Light-Scattering Study of the Coil-to-Globule Transition of Linear Poly(*N*-isopropylacrylamide) Ionomers in Water

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ABSTRACT: The coil-to-globule transition of two poly(*N*-isopropylacrylamide) (PNIPAM) ionomers with different ionic contents (0.8 and 4.5 mol %), but similar weight average molar masses, in deionized water was investigated by a combination of static and dynamic light scattering. In spite of the large difference in their ionic contents, both the ionomers have a nearly same lower critical solution temperature (LCST, ~ 32.5°C). At temperatures higher than the LCST, the ionomer chains undergo a simultaneous intrachain coil-to-globule transition and interchain aggregation to form nanoparticles thermodynamically stable in water. The average size of the nanoparticles decreases respectively as the ionic content increases and the ionomer concentration decreases. The interchain aggregation can be completely suppressed in an extremely dilute ionomer solution ($< \sim 5 \times 10^{-6}$ g/mL), so that the intrachain coil-to-globule transition leads to the collapse of the ionomer chains into individual single-chain nanoparticles. Our results clearly indicate that there is a hysteresis in the colling process (the globule-to-coil transition). © 1998 John Wiley & Sons, Inc. J Polym Sci B: Polym Phys 36: 1501–1506, 1998
Keywords: intrachain coil-to-globule transition; interchain aggregation; laser light scattering; poly(*N*-isopropylacrylamide); single-chain nanoparticle

INTRODUCTION

The coil-to-globule transition of individual polymer chains in solution is a fundamental problem in polymer physics and of special importance due to its relevance with many biological processes, such as protein folding and DNA packing.[1-5] However, the observation of the coil-to-globule transition requires narrowly distributed polymer chains (M_w/M_n = 1.1) with a very high average molar mass ($M_w = 10^7$ g/mol) and an easily accessible phase transition temperature. This is why only in one experiment a single-chain globule thermodynamically stable in water has successfully reached,[6,7] wherein an extremely narrow distributed thermosensitive water-soluble poly(*N*-isopropylacrylamide) (PNIPAM) with a lower critical solution temperature (LCST, ~ 32°C) was used. It should be noted that many investigations also used PNIPAM to study the coil-to-globule transition, but they were hampered by the interchain aggregation. To overcome this interchain interference, Ricka et al.[8,9] added a small amount of surfactant, sodium dodecyl sulfate (SDS), into the PNIPAM solution, so that the adsorption of surfactant on PNIPAM prevents the interchain aggregation at temperatures higher than the LCST, which provides another possibility to characterize individual PNIPAM chains in the globule state. However, the addition of SDS alternates the thermodynamics of PNIPAM in water.

In a previous study, we have shown that by

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introducing a very small amount of ionic groups on the PNIPAM chain backbone the interchain aggregates can be stabilized,[10,11] suggesting another way to study the coil-to-globule transition of individual PNIPAM chains. In this study, we extended the investigation to high molar mass PNIPAM ionomers, poly(N-isopropylacrylamide-co-acrylic acid). The advantage of using the PNIPAM ionomers is that at temperatures higher than the LCST the ionic groups can stabilize the collapsed hydrophobic PNIPAM chains to prevent the interchain aggregation. Another important point is that introducing a small amount of ionic groups into the chain backbone has shifted the LCST only 1–2°C. Therefore, the PNIPAM ionomer is a good candidate for the study of the coil-to-globule transition.

EXPERIMENTAL

Laser Light Scattering

A modified commercial LLS spectrometer (ALV/SP-125) with an ALV-5000 digital time correlator and a solid-state laser (ADLAS DPY425II, output power ca. 400 mW at λ = 532 nm) was used. The experimental setup and basic theory were detailed as before.[12,13] The specific refractive index increment (dn/dC) of PNIPAM in water are 0.167 mL/g and 0.172 mL/g, respectively, at 25 and 45°C.[14] In static LLS, the measurements of the angular and concentration dependence of the average excess scattering intensity lead to the weight average molar mass (M_w), the root mean square radius of gyration ($\langle R_g^2 \rangle_z^{1/2}$, or simply as $\langle R_g \rangle$), and the second virial coefficient (A_2). In dynamic LLS, the measurements of the intensity–intensity time correlation function lead to the hydrodynamic radius distribution ($f(R_h)$). All the dynamic light scattering experiments were done at θ = 15°, except otherwise stated. All the polymer solutions were clarified by 0.5-μm Millipore filter.

Ionomer Synthesis

The PNIPAM ionomer was prepared by a free radical copolymerization of N-isopropylacrylamide (NIPAM) and acrylic acid (AA) at 60°C using azobisisobutyronitrile (AIBN) as an initiator and a benzene/ethanol mixture as a reaction medium. The synthesis has been detailed before.[10] The NIPAM monomer (courtesy of Kohjin Co., Japan)

was purified by recrystallization in a benzene/n-hexane mixture. AA monomer was distilled under reduced pressure at 40°C to remove the inhabitant (hydroquinone monomethyl ether). AIBN was recrystallized in methanol. All the solvents used were analytical grade and freshly distilled. Each ionomer product was purified through three cycles of the acetone-to-hexane reprecipitation. Here, the ionomers neutralized with KOH are labeled as PNIPAM-mKAA, where m represents the average mol content of AA in each ionomer chain. The molecular parameters of the PNIPAM ionomer chains used, such as M_w, $\langle R_g \rangle$ and the ionic (AA) content, are summarized in Table I.

RESULTS AND DISCUSSION

Figure 1 shows that in the temperature range of 25–32°C $R_{vv}(\theta)/KC$ of each solution is a constant in the small range of $\sim$ 4–5 × 10^6 g/mol, very close to the molar mass of individual PNIPAM-0.8KAA chains, indicating that there was no interchain aggregation. When the temperature is raised to $\sim$ 32.5–33°C, slightly higher than the LCST of PNIPAM, an abrupt increase of $R_{vv}(\theta)/KC$ appears for the solution with a concentration higher than 9.5 × 10^{-6} g/mL, clearly indicating the interchain aggregation. Further increase of the temperature to $\sim$ 34–35°C, lead to a new $R_{vv}(\theta)/KC$ plateau. The constant $R_{vv}(\theta)/KC$ at temperatures higher than $\sim$ 35°C indicates the stop of the interchain aggregation. From the ratio of $[R_{vv}(\theta)/KC]_{T=45°C}/[R_{vv}(\theta)/KC]_{T=25°C}$, we were able to estimate the average number of the PNIPAM chains inside each aggregate (N_{chain}) to be $\sim$ 17, $\sim$ 8 and $\sim$ 4, respectively, for C = 5.0 × 10^{-4}, 1.0 × 10^{-4}, and 9.5 × 10^{-6} g/mL. In the case of C = 4.7 × 10^{-6} g/mL, $R_{vv}(q)/KC$ is nearly independent of temperature. It should be noted that $R_{vv}(q)$ is proportional to the square of the mass, i.e., a dimer scatters four times more light than an unimer. Therefore, a very small amount of the interchain aggregation would lead to a large increase of $R_{vv}(\theta)/KC$. The temperature independence of $R_{vv}(q)/KC$ indicates no interchain aggregation in the extremely dilute solution even at temperature as high as 45°C.
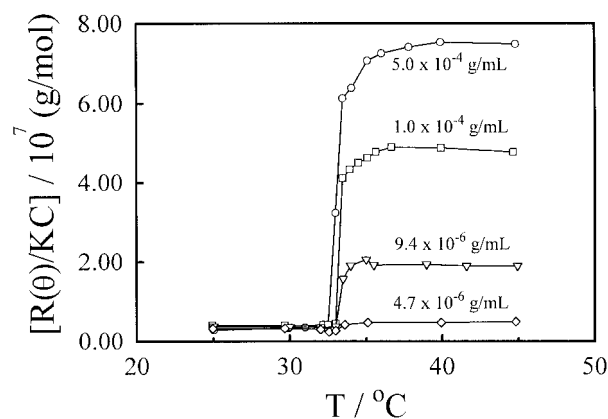
Figure 2 shows that when C = 4.7 × 10^{-6} g/mL, $\langle R_h \rangle$ decreases as the temperature increases, which actually reflects the intrachain coil-to-globule transition because we have known from Figure 1 that in this solution there is no interchain aggregation in the heating process. It is very simi-

Table I. Molecular Parameters of Poly(*N*-isopropylacrylamide-*co*-acrylic acid) Ionomers

Samples	M_w/(g/mol)	AA/mol %	$\langle R_g \rangle$/nm	M_w/M_n
PNIPAM-0.8AA	4.7×10^6	0.8	121	1.62
PNIPAM-4.5AA	2.3×10^6	4.5	102	1.73

lar to the collapsing process observed for a neutral PNIPAM homopolymer chain in an extremely dilute solution.[6,7] The difference is that the sample used here ($M_w/M_n = 1.6-1.7$) is not as narrow as the one ($M_w/M_n < 1.1$) used in refs. 6 and 7, which makes the experiment much easier. The decrease of $\langle R_h \rangle$ can be divided into three stages: (1) in the low temperature range (25–32°C), water progressively changes from a good solvent to a poor solvent, resulting a slight contraction of the PNIPAM chain and a slight smaller $\langle R_h \rangle$; (2) around the phase transition temperature (32–35°C), the PNIPAM chain undergoes the coil-to-globule transition so that $\langle R_h \rangle$ rapidly decreases; (3) at temperatures higher than ∼ 35°C, the PNIPAM chain is already in its fully collapsed globule state so that further increase of temperature has little effect on $\langle R_h \rangle$.

In the solution with a higher concentration, the intrachain coil-to-globule transition is accompanied by the interchain aggregation. When the interchain aggregation is dominate, $\langle R_h \rangle$ increases as temperature increases, leading to a peak in the temperature range of 32–35°C. At higher temperatures, the interchain aggregation stops because the increase of $R_{vv}(q)/KC$ stops at ∼ 34°C, as

shown in Figure 1. Therefore, the intrachain coil-to-globule transition becomes dominate at temperatures higher than ∼ 34°C, resulting the decrease of $\langle R_h \rangle$.

A combination of static and dynamic LLS results leads to microscopic parameters of the stable interchain aggregates at 34°C, such as the weight average molar mass ($M_{w,agg}$), the average hydrodynamic radius ($\langle R_h \rangle_{agg}$), the average number of the polymer chains inside each aggregate ($\langle N \rangle_{agg}$), the average surface area per ionic group ($\langle S \rangle_{ionic}$), and the average hydrodynamic volume of each polymer chain inside the aggregate ($\langle V \rangle_{chain}$), which are summarized in Table II. It is worth noting that the aggregates formed in different solutions have a very similar $\langle V \rangle_{chain}$, indicating that at a given temperature the average degree of the shrinking of the polymer chains is similar in spite of the interchain aggregation, so that the aggregates formed in different solutions have a similar density. This result clearly indicates that the intrachain coil-to-globule transition and the interchain aggregation are two independent, but competing, processes.

Table III summarizes the LLS results of the aggregates formed in different PNIPAM-0.8KAA solutions at 45°C. The ratio of $\langle R_g \rangle/\langle R_h \rangle$ is in the range of 0.73–0.84, indicating that the aggregates
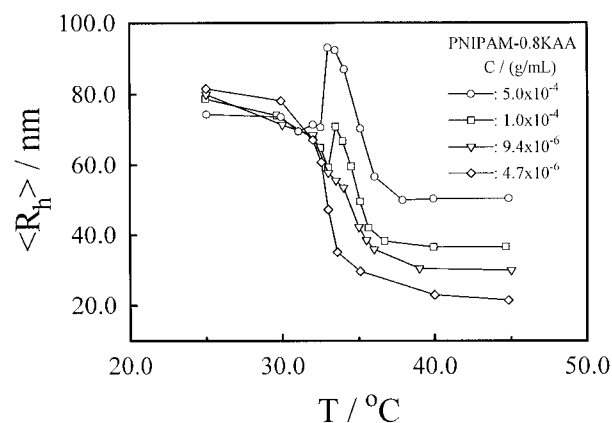

Figure 1. Temperature and concentration dependence of the excess scattering intensity $R_{vv}(\theta)/KC$ of PNIPAM-0.8KAA in deionized water, where K is a constant, and $R_{vv}(\theta)/KC$ approximately equals the weight-average molar mass (M_w) because the solution is very dilute.

Figure 2. Temperature and concentration dependence of the average hydrodynamic radius $\langle R_h \rangle$ of PNIPAM-0.8KAA in deionized water.

Table II. LLS Results of PNIPAM-0.8KAA Aggregates Formed at 34°C

C/(g/mL)	$M_{w,\mathrm{agg}}$/(g/mol)	$\langle N \rangle_{\mathrm{agg}}$	$\langle R_h \rangle$/nm	$\langle S \rangle_{\mathrm{ionic}}$/nm^2	$\langle V \rangle_{\mathrm{chain}}$/nm^3
5.0×10^{-4}	7.68×10^7	17	87	17.8	1.62×10^5
1.0×10^{-4}	3.88×10^7	8	68	20.9	1.64×10^5
9.4×10^{-6}	1.86×10^7	4	54	26.3	1.64×10^5
4.7×10^{-6}	4.97×10^6	1	35	49.1	1.80×10^5

are uniform spheres.[15,16] The average density $\langle \rho \rangle$ of the aggregates decreases as the aggregation number $\langle N \rangle_{\mathrm{agg}}$ decreases, which may be attributed to the imperfect packing of the polymer chains inside the aggregate when are only one or two chains inside each aggregate.[17] In the case of $\langle N \rangle_{\mathrm{agg}} > 8$, $\langle \rho \rangle \sim 0.34$ g/cm^3, very close to the value of the neutral PNIPAM aggregates reported by Ricka et al.[8,9] For the single-chain globule, $\langle \rho \rangle \sim 0.20$ g/cm^3, very close to what we found in the case of PNIPAM homopolymer,[6,7] indicating that the ionic groups are on the surface of the aggregates and have nearly no effect on the coil-to-globule transition.

We can reasonably picture that in the coil-to-globule transition the PNIPAM segments between two neighboring ionic groups collapse and associate with each other, while all the ionic groups stay on the surface of the aggregates to act as a stabilizer. As the aggregation proceeds, for the aggregates with a uniform density, the number of the ionic groups on each particle is proportional to the mass of the aggregate (M_{agg}) or the cubic of the size, while the surface area of the aggregate is only proportional to the square of the size or $M_{\mathrm{agg}}^{2/3}$. Therefore, the surface area per ionic group is proportional to $M_{\mathrm{agg}}^{-1/3}$, i.e., $\langle S \rangle_{\mathrm{ionic}} \propto M_{\mathrm{agg}}^{-1/3}$, indicating that $\langle S \rangle_{\mathrm{ionic}}$ decreases as the aggregation proceeds. At the same time, the intrachain coil-to-globule transition also leads to the decrease of $\langle S \rangle_{\mathrm{ionic}}$.

Figure 3 shows a sharp decrease of $\langle S \rangle_{\mathrm{ionic}}$ in the temperature range of 32.5–33°C, which exactly corresponds to the slow down of the interchain aggregation (the increase of $R_{vv}(\theta)/KC$ shown in Figure 1 and to the peak position of $\langle R_h \rangle$ shown in Figure 2. Logically, there is a minimum value of $\langle S \rangle_{\mathrm{ionic}}$, at which the surface of the aggregates is "fully covered" by the ionic groups so that further aggregation is impossible because of the ionic repulsion between different aggregates. However, the intrachain coil-to-globule transition inside the aggregates continues. This is exactly why $\langle R_h \rangle$ in Figure 2 first increases and then decreases, but $\langle S \rangle_{\mathrm{ionic}}$ in Figure 3 only decreases. It is worth noting that for aggregates with different sizes formed in different solutions, $\langle S \rangle_{\mathrm{ionic}}$ approaches a similar value at high temperatures. This is reasonable because hydrophobic particles have a tendency to aggregate in water. The stabilizers (here is the ionic groups) can reduce the surface energy. When the surface per stabilizer decreases to a certain value, i.e., the surface reaches a certain degree coverage, the aggregation stops and the particles will be stabilized. For a given type of interface (here is particle/water), this value should be a constant, independent on the particle size. Therefore, $\langle S \rangle_{\mathrm{ionic}}$ is a fundamental parameter governing the size of the aggregates.

Figures 4 shows that in spite of the large difference in the ionic content, PNIPAM-4.5KAA exhibits similar intrachain collapsing and interchain aggregation as PNIPAM-0.8KAA. In the extremely dilute solution ($C = 5.0 \times 10^{-6}$ g/mL), the collapsing process involves only the intrachain coil-to-globule transition. It should be noted that the degree of the aggregation of PNIPAM-

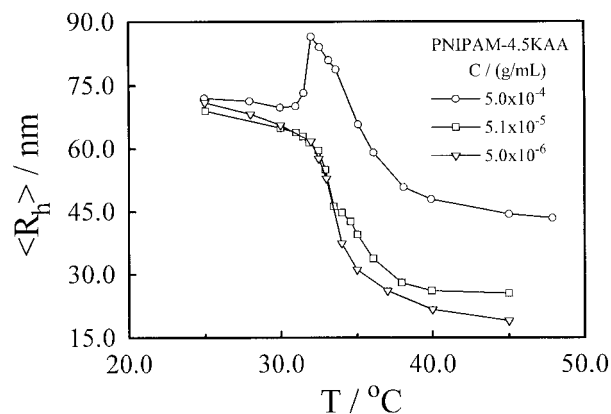**Table III.** LLS Results of PNIPAM-0.8KAA Particles Formed at 45°C

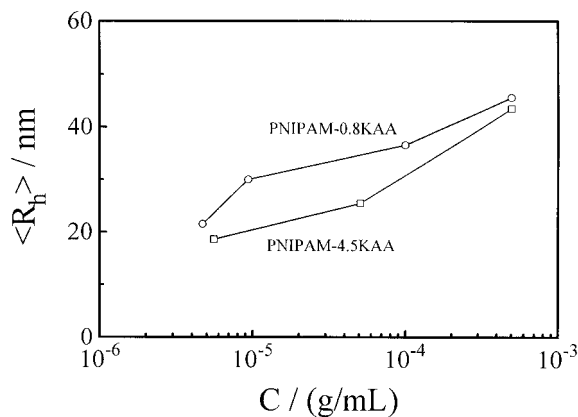| C/g/mL	M_w/(g/mol)	$\langle N \rangle_{\mathrm{agg}}$	$\langle R_h \rangle$/nm	$\langle R_g \rangle/\langle R_h \rangle$	$\langle \rho \rangle$ (g/cm^3)
5.0×10^{-4}	7.88×10^7	17	45.6	0.78	0.34
1.0×10^{-4}	4.08×10^7	8	36.6	0.73	0.34
9.4×10^{-6}	1.86×10^7	4	30.6	0.75	0.28
4.7×10^{-6}	4.97×10^6	1	21.5	0.84	0.20
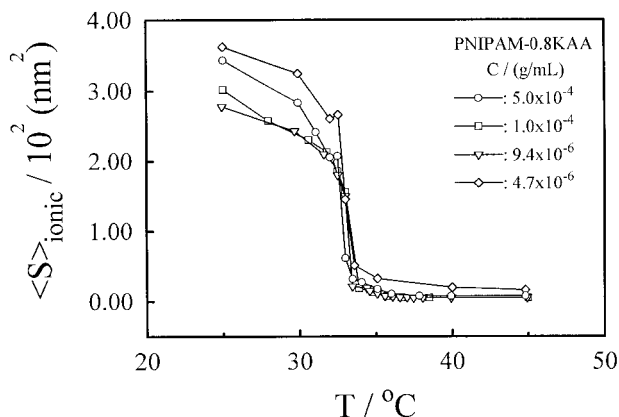
Figure 3. Temperature dependence of the average surface area $\langle S \rangle_{ionic}$ per ionic group on the PNIPAM-0.8KAA aggregates, where $\langle S \rangle_{ionic}$ is defined as 4π-$\langle R_h \rangle^2/\langle N \rangle_{ionic}$.

Figure 5. Comparison of the average size of the aggregates respectively formed in the PNIPAM-0.8KAA and PNIPAM-4.5KAA solutions.

4.5KAA is lower than that of the low ionic PNIPAM-0.8KAA, which is reflected by the smaller size (Fig. 5) and smaller aggregation peak formed in the PNIPAM-4.5KAA solution with a similar concentration. This is reasonable because PNIPAM-4.5KAA has a higher ionic content and it requires a much less degree of aggregation to reach the same minimum value of $\langle S \rangle_{ionic}$, as in the case of PNIPAM-0.8KAA.

Figure 6 shows that $\langle R_h \rangle$ returns to the starting point when the solution was cooled to 25°C, indicating that the solution returns to its initial state in which all the ionomers exist as individual chains. On the other hand, the heating rate independence of $\langle R_h \rangle$ at 45°C implies that the solution at 45°C is in a thermodynamic equilibrium state. However, around the coil-to-globule transition

temperature (32–34°C), $\langle R_h \rangle$ in the heating process is different from that in the cooling process, i.e., there is a hysteresis, which can be attributed to the association of different segments, presumably through the hydrogen bonding, in the globule state, which persist at the temperature around the transition in the cooling process, so that $\langle R_h \rangle$ is smaller. When the temperature is lower than 25°C, water becomes such a good solvent that all the intersegmental structures are destroyed and $\langle R_h \rangle$ returns to its initial value before the heating.
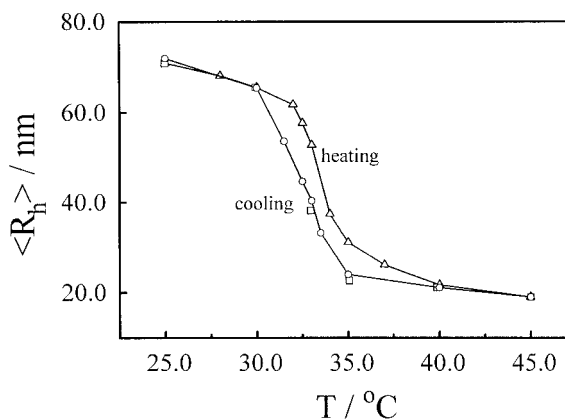

Figure 4. Temperature and concentration dependence of the average hydrodynamic radius $\langle R_h \rangle$ of PNIPAM-4.5KAA in deionized water.

Figure 6. Temperature dependence of $\langle R_h \rangle$ of a dilute PNIPAM-4.5KAA solution ($C = 5.0 \times 10^{-6}$ g/mL) respectively in the slow heating and cooling processes; "□" represents that the solution was jumped from 25 to 45°C by a single step and then slowly cooled to each measurement temperature; "△" and "○" represent that the solution was slowly heated to each measurement temperature from 25 to 45°C and then slowly cooled to each measurement temperature. Every data point was obtained after the thermodynamic equilibrium.

CONCLUSION

A combination of static and dynamic laser light-scattering study of the collapsing process of two poly(N-isopropylacrylamide) ionomers in deionized water showed that the collapsing of PNIPAM ionomer chains as temperature increases generally involves two independent and competing processes: the intrachain coil-to-globule transition and the interchain aggregation. The higher the polymer concentration, the larger the aggregates formed will be. The decrease of the ionomer concentration and the increase of the ionic content can suppress the interchain aggregation. Using an extremely dilute ionomer solution, we find another way to prepare a single polymer chain globule thermodynamically stable in water, where the requirement of a very narrowly distributed sample for the study of the coil-to-globule transition has been removed. Our results also indicate that some of the intersegment structures formed at higher temperature in the coil-to-globule transition can be preserved in the cooling process as long as the solution temperature is not too low. It should be of importance to have a further study of these intersegment structures formed at high temperatures, possibly by nuclear magnetic resonance (NMR).

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