Aggregation of Block Copolymer Microgels of Poly(*N*-isopropylacrylamide) and Poly(ethylene glycol)

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Introduction. The self-aggregation of block copolymers has attracted much attention both for its intrinsic scientific interest and for its technological importance.[1−3] Block copolymer colloids not only have similar colloidal behavior to that of low-molecular-weight surfactants but also exhibit their unique molecular architecture. The self-aggregation of block copolymers has been found to be dependent on solvent quality, concentration, and composition. Any change in temperature, ionic strength, or pH can result in selective solvent conditions. Nonionic poly(ethylene oxide)-*b*-poly(propylene oxide) and ionic poly(ethylene oxide)-*b*-poly(lactic acid) are typical examples. Spherical aggregates of block copolymers are composed of a hydrophobic core and a hydrophilic corona. These spherical aggregates may interact with each other to form networks or domain structures.

Recently, the block copolymers of poly(*N*-isopropylacrylamide) and poly(ethylene oxide) (PNIPAM-*b*-PEO) and their corresponding microgels (or cross-linked micelles) have been synthesized.[4,5] The thermally induced micellization of PNIPAM-*b*-PEO coplymers has been preliminarily reported.[4] At room temperature, PNIPAM dissolves in water to form coils that undergo a phase separation when heated to ∼31−32 °C.[6] The coil-to-globule transition of single PNIPAM chains can be observed at ∼31−32 °C if the aggregation is prevented. The conformational changes of PNIPAM exhibit similar characteristics to those of biological macromolecules. For example, the coil-to-globule transition of the PNIPAM is not a so-called *all-or-nothing* process.[7] The collapse transition of the PNIPAM chains proceeds through a set of intermediates consisting of a number of "cooperative units". In the melting of the PNIPAM globules, PNIPAM globules are also found to go through an intermediate state called the molten globule.[8]

The colloidal behavior of PNIPAM-*b*-PEO microgels has not been reported yet. We here study the aggregation of block copolymer microgels of PNIPAM and PEO in aqueous solution. Effects of the composition and concentration of the microgels on aggregation are reported.

Experimental Section. CH_3-PEO-OH (PEO) from Aldrich, with molecular weight 5000, was dissolved in water and then the solution was filtered through a 0.45 μm Millipore filter. *N*-Isopropylacrylamide (NIPAM) from Monomer-Polymer was purified by recrystallization from a 65/35 mixture of hexane and benzene. *N*,*N*′-Methylenebisacrylamide (BIS) and ceric ammonium nitrate from Aldrich were used as received.

The synthesis of block copolymer microgels of PNIPAM and PEO was carried out in aqueous solution using a redox system consisting of ceric ion $Ce^{(IV)}$ and PEO.[4] The details of preparation of block copolymers using ceric ion with polymeric reducing agent can be seen in the literature.[9] The CH_3-PEO-OH (0.5 g) and NIPAM (0.21, 0.31, 0.41, and 0.63 g) were dissolved into 40 mL of 1 N nitric acid at 50 °C, corresponding to the following molar ratios of NIPAM/PEO: 0.17, 0.25, 0.33, and 0.5, respectively. Solutions were stirred under a positive nitrogen pressure for ∼15 min, and a solution of 7.24 g of ceric ammonium nitrate in 10 mL of 1 N nitric acid was added. Solutions of BIS in 10 mL of 1 N nitric acid were added at a weigh ratio of BIS/NIPAM of 1/150 in ∼8 min after the addition of ceric ammonium nitrate solution. The precipitated copolymers were found for higher ratios of NIPAM/PEO during the polymerization. After ∼6 h, the solutions and precipitates were dialyzed at room temperature by repeated changes of fresh Milli-Q water. The precipitates were found to be gradually dissolved into water, and the solutions finally turned transparent. No polymer was formed in ∼6 h at 50 °C when a solution of ceric ammonium nitrate was added into pure NIPAM.

Dynamic light-scattering measurements were performed with an argon ion laser operating at wavelength 488 nm and at a power of 50 mW. The autocorrelation function was measured using a Malvern 4700c correlator. Hydrodynamic diameters d_h were determined using the Stokes−Einstein relation $d_h = k_B T/(3\pi\eta D)$, where k_B, T, η, and D are the Boltzmann constant, the absolute temperature, the solvent viscosity, and the diffusion coefficient. In light-scattering measurements, the solutions with different concentrations were prepared by diluting a stock solution and then were filtered through a 0.45 μm Millipore filter directly into the light-scattering cell.

Results and Discussion. The intrinsic stability of dialyzed PNIPAM-*b*-PEO microgels and their aggregates in water was checked over a period of ∼8 h at 33 and 60 °C, respectively. No precipitation was found for all the samples which were thoroughly dialyzed. The solutions were a blue at the higher temperature, as the sign of formation of stable nanoparticles, as opposed to the milky color that accompanied progressive precipitation for the corresponding samples which were not carefully dialyzed. The results imply that $Ce^{(III)}$ ions produced from polymerization can interact with PNIPAM-*b*-PEO microgels to form complexes.

Figure 1 shows the temperature and composition dependence of the normalized intensity of PNIPAM-*b*-PEO microgels at the concentration $C = 2.0 \times 10^{-4}$ g g^{-1}. It is found that the critical aggregation temperature of PNIPAM-*b*-PEO microgels is strikingly dependent on composition. For example, the intensity of NIPAM/PEO = 0.17 is almost a constant when the temperature is lower than ∼52 °C, which is taken as an indication of no interparticle interaction. An increase of intensity at 52.5 °C signals a beginning of microgel aggregation. For NIPAM/PEO = 0.50, the temperature at which the aggregation starts is 35.5 °C. The aggregation temperatures 38.5 and 46.5 °C were observed for NIPAM/PEO = 0.25 and 0.33, respectively. It is worth emphasizing that the critical aggregation temperature of PNIPAM-*b*-PEO microgels in the present work was found to be independent of composition if the samples were not thoroughly dialyzed. For PNIPAM-*b*-PEO copolymers, the low critical solution temperature (LCST) was reported to be ∼30−31 °C regardless of composition.[4]

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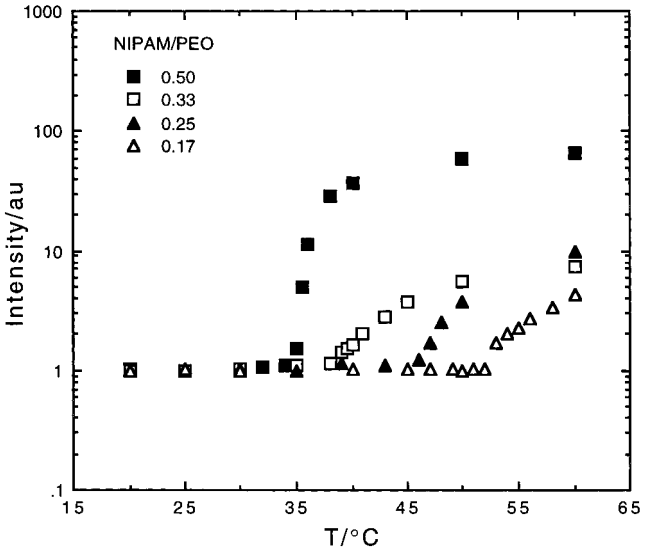

Figure 1. Temperature and composition dependence of the normalized intensity of PNIPAM-*b*-PEO microgels at $C = 2.0 \times 10^{-4}$ g/g.

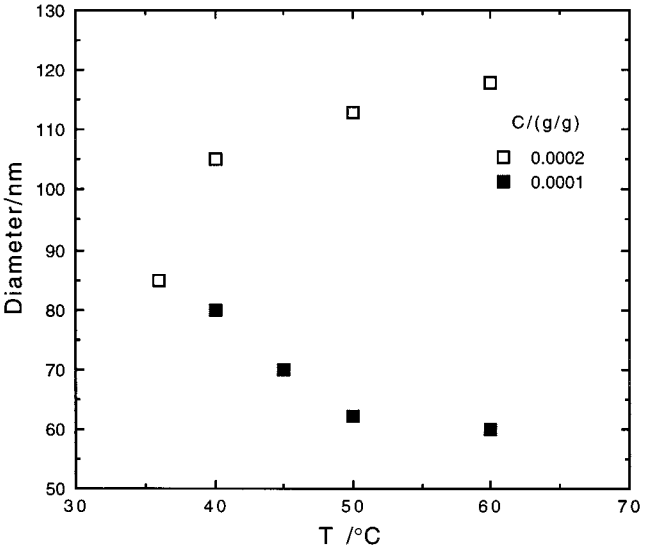

Figure 2. Temperature dependence of the hydrodynamic diameter of PNIPAM-*b*-PEO microgels with NIPAM/PEO = 0.5 at concentrations (g/g) of 2.0×10^{-4} and 1.0×10^{-4}.

Figure 2 shows the temperature dependence of the microgel aggregate size of NIPAM/PEO = 0.5 at two concentrations of 2.0×10^{-4} and 1.0×10^{-4} g g^{-1}. The samples were kept at the given temperatures for 20 min before the average aggregate sizes were measured. The aggregate size increases with temperature at $C = 2.0 \times 10^{-4}$ g g^{-1}, which is supported by a continuous increase in intensity. The progressive nature of aggregation above the critical aggregation temperature was not observed from PNIPAM-*g*-PEO copolymers.[10] The aggregate size is found to decrease with increasing temperature at $C = 1.0 \times 10^{-4}$ g g^{-1}. PNIPAM-*b*-PEO microgels exhibit thermoreversible behavior within prescribed concentrations and temperatures.

The variation of microgel aggregate size with temperature is considered to be a consequence of the competition between interparticle interaction and the intraparticle coil-to-globule transition. At the higher concentration $C = 2.0 \times 10^{-4}$ g g^{-1}, the interparticle aggregation occurs before the onset of a proper coil-to-globule transition of PNIPAM. There are several explanations for the self-aggregation of block copolymers.[2] It is generally accepted that the hydrophobic interaction plays a crucial rule. At the lower concentration $C = 1.0 \times 10^{-4}$ g g^{-1}, the intraparticle coil-to-globule transition could be generally prior to the interparticle aggregation. The localized PNIPAM clusters at the initial stage are spatially segregated inside aggregates, and their density has not reached the final globular density. Since the intraparticle coil-to-globule transition can result in a local core−corona structure, with PNIPAM globules as a core and PEO chains as a corona, the particles formed are sterically stabilized.[11] When the temperature is further increased, the collapsed PNIPAM clusters continue to shrink to a well-defined core−corona structure by internal rearrangements.

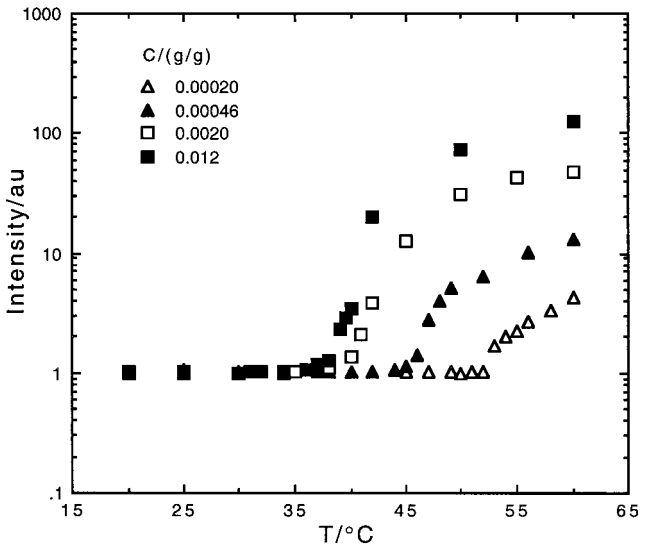

Figure 3. Temperature and concentration dependence of the normalized intensity of PNIPAM-*b*-PEO microgels with NIPAM/PEO = 0.17.

Figure 3 shows the concentration dependence of the critical aggregation temperature for the microgels with NIPAM/PEO = 0.17. It is apparent that the critical aggregation temperature increases with decreasing microgel concentration. The critical aggregation temperatures are found to be 38.5, 41.0, 45.5, and 52.5 °C, corresponding to the concentrations 1.2×10^{-2}, 2.0×10^{-3}, 4.6×10^{-4}, and 2.0×10^{-4} g g^{-1}, respectively. The concentration dependence of the critical aggregation temperature over such a broad range of temperature was not reported for PNIPAM-*b*-PEO copolymers.

Preliminary results show that the PNIPAM-*b*-PEO microgels have their unique colloidal behavior. Their critical aggregation temperature is very sensitive to the composition and concentration. The aggregation of the PNIPAM-*b*-PEO microgels above the critical aggregation temperature results in the formation of thermosensitive nanoparticles. As a material, the PNIPAM-*b*-PEO microgels are believed to have potential in bioengineering applications such as controlled release of molecular and cellular species. The colloidal behavior of PNIPAM-*b*-PEO microgels can also help us to understand more intriguing behavior such as the self-aggregation of protein hydrogels.[12]

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References and Notes

(1) Muthukumar, M.; Ober, C. K.; Thomas, E. L. *Science* **1997**, *277*, 1225.
(2) Almgren, M.; Brown, W.; Hvidt, S. *Colloid Polym. Sci.* **1995**, *272*, 2.
(3) Forster, S.; Antonietti, M. *Adv. Mater.* **1998**, *10*, 195.
(4) Topp, M. D. C.; Dijkstra, P. J.; Talsma, H.; Feijen, J. *Macromolecules* **1997**, *30*, 8518
(5) Yoshioka, H.; Mikami, M.; Mori, Y.; Tsuchida, E. *J. Macromol. Sci., Pure Appl. Chem.* **1994**, *A31*, 109.
(6) Schild, H. G. *Prog. Polym. Sci.* **1992**, *17*, 163.
(7) Tiktopulo, E. I.; Uversky, V. N.; Lushchik, V. B.; Klenin, S. I.; Bychkova, V. E.; Ptitsyn, O. B. *Macromolecules* **1995**, *28*, 7519.
(8) Wu, C.; Zhou, S. *Phys. Rev. Lett.* **1996**, *77*, 3053.
(9) Nagarajan, S.; Srinivasan, K. S. V. *J. Polym. Sci., Part A, Polym. Chem.* **1995**, *33*, 2925.
(10) Qiu, X.; Wu, C. *Macromolecules* **1997**, *30*, 7921.
(11) Napper, D. H. *Polymeric Stabilization of Colloidal Dispersions*; Academic: New York, 1983.
(12) Petka, W. A.; Harden, J. L.; McGrath, K. P.; Wirtz, D.; Tirrel, D. A. *Science* **1998**, *281*, 389.

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