The Coil-to-Globule-to-Coil Transition of Linear Polymer Chains in Dilute Aqueous Solutions: Effect of Intrachain Hydrogen Bonding

Kejin Zhou,[†] Yijie Lu,[‡] Junfang Li,[‡] Lei Shen,[‡] Guangzhao Zhang,*[,‡] Zuowei Xie,[†,§] and Chi Wu*[,§]

Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China; The Hefei National Laboratory for Physical Sciences at Microscale, Department of Chemical Physics, University of Science and Technology of China, Hefei, China; and Department of Chemistry, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China

Received August 22, 2008; Revised Manuscript Received September 13, 2008

ABSTRACT: Our previous studies of the captioned transition have shown that thermally sensitive poly(*N*-isopropylacrylamide) (PNIPAM) in water can form stable individual single-chain globules, but not for polystyrene (PS) in cyclohexane. In the current study, using poly(*N*,*N*-diethylacrylamide) (PDEAM) ($M_w = 1.7 \times 10^7$ g/mol and $M_w/M_n = 1.06$) with no hydrogen donator site, we intend to find whether the intrachain hydrogen bonding plays a role in stabilizing individual collapsed PNIPAM single-chain globules. We found that PDEAM can also form stable single-chain globules in water even though the transition is less sharp. The resultant individual PDEAM single-chain globules are less compact, reflecting in a lower chain density and a higher ratio of the radius of gyration to hydrodynamic radius, presumably due to the lack of intrachain hydrogen bonding. Our result also shows that, unlike PNIPAM, there is no hysteresis in the transition, indirectly supporting our previous assumption that the hysteresis observed for PNIPAM is due to the formation of some intrachain additional hydrogen bonds formed in the collapsed state.

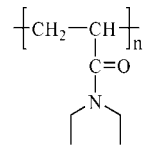
Introduction

Since Stockmayer predicted the collapse of a linear polymer chain from an expanded coil to a rather dense globule,[1] the coil-to-globule transition as a fundamental problem has been extensively studied[2−11] because it was thought to be potentially or maybe remotely related to many phenomena, such as the protein folding[12] and the DNA packing.[13] Later on, it has been gradually realized that the folding and packing biopolymers involve some active process and are helped by other proteins, much more complicate. In most of previous studies of the coil-to-globule transition, polystyrene (PS) or poly(methyl methacrylate) (PMMA) in different organic solvents was used. However, the interchain aggregation always spoils the observation of the coil-to-globule transition of individual chains.[14−17] In other words, there were only some limited success in the observation of single-chain globules formed in a kinetic process, but no one, to our knowledge, has made individual PS or PMMA chains to reach their thermodynamically stable single-chain globular state; i.e., no data have been reported to show that single-chain PS or PMMA globules are stable over a reasonable time period.

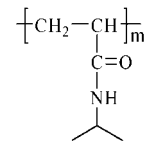
In the middle 1990s, we had, for the first time, made that individual poly(*N*-isopropylacrylamide) (PNIPAM) chains with a lower critical solution temperature (LCST ∼ 32 °C) collapse into stable single-chain globules in a dilute aqueous solution upon heating.[18] Further, we systematically studied such a coil-to-globule transition and its reverse globule-to-coil process.[19−22] Recently, we investigated the coil-to-globule transition of some hydrophilically or hydrophobically modified PNIPAM chains.[23−29] It was reported that the intrachain hydrogen bonding in the core−shell microgel systems could led to a marked depression of the phase transition temperature.[30–32]

However, we always question whether the formation of stable single-chain globules is somehow related to or affected by the intrachain hydrogen bonding because PNIPAM has ⟩C═O and H–N⟨ motifs. In order to answer this question, we have to find another water-soluble polymer without any intrachain hydrogen bonding site. Our own experience tells us that the most difficult part is not to find such a polymer, but to prepare narrowly distributed ultralong polymer chains with their molar mass high than 1.0×10^7 g/mol and polydispersity index (M_w/M_n) less than 1.10. It is even better if such a polymer is also thermally sensitive with a convenient LCST, similar to PNIPAM.

There are several choices related to N-subsituted polyacrylamides with different LCSTs. Among them, poly(*N*,*N*-diethylacrylamide) (PDEAM) is particularly interesting because it has a monomer molar mass and a LCST similar to PNIPAM.[33−38] The following chemical structures comparatively show that PDEAM has no hydrogen donator site H−N⟨ for the intrachain hydrogen bonding.



Poly(*N*,*N*-diethylacrylamide)
(PDEAM)



Poly(*N*-isopropylacrylamide)
(PNIPAM)

The objectives of the current study are to find whether the intrachain hydrogen boding plays a role in stabilizing individual collapsed single-chain globules, in the formation of the molten globular state during the coil-to-globule transition, and in the hysteresis of the globule-to-coil transition.

Experimental Section

Sample Preparation. The synthetic detail and purification of monomer *N*,*N*-diethylacrylamide (DEAM) can be found elsewhere.[37] PDEAM was prepared via free radical polymerization in

* Corresponding authors. The Hefei address should be used for all correspondence.
[†] Chinese Academy of Sciences.
[‡] University of Science and Technology of China.
[§] The Chinese University of Hong Kong.

10.1021/ma8019128 CCC: $40.75
Published on Web 10/21/2008

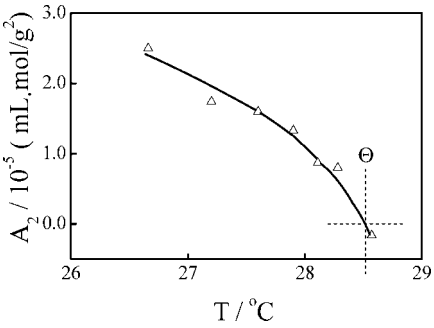


Figure 1. Temperature dependence of second virial coefficient (A_2) for poly(*N*,*N*-diethylacrylamide) (PDEAM) in water.

bulk at 25 °C for 30 days with azobis(isobutyronitrile) as an initiator. The resultant poly(*N*,*N*-diethylacrylamide) (PDEAM) was successively fractionated in an acetone/*n*-hexane (~1:2) mixture. In each cycle, the fraction with the highest molar mass was used for the next run. In this way, we successfully obtained a fractionation of narrowly distributed PDEAM chains with $M_w/M_n = 1.06$ and $M_w = 1.7 \times 10^7$ g/mol. With this sample, we prepared an aqueous stock solution of 1.0×10^{-3} g/mL and let the solution stand at the room temperature for 1 week to ensure a complete dissolution. The solution was further diluted to 1.2×10^{-6} g/mL and then clarified with a 0.45 μm Millipore Millex-LCR filter to remove dust prior to our LLS experiments.

Laser Light Scattering. In static LLS,[39] 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 polymer chains in an dilute solution can be determined from the angular dependence of the excess absolute time-averaged scattering intensity, known as the Rayleigh radio $R_{vv}(q)$, on the basis of

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

where $K = 4\pi^2 n^2 (dn/dC)^2/(N_A\lambda_0^4)$ and $q = (4\pi n/\lambda_0)\sin(\theta/2)$, with n, dn/dc, N_A, λ_0, and θ the solvent refractive index, the specific refractive index increment, the Avogadro's number, the wavelength of light in vacuum, and the scattering angle, respectively. The extrapolations of both $C \rightarrow 0$ and $q \rightarrow 0$ lead to M_w. The plots of $[KC/R_{vv}(q)]_{C\rightarrow 0}$ vs q^2 and $[KC/R_{vv}(q)]_{q\rightarrow 0}$ vs C lead to $\langle R_g^2\rangle$ and A_2, respectively. In an extremely dilute solution, the $2A_2C$ term can be ignored. For small scattering objects, the Zimm plot on the basis of eq 1 is usually used, which incorporates the extrapolations of $C \rightarrow 0$ and $q \rightarrow 0$ in a single grid. For long polymer chains, the Berry plot is normally used as follows:

$$\left(\frac{KC}{R_{vv}(q)}\right)^{1/2} \cong \left(\frac{1}{M_w}\right)^{1/2}\left(1 + \frac{1}{6}\langle R_g^2\rangle q^2\right) \qquad (2)$$

In dynamic LLS,[40] the cumlant analysis of the measured intensity−intensity time correlation function $G^2(t)$ of narrowly dispersed polymer chains in a dilute solution is sufficient for an accurate determination of the average line width ($\langle\Gamma\rangle$). For a diffusive relaxation, $\langle\Gamma\rangle$ can be further related to the average translational diffusive coefficient ($\langle D\rangle$) using $\langle D\rangle = (\langle\Gamma\rangle/q^2)_{q\rightarrow 0}$ or the average hydrodynamic radius ($\langle R_h\rangle$) using $\langle R_h\rangle = k_BT/(6\pi\eta\langle D\rangle)$ with k_B, η, and T being the Boltzmann constant, the solvent viscosity, and the absolute solution temperature, respectively. The hydrodynamic radius distribution $f(R_h)$ can also be calculated for the Laplace inversion of $G^2(t)$ by using the CONTIN program. It is should be state once more that the solution was so dilute that the extrapolation of $C \rightarrow 0$ was not necessary. The long-term temperature fluctuation inside the scattering cell is less than ± 0.02 °C.

Results and Discussion

Figure 1 shows that the second virial coefficient A_2 of PDEAM in water decreases as the solution temperature increases, a characteristic of some aqueous polymer solutions because of the negative entropy change. The interpolation of $A_2 \rightarrow 0$ leads to the Flory Θ-temperature (28.5 °C) that is slightly lower than 30.5 °C for PNIPAM in water. Therefore, PDEAM is slightly more hydrophobic than PNIPAM for a given solution temperature. Note that this is the first serious measurement of the Flory Θ-temperature for PDEAM in water. Figure 1 establishes a starting point for the current study because we are more interested in how PDEAM behaves in water under the poor solvent condition, i.e., $T > \Theta$.

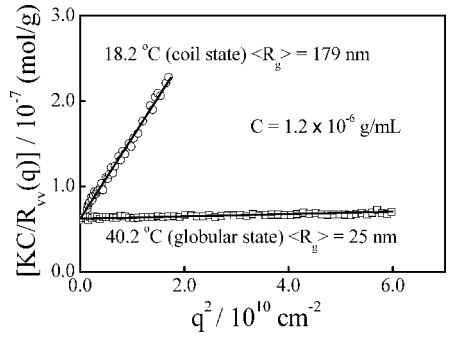


Figure 2. Scattering vector dependence of Rayleigh ratio ($KC/R_{vv}(q)$) of poly(*N*,*N*-diethylacrylamide) (PDEAM) in water, where the concentration is ~1.2×10^{-6} g/mL.

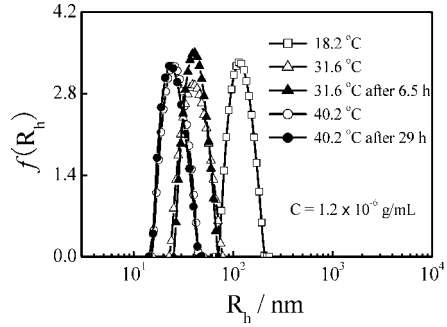


Figure 3. Temperature and aging time dependence of hydrodynamic radius distributions ($f(R_h)$) of poly(*N*,*N*-diethylacrylamide) (PDEAM) chains in water.

Figure 2 shows that the extrapolation of $KC/R_{vv}(q)$ to $q \rightarrow 0$ at two different solution temperatures, much lower and higher than the Γ-temperature, leads to an identical intercept but very different slopes. On the basis of eq 1, this indicates that there is no change in M_w, even though $\langle R_g\rangle$ significantly decreases. In other words, the observed chain contraction is a pure intrachain process. It should be emphasized that in the globule state the average scattered light intensity ($\langle I\rangle$) remains a constant over a long time, indicating that individual single-chain globules are stable and there is no interchain association because $\langle I\rangle$ is proportional to M_w ($= \sum n_i M_i^2$) that is extremely sensitive to a trace amount of interchain association according to eq 1.

Figure 3 shows typical hydrodynamic radius distribution $f(R_h)$ of PDEAM in water at different solution temperatures and after different aging times. As the temperature increases, the decrease of $\langle R_h\rangle$ clearly shows the chain contraction. It should be stated that even at the globular state $f(R_h)$ is independent of the aging time, further indicating that individual collapsed single-chain globules are stable. A combination of Figures 2 and 3 clearly shows that the individual PDEAM chains can also collapse into stable single-chain globules without our previously speculated help of intrachain hydrogen bonding. In comparison with polystyrene or PMMA in organic solvents, the stronger intrachain hydrophobic interaction in water seems to be the main force to drive individual PNIPAM or PDEAM chains into a

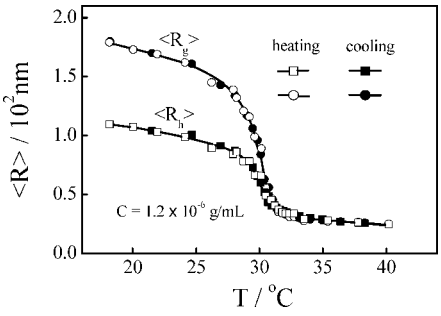


Figure 4. Temperature dependence of average radius of gyration ($\langle R_g \rangle$) and hydrodynamic radius ($\langle R_h \rangle$) of poly(*N*,*N*-diethylacrylamide) (PDEAM) chains in water in one heating-and-cooling cycle.

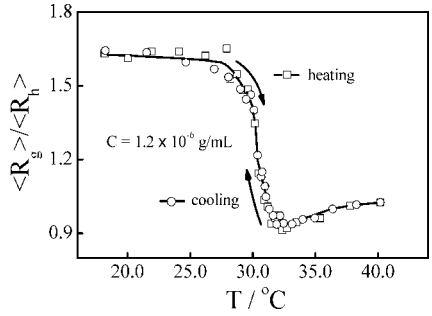


Figure 5. Temperature dependence of ratio of average radius of gyration to average hydrodynamic radius ($\langle R_g \rangle / \langle R_h \rangle$) of poly(*N*,*N*-diethylacrylamide) (PDEAM) chains in water in one heating-and-cooling cycle.

collapsed state. Moreover, the amphiphilic nature of NIPAM and DEAM monomers and a delicate balance between the hydrophobic backbone and hydrophilic motif might also play a role in the stabilization of individual single-chain globules in water.

Figure 4 summarizes the temperature dependence of $\langle R_g \rangle$ and $\langle R_h \rangle$ in one heating-and-cooling cycle, where each data point was obtained at least 2 h after the solution reached each desired temperature. Our measurements show that $\langle R_g \rangle$ and $\langle R_h \rangle$ become stable as soon as the solution temperature reaches its equilibrium. The contraction of individual coiled chains in the heating process and the swelling of individual single-chain globules in the cooling processes can be attributed to the negative entropy change in the dissolution of PDEAM in water. The solution has a lower critical solution temperature (LCST $\sim$ 30 °C). As shown in Figure 4, both $\langle R_g \rangle$ and $\langle R_h \rangle$ in the heating process gradually decrease in the range 18−28.5 °C but drop in the narrow range 28.5−32.5 °C. After 32.5 °C, they change a little and approach a constant at $\sim$37 °C, indicating the formation of individual stable single-chain globules. Also note that $\langle R_g \rangle$ decreases much faster than $\langle R_h \rangle$ in the temperature range 28.5−32.5 °C. It is known that $\langle R_g \rangle$ and $\langle R_h \rangle$ are critically dependent on how a chain is distributed in real space, whereas $\langle R_h \rangle$ is also influenced by the hydrodynamic draining. Such a difference can be better viewed in terms of the ratio $\langle R_g \rangle / \langle R_h \rangle$, as shown in Figure 5.

In the heating process, $\langle R_g \rangle / \langle R_h \rangle$ remains a constant ($\sim$1.60) when $T < 26$ °C in spite that both $\langle R_g \rangle$ and $\langle R_h \rangle$ decrease, as shown in Figure 4, indicating that individual PDEAM chains have kept an expanded conformation. As the temperature increases in the range 26−28.5 °C, $\langle R_g \rangle / \langle R_h \rangle$ slightly changes from $\sim$1.60 to $\sim$1.51, very close to 1.504 predicted for a random coil in the Θ state. Further increase of the solution temperature in the range 28.5−32.5 °C leads to a drop of $\langle R_g \rangle / \langle R_h \rangle$ from $\sim$1.51 to $\sim$0.92, clearly revealing the contraction of individual chains in the poor solvent. The minimum of $\langle R_g \rangle / \langle R_h \rangle \sim 0.92$ at 32.5 °C should be noted. In previous studies of PNIPAM,[21] we repeatedly observed such a minimum for the temperature dependence of $\langle R_g \rangle / \langle R_h \rangle$, which was attributed to the formation of the "molten" globular state; namely, the contraction of a linear polymer chain eventually results in many small loops on its periphery. It is these small loops that lead to a higher $\langle R_h \rangle$ but have less effect on $\langle R_g \rangle$. At high temperatures, these small loops finally collapse so that $\langle R_h \rangle$ further decreases, but not $\langle R_g \rangle$. This explains why $\langle R_g \rangle / \langle R_h \rangle$ finally increases and approaches a constant after passing the minimum point.

It is important to note that for PDEAM $\langle R_g \rangle / \langle R_h \rangle$ finally reaches $\sim$1.0, higher than 0.774 predicted for a uniform nondraining sphere. This means that individual PDEAM single-chain globules are not hard sphere, but still partially draining, less compact than those PNIPAM single-chain globules because its $\langle R_g \rangle / \langle R_h \rangle$ reaches $\sim$0.78 at high temperatures.[21] We can attribute such a difference to the lacking of intrachain hydrogen bonding in PDEAM. It has been known that the hydrogen bonding involving the $\rangle$C═O and H−N$\langle$ motifs on a protein backbone result in a large number of *native contacts* in a folded chain. It is these intrachain hydrogen bonds that determine how compact a folded protein chain is.[41−43] Also note that the contraction of individual PNIPAM chains favors the formation of more intrachain hydrogen bonds, leading to further chain contraction and a more compact conformation, a self-promoting process.[42]

In Figures 4 and 5, the heating and cooling curves nearly superpose with each other, indicating that in the temperature range studied, there is no hysteresis in one heating-and-cooling cycle; i.e., the coil-to-globule transition is completely reversible. In contrast, there is a clear hysteresis in our previous studies of the coil-to-globule-to-coil transition of PINIPAM chains in water. We attributed it to the formation of additional intrachain hydrogen bonds in the collapsed state.[21] The current experiment confirms our previous speculation.

Using the modified Flory theory, one can formulate the chain contraction is formulated in the terms of the expansion factor ($\alpha = \langle R \rangle_T / \langle R \rangle_\Gamma$) as[44]

$$\frac{7(1-\alpha^2)}{3r} = \frac{1}{2}(\Theta/T)\phi + \frac{\ln(1-\phi)}{\phi} + 1 \qquad (3)$$

where $\phi \equiv \phi_0/\alpha^3$ with ϕ_0 the fraction of space occupied by an idea chain with a radius of gyration R_g; r is the number of residues that can be one monomer or a number of connected monomers; and $\langle R \rangle_T$ and $\langle R \rangle_\Theta$ are the radius of gyration or the hydrodynamic radius at T and Θ, respectively. $\phi < 1$ so that $\alpha > \phi_0^{1/3}$ if $r \rightarrow \infty$, $\phi_0 \rightarrow (19/27)^{1/2} r^{-1/2}$. In a good solvent, $\alpha > 1$ and $\phi \neq 1$. After expanding $\ln(1-\phi)$, we rewrite eq 3 in a useful and familiar form as[45]

$$\alpha^6(1-\alpha^2) + 0.102 + \ldots = 0.180\alpha^3(M_w/M_o)^{1/2} \qquad (4)$$

where τ [$= (T-\Theta)/\Theta$] is the reduced temperature; we have replaced r by the ratio of masses of polymer and "residues", M_w/M_o.

Figure 6 shows a comparison of the temperature dependence of the static expansion factor α_s of PDEAM and PNIPAM. When $T < \Theta$ (good solvent), the experimental results of both PDEAM and PNIPAM are well represented by the lines with $r = 1.3 \times 10^5$ and $r \sim 1.0 \times 10^5$, respectively. A similar result was also obtained for polystyrene in cylcohexane.[46,47] The theory works fairly well in good solvent wherein ϕ_0 is expected to be a weak function of T. In contrast, when $T > \Theta$ (poor solvent), the measured α_s drops much faster than those lines predicted for either PDEAM or PNIPAM. To our knowledge, there is no explanation for such a discrepancy. Originally, we thought that this might be attributed to the formation of some additional intrachain hydrogen bonds; namely, the chain con-

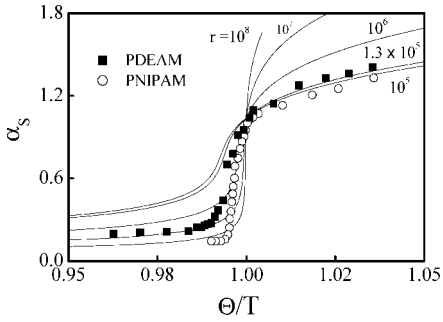


Figure 6. Temperature dependence of static expansion factor α_s ($\langle R_g\rangle_T/\langle R_g\rangle_\Theta$) of poly(*N*,*N*-diethylacrylamide) (PDEAM) in water. The lines represent the calculations on the basis of eq 3 with three different *r* values. For comparison, previous PNIPAM data are also plotted.

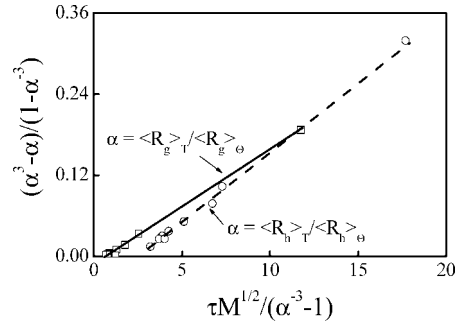


Figure 7. $(\alpha^3 - \alpha)/(1 - \alpha^{-3})$ vs $\tau M^{1/2}/(\alpha^{-3} - 1)$, where lines represent the best fittings of $\alpha - \alpha^3 + C(\alpha^{-3} - 1) = B\tau M_w^{1/2}$.

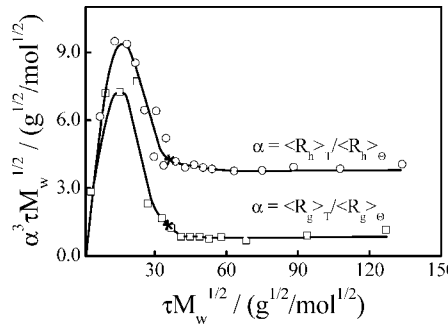


Figure 8. Scaled contraction factor $\alpha^3\tau M_w^{1/2}$ vs $\tau M_w^{1/2}$, where $\tau = (T - \Theta)/\Theta$ and each asterisk (∗) marks a crossover point from the coil state to the globular state.

traction would lead to a self-promoting process, resulting in a more sharp decrease of α_s. However, the current result invalidates such a proposal because PDEAM is not able to form any intrachain hydrogen bonds. There are two more possibilities: (1) the exiting theory for polymer chains in good solvents has to be modified to describe polymer chain conformations in poor solvents, or (2) we has to consider water as a strange solvent because water molecules are able to associate/disassociate with a polymer chain and form some clusters by themselves. At higher temperatures (small τ), α_s approaches a plateau predicted in eq 3; namely, $\alpha_s \rightarrow 0.20$ for PDEAM and $\alpha_s \rightarrow 0.14$ for PNIPAM. The different plateau values further indicate that individual single-chain PDEAM globules are less compact than those made of PNIPAM.

Considering a remarkable similarity between the coil−helix and the current coil-to-globule transitions, it has been suggested that the steepness of the sigmoidal curves might be caused by cooperativity.[48] Namely, there might be an activating step that involves a constraint. It is this constraint that causes a specific local change of a randomly formed segment to a conformation that is compatible to the constraint. Instead of a random process, once such a conformer is created, it will induce a neighboring segment to change into the required compatible conformation. Therefore, there is no need for hydrogen bonding or another type of associative equilibrium since the cooperativity is enhanced if the neighboring conformation remained fixed in the constraint compatible state. Clearly, this effect is seen in the comparison of PINIPAM and PEDEAM. This activated cooperative mechanism is a more convincing approach than any mean-field theory. The real theory for the coil-to-globule transition should be much more complicated than the existing ones because the constraint does not remain a constant but increases as the coil shrinks to a more ordered state.

Birstshtein and Proyamistyn[49]suggested that α is related to the reduced temperature τ and the molar mass of a polymer chain (M) as

$$\alpha - \alpha^3 + C(\alpha^3 - 1) = B\tau M^{1/2} \tag{5}$$

where B and C are two constants, independent of M and T for a given polymer solution. The plot of $(\alpha - \alpha^3)/(\alpha^{-3} - 1)$ vs $\tau M^{1/2}/(\alpha^{-3} - 1)$ should be a straight line whose slope and intercept lead to B and C, respectively. In Figure 7, the solid and dotted lines represent the best fitting of $B = 1.71 \times 10^{-2}$ and $C = 1.01 \times 10^{-2}$ and $B = 2.11 \times 10^{-2}$ and $C = 5.45 \times 10^{-2}$, respectively, for $\langle R_g\rangle_T/\langle R_g\rangle_\Theta$ and $\langle R_h\rangle_T/\langle R_h\rangle_\Theta$. Equation 5 shows that the free energy change associated with the coil-to-globule transition contains two parts: $\alpha - \alpha^3$ is related to the deformation of a Gaussian chain from its unperturbed sate, while $C(\alpha^{-3} - 1)$ is related to the total volume of the chain. The balance between them, i.e., $\alpha - \alpha^3 = C(1 - \alpha^{-3})$, is defined as the crossover point in the coil-to-globule transition. Equation 5 is useful for a phenomenological analysis of transition curves. It predicts an asymptotic behavior at large $\tau M^{1/2}$ as $\alpha^3\tau M^{1/2} \sim C/B$.

Figure 8 shows a plot of the scaled expansion factor $\alpha^3\tau M^{1/2}$ as a function of $\tau M^{1/2}$. Such a plot was previously reported for polystyrene and PMMA in various solvents[9,11] and also for PNIPAM in water.[10,18] The theory predicts that $\alpha^3\tau M^{1/2}$ should level to two asymptotic values of $C/B = 0.59$ and 2.59, respectively, for $\langle R_g\rangle_T/\langle R_g\rangle_\Theta$ and $\langle R_h\rangle_T/\langle R_h\rangle_\Theta$. Two asymptotic values of $\alpha^3\tau M^{1/2}$ from the current study are 1.2 and 4.1, respectively, for $\langle R_g\rangle_T/\langle R_g\rangle_\Theta$ and $\langle R_h\rangle_T/\langle R_h\rangle_\Theta$. Note that for stable single-chain PNIPAM globules the corresponding values of C/B are 0.22 and 0.91, respectively, It further indicates that stable single-chain PDEAM globules are less compact, presumably due to the lack of the intrachain hydrogen bonding. Finally, it is also worth noting that such a crossover point is between Θ and the temperature at which $\langle R_g\rangle$ approaches a constant.

Conclusion

Individual poly(*N*,*N*-diethylacrylamide) (PDEAM) chains can undergo a reversible coil-to-globule-to-coil transition in an extremely dilute aqueous solution even without any intrachain hydrogen bonds, which answers our previous question whether the intrachain hydrogen bonding plays a role in the formation of stable single-chain poly(*N*-isopropylacrylamide) (PNIPAM) globules. On the other hand, no formation of intrachain hydrogen bonds leads to less compact chain segments inside each single-chain PDEAM globule. The lack of intrachain hydrogen bonding affects the transition, especially the unfolding process. Unlike PNIPAM, there is no hysteresis in one coil-to-globule-to-coil transition of PDEAM chains in water. The current results confirm that the previous speculation that the hysteresis observed in the coil-to-globule-to-coil transition of PNIPAM chains in water is related to the formation of some additional hydrogen bonds in the collapsed state.

Acknowledgment. This work was supported by the Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis and the Ministry of Science and Technology of China (2007CB936401), the National Natural Science Foundation of China (Project 20574065), and the Hong Kong Special Administration Region Earmarked Grant (Project CUHK4037/06P, 2160298). Z.K. thanks the Croucher Studentship. We also thank Prof. Tang Yong for some helpful discussions and one reviewer for his/her qualitative discussion about the nature of the steepness of the sigmoidal curves in Figure 6.

References and Notes

(1) Stockmayer, W. H. *Macromol. Chem.* **1960**, *35*, 54.
(2) Lifshitz, I. M. *Zh. Eksp. Teor. Fiz.* **1968**, *55*, 2408; *Sov. Phys. JETP* **1969**, *28*, 1280.
(3) Ptitsyn, O. B.; Kron, A. K.; Eizner, Y. Y. *J. Polym. Sci., Part C* **1968**, *16*, 3509.
(4) de Gennes, P. G. *J. Phys., Lett.* **1975**, *36*, 55.
(5) Yamakawa, H. *Modern Theory of Polymer Solutions*; Harper & Row: New York, 1971; *Macromolecules* **1993**, *26*, 5061.
(6) Grosberg, A. Y.; Khokhlov, A. R. *Statistical Physics of Macromolecules*; AIP Press: Woodbury, NY, 1994.
(7) Post, C. B.; Zimm, B. H. *Biopolymers* **1979**, *18*, 1487; **1982**, *21*, 2123.
(8) Sun, S. T.; Nishio, I.; Swislow, G.; Tanaka, T. *J. Chem. Phys.* **1980**, *73*, 5971.
(9) Chu, B.; Park, I. H.; Wang, Q. W.; Wu, C. *Macromolecules* **1987**, *20*, 1965.
(10) Kubota, K.; Fujishige, S.; Ando, I. *J. Phys. Chem.* **1990**, *94*, 5154.
(11) Nakata, M. *Phys. Rev. E* **1995**, *51*, 5770.
(12) Creighton, T. E. *Protein Folding*; Freeman: New York, 1992.
(13) Chan, H. S.; Dill, K. A. *Phys. Today* **1993**, *46*, 24.
(14) Yu, J.; Wang, Z. L.; Chu, B. *Macromolecules* **1992**, *25*, 1618.
(15) Chu, B.; Ying, Q.; Grosberg, A. Y. *Macromolecules* **1995**, *28*, 180.
(16) Nakamura, Y.; Sasaki, N.; Nakata, M. *Macromolecules* **2002**, *35*, 1365.
(17) Maki, Y.; Sasaki, N.; Nakata, M. *Macromolecules* **2004**, *37*, 5703.
(18) Wu, C.; Zhou, S. *Macromolecules* **1995**, *28*, 5388.
(19) Wu, C.; Zhou, S. *Macromolecules* **1995**, *28*, 8381.
(20) Wu, C.; Zhou, S. *Phys. Rev. Lett.* **1996**, *77*, 3053.
(21) Wang, X.; Qiu, X.; Wu, C. *Macromolecules* **1998**, *31*, 2972.
(22) Wu, C.; Wang, X. *Phys. Rev. Lett.* **1998**, *80*, 4092.
(23) Qiu, X.; Wu, C. *Macromolecules* **1997**, *30*, 7921.
(24) Wu, C.; Qiu, X. P. *Phys. Rev. Lett.* **1998**, *80*, 620.
(25) Wu, C.; Zhou, S. Q. *Macromolecules* **1996**, *29*, 1574.
(26) Siu, M.; Zhang, G. Z.; Wu, C. *Macromolecules* **2002**, *35*, 2723.
(27) Chen, H.; Li, J.; Ding, Y.; Zhang, Q.; Wu, C. *Macromolecules* **2005**, *38*, 4403.
(28) Hong, L.; Zhu, F.; Li, J.; Ngai, T.; Xie, Z.; Wu, C. *Macromolecules* **2008**, *41*, 2219.
(29) Zhang, Q.; Ye, J.; Lu, Y.; Nie, T.; Xie, D.; Song, Q.; Chen, H.; Zhang, G.; Tang, Y.; Wu, C.; Xie, Z. *Macromolecules* **2008**, *41*, 2228.
(30) Berndt, I.; Pedersen, J. S.; Richtering, W. *J. Am. Chem. Soc.* **2005**, *127*, 9372.
(31) Keerl, M.; Richtering, W. *Colloid Polym. Sci.* **2007**, *285*, 471.
(32) Keerl, M.; Smirnovas, V.; Winter, R.; Richtering, W. *Angew. Chem. Int Ed.* **2008**, *47*, 338.
(33) Idziak, I.; Avoce, D.; Lessard, D.; Gravel, D.; Zhu, X. X. *Macromolecules* **1999**, *32*, 1260.
(34) Itakura, M.; Inomata, K.; Nose, T. *Polymer* **2000**, *41*, 8681.
(35) Cai, W. S.; Gan, L. H.; Tam, K. C. *Colloid Polym. Sci.* **2001**, *279*, 793.
(36) Maeda, Y.; Nakamura, T.; Ikeda, I. *Macromolecules* **2002**, *35*, 10172.
(37) Lessard, D. G.; Ousalem, M.; Zhu, X. X.; Eisenberg, A.; Carreau, P. J. *J. Polym. Sci., Part B Polym. Phys.* **2003**, *41*, 1627.
(38) Mao, H.; Li, C.; Zhang, Y.; Bergbreiter, D. E.; Cremer, P. S. *J. Am. Chem. Soc.* **2003**, *125*, 2850.
(39) Chu, B. *Laser Light Scattering*, 2nd ed.; Academic Press: New York, 1991.
(40) Pecora, R. *Dynamic Light Scattering*; Plenum Press: New York, 1976.
(41) Dill, K. A. *Biochemistry* **1990**, *29*, 7133.
(42) Chan, H. S.; Dill, K. A. *Annu. Rev. Biophys. Biophys. Chem.* **1991**, *20*, 447.
(43) Deechongkit, S.; Dawson, P. E.; Kelly, J. W. *J. Am. Chem. Soc.* **2004**, *126*, 16762.
(44) Sanchez, I. C. *Macromolecules* **1979**, *12*, 980.
(45) Akcasu, A. Z.; Han, C. C. *Macromolecules* **1979**, *12*, 276.
(46) Yamamoto, I.; Iwasaki, K.; Hirotsu, S. *J. Phys. Soc. Jpn.* **1989**, *58*, 210.
(47) Zhou, S. Q.; Fan, S. Y.; Au-yeung, S. T. F.; Wu, C. *Polymer* **1995**, *36*, 1341.
(48) This paragraph of discussion is composed of the comments of one reviewer.
(49) Birshtein, T. M.; Pryamitsyn, V. A. *Macromolecules* **1991**, *24*, 1554.

MA8019128