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# Microcalorimetric Investigation on Association and Dissolution of Poly(*N*-isopropylacrylamide) Chains in Semidilute Solutions

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ABSTRACT: The concentration ($C$) effect on association and dissolution of linear poly(*N*-isopropylacrylamide) (PNIPAM) chains in dilute and semidilute aqueous solutions was investigated by using ultrasensitive differential scanning calorimetry (US−DSC). When $C$ is below the overlap concentration ($C^*$), both the phase-transition temperature ($T_p$) and enthalpy change ($\Delta H$) in the heating process decrease as the solution becomes more dilute, while $T_p$ and $\Delta H$ become independent of $C$ in the semidilute regime ($C > C^*$). Such a difference can be attributed to different contributions of interchain association and intrachain contraction in dilute and semidilute solutions. In the cooling process, $T_p$ nearly remains a constant, but $\Delta H$ decreases as $C$ increases in dilute solutions, but both of them slightly vary in the range $C > C^*$. A hysteresis was observed in one heating-and-cooling cycle. Such a hysteresis becomes more obvious as $C$ increases. The effect of scanning rate on both $T_p$ and $\Delta H$ further confirms that the hysteresis is due to incomplete disruption of additional hydrogen bonds formed when the chains are in the collapsed state.

## Introduction

Thermodynamics and dynamics of polymers in solutions are important for a correlation between their structure and properties. Polymer chains are well studied in dilute solutions, while polymer behaviors in semidilute and concentrated solutions are less understood because of the difficulties in theoretical treatment and experimental characterization.[1] For example, the scaling theory predicted one fast dynamical relaxation process related to the cooperative diffusion of the subchains between two neighboring entangled points in semidilute polymer solutions.[2] However, some of previous laser light scattering experiments revealed an additional slow mode that is not due to the slower reptation of the chains inside the "tubes" because they are invisible there.[3−8] Recently, some cleverly designed studies show that such a slow mode is not due to dust particles or concentration inhomogeneity but due to a mobility difference between the chain segments near and away from the entanglement points.[8] When the solvent quality changes from good to poor, the chain overlapping and entanglement in semidilute and concentrated solutions are expected to result in different chain contraction and association behaviors in comparison with those in dilute solutions. It should be noted that the folding and association of proteins inside cells often occur in a concentrated solution.[9]

Since poly(*N*-isopropylacrylamide) (PNIPAM) aqueous solutions exhibit a lower critical solution temperature (LCST) at ~32 °C, the collapse and association of PNIPAM chains can be conveniently examined by adjusting the solvent quality via the solution temperature.[10−17] Previously, we investigated the association and dissolution of PNIPAM chains in dilute aqueous solutions.[18] Our results revealed that intrachain contraction and interchain association play important roles in the phase transition. In our recent experiments, we found that the association of PNIPAM chains has no noticeable effect on the calorimetric measurements at high PNIPAM concentrations since the aggregates do not precipitate, that is, they behave like colloidal particles. This enables us to conduct the present study. Our main objective is to understand the roles that chain entanglement and additional hydrogen bonding played in the intrachain contraction and interchain association.

## Experimental Section

**Sample Preparation.** PNIPAM was synthesized by a radical polymerization.[19] The resultant PNIPAM was fractioned in an acetone/hexane mixture. The weight-average molecular weight ($M_w = 1.6 \times 10^6$ g/mol) and the $z$-average gyration radius ($\langle R_g \rangle = 66$ nm) of the fraction used in this study were determined by static laser light scattering. The polydispersity index ($M_w/M_n = 1.5$) is estimated from the relative width of characteristic relaxation time distribution measured in dynamic laser light scattering.[20]

**US-DSC Measurements.** PNIPAM solutions were measured on a VP-DSC microcalorimeter from Microcal Inc. with deionized water as the reference. Each PNIPAM solution and the reference were degassed at 25.0 °C for 30 min and then equilibrated at 10.0 °C for 120 min before heating. In the cooling process, they were equilibrated at 60 °C for 120 min to eliminate the effect of thermal history. The PNIPAM concentrations used were in the range 1.0−25.0 mg/mL. Data were analyzed by use of the software supplied by the manufacturer. The phase-transition temperature ($T_p$) was taken as that corresponding to the maximum specific heat capacity ($C_p$) during the transition. The enthalpy change ($\Delta H$) during the transition was calculated from the area under each peak.

## Results and Discussion

Figure 1 shows the temperature dependence of specific heat capacity ($C_p$) of PNIPAM aqueous solutions with different concentrations in one heating-and-cooling cycle, where both the heating and cooling rates were 1.0 °C/min. As the concentration increases, the peak shifts to the left, that is, the transition occurs at a lower temperature. This is because the interchain association is enhanced in the heating process when the concentration is higher. As a result, more chains are trapped inside each aggregate. Thus, a lower temperature is required for dissolution of such aggregates in the cooling process. Further increasing

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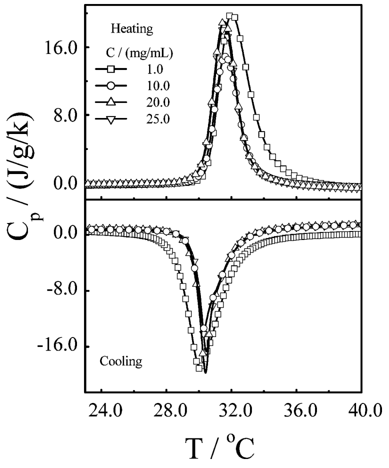

**Figure 1.** Temperature dependence of specific heat capacity ($C_p$) of PNIPAM solutions with different concentrations in one heating-and-cooling cycle, where the heating and cooling rates were 1.0 °C/min.

the polymer concentration leads to the chain overlapping in the solution. Note that the overlap concentration ($C^*$) has previously been defined in the literature as $3M/(4\pi N_A R_g^3)$ or $M/(N_A R_g^3)$ or $[\eta]^{-1}$, where $M$ and $R_g$ are the molar mass and the radius of gyration of polymer chains, $N_A$ is the Avogadro constant, and $[\eta]$ is the intrinsic viscosity.[1] Generally, $3M/(4\pi N_A R_g^3) < C^* < M/(N_A R_g^3)$. In this case, $\langle R_g \rangle = 66$ nm and $M_w = 1.6 \times 10^6$ g/mol, so that $3M/(4\pi N_A R_g^3) = 2.2$ mg/mL and $M/(N_A R_g^3) = 9.3$ mg/mL. Therefore, the solution with a concentration ($C$) higher than 10.0 mg/mL can be considered as semidilute.

Figure 1 also shows a hysteresis reflecting in the transition temperature ($T_p$) in the heating-and-cooling cycle. Such a phenomenon was previously observed in the folding-and-unfolding of individual PNIPAM chains in an extremely dilute solution and the association-and-dissolution of PNIPAM chains in dilute solutions.[17,18] Recent experimental results revealed that the additional hydrogen bondings between PNIPAM segments formed in the collapsed state due to the dehydration and a shorter average interchain distance at an elevated temperature is responsible for the hysteresis.[18,21] When $C > C^*$, a bimodal transition can be observed in the cooling process with one exothermic peak centered at ~30.2 °C and the other at ~31.0 °C. Such a bimodal transition was also observed in dilute aqueous solutions of PNIPAM in the cooling process when the temperature scanning rate was lower than 0.328 °C/min. The two peaks were attributed to the disruption of the additional hydrogen bonding and the dissolution of the collapsed chains, respectively.[18] In the semidilute solution, more PNIPAM chains can associate together to form larger aggregates in the heating process. When the solution is cooled down, the aggregates are swollen before the chains inside diffuse out and dissolve into the solution as individual chains. A bigger lag is expected when the aggregates contain more chains. This explains why the separation of two peaks is visible even when the cooling rate is greater than 1.0 °C/min.

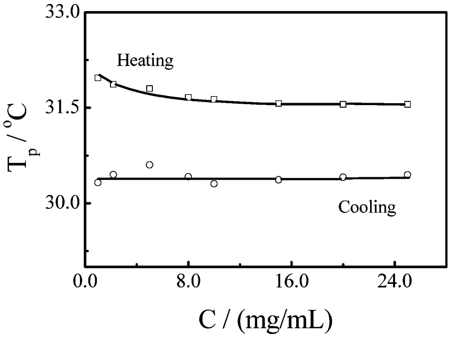

**Figure 2.** Concentration dependence of the transition temperature ($T_p$), where both the heating and cooling rates were kept at 1.0 °C/min.

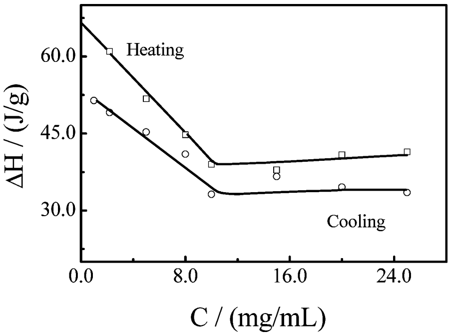

**Figure 3.** Concentration dependence of the transition enthalpy change ($\Delta H$) during the phase transition of PNIPAM solutions, where both the heating and cooling rates were kept at 1.0 °C/min.

Figure 2 shows that $T_p$ gradually decreases as the concentration increases in the heating process when $C < C^*$. It is known that the dehydration involves both intrachain contraction and interchain association. The former is more difficult than the latter because it requires a cost of conformational entropy. As concentration increases, the chains have more chance to undergo interchain association instead of intrachain contraction. On the other hand, the hydration surface of the chains also increases with the concentration. Thus, less energy is needed for the phase transition at a higher concentration, and $T_p$ shifts to a lower temperature. $T_p$ levels off in the range $C > C^*$. This is because the interchain association dominates the intrachain contraction in semidilute solutions. On the other hand, $T_p$ is independent of the polymer concentration in the cooling process. As discussed before, both the swelling of the aggregates with some disruption of additional hydrogen bonding and the dissolution of the chains in the aggregates occur in the cooling process. If the solutions at $T < T_p$ are used as references, more additional hydrogen bonding is expected at $T > T_p$ in a more dilute solution. This is because some hydrogen bonding is already formed in a semidilute solution even at $T < T_p$ due to the chain entanglement. Note that the difference between the values of $T_p$ in the heating and cooling processes increases with decreasing concentration in the range $C < C^*$. As discussed above, $T_p$ in the cooling process slightly changes with temperature. However, in the heating process, as the concentration decreases, more intrachain contraction with an entropy cost occurs instead of interchain association, leading $T_p$ to increase. This explains the larger $T_p$ difference or hysteresis at a lower concentration. The fact also suggests less additional hydrogen bonds formed in a more concentrated solution in the range $C < C^*$.

Figure 3 shows the concentration dependence of the enthalpy change ($\Delta H$). In dilute solutions ($C < C^*$), $\Delta H$ decreases with increasing polymer concentration in either heating or cooling process. Note that both the intrachain contraction and interchain association of PNIPAM contribute to $\Delta H$ during the phase transition. More interchain association is expected as polymer concentration increases. The decrease in $\Delta H$ implies that the interchain association involves less $\Delta H$ than intrachain contraction. The extrapolation of $\Delta H$ to zero concentration leads to the enthalpy change ($\Delta H_c$) concerning only intrachain contraction in the heating process; namely, $H_c$ reflects the energy change of coil-to-globule transition of the individual chains. In the range $C > C^*$, $\Delta H$ is nearly independent of the concentration. This is understandable because interchain association is dominant when the chains overlap each other. Enthalpy change

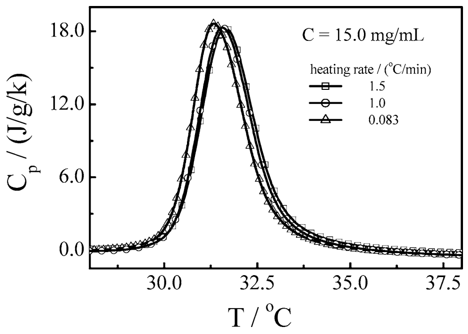

**Figure 4.** Temperature dependence of specific heat capacity ($C_p$) of a PNIPAM semidilute solution at different heating and cooling rates.

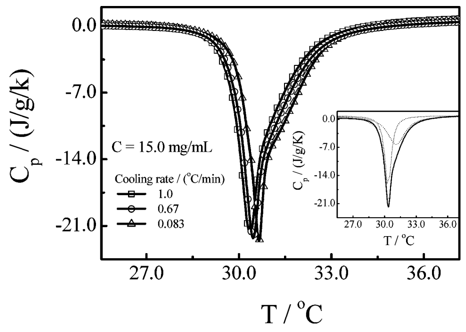

**Figure 5.** Temperature dependence of specific heat capacity ($C_p$) of PNIPAM semidilute solution in a cooling process. (Inset) Deconvolution of the peak at the cooling rate of 1.0 °C/min.

($\Delta H_a$) at $C > C^*$ can be considered to be related only to the interchain association. Obviously, $\Delta H_c > \Delta H_a$. This could be attributed to the fact that intrachain contraction involves a larger change in the chain conformation and the chain collapse induces more stress inside. The difference indicates that single chain events cannot simply be treated as a phase transition. Note that $\Delta H$ obtained by extrapolating concentration to zero in the cooling process cannot be taken as the energy change with respect to the globule-to-coil transition of the individual chains because the starting point cannot be defined here.

Figure 4 shows the scanning rate dependence of specific heat capacity ($C_p$) of a PNIPAM semidilute solution in heating process, where $C = 15.0$ mg/mL. It is helpful to note that PNIPAM dilute solutions exhibit a symmetrical peak when the heating rate is lower than 0.081 °C/min. As the heating rate increases, the peak becomes asymmetrical because interchain association and intrachain contraction do not occur simultaneously.[18] As expected, the faster the heating, the more the intrachain contraction will occur. Therefore, it is the intrachain contraction that leads to the asymmetry. In semidilute solutions, the chains overlap each other independent of the heating rate, so that the interchain association is dominant and the intrachain contraction is suppressed. That is why more symmetrical peaks are observed in Figure 4.

On the other hand, Figure 5 shows that the peaks are asymmetrical in the cooling process. As the cooling rate decreases in the range 1.0−0.083 °C/min, the asymmetry increases. Particularly, when the cooling rate is lower than 1.0 °C/min, a bimodal transition is observed after the deconvolution (inset). As we discussed before, the peak at the lower temperature and the shoulder at higher temperature can be attributed to the swelling of the aggregates with the disruption of the additional hydrogen bonding and the dissolution of the chains inside the aggregates, respectively. As expected, the aggregates swell before the chain dissolution. The area of the shoulder peak increases as the cooling rate decreases. This is because a slower cooling provides sufficient time for the aggregates to swell before the inside chains dissolve and diffuse into the solution.

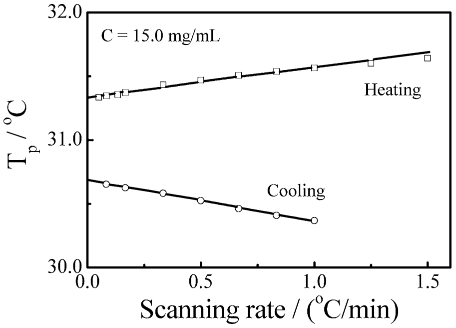

**Figure 6.** Scanning rate dependence of transition temperature ($T_p$) of a PNIPAM semidilute solution.

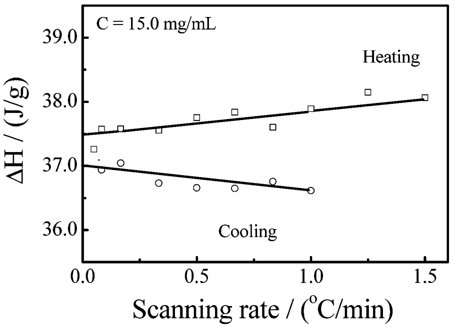

**Figure 7.** Scanning rate dependence of enthalpy change ($\Delta H$) of a PNIPAM semidilute solution.

Figure 6 shows that $T_p$ of the PNIPAM semidilute solution increases linearly with the heating rate, indicating that the chain association lags behind the temperature change. On the other hand, the linear decrease of $T_p$ with the cooling rate in the cooling process suggests that the swelling and dissolution of the associated PNIPAM chains are slower than the temperature change. The extrapolation of $T_p$ to zero scanning rate leads to $T_{p,0} = 31.4$ and 30.7 °C in the heating and cooling processes, respectively. $T_{p,0}$ in the heating process here is fairly close to that observed in the folding of individual chains in extremely dilute solution.[17] However, there is a difference ($\Delta T_p \sim 0.7$ °C) in $T_{p,0}$ in the heating and cooling processes. It is known that dilute PNIPAM solutions almost do not exhibit such a difference.[18] The difference in $T_{p,0}$ in semidilute solutions suggests that the interchain association cannot be completely removed by the cooling in the time we investigated due to the chain entanglement.

Figure 7 shows that $\Delta H$ of the PNIPAM semidilute solution linearly increases with the heating rate, which is similar to that in dilute PNIPAM solutions.[18] It is known that interchain association and intrachain contraction in the heating process involving dehydration, which is endothermic, lead $\Delta H$ to increase. The formation of additional hydrogen bonds in the collapsed state leads to a decrease of $\Delta H$ because it is exothermic. In a slow heating process, PNIPAM segments have more time to form additional hydrogen bonds, resulting in a lower $\Delta H$. In the cooling process, the swelling and dissolution related to hydration are exothermic, while the disruption of the additional hydrogen bonds among chain segments is endothermic. Their counteraction leads the absolute value of $\Delta H$ to decrease. As the cooling rate increases, the aggregates can be more quickly cooled so that more additional hydrogen bonds are disrupted. This explains why $\Delta H$ decreases as the cooling rate increases. A similar behavior was also observed in the denaturation of some plant proteins.[22] Figure 7 also shows that

$\Delta H$ in the cooling process is smaller than that in the heating process. The difference increases with the scanning rate, further indicating that the swelling and dissolution in the cooling process is relatively slower than the temperature change, and the additional hydrogen bonding cannot be disrupted in the time we investigated due to the chain entanglement.

## Conclusions

The present study of the concentration effect on the association and dissolution of poly(*N*-isopropylacrylamide) (PNIPAM) chains in dilute and semidilute aqueous solutions by using an ultrasensitive differential scanning calorimeter leads to the following conclusion. Fast heating results in less additional hydrogen bonding between PNIPAM segments in the heating process, while fast cooling leads the additional hydrogen bonds to disrupt more quickly in the cooling process. In semidilute solutions, the chain overlapping suppresses the intrachain contraction so that the transition temperature ($T_p$) and the enthalpy change ($\Delta H$) become independent of the polymer concentration. Moreover, the intrachain contraction involves a larger change in $\Delta H$ than interchain association, so that $\Delta H$ increases as the polymer concentration decreases in dilute solutions. The hysteresis observed in one heating-and-cooling cycle can be attributed to the incomplete disruption of additional hydrogen bondings between PNIPAM segments, especially in semidilute solutions where the chains are highly entangled each other.

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