

## Structure of a Collapsed Polymer Chain with Stickers: A Single- or Multiflower?

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Using an amphiphilic copolymer with evenly spaced hydrophobic styrene segments (stickers), poly(*N*-isopropylacrylamide-*s*-styrene), we recently confirmed a long-standing prediction that such a copolymer chain in a solvent selectively poor for the stickers could self-fold from a random coil to a single-flowerlike core-shell nanostructure. Moreover, we found that the self-folding involves the movement of the sticks to the center and the transition from the random coil to the collapsed globule passes through a proposed ordered coil state.

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The presence of a few molar per cent of hydrophobic monomer units (stickers) in a hydrophilic polymer chain can trigger chain association in water or in a selective solvent to form gels or clusters, depending on solvency and polymer concentration. Such associating copolymers are widely used as viscosity modifiers, colloidal stabilizers, and surface-active agents [1–3]. This type of copolymer chain can adopt a more complicated conformation in solution than the corresponding homopolymer. It has been predicted and observed that in a solvent selectively poor for the stickers the chain can fold upon itself into a multiflower nanostructure; namely, each or a number of neighboring stickers undergoes intrachain association to form a string of micellelike flowers along the chain backbone [3–7]. However, it has also been suggested that the self-folding could lead to a single-flowerlike core-shell nanostructure with all stickers condensed in the center and the chain segments between stickers swollen like a flower petal (chain loop) [3–5,7]. It is expected that such a chain folding may provide a simple model for the study of more complicated problems, such as protein folding and DNA packing.

However, due to various experimental difficulties, especially in sample preparation, few experimental studies have been reported clarifying this point. In most cases, interchain association taking places prior to a complete intrachain self-folding spoils the study, in which multichain micelles coexisted with single-chain micelles [8,9]. To our knowledge, only Kikuchi and Nose [10], in their studies of polystyrene-*graft*-poly(methyl methacrylate), observed the formation of a thermodynamically stable single-chain multiflower structure. Their results revealed that the structure was rigid and on average consisted of c.a. five flowerlike micelles on each chain, resembling a string of closely packed pearls. Experimentally, there has been no report as yet on the formation of a *single flower-*

*like single-chain nanostructure*. The prediction has remained a challenge in polymer physics.

In recent years, we studied the coil-to-globule transition of long thermally sensitive linear poly(*N*-isopropylacrylamide) (PNIPAM) homopolymers and copolymers grafted with short polyethylene oxide chains, on the basis of the fact that PNIPAM in water can change from a hydrophilic random coil to a hydrophobic collapsed globule when the solution is heated to a temperature higher than 32 °C [11–13]. For the present study we have prepared by a micellar polymerization process, as developed by Candau *et al.* [14], copolymers consisting of short hydrophobic styrene segments (stickers) inserted, equally spaced, into a PNIPAM chain. Our original objective was to determine whether such a copolymer chain can self-fold into the predicted single-flowerlike core-shell nanostructure.

In the micellar polymerization method employed, hydrophobic styrene (St) monomers were solubilized inside micelles of the surfactant, hexadecyltriethylammonium bromide (CTAB) [15]. Potassium persulfate (KPS) and *N, N, N', N'*-tetramethylethylenediamine (TMED) were used to initiate the polymerization of the hydrophilic *N*-isopropylacrylamide (NIPAM) monomers dissolved in the continuous aqueous medium. When the free radical end of a growing PNIPAM chain enters a micelle, styrene monomers entrapped inside polymerize forming a short hydrophobic segment (sticker). The free radical end then reenters the continuous aqueous medium to polymerize NIPAM further until it hits another micelle. Since the mean distance between two micelles is constant for a given micelle concentration, we can assume that the distance between two neighboring stickers along the resultant PNIPAM chain is similar. In principle, by varying the average number of styrene monomers inside each micelle and either the NIPAM or the micelle

concentration, we can control, respectively, the average length of the sticker or that of the PNIPAM chain between two neighboring stickers.

The initial concentrations of NIPAM, styrene, CTAB, KPS, and TMED were 0.16 M, 5.24 mM, 17.3 mM, 0.34 mM, and 0.67 mM, respectively. The resultant segmented copolymer, denoted hereafter as PNIPAM-*seg*-St, has a styrene content of 3.9 mol%, as determined by pyrolysis gas chromatography. The average degree of polymerization between two styrene segments is *c.a.* 500. After purification, the copolymer was fractionated by six successive dissolution/precipitation cycles in a mixture of extremely dried acetone and *n*-hexane at 25 °C. In each cycle, only the very first fraction obtained was used in the next cycle. This combination of fractionation and filtration enabled us to obtain ultralong PNIPAM-*seg*-St chains with a weight-average molar mass of  $1.33 \times 10^7$  g/mol and a polydispersity index of  $M_w/M_n < 1.1$ . On average, each chain had *ca.* 230 hydrophobic stickers and each sticker had *ca.* 20 styrene units. The copolymer was placed in deionized water for 10 d to ensure complete dissolution. The final concentration used for laser light scattering (LLS) was  $7.2 \times 10^{-7}$  g/ml and the solution was clarified with a 0.5  $\mu$ m Millipore Millex-LCR filter to remove dust. It is helpful to note that there were  $10^5$ – $10^6$  chains inside the scattering volume ( $\sim 10$   $\mu$ L) so that the number density fluctuation was not a problem even in such a dilute solution.

Figure 1 shows that the slope of  $KC/R_{vv}(q)$  vs  $q^2$  sharply decreases as the temperature increases. It is known in LLS that the slope of this line is related to

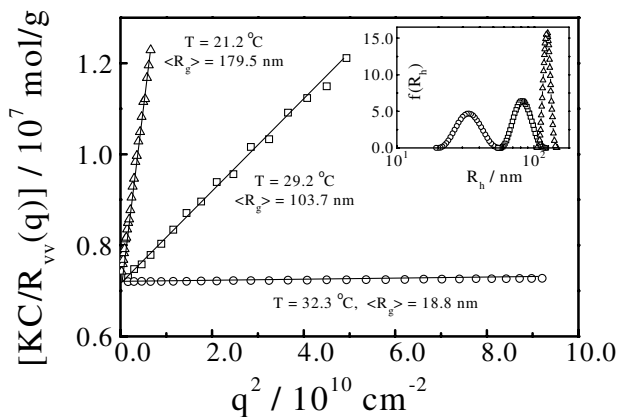


FIG. 1. Angular dependence of the Rayleigh ratio  $R_{vv}(q)$  of the segmented copolymer PNIPAM-*seg*-St in water measured by static laser light scattering, where  $K$  is a constant related to the light wavelength, solvent refractive index, and specific refractive index increment of solution  $q$  is the scattering vector, and the polymer concentration ( $C$ ) is  $7.2 \times 10^{-7}$  g/ml. The inset shows the temperature dependence of the hydrodynamic radius distribution  $f(R_h)$  determined from dynamic laser light scattering.

the  $z$ -average root-mean-square radius of gyration ( $\langle R_g^2 \rangle^{1/2}$  or written as  $\langle R_g \rangle$ ) of a polymer chain [16]. A decrease of  $\langle R_g \rangle$  indicates shrinking of the chains. Such a shrinking can be viewed directly in terms of the shift of the hydrodynamic radius distribution  $f(R_h)$  from  $\sim 124$  to  $\sim 31$  nm, as shown in the inset of Fig. 1, where  $f(R_h)$  was calculated from the time correlation function measured in dynamic LLS [17]. On the other hand, the extrapolation to  $q \rightarrow 0$  leads to  $M_w$ . The same intercept clearly reveals no change in  $M_w$ , *i.e.*, no interchain association. Therefore, the shrinking of the chains with increasing temperature is purely a single-chain (intrachain) process. The plot of  $qR_{vv}(q)/KC$  versus  $q\langle R_g \rangle$  (not shown) reveals the increase of the chain segment density at higher temperatures [18].

Figure 2 shows that both  $\langle R_g \rangle$  and  $\langle R_h \rangle$  decrease as the temperature increases. Each data point was obtained only after the solution had reached thermodynamically equilibrium and the measured value was stable. Note that in each curve there exists a small kink at  $\sim 29.4$  °C and that  $\langle R_g \rangle / \langle R_h \rangle$  remains constant at  $\sim 1.15$  in the range (29–30.6) °C, representing an additional transition prior to the collapse of the PNIPAM chain segments. The decreases of both  $\langle R_g \rangle$  and  $\langle R_h \rangle$  after the kink become faster. Corresponding curves drawn for the coil-to-globule transition of PNIPAM homopolymer chains do not present such a “kink” [13]. It is known that for a random coil chain in a good solvent  $\langle R_g \rangle / \langle R_h \rangle \sim 1.5$ , while for a uniform hard sphere,  $\langle R_g \rangle / \langle R_h \rangle \sim 0.774$  [19]. The decrease of  $\langle R_g \rangle / \langle R_h \rangle$  from  $\sim 1.5$  to  $\sim 0.6$  (Fig. 2) confirms the coil-to-globule transition of individual copolymer chains. However, a careful examination of Fig. 2 raises a number of questions.

The first question concerns the association of the stickers: do they associate into a string of micellelike flowers or as one core-shell-like flower? If a string of flowers were

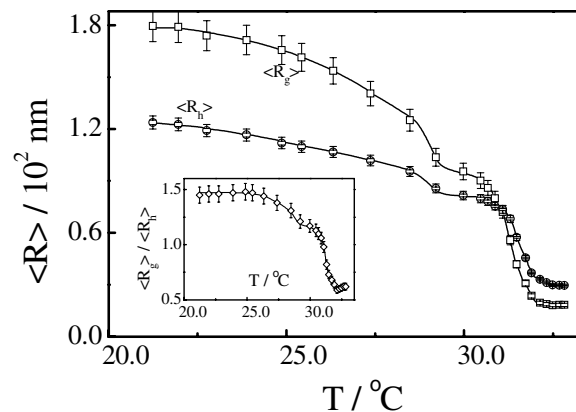


FIG. 2. Temperature dependence of the  $z$ -average root-mean square radius of gyration ( $\langle R_g \rangle$ ) and the average hydrodynamic radius ( $\langle R_h \rangle$ ) of the copolymer PNIPAM-*seg*-St in water; the inset shows the temperature dependence of the ratio of  $\langle R_g \rangle / \langle R_h \rangle$ .

formed, the overall chain structure would become more rigid and, hence,  $\langle R_g \rangle / \langle R_h \rangle$  should increase. In addition, these micellelike flowers would collapse and pack together at higher temperatures to form a uniform globule. In contrast, if only one micellelike flower was formed, the hydrophobic stickers would condense in the center so that the resultant globule should have a core denser than the shell. According to the definitions of  $\langle R_g \rangle$  and  $\langle R_h \rangle$ , a hard sphere with a denser core has a smaller  $\langle R_g \rangle$  than a uniform sphere with the same size, but the density distribution has no effect on  $\langle R_h \rangle$ . In our experiment, the ratio  $\langle R_g \rangle / \langle R_h \rangle$  decreases from  $\sim 1.5$  to  $\sim 1.1$  in the range (25–29.8) °C (Fig. 2) and, at higher temperatures, becomes much smaller than 0.774. Previously, we measured the ratios of  $\langle R_g \rangle / \langle R_h \rangle$  for surfactant-free polystyrene nanoparticles before and after grafting a layer of linear polymer chains. We found that  $\langle R_g \rangle / \langle R_h \rangle$  decreases from  $\sim 0.8$  to  $\sim 0.6$ , which was due to the hydrodynamic draining of the grafted layer [20]. The values of  $\langle R_g \rangle / \langle R_h \rangle$  much lower than 0.8 suggests that the resultant single-chain nanostructure with a dense core, presumably made of the hydrophobic stickers.

The second question relates to the existence of the additional transition at  $\sim 29.4$  °C. As expected, hydrophobic styrene stickers tend to associate in water. But, at lower temperatures, water is such a good solvent for PNIPAM that the copolymer chain adopts a random coil conformation and the movement of one sticker is not correlated to other stickers because the PNIPAM chain backbone randomly fluctuates in solution. As the temperature increases in the range (25–30.6) °C, the solvency of water for PNIPAM gradually decreases and the hydrophobic stickers tend to gather towards the center and to move in a more correlated fashion. Since water is not a poor solvent yet, the PNIPAM chain segments are still in the swollen and coiled state, as reflected by the fact that the decrease of  $\langle R \rangle$  is rather small (only  $\sim 30\%$ , Fig. 2). In order to distinguish this copolymer conformation from the normal random coil, we name it “ordered coil.”

Figure 3 schematically shows such a conformation transition from the random coil to the ordered coil. As the temperature approaches  $\sim 30.6$  °C (the Flory  $\Theta$ -point), the stickers start to gather towards the center and each PNIPAM chain segment between two neighboring stickers forms a flower petal (loop). The overall chain conformation becomes flowerlike. Further increase of the temperature leads to the condensation of the stickers and the shrinking of the PNIPAM loops, resulting in a collapsed core-shell nanoparticle. To provide a direct evidence of the association of the stickers, we are changing the stickers to hydrophobic fluorescence labeling. The preliminary result supports the schematic presented in Fig. 3. The detail will be reported in the coming full paper.

In order to confirm the existence of such two transitions, we also carried out a thermal analysis of a co-

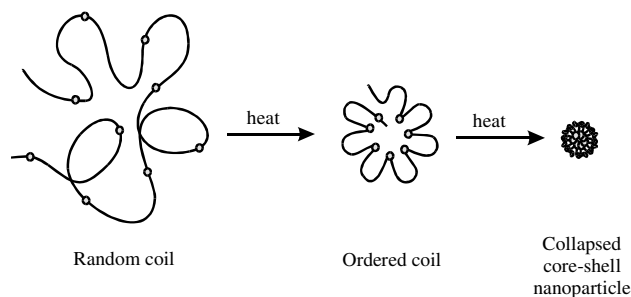


FIG. 3. Schematic representation of the chain conformation transitions of a segmented copolymer chain with stickers in dilute solution from the random coil to the ordered coil and then from the ordered coil to the collapsed core-shell globule as the solvency for the major component of the copolymer chain decreases.

polymer aqueous solution (0.157 ml) using a differential scanning microcalorimeter (VP-DSC, MicroCal Inc, USA) with a heating rate of 0.5 °C/min and a response time of 5.6 s. Note that the copolymer concentration used here is much higher than that in LLS (Fig. 1). Figure 4 shows that, for PNIPAM homopolymer, the endotherm corresponding to the transition is slightly skewed towards the high temperature side, whereas the endotherm registered for a solution of PNIPAM-*seg*-St is abnormally skewed towards the low temperature side and, surprisingly, the transition occurs at a higher temperature. It is known that copolymerization of hydrophobic monomers into PNIPAM should decrease, but not increase, its shrinking temperature. We had in hand a random copolymer, PNIPAM-*co*-St, of composition similar to that PNIPAM-*seg*-St and recorded a DCS curve of its aqueous solution. Figure 4 shows that the endotherm of a

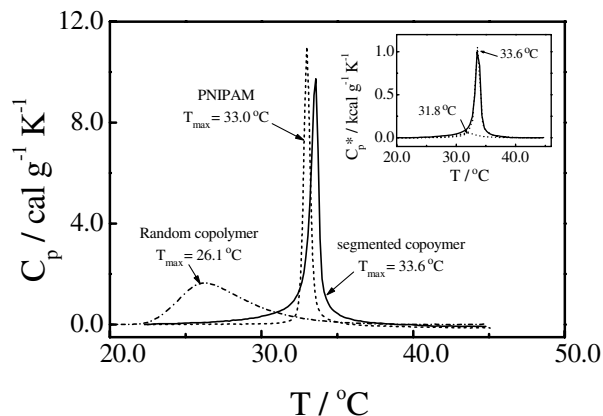


FIG. 4. Temperature dependence of the partial heat capacity ( $C_p$ ) of PNIPAM homopolymer, PNIPAM-*co*-St (4.1 mol%) random copolymer and PNIPAM-*seg*-St (3.9 mol%) segmented copolymer in water; the polymer concentration was 1.0 g/L and the heating rate was 0.5 °C/min. The inset shows the deconvolution of stand partial heat capacity ( $C_p^*$ ) of PNIPAM-*seg*-St.

PNIPAM-*co*-St solution has the normal skew and is shifted to lower temperatures, compared to that of aqueous PNIPAM. Considering the kink in Fig. 2, we attributed the abnormal skew to a transition prior to the shrinking of PNIPAM.

The inset in Fig. 4 shows that endotherm corresponding to the collapse of the segmented copolymer can be deconvoluted into two peaks. A small peak appears  $\sim 1.2^\circ\text{C}$  before the homopolymer peak. We ascribe it to the transition from the random coil to the ordered coil, while the large peak is related to the collapse of PNIPAM. Note that in comparison with the transition temperatures obtained in LLS, all the peak temperatures in DSC were  $\sim 1^\circ\text{C}$  higher. This is because the transitions in DSC were slightly behind the temperature scanning, while the measurement in LLS could be considered as an infinitely slow scanning. Therefore, the small peak in DSC corresponds well with the kink in LLS. Also note that the collapse temperature of the short PNIPAM chain segments, the flower petals, is  $\sim 0.6^\circ\text{C}$  higher than that of long PNIPAM homopolymer chains. This could be ascribed to the chain length dependence of the phase transition temperature and also to the fact that the collapse of the small PNIPAM petals (looped chain) has to overcome an additional internal stress [13,19]

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