Formation of Mesoglobular Phase of PNIPAM-*g*-PEO Copolymer with a High PEO Content in Dilute Solutions

Hongwei Chen,[†,§] Qijin Zhang,[*,†] Junfang Li,[§] Yanwei Ding,[†] Guangzhao Zhang,[*,‡,§] and Chi Wu[*,‡,§,⊥]

Structure Research Laboratory, Department of Polymer Science and Engineering, University of Science and Technology of China, Hefei, Anhui, China; Department of Chemical Physics, University of Science and Technology of China, Hefei, Anhui, China; Hefei National Laboratory for Physical Sciences at Microscale, Hefei, Anhui, China; and Department of Chemistry, The Chinese University of Hong Kong, Shatin, N. T., Hong Kong

Received May 12, 2005; Revised Manuscript Received June 29, 2005

ABSTRACT: Free radical copolymerization of *N*-isopropylacrylamide (NIPAM) and poly(ethylene oxide) (PEO) macromonomer (M_w = 5000) end-capped with methacrylate in water at 45 °C, higher than PNIPAM's lower critical solution temperature (~32 °C), resulted in (PNIPAM-*g*-PEO) copolymer with 48 wt % of PEO. As expected, the grafting of PEO on the PNIPAM chain backbone was heterogeneous because PEO is hydrophilic and stayed on the periphery of the PNIPAM segments collapsed at the reaction temperature. The copolymer is soluble in water at lower temperatures. When the solution temperature is raised to ~34 °C, a limited number of the copolymer chains can collapse and associate to form stable narrowly distributed mesoglobules with a collapsed PNIPAM core and a swollen PEO shell, different from either individual single-chain globules or macroscopic precipitation. The formation of such mesoglobules was studied by a combination of static and dynamic laser light scattering. We found that the mesoglobular formation has two transition stages, occurring at ~34 and ~47 °C. The transition at ~34 °C is related to the contraction of the PNIPAM segment between two grafted PEO chains. The high-temperature transition is attributed to the stretch and collapse of the grafted PEO chains on the periphery. The fast heating generally resulted in smaller mesoglobules, which is due to a competition between intrachain contraction and interchain association as well as the viscoelastic effect.

Introduction

It is well-known that polypeptide or protein chains can assemble and associate into stable quaternary structures without macroscopic precipitation under a proper condition.[1] Biological functions of a protein or peptide chain are intimately related to its chain folding and assembly, depending not only on its primary structure but also on some complex interaction among its residues or even its initial conformation (starting point).[2] The aggregation of a limited number of protein chains can be induced by a variation of different experimental conditions, such as temperature, salt concentration, pH, and cosolvent.[3−7] Polymer researchers have tried to prepare protein-like copolymer chains made of hydrophilic and hydrophobic comonomers in both computer simulation and real experiments.[8−11] In dilute heteropolymer solutions, a limited number of such chains could also collapse and associate to form stable mesoglobules, which exist between individual single-chain globules and macroscopic precipitation.[12−18] Timoshenko et al.[12−14] explained the stability of such mesoglobules on the basis of an extended version of the Gaussian variational theory and determined the histograms of its size distributions by lattice Monte Carlo simulation. Siu et al.[15,16] studied the effects of both comonomer distribution and composition on the formation of such mesoglobules made of amphiphilic thermally sensitive copolymers P(NIPAM-*co*-VP) and P(DEA-*co*-DMA) in dilute aqueous solutions. They found that P(NIPAM-*co*-VP) with a segmented VP distribution aggregated more readily to form smaller mesoglobules with a core−shell structure than its counterpart with a random VP distribution.[15] The higher content of hydrophilic DMA could lead to the formation of mesoglobules with a larger aggregation number.[16] On the other hand, Wu et al.[17,18] found some unexpected results; namely, copolymerizing more hydrophobic comonomers on a thermally sensitive PNIPAM chain backbone could lead to less aggregation and smaller mesoglobules at higher temperatures in dilute aqueous solutions. These unexpected results were attributed to the viscoelastic effect. Moreover, Qiu et al.[19] revealed that the fast heating could suppress interchain aggregation and lead to smaller aggregates or even to individual single-chain core−shell nanoparticles. Itakura et al.[20] studied the effect of solvent composition on the association of poly(*N*,*N*-dimethylacrylamide)-*g*-poly(methyl methacrylate) (PDMA-*g*-PMMA) in a methanol/water mixture and found that a quick change of the solvent quality from good to poor could also lead to smaller aggregates with a unimodal size distribution, while a slow change of the solvent quality resulted in larger aggregates with a bimodal size distribution. Grinberg et al.[21] used DSC to study the heating rate dependence of the transition temperature, the enthalpy change, and the half-width of the transition involved in the collapse of PNIPAM gels in a dispersion and found that these parameters were linearly dependent on the heating rate.

Following up a previous study on the intrachain coil-to-globule transition of individual PNIPAM-*g*-PEO chains in extremely dilute solutions, we extended the present

[†] Department of Polymer Science and Engineering, University of Science and Technology of China.
[‡] Department of Chemical Physics, University of Science and Technology of China.
[§] Hefei National Laboratory for Physical Sciences at Microscale.
[⊥] The Chinese University of Hong Kong.
* The Hong Kong address should be used for correspondence.

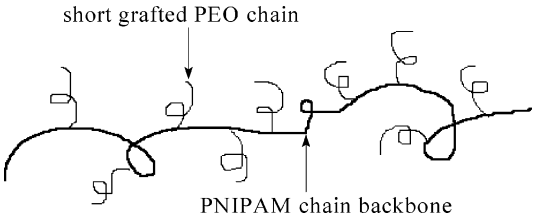
10.1021/ma050994j CCC: $30.25
Published on Web 08/19/2005

study to the interchain association, namely the formation of stable mesoglobules. It has been known that PNIPAM-*g*-PEO chains with a high PEO content can be prepared by free radical copolymerization of *N*-isopropylacrylamide and poly(ethylene oxide) macromonomer end-capped with an active group in water at a temperature (45 °C) higher than the lower critical solution temperature (LCST) of PNIPAM. As expected, short hydrophilic PEO chains are heterogeneously grafted on the PNIPAM chain backbone because the PNIPAM segment becomes hydrophobic and collapses at temperatures higher than its LCST. The formation of stable mesoglobules can be generally explained on the basis of a competition between intrachain contraction and interchain association during the phase transition.

Experimental Section

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 in water. Other chemicals were used without further purification. In the preparation of the PEO macromonomers end-capped with methacrylate, PEO with 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. The macromonomers were recovered by further purification. The details of the synthesis can be found elsewhere.[22]

Short PEO chains grafted on poly(*N*-isopropylacrylamide) by free radical copolymerization of *N*-isopropylacrylamide monomer with the PEO macromonomer in water at 45 °C. The reaction was conducted in a 250 mL two-necked flask equipped with a nitrogen inlet tube and a magnetic stirrer. 22 mmol of NIPAM and 0.22 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 6.6 and 33 mM, respectively. 5 mL of 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 reaction mixture was heated to 45 °C, 1 mL of TEMED solution was added, and the reaction was carried out at this temperature for 45 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. The copolymer was further fractionated by precipitation from an acetone solution to *n*-hexane at 35 °C. The fraction was characterized by LLS and ^{1}H NMR (Bruker DPX-400 spectrometer). The ^{1}H NMR of the copolymer is shown in Figure 1. The detailed assignment of each proton is consistent with the expected copolymer structure. By using the area ratio of the two peaks located at 3.63 and 4.00 ppm, it is estimated that the weight percentage of PEO in the copolymer is 48 ± 2 wt %. Therefore, the copolymer chains actually have a branched conformation as follows.



Laser Light Scattering. A commercial LLS spectrometer (ALV/DLS/SLS-5022F) equipped with a multi-tau digital time correlation (ALV5000) and a cylindrical 22 mW He−Ne laser (λ_0 = 632 nm, UNIPHASE) as the light source was used. In static LLS,[23] we can obtain the weight-average molar mass (M_w) and the *z*-average root-mean-square radius of gyration ($\langle R_g^2\rangle^{1/2}$or written as $\langle R_g\rangle$) of scattering objects in a dilute solution or dispersion from the angular dependence of the excess scattering intensity, known as Rayleigh ratio $R_{vv}(q)$, as

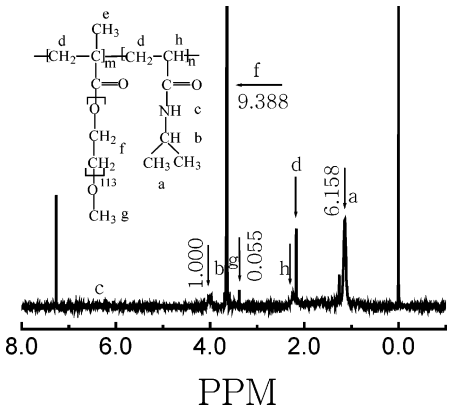


Figure 1. Typical ^{1}H NMR spectrum of PNIPAM-*g*-PEO in $CDCl_3$ at 25 °C, where every number represents the peak area of each corresponding proton.

$$\frac{KC}{R_{vv}(q)} \approx \frac{1}{M_w}\left(1 + \frac{1}{3}\langle R_g^2\rangle q^2\right) + 2A_2C \qquad (1)$$

where $K = 4\pi n^2(dn/dC)^2/(N_A\lambda_0^4)$ and $q = (4\pi n/\lambda_0)\sin(\theta/2)$ with N_A, dn/dC, n, and λ_0 being the Avogadro number, the specific refractive index increment, the solvent refractive index, and the wavelength of the light in a vacuum, respectively, and A_2 is the second virial coefficient. In this study, the solution was so dilute that the extrapolation of $C \rightarrow 0$ was not necessary, and the second term in eq 1 $2A_2C$ could be dropped.

In dynamic LLS,[24] the Laplace inversion (we used the CONTIN method in the correlator) of each measured intensity−intensity time correlation function $G^{(2)}(q,t)$ in the self-beating mode can lead to a line-width distribution $G(\Gamma)$. For a diffusive relaxation, Γ is related to the translational diffusion coefficient D by $(\Gamma/q^2)_{C\rightarrow 0, q\rightarrow 0} \rightarrow D$, so that $G(\Gamma)$ can be converted into a transitional diffusion coefficient distribution $G(D)$ or further a hydrodynamic radius distribution $f(R_h)$ via the Stokes−Einstein equation, $R_h = (k_BT/6\pi\eta)/D$, where k_B, T, and η are the Boltzmann constant, the absolute temperature, and the solvent viscosity, respectively. Note that for a broadly distributed sample the average $\langle R_h\rangle$ (= $(k_BT/6\pi\eta)\langle 1/D\rangle$) is different from $(k_BT/6\pi\eta)/\langle D\rangle$. Such a common mistake should be avoided. In this study, the resultant mesoglobules are narrowly distributed with a relative width no more than 10%. The cumulant analysis of $G^{(2)}(t)$ of a narrowly distributed sample can actually result in an accurate average line width ($\langle\Gamma\rangle$) with a sufficient accuracy. The copolymer solution (2.0×10^{-5} g/mL) was clarified with a 0.45 μm Millipore Millex-LCR filter to remove dust.

Micro-Differential Scanning Calorimetry (Micro-DSC). The copolymer solution was measured by a VP-DSC microcalorimeter (MicroCal Inc.) at an external pressure of ~180 kPa. The cell volume was 0.157 mL. The instrument response time was set at 5.6 s. All the micro-DSC data were corrected for instrument response time and analyzed using the software in the calorimeter. The polymer concentration used in DSC was kept at 1.0 mg/mL, much higher than those used in laser light scattering.

Results and Discussion

Figure 2 shows a typical temperature dependence of the apparent weight-average molar mass ($M_{w,app}$) of the copolymer chains or resultant mesoglobules in one heating-and-cooling cycle. Note that each data point was

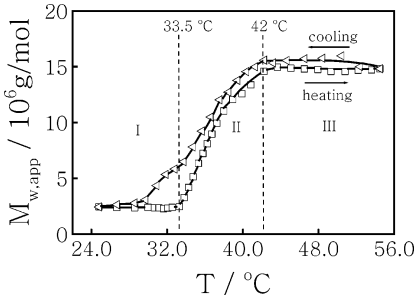


Figure 2. Temperature dependence of apparent weight-average molar mass ($M_{w,app}$) of PNIPAM-*g*-PEO copolymer chains or resultant mesoglobules in water in one heating-and-cooling cycle, where the copolymer concentration was 2.0×10^{-5} g/mL.

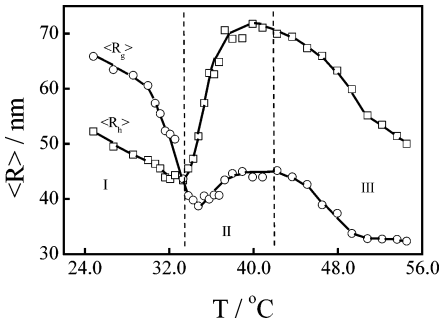


Figure 3. Temperature dependence of average radius of gyration ($\langle R_g \rangle$) and average hydrodynamic radius ($\langle R_h \rangle$) of PNIPAM-*g*-PEO copolymer chains or resultant mesoglobules in water in a heating process.

obtained after the solution temperature reached its equilibrium. Let us first examine the heating effect. An abrupt increase of $M_{w,app}$ at ~33 °C clearly reveals the interchain association. At ~42 °C, $M_{w,app}$ approaches a constant, indicating that interchain association stops and stable mesoglobules are formed. On the basis of this constant value (1.5×10^7 g/mol) and the average molar mass of individual PNIPAM-*g*-PEO chains (2.4×10^6 g/mol), we estimated that each mesoglobule was, on average, consisting of six copolymer chains. In comparison with the study of the PNIPAM-*g*-PEO chains with a much lower grafting density in a similar aqueous solution,[25] we found that the PEO content has less influence on the coil-to-globule transition temperature, revealing that for the copolymer chains prepared at higher temperatures the transition temperature is mainly determined by the PNIPAM chain backbone.[26] On the other hand, Tenhu et al.[10,11] found that the copolymer chains synthesized at different temperatures had different transition temperatures; namely, the copolymer chains prepared at temperatures lower than the LCST (~32 °C) of PNIPAM have randomly distributed PEO chains and a higher transition temperature.

Figure 3 shows the temperature dependence of both $\langle R_g \rangle$ and $\langle R_h \rangle$ of the copolymer chains or resultant mesoglobules in water during the heating. Also, note that each data point was obtained after the solution temperature reached its equilibrium. The change of $\langle R_g \rangle$ and $\langle R_h \rangle$ can be divided into three regions. A combination of Figures 2 and 3 shows that in region I (25−33.5 °C) the copolymer chains undergo intrachain contraction because $M_{w,app}$ remains a constant; in region II (33.5−42 °C), interchain association starts, but it competes with intrachain contraction, reflecting in the increases of $M_{w,app}$ and $\langle R_h \rangle$; in region III (>42 °C), interchain association nearly stops, but intrachain contraction

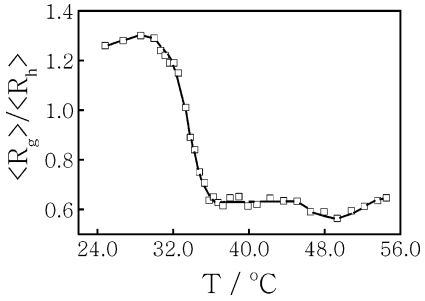


Figure 4. Temperature dependence of $\langle R_g \rangle / \langle R_h \rangle$ of PNIPAM-*g*-PEO copolymer chains or resultant mesoglobules in water in a heating process, where $\langle R_g \rangle$ is the average radius of gyration and $\langle R_h \rangle$ is the average hydrodynamic radius.

inside each mesoglobule continues, as evidenced by a constant value of $M_{w,app}$ and the decreases of $\langle R_g \rangle$ and $\langle R_h \rangle$.

In comparison with the PNIPAM-*g*-PEO chains with a relatively low PEO content[25] or a randomly distributed PEO chains,[27] the temperature dependence observed here is different, which should be related to the unevenly distributed high PEO content. It is interesting to note that when $T > 50$ °C, $\langle R_g \rangle$ approaches a constant, but $\langle R_h \rangle$ continually decreases. This could be attributed either to the shrinking of small intrachain contraction induced PNIPAM loops on the periphery or to the *n*-clustering induced collapse of the stretched PEO chains in the shell because the density of PEO chains in the shell is as high as 0.056 g/cm^3.

To have a better view of such a chain conformation change, we plot the temperature dependence of $\langle R_g \rangle / \langle R_h \rangle$ in Figure 4. At room temperature, where water is a fairly good solvent for PNIPAM and PEO, $\langle R_g \rangle / \langle R_h \rangle$ is ~1.25, instead of ~1.5 for linear flexible coil chains, because of the branched chain structure. The slight increase of $\langle R_g \rangle / \langle R_h \rangle$ in the range 25−30 °C could be attributed to the increase of chain stiffness because of the shrinking of every PNIPAM segment between two grafted PEO chains. The decrease of $\langle R_g \rangle / \langle R_h \rangle$ from ~1.3 to ~0.6 reflects the collapse of the PNIPAM chain backbone from an extended coil conformation to a collapsed compact globule because the average chain density ($\langle \rho \rangle$), defined as $M_{w,app}/(4\pi \langle R_h \rangle^3 N_A/3)$, increases ~10 times. It is helpful to note that $\langle R_g \rangle / \langle R_h \rangle$ of a uniform solid sphere is ~0.774. The lower $\langle R_g \rangle / \langle R_h \rangle$ ratio can be related to a core−shell nanostructure with a dense core and a loose shell. As expected, when the temperature is higher than ~32 °C, every PNIPAM segment between two grafted PEO chains collapse, which forces the soluble PEO chains to stay on the periphery of the collapsed PNIPAM core to form a swollen PEO shell. The collapsed PNIPAM core has a higher chain density than the swollen PEO shell so that such a core−shell structure has a smaller $\langle R_g \rangle$ than a uniform sphere. This explains why $\langle R_g \rangle / \langle R_h \rangle$ is lower than 0.774.

In the temperature range 35−45 °C, $\langle R_g \rangle / \langle R_h \rangle$ is nearly a constant, reflecting that both the densities of the PNIPAM core and the PEO shell increase in a similar fashion. The decrease and increase of $\langle R_g \rangle / \langle R_h \rangle$ in the temperature range 45−55 °C could be attributed to the steric-repulsion induced stretching, followed by the *n*-cluster-induced shrinking of the PEO chains. This is because the continuous shrinking of the PNIPAM core increases the density of the PEO chains on the periphery. It is known that the PEO chains have a hydrody-

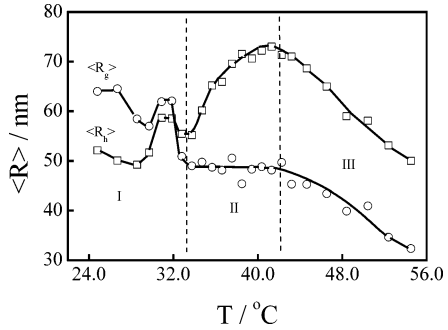


Figure 5. Temperature dependence of average radius of gyration ($\langle R_g \rangle$) and average hydrodynamic radius ($\langle R_h \rangle$) of PNIPAM-*g*-PEO copolymer chains or resultant mesoglobules in water in a cooling process.

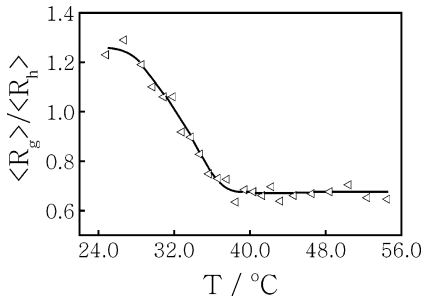


Figure 6. Temperature dependence of $\langle R_g \rangle / \langle R_h \rangle$ of PNIPAM-*g*-PEO copolymer chains or resultant mesoglobules in water in a cooling process, where $\langle R_g \rangle$ is the average radius of gyration and $\langle R_h \rangle$ is the average hydrodynamic radius.

namic radius of ~2−3 nm or a cross section of ~30 nm^2.[25] The average surface area per PEO chain estimated on the basis of the aggregation number, the average size of mesoglobules, and the PEO content at ~49 °C is ~25 nm^2, smaller than the cross section of the PEO chain free in water. The stretching of the PEO chains in the shell and the collapse of the PNIPAM chain backbone in the core compete with each other. The slight decrease of $\langle R_g \rangle / \langle R_h \rangle$ indicates that the stretching of the PEO chains is dominant at this stage, which results in a decrease in the shell density. The slight increase of $\langle R_g \rangle / \langle R_h \rangle$ at higher temperatures can be attributed to the *n*-clustering induced collapse of the PEO chains and the increase of the shell density.

Figure 5 shows the complicated temperature dependence of both $\langle R_g \rangle$ and $\langle R_h \rangle$ of the copolymer chains or the resultant mesoglobules in water during the cooling process. Again note that each data point was obtained after the solution temperature reached its equilibrium. The change can also be divided into three regions as those in Figures 2 and 3. In region III, both the PNIPAM core and the PEO shell swell, but no dissolution of the mesoglobules during the cooling of the solution from ~54 to ~41 °C because there was no change in $M_{w,app}$, as shown in Figure 2. On the other hand, Figure 6 shows that $\langle R_g \rangle / \langle R_h \rangle$ is nearly a constant in this region, indicating a uniform swelling of the mesoglobules. In region II, the decrease of $M_{w,app}$ in Figure 2 reveals the dissolution of the chains from each mesoglobule. As expected, the swelling of the chains inside each mesoglobule is continuous as the temperature decreases.

However, it is interesting to note that in this region $\langle R_g \rangle$ remains nearly a constant, but $\langle R_h \rangle$ decreases. This can be explained as follows. The dissolution decreases both $\langle R_g \rangle$ and $\langle R_h \rangle$. One the other hand, the swelling increases $\langle R_g \rangle$ but leads to a decrease in $\langle R_h \rangle$ because a

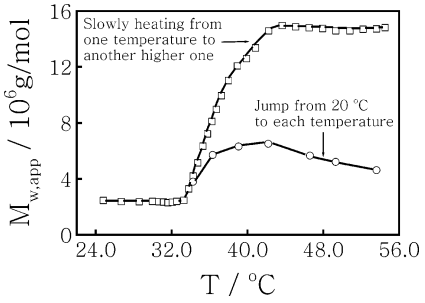


Figure 7. Temperature dependence of apparent weight-average molar mass ($M_{w,app}$) of PNIPAM-*g*-PEO copolymer chains or resultant mesoglobules in water under different heating rates.

swollen mesoglobule is more draining. The two effects are opposite to each other for $\langle R_g \rangle$ but have the same influence on $\langle R_h \rangle$. This is why $\langle R_h \rangle$ decreases sharply. Further, in the temperature range 34−31 °C, the swelling becomes so dominant that both $\langle R_g \rangle$ and $\langle R_h \rangle$ increase, but $M_{w,app}$ only slightly depends on the temperature, as shown in Figure 2. It seems that the dissolution of the chains from the center of the core is more difficult than those near the periphery. In the range 31−29 °C, water becomes a good solvent for PNIPAM so that both $\langle R_g \rangle$ and $\langle R_h \rangle$ decrease. When the temperature is lower than ~29 °C, the mesoglobules are completely dissolved into individual chains in water. The increase of both $\langle R_g \rangle$ and $\langle R_h \rangle$ can be attributed to the swelling of individual copolymer chains.

Figure 7 shows the heating rate dependence of $M_{w,app}$ of the copolymer chains or the resultant mesoglobules. When the temperature is higher than 34 °C, the copolymer chains start to associate to form stable mesoglobules. In general, the fast heating leads to smaller mesoglobules. The maximum $M_{w,app}$ occurs at a similar temperature (~42 °C) despite the heating rate. First, let us explain why the fast heating could lead to smaller mesoglobules. The mesoglobule formation involves a competition between intrachain contraction and interchain association. On the other hand, it also involves the formation of a hydrophobic PNIPAM core and a hydrophilic PEO shell. For homopolymer, Tanaka[30,31] and Picarra et al.[32] showed that the collision of small polymer aggregates ("particles") would not be effective to lead a merge of them together if the collision (or contact) time (τ_c) is much shorter than the entanglement time (τ_e) of the chains inside two approaching "particles". Quantitatively, Tanaka[30,31] showed that τ_c and τ_e could be roughly estimated as

$$\tau_e \sim \frac{\alpha_m^{\,2} N_m^{\,3} \varphi_p^{\,3/2}}{D_m} \qquad (2)$$

where r_0 is the interaction range, $\langle v \rangle$ is the particle average thermal velocity, $\langle D \rangle$ is the average transition diffusion coefficient of the particles, φ_p is the local concentration of the chains inside each particle, and α_m, N_m, and D_m are the length, number, and translation diffusion coefficient of the monomer, respectively. α_m, N_m, and D_m are constants for a given polymer solution. The formation of stable mesoglobules can be mainly attributed to the PEO shell, which greatly decreases the interaction range r_0. In the fast heating, intrachain contraction becomes so dominant that the resultant mesoglobules on average are smaller and contain a few copolymer chains inside, as shown in Figures 7 and 8.

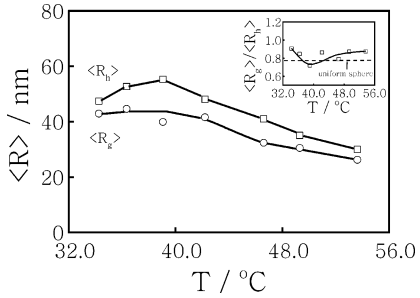


Figure 8. Temperature dependence of average radius of gyration ($\langle R_g \rangle$) and average hydrodynamic radius ($\langle R_h \rangle$) of PNIPAM-*g*-PEO copolymer chains or resultant mesoglobules in water, where the solution temperature was abruptly changed from 20 °C to each measured temperature.

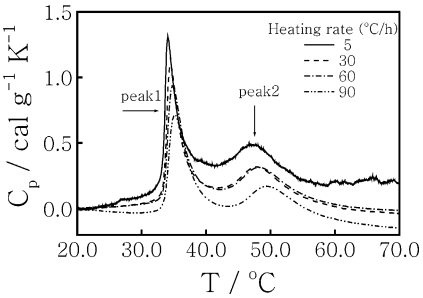


Figure 9. Temperature dependence of partial heat capacity (C_p) of PNIPAM-*g*-PEO copolymer chains or resultant mesoglobules in water under different heating rates.

Small particles have a larger $\langle D \rangle$ so that τ_c is shorter. At the same time, the fast intrachain contraction also sharply increases φ_p so that τ_e becomes much longer. Note that in the fast heating φ_p reaches 22 wt %, while in the slow heating φ_p is only 15 wt %. This leads to $\tau_c < \tau_e$ so that further interchain association becomes more difficult.

Next, let us explain why there exists a maximum $M_{w,app}$. We can definite $\Delta T = T_{final} - T_{LCST}$. ΔT represents the quenching depth. When ΔT is small, the solution is in the metastable region so that the mesoglobules grow with time. When ΔT is sufficiently large, the solution undergoes the phase separation, and the copolymer chains inside each mesoglobule are in such a collapsed state that τ_e becomes much longer than τ_c. Further interchain association becomes impossible. Further decreases of both $\langle R_g \rangle$ and $\langle R_h \rangle$ in Figure 8 at $T > 42$ °C are due to intrachain contraction inside each mesoglobule. The inset shows that $\langle R_g \rangle / \langle R_h \rangle$ is around 0.8 ± 0.1, much larger than that in Figure 4 in the same temperature range, which indicates that the mesoglobules formed in the fast heating have a more uniform density. Presumably, this can be related to the entrapping of some PEO chains inside the core because they have no chance or time to rearrange themselves on the periphery during the coil-to-globule transition in the fast heating. In the cooling process, the continuous increases of $\langle R_g \rangle$, $\langle R_h \rangle$, and $\langle R_g \rangle / \langle R_h \rangle$ (not shown) of the mesoglobules formed in the fast heating also support our conclusion that the fast heating leads to more uniform mesoglobules.

Figure 9 shows the heating rate dependence of partial heat capacity (C_p) of the copolymer aqueous solution in the heating process. There are two endothermic peaks located at ~34 and ~47 °C. The low-temperature peak (peak 1) is due to the collapse of the PNIPAM chain backbone, while the high-temperature peak (peak 2) is

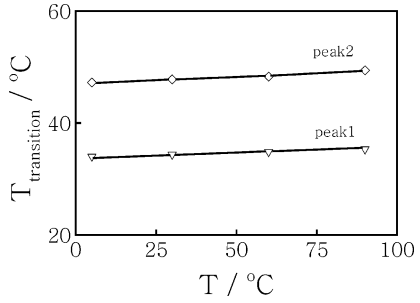


Figure 10. Heating rate dependence of transition temperatures of peak 1 and peak 2, as indicated in Figure 9.

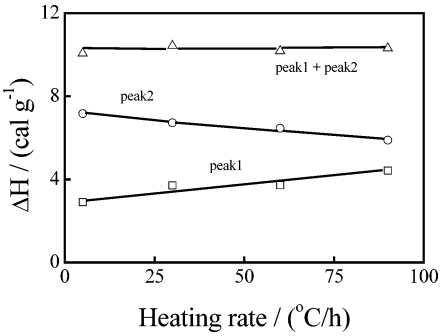


Figure 11. Heating rate dependence of endothermic heat (ΔH) related to peak 1, peak 2, and their sum (total endothermic heat).

related to the stretching and collapsing of the PEO chains grafted on the chain backbone. This is because interchain association already stops in this high-temperature range, and the contraction of the PNIPAM segments inside the mesoglobule reduces the surface area and forces the PEO chains on the periphery to stretch and overlap. We know that linear and flexible polymer chains in bulk are coiled and in the θ state. The overlapping of the PEO chains forces water out and increases the local PEO concentration. Up to a certain point, the PEO chains are coiled (collapsed) again, but by a different reason in comparison with they are in a good solvent (water at lower temperatures).

Figure 10 shows that both the peak positions shift to higher temperatures and the shift of the peak position is linear with the heating rate. This is expected because the conformational changes of both the PNIPAM chain backbone and the grafted PEO side chains are lagged behind the temperature sweeping in the heating process. Defining the area under each peak as the total endothermic heat (ΔH) associated with each transition, we obtained the heating rate dependence of ΔH in Figure 11. $(\Delta H)_{peak1}$ increases while $(\Delta H)_{peak2}$ decreases. The faster the heating rate, the more the PEO chains are entrapped inside the PNIPAM core. This makes the collapse of the core more difficult and requires an additional energy. At the same time, fewer PEO chains on the periphery also reduce the energy required for the corresponding stretching-and-collapsing transition. The results of micro-DSC and LLS support each other.

Conclusion

Grafting short poly(ethylene oxide) (PEO) chains (48 wt %) on the periphery of the collapsed poly(*N*-isopropylacrylamide) (PNIPAM) chain backbone in free radical copolymerization of NIPAM and PEO at a temperature higher than the lower critical solution temperature (LCST) of PNIPAM can lead to an unevenly distributed

PEO chains on a resultant PNIPAM-*g*-PEO copolymer. The heating-induced association and the cooling-induced dissolution of such copolymer chains in dilute aqueous solution can be well studied by using a combination of static and dynamic laser light scattering (LLS) as well as micro-differential calorimetry (micro-DSC). At temperatures higher than (~34 °C), such copolymer chains can form stable core−shell mesoglobules with a collapsed PNIPAM core and a swollen PEO shell existing between single-chain globules and macroscopic precipitation. The faster the heating rate, the smaller the resultant mesoglobules are. This can be attributed to a competition between intrachain contraction and interchain association as well as the viscoelastic effect described by Tanaka for homopolymer chains.[30,31] Both the LLS and micro-DSC results reveal that the formation of such mesoglobules at temperatures much higher than the LCST involves two different transitions, namely, the coil-to-globule transition (contraction or collapse) of the PNIPAM chain backbone at a lower temperature (~34 °C) and the steric repulsion-induced stretching followed by the *n*-clustering-induced collapse of the PEO chains at a higher temperature (~47 °C). If the heating rate is too fast, some of the grafted PEO chains are entrapped inside the PNIPAM core so that the mesoglobules become more uniform, and the collapse of the core is relatively more difficult.

Acknowledgment. The financial support of the National Natural Science Foundation of China (20274045, 50025309, and 90201016) and the Research Grants Council of the Hong Kong Special Administration Region Earmarked Grant 2003/04 (CUHK4029/03P, 2160206) is gratefully acknowledged.

References and Notes

(1) Stryer, L. *Biochemistry*, 3rd ed.; W.H. Freeman: New York, 1988.
(2) Leach, A. R. *Molecular Modeling*; Longman: United Kingdom, 1996.
(3) Broide, M. L.; Tominc, T. M.; Saxowsky, M. D. *Phys. Rev. E* **1996**, *53*, 6325.
(4) Gast, K.; Zirwer, D.; Damaschun, G. *Eur. Biophys. J.* **2003**, *31*, 586.
(5) Shastry, M. C. R.; Udgaonkar, J. B. *J. Mol. Biol.* **1995**, *247*, 1013.
(6) Beretta, S.; Chirico, G.; Baldini, G. *Macromolecules* **2000**, *33*, 8663.
(7) Aymard, P.; Nicolai, T.; Durand, D.; Clark, A. *Macromolecules* **1999**, *32*, 2542.
(8) Khokhlov, A. R.; Khalatur, P. G. *Physica A* **1998**, *249*, 253.
(9) Khokhlov, A. R.; Khalatur, P. G. *Phys. Rev. Lett.* **1999**, *82*, 3456.
(10) Virtanen, J.; Baron, C.; Tenhu, H. *Macromolecules* **2000**, *33*, 336.
(11) Virtanen, J.; Tenhu, H. *Macromolecules* **2000**, *33*, 5970.
(12) Timoshenko, E. G.; Kuznetsov, Y. A. *J. Chem. Phys.* **2000**, *112*, 8163.
(13) Timoshenko, E. G.; Basovsky, R.; Kuznetsov, Y. A. *Colloids Surf., A* **2001**, *190*, 129.
(14) Timoshenko, E. G.; Kuznetsov, Y. A. *Europhys. Lett.* **2001**, *53*, 322.
(15) Siu, M.; Liu, H. Y.; Zhu, X. X.; Wu, C. *Macromolecules* **2003**, *36*, 2103.
(16) Siu, M.; Cheng, H.; Wu, C. *Macromolecules* **2003**, *36*, 6588.
(17) Wu, C. *Chin. J. Polym. Sci.* **2003**, *21*, 117.
(18) Wu, C.; Li, W.; Zhu, X. X. *Macromolecules* **2004**, *37*, 4989.
(19) Wu, C.; Qiu, X. P. *Phys. Rev. Lett.* **1998**, *80*, 620.
(20) Itakura, M.; Inomata, K.; Nose, T. *Polymer* **2001**, *42*, 9261.
(21) Grinberg, N. V.; Dubovik, A. S.; Grinberg, V. Y.; Kuznetsov, D. V.; Makhaeva, E. E.; Grosberg, A. Y.; Tanaka, T. *Macromolecules* **1999**, *32*, 1471.
(22) Wang, P. H.; Pan, C. Y. *J. Appl. Polym. Sci.* **2002**, *86*, 2732.
(23) Chu, B. *Laser Light Scattering*, 2nd ed.; Academic Press: New York, 1991.
(24) Berne, B. J.; Pecora, R. *Dynamic Light Scattering*; Wiley-Interscience: New York, 1976.
(25) Qiu, X. P.; Wu, C. *Macromolecules* **1997**, *30*, 7921.
(26) Yoshioka, H.; Mikami, M.; Mori, Y.; Tsuchida, E. *J. Macromol. Sci., Pure Appl. Chem.* **1994**, *A31*, 109.
(27) Liang, D. H.; Zhou, S. Q.; Song, L. G.; Zaitsev, V. S. Chu, B. *Macromolecules* **1999**, *32*, 6326.
(28) Hu, T.; Wu, C. *Macromolecules* **2001**, *34*, 6802.
(29) Hu, T.; Wu, C. *Phys. Rev. Lett.* **1999**, *83*, 4105.
(30) Tanaka, H. *Phys. Rev. Lett.* **1993**, *71*, 3158.
(31) Tanaka, H. *Macromolecules* **1992**, *25*, 6377.
(32) Picarra, S.; Martinho, J. M. G. *Macromolecules* **2001**, *34*, 53.

MA050994J