

Note

Thermo-induced formation of physical “cross-linking points”
of PNIPAM-*g*-PEO in semidilute aqueous solutions

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Abstract

Linear poly(*N*-isopropylacrylamide) chains grafted with short poly(ethylene oxide) chains (PNIPAM-*g*-PEO) were prepared by free radical copolymerization of NIPAM and PEO macromonomers ($M_w = 5000$ g/mol) end-capped with methacrylate in water. Temperature effects on the solution viscosity of thermally sensitive copolymer were studied in different aqueous concentrations. A specific transition was observed during the measurement of the reduced viscosities of PNIPAM-*g*-PEO copolymer at a certain concentration (C_0) in semidilute aqueous solutions: the reduced viscosities increased sharply (namely, thermothickening behavior) at LCST when concentrations were higher than C_0 , or decreased sharply at LCST when concentrations lower than C_0 . A plateau was also found near C_0 when temperature was closing to LCST from low temperature, showing there is no change in reduced viscosity under this circumstance. The inverse increase of the viscosities at higher temperatures in higher concentration ($> \sim 3$ g/L) is attributed to the forming of physical “cross-linking points” composed of collapsed PNIPAM core and expanded PEO shell. The sharp decrease of the viscosities at higher temperatures in lower concentration ($< \sim 3$ g/L) is attributed to the forming of independent globules. The plateau could be attributed to the equilibrium competition between forming of physical “cross-linking points” and independent globules depending on the copolymer solution concentrations.

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1. Introduction

Microphase separation in aqueous polymer solution can lead to rich and complex rheological properties. Thermothickening polymers, in particular (leading to an increase of viscosity with temperature), have attracted attention in the past decade as a result of their original behavior, which is opposite to the behavior of conventional liquids. In recent years, many researchers have paid more and more attention to thermothickening or gelling properties not only for scientific interest but also for practical biomedical or pharmaceutical applications [1]. Such thermogelation may provide a convenient means of injectable drug delivery, particularly for biomacromolecules labile to denaturation [2].

Thermally reversible gelation upon heating is relatively rare and is mainly reported with modified polysaccharide [3],

commercially available family of poly(ethylene oxide)–poly(propylene oxide)–poly(ethylene oxide) triblock copolymers PEO–PPO–PEO [4], poly(EOVE-*b*-HOVE) block copolymers [5,6], and based thermosensitive PNIPAM copolymers in aqueous solution [7–11]. Desbrieres et al. [3] studied the thermogelation of hydrophobic modified methylcellulose and attributed the thermogelation to hydrophobic interactions between highly substituted units. Okabe et al. [5,6] observed a thermoreversible sol–gel transition around 20 °C in a 17 wt% PEOVE-*b*-PHOVE aqueous solution. After study of rheology, dynamic light scattering, and small-angle neutron scattering, they concluded that the crystallike structure with macrolattice was the reason for thermogelation. Recently Bossard et al. [12] reported a novel thermoreversible gelation phenomenon of a long central poly-(2-vinylpyridine) block end-capped by two shorter poly(acrylic acid) blocks (PAA₁₃₅–P2VP₆₂₈–PAA₁₃₅), and they attributed these unexpected thermal response behaviors from the competition between the significant swelling of the PAA outer blocks, which favors intermolecular interactions responsible

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for the pronounced thermothickening behavior and the thermal motion, which weaken the rheological properties of the polymer solution by speeding up the molecular dynamics. Ma et al. [13] studied pH-responsive physical gels based on ABA triblock copolymers and attributed the gelation to the forming of a micellar gel network in higher concentration and at pH 8. Poly(*N*-isopropylacrylamide) (PNIPAM) is a thermally sensitive polymer with a lower critical solution temperature (LCST $\sim 32^\circ\text{C}$) in water solution [14–16]. PNIPAM and its copolymers with special structures and architectures are included in the class of the so-called “smart” materials that are responsive to internal or external stimuli. Reports in the literature about thermogelation of PNIPAM include PNIPAM homopolymer [17] and copolymer aqueous solutions of poly(NIPAM-co-AAc) [7], star copolymer composed of PEO and PNIPAM [8], PAM-*g*-PNIPAM [9], PNIPAM-*g*-MC [10], and CMC-*g*-PNIPAM copolymers [11]. The reversible gelation was mainly caused by the hydrophobic association of collapsed PNIPAM chains at temperatures higher than its LCST.

In the experimental work reported, scattering techniques including laser light scattering, small-angle neutron scattering (SANS), and small-angle X-ray scattering in conjunction with rheological techniques have been applied frequently to explore the thermothickening or gelling process [5,6,18–22]. In addition, the macroscale properties and the microscale transition assessed by means of thermal analysis, viscoelasticity study, and surface force analysis have been used to study the nature of the physical gelation [23–25]. As a simple and convenient method, viscosity measurements [7,26,27] could also be used to investigate copolymer aqueous solution properties. Virtanen and Tenhu [27] gave the temperature dependence of the reduced viscosities of the 1.0 g/L aqueous polymer solutions, which showed that reduced viscosities would decrease sharply with temperature above the transition temperature.

Our previous studies of poly(*N*-isopropylacrylamide)-*graft*-poly(ethylene oxide) (PNIPAM-*g*-PEO) amphiphilic copolymer chains in dilute aqueous solutions showed that when the temperature is lower than the PNIPAM's LCST, PNIPAM-*g*-PEO is hydrophilic in water, while at higher temperatures, the PNIPAM backbones become hydrophobic and collapse into individual single-chain globules or stable multichain aggregates (mesoglobules), depending on the solution conditions [28,29]. For semidilute solutions of copolymer, the viscosity measurements were performed at different temperatures and in different concentrations, from which the state of the polymer chains can be speculated. A specific transition was observed during the measurement of the reduced viscosities of PNIPAM-*g*-PEO copolymer at a certain concentration (C_0) in semidilute aqueous solutions at different temperatures: The reduced viscosities increased sharply at LCST when concentrations were higher than C_0 , or decreased sharply at LCST when concentrations were lower than C_0 . A plateau was also found near C_0 when temperature was closing to LCST from low temperature, showing there was no change in reduced viscosity in this circumstance. The plateau could be attributed to the equilibrium competition between formation of physical “cross-linking points” and independent globules, depending on the copolymer solu-

tion concentrations. In order to confirm that the existence of the “plateau” is intrinsic to the transition, two PNIPAM-*g*-PEO copolymers were synthesized in water under similar conditions: 21 and 29°C , respectively.

2. Materials and methods

2.1. Sample preparation

N-Isopropylacrylamide (NIPAM) was purified by recrystallization in a benzene/*n*-hexane (v/v = 35/65) mixture. Narrowly distributed monohydroxyl poly(ethylene oxide) (PEO) ($M_w = 5000$ g/mol, $M_w/M_n = 1.14$) from Fluka was used as received. Potassium persulfate (KPS) was purified by recrystallization in water. Other chemicals were used without further purification. In the preparation of PEO macromonomers end-capped with methacrylate, PEO with a hydrophilic (–OH) end was dissolved in anhydrous dichloromethane. An excess amount of methacryloyl chloride was added dropwise to convert the –OH chain end to a methacrylic-terminated one. Triethylamine was added to remove HCl produced. The resultant salt was removed by filtration and further absorption of Al_2O_3 .

The grafting of PEO onto poly(*N*-isopropylacrylamide) was done by free radical copolymerization of *N*-isopropylacrylamide monomer with the PEO macromonomer in water at 29 and 21°C , respectively. The reaction was conducted in a 250-mL two-neck flask equipped with a nitrogen inlet tube and a magnetic stirrer. Amounts of 19 mmol of NIPAM and 0.12 mmol of PEO macromonomer were added to 180 mL of deionized water. The KPS/*N,N,N',N'*-tetramethylethylenediamine (TEMED) redox was used as initiator. The molar ratio of KPS/TEMED was 1:1. The KPS and TEMED were dissolved in water with concentrations 15.2 and 76 mM respectively. A 5-mL KPS solution was added into the reaction mixture. The solution was repeatedly degassed at 20°C and then purged with nitrogen for 0.5 h before reaction. After the mixture was heated to reaction temperature, 1 mL of TEMED solution was added and the reaction was carried out at this temperature for 60 min in a water bath. The PNIPAM-*g*-PEO copolymer was purified in dialysis (with cutoff 8000) in a large amount of water. The final product was dried under reduced pressure at 40°C . ^1H NMR (BRUKER DPX-400 spectrometer) and laser light scattering (LLS) were used to characterize the resultant copolymers using the area ratio of the two peaks located at 3.63 and 4.00 ppm. The weight-average molar mass (M_w), the z -average root-mean square radius of gyration (R_g), and the average hydrodynamic radius (R_h) of the copolymer were measured in dilute solution (2×10^{-5} g/mL). Table 1 summarizes the characteristics of PNIPAM-*g*-PEO copolymers in detail.

2.2. Viscosity measurements

The viscosity measurements were carried out with a precision of 0.1°C using a conventional Ubbelohde viscometer that was placed in a thermostatically controlled water bath. At each temperature the samples were equilibrated for 30 min before

Table 1
Characteristics of poly(*N*-isopropylacrylamide)-*g*-PEO copolymers

Samples	$T_{\text{synthesized}}$ (°C)	M_w^a (g/mol)	[NIPAM]/ [PEO] ^b	N_{PEO}	$\langle R_g \rangle$ (nm)	$\langle R_h \rangle$ (nm)
a	21	4.5×10^6	260	131	167.1	103.5
b	29	6.4×10^6	213	220	175.4	115.6

^a Measured by LLS at 25 °C.

^b [NIPAM]/[PEO] refers to number ratio of NIPAM monomers to PEO and measured by ¹H NMR.

measurement. The flow time of the pure water, namely t_0 was measured using a thoroughly cleaned viscometer and the flow time of the copolymer–water solution at concentration C was t , so that the reduced viscosity was calculated from

$$\frac{\eta_{\text{sp}}}{C} = \frac{(t/t_0) - 1}{C}. \quad (1)$$

3. Results and discussion

Fig. 1 shows the temperature dependence of reduced viscosities of two copolymers in different concentrations. The results reveal that the reduced viscosity decreased gradually with temperature before reaching two samples' LCST. Such great decrease in viscosity could not be caused by thermomotion of polymer chains alone. It is worth noting that the relative value of the decrease during this stage is decreased as the concentration is lowered. And combining our recent LLS studies (to be shown later), the total scattering light intensity of the solution increased gradually during this stage; this great decrease in viscosity, especially of higher concentration, is attributed to disentanglement of the chains induced by gradual shrinking of PNIPAM chains. However, the temperature dependence of the reduced viscosities above LCST in different concentrations is complicated. At 6 and 10 g/L, the reduced viscosity increased sharply with temperature, forming thermothickening behavior and revealing the formation of “cross-linking points” composed of collapsed PNIPAM core and expanded PEO shell. When we increased the concentration to 30 g/L, a physical gel was formed at 37 °C, confirmed by inverting the tube as shown in the inserts. Then at 3.0 and 2.0 g/L, the reduced viscosity decreased sharply with temperature, revealing the forming of independent globules with PNIPAM core and PEO shell [27]. At 3.0 g/L, another noticeable phenomenon is that the reduced viscosity is nearly unchanged with temperature when the system is close to its LCST from low temperature; namely a plateau was observed in the curve giving the viscosity as a function of temperature. To our knowledge, this characteristic transition was first observed by viscosity measurements. The plateau of viscosity around the transition temperature of PNIPAM-*g*-PEO copolymer in semidilute aqueous solution was attributed to the competition between forming physical “cross-linking points” and independent globules.

To explain the forming of physical “cross-linking points” or independent globules in detail, a scheme is given shown in Fig. 2. When concentration is high enough, copolymer chains entangle with each other. When heated, the PNIPAM backbone chains collapse. Both the hydrophilic PEO located on the

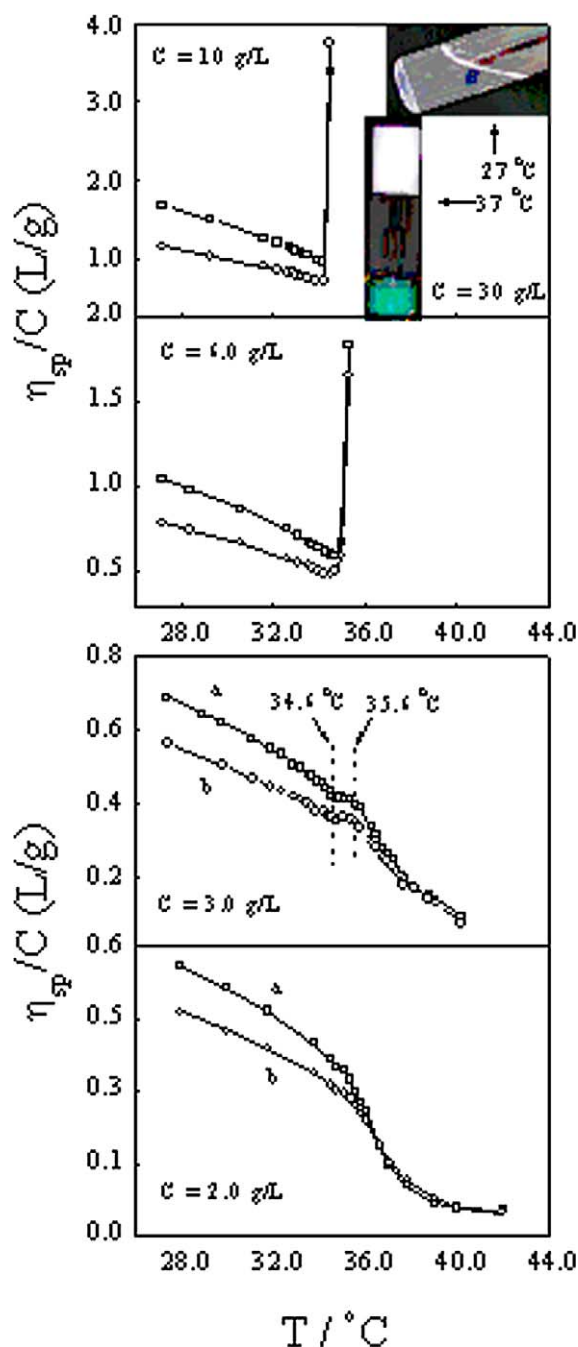


Fig. 1. Temperature dependence of reduced viscosities of PNIPAM-*g*-PEO copolymers prepared at 21 °C (a) and 29 °C (b) in semidilute aqueous solutions.

periphery of the collapsed PNIPAM globule and the entanglements of the copolymer chains will prevent further aggregation and form physical “cross-linking points,” which makes the viscosity increase greatly at higher temperatures. As the concentration decreases, the entanglement weakens, so it is beneficial to the formation of independent globules, which decreases the viscosity of the solution greatly. The two strengths will compete with each other at a certain concentration, C_0 . The equilibrium competition between them may be attributed to the appearance of the plateau in the curve from viscosity measurement.

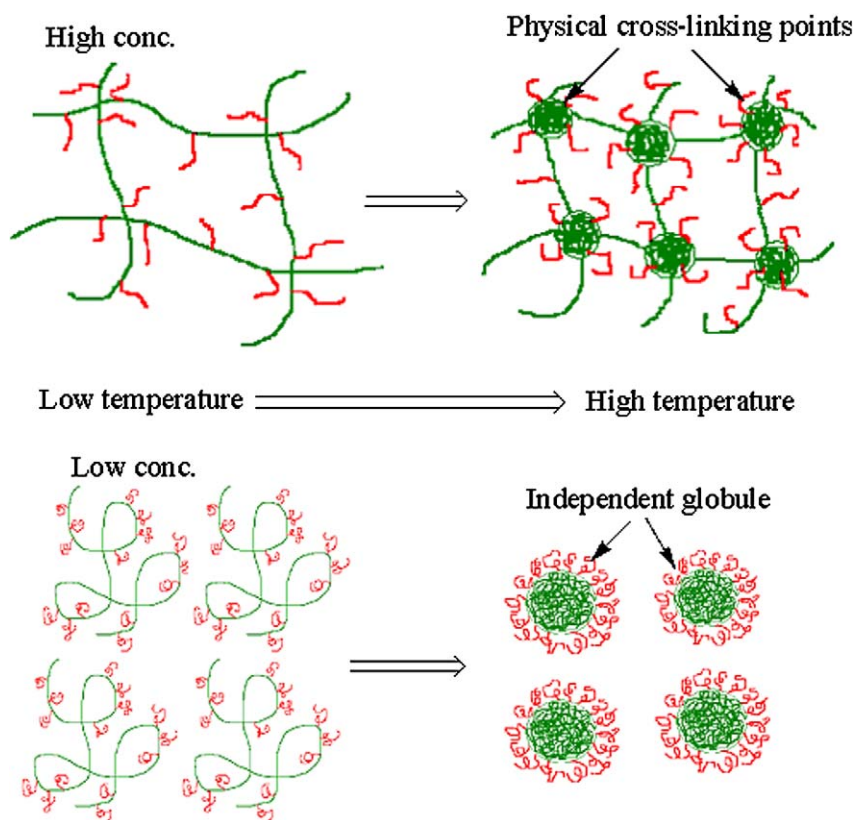


Fig. 2. Schematic of formation of physical “cross-linking points” and independent globule of PNIPAM-g-PEO copolymer chains in semidilute aqueous solutions above and below a certain concentration; curve in green represents PNIPAM backbone and curve in red represents PEO chain.

4. Conclusions

In summary, a specific transition was observed during the measurement of the reduced viscosities of PNIPAM-g-PEO copolymer in semidilute aqueous solution at different temperatures. The inversely increase of the viscosities at higher temperatures in higher concentration (6 g/L) is attributed to the forming of the physical “cross-linking points.” And the thermo-induced physical gelation of an aqueous solution (30 g/L) of PNIPAM-g-PEO copolymer at 37 °C was attributed to the forming of the “cross-linking points.” The sharp decrease of the viscosities at higher temperatures in lower concentration (3 g/L) is attributed to the formation of independent globules. The plateau could be attributed to the equilibrium competition between formation of physical “cross-linking points” and independent globules, depending on the copolymer solution concentrations.

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