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Folding of a single polymer chain and phase transition

DING YanWei & ZHANG GuangZhao†

Hefei National Laboratory for Physical Sciences at the Microscale, Department of Chemical Physics, University of Science and Technology of China, Hefei 230026, China

Using an ultra-sensitive differential scanning calorimetry (US-DSC), we have investigated the folding and aggregation behaviors of poly(N-isopropylacrylamide) (PNIPAM) chains in dilute and semidilute solutions. In the heating process, the intrachain folding and interchain aggregation simultaneously occur in the dilute solutions, and the ratio of intrachain folding increases with decreasing concentration. In the semidilute solutions, PNIPAM chains show limited interchain aggregation with elevated temperature, because most of the PNIPAM chains have been collapsed at lower temperature. In an extremely dilute solution, PNIPAM chains undergo a single folding transition in the heating process. By extrapolating heating rate and concentration to zero, we have obtained the phase transition temperature (T_S) and enthalpy change (ΔH_S) of the single chain folding. ΔH_S is higher than that for a phase transition involving intrachain collapse and interchain aggregation, indicating that a single chain folding can not be taken to be a macroscopic phase transition.

Ultra-sensitive differential scanning calorimetry, interchain aggregation, single chain folding

Studies of the thermodynamic and dynamic behaviors of polymer chains in solutions are important for understanding the structure-property relations of polymers[1]. Theoretically, a flexible polymer chain can collapse into a compact globule or undergo a coil-to-globule transition as solvent becomes poor. Actually, such a coil-to-globule transition can only be observed in an extremely dilute solution[2,3], because interchain association often occurs before the full collapse of a single chain[4,5]. The intrachain folding and interchain association of polymer chains are of significance for understanding protein folding, protein aggregation and DNA packing[6,7]. Yet, how to differentiate the polymer folding and aggregation experimentally is one of the unsolved problems in physical chemistry of polymers.

Poly(N-isopropylacrylamide) (PNIPAM) exhibits a lower critical solution temperature (LCST) at ~32℃ in aqueous solution because of its dehydration at an elevated temperature[8]. Accordingly, PNIPAM is often used as a model to study the conformation change of macromolecular chains in solution. The LCST of PNIPAM solution often shifts when some hydrophobic or hydrophilic monomers are copolymerized into PNIPAM chains[9]. The LCST is also related to the solvent composition[10]. We have observed the coil-to-globule-to-coil transition of PNIPAM chains in water/methanol mixtures[11,12].

Recently, we have investigated the effects of concentration and heating/cooling rate on the phase transitions of PNIPAM chains in water by use of US-DSC[13–15]. By extrapolating concentration to zero, we obtained the transition temperature (T_p) and enthalpy change (ΔH) for the folding of a single PNIAM chain. However, because of the effects of heating rate, the measurements of such parameters are not in a thermodynamic equilibrium state[13]. In the present work, we have investigated the effects of concentrations and heating rates on the intrachain collapse and interchain association of PNIPAM chains by use of US-DSC. By extrapolating both con-

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†Corresponding author (email: gzzhang@ustc.edu.cn)

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centration and heating rate to zero, we obtained the T_p and ΔH for the folding of a single chain in a thermodynamic equilibrium state so that the single chain event and phase transition are thermodynamically differentiated.

1 Experimental Section

1.1 Preparation and Characterization of PNIPAM Samples

PNIPAM was synthesized by free radical polymerization with azobis(isobutyronitrile) (AIBN) as the initiator in benzene. The resultant product was fractioned by a dissolution/precipitation process.

The absolute weight-average molecular weight (M_W = 2.35×10^6 g/mol), the *z*-average radius of gyration ($\langle R_g \rangle$= 60 nm) and the polydispersity index (M_W/M_n = 1.4) were determined by the laser light scattering, respectively.

The dried PNIPAM was weighed and dissolved in redistilled water to prepare different concentration solutions. The polymer solutions were stored at 4℃ after complete dissolution.

The overlap concentration (C^*) was estimated to be 4.3 mg/mL by $C^* = 3M/(4\pi N_A R_g^3)$, where M and R_g are the molar mass and the radius of gyration of polymer chains, N_A is the Avogadro constant[1].

1.2 US-DSC Measurements

US-DSC measurements were performed on a VP-DSC microcalorimeter from Microcal LLC, USA with two identical volume cells (0.509 mL). PNIPAM solution and the reference (redistilled water) were degassed at 25.0℃ for 30 min. By use of a special Hamilton injector, 0.75 mL of sample solution and water were added into the sample and reference cells, respectively. The cells were sealed after removing the superfluous liquid and then equilibrated at 10.0℃ for 120 min before heating.

The obtained US-DSC curves were calibrated by using water-water measurements as the reference. T_p was taken as that centered at the transition. ΔH during the transition was calculated from the area under each peak[16].

2 Results and discussions

Figure 1 shows the heating rate dependence of specific heat capacity (C_p) of PNIPAM solutions, where the curves have been normalized by concentration and heating rate. The endothermic peak located at ~32℃ was attributed to the disruption of the additional hydrogen bonds around PNIPAM chains[8]. It can be seen that a higher heating rate leads to a more asymmetrical peak and higher T_p. This is because the temperature varies faster than intrachain folding and interchain association of PNIPAM chains. That is, the chain folding and association can not follow the temperature change, and the chains do not have enough time to associate even at the phase transition temperature[13]. Thus, T_p and ΔH at a certain heating rate are those in a nonequilibrium state. Only when the heating rate is zero can we obtain such parameters in thermodynamic equilibrium.

PNIPAM concentration also has effects on the phase transition[17,18]. Figure 2 shows the concentration dependence of specific heat capacity (C_p) of PNIPAM solutions, where the heating rate is 1.0℃/min. Clearly, either T_p or ΔH increases as concentration decreases in a dilute solution ($C<C^*$). As discussed above, the phase

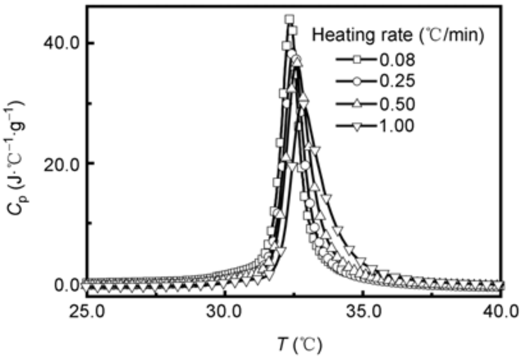

Figure 1 Heating rate dependence of specific heat capacity (C_p) of PNIPAM solutions, where the concentration of PNIPAM is 1.0 mg/mL.

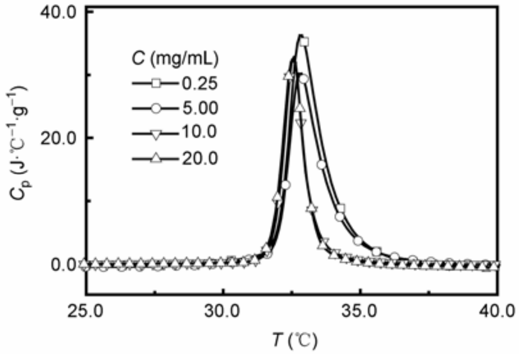

Figure 2 Concentration dependence of specific heat capacity (C_p) of PNIPAM solutions, where the heating rate of PNIPAM was 1.0°C/min.

transition involves intrachain collapse and interchain association in dilute solutions. The intrachain folding needs more energy because of the conformation entropy cost. Since the weighing of interchain association decreases as concentration decreases, either T_p or ΔH decreases with concentration. In addition, the endothermic peak in Figure 2 becomes more symmetric as concentration increases, indicating that the interchain association becomes dominant at a higher concentration.

In a dilute solution, T_p and ΔH have a linear dependence on the concentration of PNIPAM. Thus, by extrapolating concentration to zero, we can obtain T_p and ΔH for the folding of a single chain. Note that PNIPAM solution with a concentration below 0.25 mg/mL can not be measured due to the limited accuracy of US-DSC. Otherwise, such an extrapolation is more reliable.

As discussed above, T_p and ΔH for the folding of a single chain in equilibrium can not be determined by extrapolating of either heating rate or concentration to zero. Only when both of them are extrapolated to zero can we obtain the parameters for the single chain event in equilibrium state. Here, we use a Zimm-like plot[19] to combine the dependences of concentration and heating rate in one plot, namely, T_p (or ΔH) serves as the y-coordinate and heating rate + K as that of x-axis, where K is a constant arbitrarily selected for convenience.

Figure 3 shows the concentration dependence on T_p at different heating rates, where the concentration ranges from 0.25 to 20.0 mg/mL and heating rate is in the range 0.081 to 1.49℃/min. The extrapolating of T_p to zero leads to the phase transition temperature ($T_{p,0}$) in equilibrium at a certain concentration. It is shown that $T_{p,0}$ decreases with concentration at $C < C^*$. When $C > C^*$, $T_{p,0}$ holds a constant (~32.32℃). Thus, the constant $T_{p,0}$ can be taken as the temperature (T_a) for the phase transition involving only interchain association.

The extrapolating of $T_{p,0}$ to zero concentration leads to the transition temperature (T_s ~ 32.44℃) for the single chain folding. This is reasonable because PNIPAM chains are expected to undergo intrachain folding or coil-to-globule transition in an extremely dilute solution. The higher T_s shows more energy is required for an intrachain folding than an interchain association. Obviously, the coil-to-globule transition can not be simply treated as a phase transition.

The concentration dependence on ΔH at different heating rates is shown in Figure 4. The enthalpy change (ΔH_0) in equilibrium at a certain concentration is obtained by the extrapolating of ΔH to zero heating rate. It is shown that ΔH_0 holds a constant (ΔH_a ~ 38.8 J/g) in a semidilute PNIPAM solution. Clearly, it is smaller than that in a dilute solution. This is because the interchain association dominates the intrachain folding when the chains overlap each other and less energy is required for the dehydration. At $C < C^*$, ΔH_0 increases as concentration decreases. The enthalpy change (ΔH_s ~ 61.0 J/g) for the coil-to-globule transition of single PNIPAM chain is obtained by the extrapolation of ΔH_0 to zero concentration. Figure 4 shows $\Delta H_s > \Delta H_a$, further indicating that a coil-to-globule transition is different from a phase transition involving both intrachain collapse and interchain association.

3 Conclusion

The current study leads to the following conclusions.

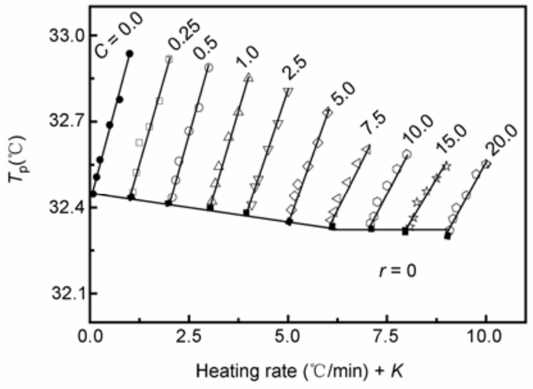

Figure 3 Concentration dependence on transition temperature (T_p) at different heating rate.

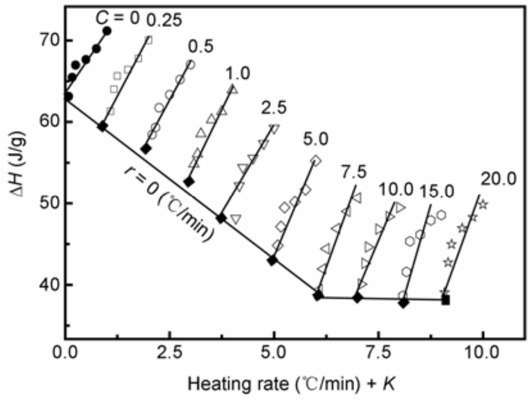

Figure 4 Concentration dependence on transition enthalpy (ΔH) at different heating rate.

Polymer chains undergo intrachain folding and interchain association in dilute solutions. In semidilute solutions, the interchain association is dominant. In an extremely dilute solution, the chains undergo coil-to-globule transition. By extrapolating heating rate and concentration to zero, the temperature (T_s) and enthalpy change (ΔH_s) for the folding of a single polymer chain can be obtained.

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