Single Chain Core-Shell Nanostructure

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A combination of static and dynamic laser light scattering has revealed that at temperatures higher than ~33 °C a linear poly(*N*-isopropylacrylamide) chain grafted with poly(ethylene oxide) (PNIPAM-g-PEO) in water can undergo a “coil-to-globule” transition to form a stable single chain core-shell nanostructure with the collapsed PNIPAM chain backbone as the hydrophobic core and the grafted PEO branches as the hydrophilic shell. It was also found that there still exists ~75% of water in the collapsed hydrophobic core which might be useful for biomedical applications because the core-shell nanostructure can be easily switched on and off by a simple temperature variation of 1–2 °C. [S0031-9007(97)05032-1]

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Recently, there has been considerable interest in the study of the amphiphilic copolymers, including block copolymers and graft copolymers, in selected solvents because these copolymers can form stable aggregates with a core-shell structure in solution [1–7]. For example, the amphiphilic graft copolymers made up of the hydrophobic backbone and hydrophilic branches can form stable colloidal particles in water by one-step nanoprecipitation or solvent exchange because the hydrophobic backbone chains tend to aggregate to form a hydrophobic core, while the grafted hydrophilic branches become a hydrophilic corona shell [7–10]. Such formed core-shell particles are sterically stabilized. The average size of the particles is normally in the range of 10–100 nm, depending on the formation conditions and the copolymer structure. This has provided a new method for preparing stable surfactant-free polymeric nanoparticles.

On the basis of our previous study of the coil-to-globule transition of poly(*N*-isopropylacrylamide) (PNIPAM) [11], we know that when the temperature is lower than the lower critical solution temperature (LCST) ~32 °C, PNIPAM is hydrophilic and exists as individual random coil chains in water, while at higher temperatures, PNIPAM becomes hydrophobic and collapses into a molecular globule. Qualitatively, this is due to the existence of a delicate balance between the hydrophobic portion (the chain backbone and the *N*-isopropyl groups) and the hydrophilic portion (the acrylamide groups). The increase of temperature breaks this balance and the free energy change becomes positive because the dissolution of PNIPAM in water has a negative entropy change, which is unusual, but typical for water-soluble polymers. Our recent NMR studies showed that, at temperatures below the LCST, some water molecules are associated with the amide group; and during the transition, the associated water molecules dissociate. Utilizing this special phase behavior, we have prepared a set of poly(*N*-isopropylacrylamide)s grafted with different amounts of poly(ethylene oxide) (PEO) chains (PNIPAM-g-PEO). Both the PNIPAM chain backbone and the grafted PEO branches are hydrophilic in cold water. Simply increasing the temperature to ~32 °C or higher can induce the coil-to-globule transition of the PNIPAM chain backbone to form a stable colloidal nanoparticle with a hydrophobic PNIPAM core and a soluble hydrophilic PEO shell. The core-shell structure can be switched on and off simply by a small temperature variation of 1–2 °C. The experimental details are as follows.

The poly(ethylene oxide) macromonomers end capped with methacrylate were synthesized by anionic ring-opening polymerization of ethylene oxide in tetrahydrofuran using potassium methoxide as the initiator [12]. The weight average molar mass and polydispersity of the PEO macromonomers were determined by gel permeation chromatography using chloroform as the eluent and PEO as standards. The PEO macromonomers used in this study have a weight average molar mass of 7000–8000 g/mol and a polydispersity index (M_w/M_n) of 1.15.

The poly(*N*-isopropylacrylamide) grafted with the PEO macromonomers was prepared by free-radical copolymerization of the PEO macromonomers and *N*-isopropylacrylamide (NIPAM) in water at 60 °C using $K_2S_2O_8$ as the initiator. The monomer conversion was controlled to be less than 50%. The apparent weight average molar mass (M_w) of PNIPAM-g-PEO was determined by laser light scattering and the copolymer composition was estimated by ^{1}H NMR. The NMR spectra were recorded in $CDCl_3$ on a Bruker DPX-300 (300 MHz) spectrometer. For the PNIPAM-g-PEO used in this study, $M_w = 7.29 \times 10^6$ g/mol. On average, each PNIPAM chain backbone was grafted with ~70 PEO macromonomer chains.

A modified commercial laser light scattering (LLS) spectrometer (ALV/SP-125) equipped with a multi-τ digital correlator (ALV-5000) and a solid-state laser (ADLAS DPY425II, output power ~400 mW at $\lambda_0 = 532$ nm) was used. The modified LLS spectrometer has an unusual small angular range of 6°–15°, which is particularly useful

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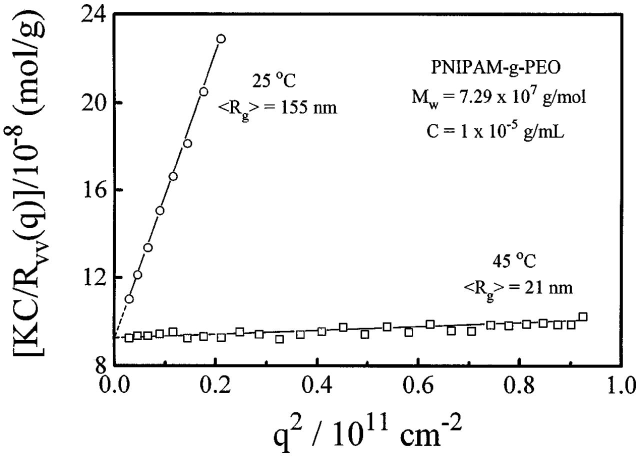

FIG. 1. Angular dependence of the excess scattered light intensity $KC/R_{vv}(q)$ at two different temperatures, respectively, lower and higher than the lower critical solution temperature (~32 °C), where $C = 1.00 \times 10^{-5}$ g/ml.

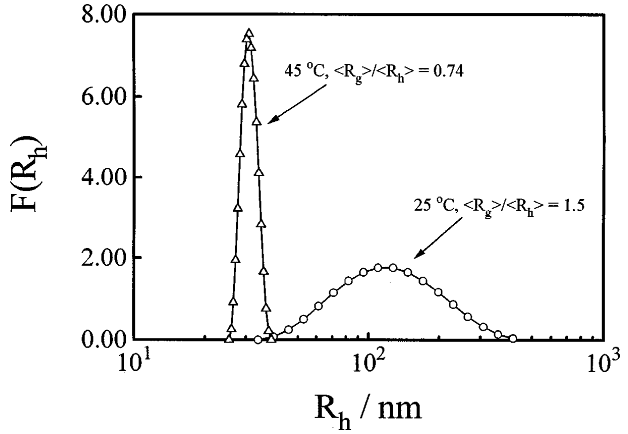

FIG. 2. Hydrodynamic radius distributions of PNIPAM-g-PEO in deionized water at two different temperatures, respectively, lower and higher than the lower critical solution temperature (~32 °C), where $C = 1.00 \times 10^{-5}$ g/ml.

in studying a longer polymer chain [11]. In static LLS, the root-mean-square z-average radius ($\langle R_g^2\rangle_z^{1/2}$ or written as $\langle R_g\rangle$) of the polymer chain in solution can be determined from the angular dependence of the access absolute time-averaged scattered light intensity [i.e., the Rayleigh ratio, $R_{vv}(q)$] on the basis of $[KC/R_{vv}(q)]_{C\to 0} \approx (1/M_w)[1 + (\frac{1}{3})\langle R_g^2\rangle q^2]$, where $K = 4\pi^2 n^2 (dn/dC)^2/(N_A \lambda_0^4)$ and $q = (4\pi n/\lambda_0)\sin(\frac{\theta}{2})$ with n, dn/dC, N_A, λ_0, and θ being the solvent refractive index, the specific refractive index increment, Avogadro's number, the wavelength of the laser light in vacuum, and the scattering angle, respectively [13]. In dynamic LLS, for a pure diffusive relaxation, the linewidth distribution $G(\Gamma)$, calculated from the Laplace inversion of a measured time correlation function, can lead to a hydrodynamic radius distribution $f(R_h)$ and, further, to an average hydrodynamic radius $\langle R_h\rangle [= \int_0^\infty f(R_h) R_h \, dR_h]$ [14–16]. All of the solutions and dispersions were clarified using 0.5-μm or 0.1-μm Millipore filters depending on the size of the particles, so that dust was removed, but not the polymer chains.

Figures 1 and 2, respectively, show the angular dependence of $KC/R_{vv}(q)$ and the hydrodynamic radius distribution $f(R_h)$ of PNIPAM-g-PEO in deionized water at two temperatures, respectively, lower and higher than its LCST (~32 °C). The decrease of the slope (i.e., $\langle R_g\rangle$ from 155 to 21 nm) in Fig. 1 and the shift of the peak in Fig. 2 clearly indicate the shrinking of the PNIPAM-g-PEO chains when the temperature increases from 25 to 45 °C. The change of the $\langle R_g\rangle/\langle R_h\rangle$ ratio from 1.5 to 0.74 shows that the chain conformation of PNIPAM-g-PEO changes from a random coil to a globule when the temperature rises from 25 to 45 °C. It is worth noting that, in Fig. 1, the two least-square fitting lines have the same intercept, revealing that there is no change in M_w, or in other words, this is only an intrachain conformation change and involves no interchain aggregation.

Figure 3 shows a schematic of the formation of a single chain core-shell nanostructure. It is known that the PEO macromonomer chains have an average hydrodynamic radius of ~3 nm. Assuming that the PEO chains free in water and on the nanostructure have a similar chain conformation, we can estimate the shell thickness (L_{shell}) and the radius of the core to be ~6 and ~23 nm, respectively. Further, using the molar mass of the PNIPAM chain backbone, we found that the chain density of the core is only 0.25 g/cm^3, which is significantly lower than the chain density (~1 g/cm^3) of conventional polymeric latex particles. This finding implies that the hydrophobic core made of a single fully collapsed PNIPAM chain still contains ~75% water. Therefore, this core-shell nanostructure might be used as a carrier to load a large amount of drugs or catalysts because of the large free volume inside the core. Another advantage of using it as a carrier is that this single chain core-shell nanostructure can be easily and quickly switched on and off by a simple temperature variation of only 1–2 °C.

Figure 4 shows an imitation of the releasing and encapsulation of drugs or catalysts in terms of the temperature dependent fluorescence intensity ratio (I_1/I_3) of pyrene in the presence of PNIPAM-g-PEO, where the pyrene concentration is $\sim 2 \times 10^{-7} M$. It has been known that I_1/I_3, the highest energy vibrational band I_1 (373 nm) to the third

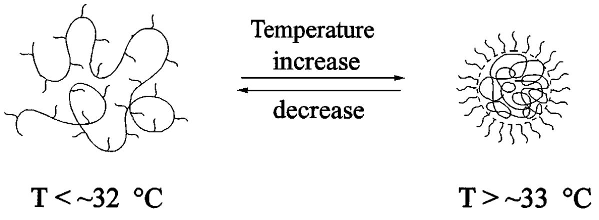

FIG. 3. Schematic of the formation of a single chain core-shell nanostructure through the coil-to-globule transition of the chain backbone of PNIPAM-g-PEO.

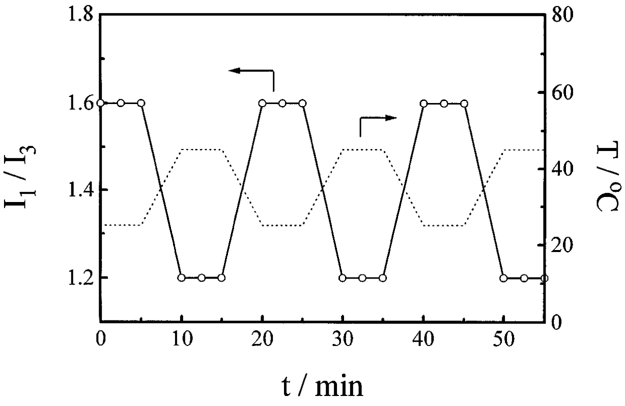

FIG. 4. Temperature dependence of the fluorescence intensity ratio (I_1/I_3) of pyrene in deionized water in the presence of PNIPAM-g-PEO, where the concentration of pyrene is $\sim 2 \times 10^{-7} M$.

highest energy vibrational band I_3 (385 nm), is very sensitive to microenvironmental polarity [17]; namely, in pure water, $I_1/I_3 \sim 1.8$, while, in a hydrophobic domain, I_1/I_3 could be as low as 1.2. The change of I_1/I_3 between ~1.6 and ~1.2 in Fig. 4 clearly shows that PNIPAM-g-PEO can release and encapsulate pyrene when the temperature changes from 25 to 45 °C. It should be noted that the change of I_1/I_3 in Fig. 4 would be a sharp step function if we were able to jump the temperature instantly.

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