs and, consequently, exhibiting a sharp one-step transition, when we carry out the polymerization by adding AAc continuously to the reaction system throughout the polymerization. The result of this experiment strongly supported the second explanation because the shoulder in lower temperature range disappeared on the hydrodynamic diameter vs. temperature curve of the product.

Because H[1.0] exhibited discontinuous change in HD under the condition where a small fraction of COOH was dissociated, we expected that we can obtain the particles which sharply respond to the temperature change even at neutral pH if we prepare particles whose shell contains a small amount of AAc. This was confirmed by measuring the temperature dependence of HD of PNIPAM hair-bearing microspheres with lower AAc content, H[0.1] and H[0.02]. As expected, these microspheres exhibited clear transition at higher pHs than H[1.0] did. The pHs were about 5 and 7 for H[0.1] and H[0.02], respectively as shown in Figure 6.
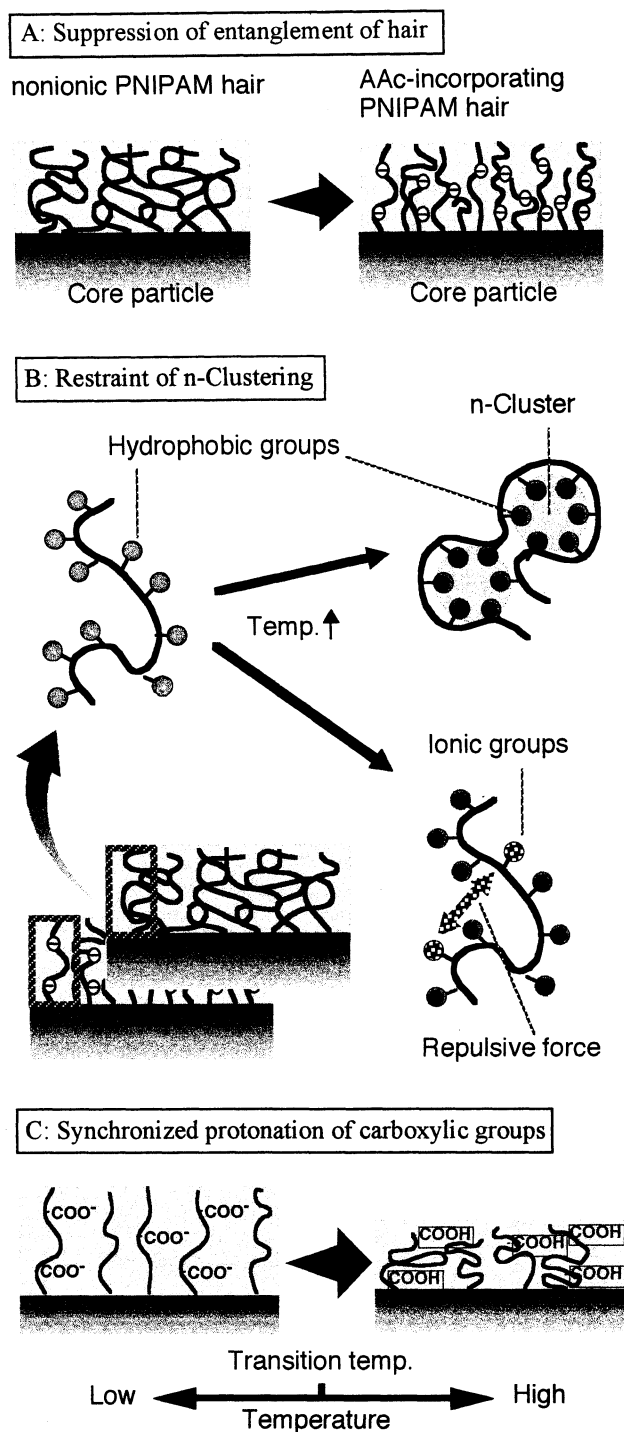
It was reported that, in PNIPAM bulk gel, at least several percent AAc was necessary to be copolymerized for its

sharp volume change. On the contrary, in the present case of PNIPAM hair grafted on microsphere, 0.02 % AAc was enough to make the volume change discontinuous at the LCST. Yoshida et al. reported that free end chain in gel responds to temperature change more than hundred times faster than crosslinked one[10]. It is very probable that slightly ionic free end chain would contribute not only to quickness but also to sharpness of response to environmental changes, in this case, to the temperature change through the LCST of PNIPAM.

The effect of ionic strength on the sharpness of slightly ionic hair-carrying microspheres was examined by

Figure 7. Mechanism of sharp response brought about by AAc incorporation into PNIPAM hair.

Figure 6. Highest discontinuity in hydrodynamic size vs. temperature of particles containing different amounts of AAc in their shells.

1142

Polym. J., Vol. 31, No. 11-2, 1999

measuring the response in the presence of calcium chloride. The HD change of the microsphere with temperature decreased with increasing calcium ion concentration up to 2 mole/L but the discontinuity at the LCST was maintained. The LCST was not affected by the calcium ion and kept to be 32°C in the calcium ion concentration range examined.

Figure 7 summarizes the mechanisms for sharp transition presented by slightly ionic, hairy shell. A small amount of ionic groups in PNIPAM hair seemed to restrain the entanglement of inter- and intra-chains and expand the chains due to repulsive force or exclusion volume effect (Figure 7A). The repulsive force is also effective in preventing n-clustering in the temperature range below LCST (Figure 7B). In addition to these effects, one more factor that affects the sharpness of thermosensitivity would be pointed out. When the microspheres are warmed up, the vicinity of AAc units in hairs becomes hydrophobic and then the dissociation constant decreases, that is, the carboxylic group is protonated. Loss of ionized groups in hair accelerates the shrinking of hairy layer and thus the response can progress almost all at once (Figure 7C).

The reason for that too large amount of AAc made the response dull would be that excess of AAc weakens the repulsive force and suppresses the rapid hydrophobization at the LCST.

Volume Phase Transition of PNIPAM Shell-Carrying Microsphere Caused by Solvent Composition Change

There have been some reports on volume phase transitions of PNIPAM gels in mixed water-organic solutions.[7,11] The organic solvents used so far were methanol, ethanol, iso-propanol, and N,N-dimethylform-amide. No report has presented discontinuous volume transition of the gels in mixed water-organic solutions.

We have confirmed that the PNIPAM shell-carrying particles undergo volume-phase transition in response to the change in water-ethanol composition as well as temperature. Namely, the PNIPAM shell on the particle once collapsed in the solvents with low ethanol fractions and swelled again in the solvents with high ethanol fractions[7]. But the change was not sharp for X(x) particles as shown by square plots in Figure 8, as well as other results previously reported. The HD of PNIPAM hair-carrying particle (H[0]) also did not change sharply (triangle plots in Figure 8). The smaller change in HD of hairy shell-carrying particles than crosslinked shell-carrying one, shown in Figure 8, would be attributed to no electrorepulsive force in the former.

The above-mentioned results, that is, continuous volume change with changing water-ethanol composition, were supposed to result from the suppressed motion of PNIPAM chains due to crosslinking and chain entanglement, or they might be attributed to the mechanism different from dehydration / hydrophobic interaction effect which occurred at the transition temperature in water.

Differing from two kinds of particles, X(x) and H[0], the change was very sharp and discontinuous for the particles which carry the shell composed of AAc containing PNIPAM (H[y], circles in Figure 8). Among the series of H[y], the less the particle contained AAc, the sharper the response was in the range examined. And the result was again attributed to the effective intra- and inter-chain

repulsion due to suitable amount of AAc. Contribution of elecrtorepulsive force to the extension of polymer chains even in aqueous ethanol was confirmed by an experiment to measure the HD in the presence of additional electrolyte.

Thus, it was concluded that a small amount of ionic group-carrying hairs perform very sharp transitions at the critical low and high compositions of solvent (CL and CH, respectively) as well as at the critical temperature (LCST).

An increase in the fraction of ethanol up to CL causes taking water from PNIPAM and consequently plays the same role as an increase in the temperature, Therefore, the CL is a function of temperature. At a higher temperature, less fraction of ethanol is sufficient for the collapse of PNIPAM shell. The CL values was 0.19 at 20°C and 0.14 at 25°C for H[0.02]. As the LCST increased with the AAc content in PNIPAM, the CL also increased with the AAc content, for example, the CL of H[1.0] was 0.22 at 20°C.

The role of ethanol in the range around CH is to contact the collapsed PNIPAM directly and dissolve them. The solvent power of ethanol is less sensitive to temperature and the CH values were little dependent on temperature in most cases. The CH decreased with increasing AAc in the PNIPAM shell. The result implied that AAc units have more affinity to ethanol than NIPAM units.

CONCLUSIONS

Several core-shell particles were prepared and their stimuli-responsivity was studied as a function of the architecture of poly(N-isopropylacrylamide) (PNIPAM) shells. The particles having crosslinked or nonionic hairy shells did not exhibit discontinuous response at the transition temperature. On the contrary, the particles having slightly ionic hairy shells exhibited sharp response. The necessary fraction of acrylic acid for the sharp response was only 0.02% in PNIPAM and the incorporation of more acrylic acid rather decreased the sharpness. The sharp response brought about by the small amount of acrylic acid would be due to a) suppression of entanglement or physical
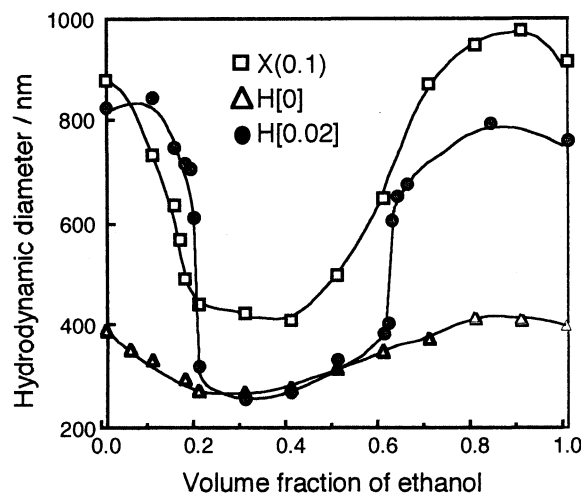

Figure 8. Dependence of hydrodynamic size of PNIPAM shell-carrying particles on ethanol content in mixed solvent.

crosslinking of PNIPAM hair, b) restraint of n-clustering due to electrorepulsive force, and c) synchronized protonation of carboxyl groups when PNIPAM started to dehydrate above the transition temperature.

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1144

Polym. J., Vol. 31, No. 11-2, 1999