# Inverse Molecular Weight Dependence of Cloud Points for Aqueous Poly(*N*-isopropylacrylamide) Solutions

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**Introduction.** Poly(*N*-isopropylacrylamide) (PNIPAm) becomes an attractive polymeric material both academically and industrially due to the thermosensitivity found in its aqueous solutions and cross-linked hydrogels.[1,2] It is well-known that PNIPAm/water solution undergoes phase separation upon raising temperature beyond about 32 °C induced by the hydrophobic interaction.[3] PNIPAm can also act as a model compound for revealing the phase behavior of solutions with hydrophobic bonding since it contains both hydrophilic amide groups and hydrophobic isopropyl groups. Fully understanding the hydrophobic bonding induced phase separation would help the design for intelligent materials based on this phase change and the recognition to the heating-induced denaturation process of proteins as well.

The thermosensitivity behavior of this system is commonly believed on the base of its lower critical solution temperature (LCST) which is a common phenomenon for all polymer solutions.[4−9] However, the information about the phase diagram for the aqueous solution of PNIPAm is still confusing. By visible observation of the phase separation upon heating on only one sample, Heskins and Guillet[10] determined the cloud point temperature as a function of the polymer concentration. From optical transmittance measurements Fujishige et al.[11] showed that the cloud point curves for PNIPAm ranging in molecular weight from 50 000 to 8 400 000 were superimposable. The curve for the highest molecular weight was almost flat, i.e., parallel to the concentration axis. In contrast, Schild and Tirrell[12] argued that the cloud point for PNIPA in water depends on polymer molecular weight and concentration. To be more serious, neither the concentration of the lower critical point nor binodals for this system are available as yet. This entire situation is due to the lack of monodisperse PNIPAm samples, which are considerably difficult to be acquired by usual precipitation fractionation because it is amphiphilic.

Recently, we were successful in fractionation of PNIPAm and obtained a series of samples of different molecular weights with $M_w/M_n$ less than 1.3.[13] Using these narrowly distributed PNIPAm samples, we determined the cloud point temperature of its aqueous solutions covering the concentration from 0.58 up to 70 wt % and found a novel molecular weight dependence, in contrast to common polymer solutions with the LCST at solvent elevated temperatures.

**Experimental Procedures.** *N*-Isopropylacrylamide (NIPA) monomer provided by Kohjin Co., Japan, was recrystallized twice from a benzene/*n*-hexane mixture prior to use. The polymerization was conducted in *tert*-butyl alcohol at 55 °C for 8 h with the monomer concentration of 1.073 mol/L and the initiator azobis(isobutylonitrile) of 0.58 mol %. The obtained poly(*N*-isopropylacrylamide) (PNIPAm) sample was purified by precipitation three times from acetone solution into *n*-hexane and then fractionated by phase separation in acetone/*n*-hexane mixtures at 30 °C several times. The first fraction was produced at the volume fraction of *n*-hexane of 0.51 in the mixture, and the following fractions were obtained by adding *n*-hexane. Two fractions T-49 and T-101 were chosen to be used in this study. Their weight-average molecular weight $M_w$ determined by light scattering in tetrahydrofuran at 25 °C was 49 400 and 101 000, respectively.[14] The index of molecular weight distribution $M_w/M_n$ was 1.21 and 1.23 as estimated by a Waters-150C gel permeation chromatograph using narrowly distributed polystyrene as the standards.

After being completely dissolved in doubly distilled water, the PNIPAm/water solution was sealed in cylindrical cells of outside diameter 8 mm for cloud point measurement following the method described by Tsuyumoto et al.[15] The cell containing a test solution was mounted quiescently in a water bath thermostatically controlled with precision of ±0.05 °C under continuous stirring, and the temperature was increased or decreased at the rate about 2 °C/h near the cloud point. Cloud points were determined by monitoring the transmittance of a He−Ne laser beam passing through the solution as a function of temperature. The intensity of the transmitted light decreased sharply when temperature passed through the cloud point, and the largest uncertainty is less than ±0.05 °C.

**Results and Discussion.** Figure 1 illustrates the appearance change during phase separation in aqueous PNIPAm solutions of the samples T-49 and T-101 at the same concentration of 31 wt %. At 29.8 °C (a) both solutions are transparent while at 31.7 °C (c) they become uniformly milky white, indicating the occurrence of phase separation. It is clearly shown that at 31.2 °C (b) the solution of sample T-49 with lower $M_w$ turns to opaque while the solution of sample T-101 with higher $M_w$ is still homogeneous. The term phase separation means that the aqueous PNIPAm solution changes from a transparent homogeneous state into a uniformly milky state upon heating. However, the milky solution cannot separate into two transparent homogeneous liquid phases even when maintained at a controlled temperature for more than 1 week. Only when the PNIPAm/water solution is subjected to an ultracentrifuge at 4000 rpm at temperatures above 33 °C can a transparent liquid and a white gel be yielded.[16] Therefore, equilibrated two phases in usual meaning have not yet been obtained for this special system upon gravitation up to now.

The phase diagram for these two samples in water determined by observing the solution transmittance is depicted in Figure 2. In the complete concentration range studied from 0.58 up to 70 wt %, the cloud point temperature for a given PNIPAm sample gradually

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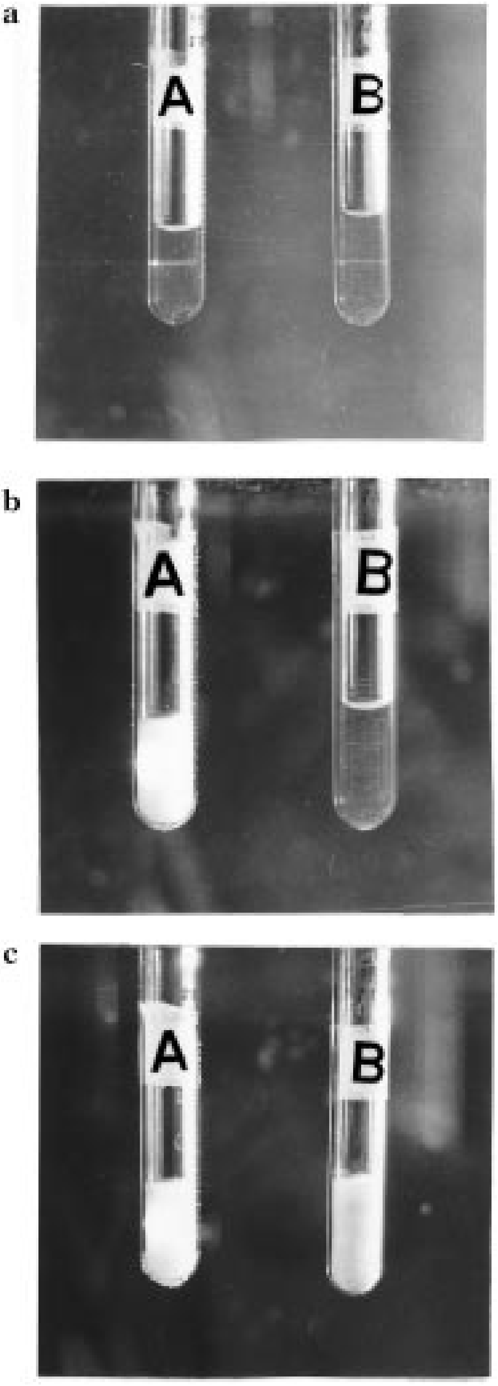

**Figure 1.** Appearance of 31 wt % aqueous solutions of poly(*N*-isopropylacrylamide) samples T-49(A) and T-101(B): (a) at 29.8 °C both solutions are homogeneous and transparent; (b) at 31.2 °C, the solution of lower molecular weight sample T-49 becomes opaque exhibiting phase transition, but the solution of higher molecular weight sample T-101 remains homogeneous; (c) at 31.7 °C the phase transition occurs in both solutions.

decreases with increasing concentration from about 33 °C down below 30 °C. Consequently, we cannot determine the critical point on account of the shape of this observed cloud point curve. It is surprising if one looks at the figure carefully that the cloud point temperature is obviously higher for the sample T-101 with higher $M_w$ than that for the sample T-49 with lower $M_w$ when compared at the same concentration. Therefore, the cloud point curve for the solution of sample T-101 is located above that for sample T-49. To confirm that the above cloud point temperature is free from heating kinetics, we also determined the cloud point temperature for some solutions by the lowering temperature, and the difference is within the experimental precision, i.e., ±0.05 °C.

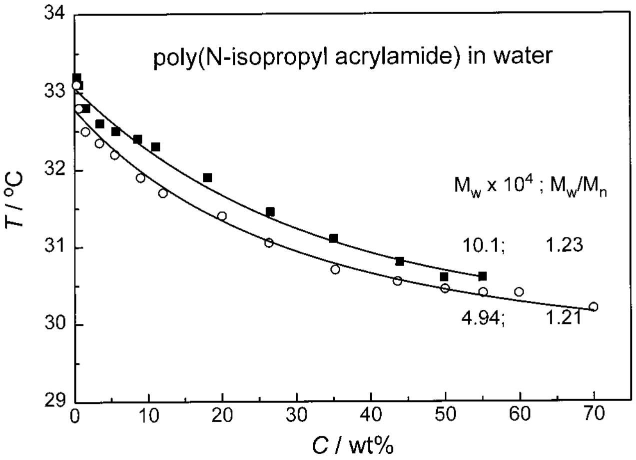

**Figure 2.** Cloud point temperatures plotted against the solution concentration for the poly(*N*-isopropylacrylamide) in water: filled square, sample T-101; open circle, sample T-49.

This is the first report on the molecular weight dependence of phase behavior in the PNIPAm aqueous solution covering such a wide concentration, which is just in contrast to the phase separation occurring in most synthetic polymer solutions with the LCST. For example, the polystyrene/cyclohexane solution separates into two liquid phases at an elevated temperature about 237 °C, close to the solvent critical.[9] Flory and collaborators[17−19] reasonably interpreted the latter phenomenon with the equation of state, which is due to the dissimilarity in the free volume of polymer and solvent, i.e., that the solvent is much more expandable than the polymer. Therefore, the difference is more obvious for the polymer with longer chain, and its phase separation appears at lower temperature.

On the other hand, there is another type of phase separation occurring in aqueous polymer solutions involving hydrogen bonds and hydrophobic residues at moderate temperatures, similar to the protein unfolding by heating.[20] The hydrophobic bonding, which already exists in small molecule solutions of amino acid,[21−23] causes this transition. The transition temperature is even used as a hydrophobicity scale for comparing amino acid residues.[24] The hydrophobic bonding is usually considered to be a local interaction acting on repeat units and thus without relation to the chain length. But there is no any experimental evidence up to now. The above results suggest that the phase behavior induced by the synergistic effect of local hydrophobic bonding be affected by the polymer molecular weight.

At present, we can classify the origin of the phase separation induced by increasing temperature into two categories: dissimilarity in the free volume of polymer and solvent and the formation of hydrophobic bonding among polymer side chains in aqueous solutions. The former occurs at the temperature close to the solvent critical and has been comprehensively understood. However, few are known for the latter appearing at moderate temperatures despite its analogy to the protein unfolding and denaturation.[25]

We have found that in aqueous PNIPAm solutions the hydrophobic bonding among isopropyl groups leads to the phase transition[26] and causes the formation of physical networks during the phase transition.[27] The present results reveal the chain length effect on the phase transition in aqueous PNIPAm solutions. All of these facts suggest that upon heating the PNIPAm chains in water aggregate together to form flocci leading to the milky appearance, and these flocci are connected to each other through bridging chains showing an equilibrium modulus. This delicate "inverse" molecular weight dependence of phase separation may be useful in developing new drug release and/or solute recovery systems with this PNIPAm/water system to control the action temperature precisely.

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## References and Notes

(1) Schild, H. G. *Prog. Polym. Sci.* **1992**, *17*, 163.
(2) Hirokawa, Y.; Tanaka, T. *J. Chem. Phys.* **1984**, *81*, 6379.
(3) (a) Kubota, K.; Fujishige, S.; Ando, I. *J. Phys. Chem.* **1990**, *94*, 5154. (b) Marchetti, M.; Pranger, S.; Cussler, E. L. *Macromolecules* **1990**, *23*, 1760 and 3445. (c) Oh, K. S.; Oh, J. S.; Choi, H. S.; Bae, Y. C. *Macromolecules* **1998**, *31*, 7328.
(4) Malcolm, G. N.; Rowlinson, J. S. *Trans. Faraday Soc.* **1957**, *53*, 921.
(5) Freeman, P. I.; Rowlinson, J. S. *Polymer* **1960**, *1*, 20.
(6) Delmas, G.; Patterson, D. *J. Polym. Sci.* **1962**, *57*, 79.
(7) Delmas, G.; Patterson, D. *Polymer* **1966**, *7*, 513.
(8) Saeki, S.; Kuwahara, N.; Konno, S.; Kaneko, M. *Macromolecules* **1973**, *6*, 246.
(9) Konno, S.; Saeki, S.; Kuwahara, N.; Nakata, M.; Kaneko, M. *Macromolecules* **1975**, *8*, 799.
(10) Heskins, M.; Guillet, J. E. *J. Macromol. Sci. Chem.* **1968**, *A2*, 1441.
(11) Fujishige, S.; Kubota, K.; Ando, I. *J. Phys. Chem.* **1989**, *93*, 3311.
(12) Schild, H. G.; Tirrell, D. A. *J. Phys. Chem.* **1990**, *94*, 4352.
(13) Xie, X.; Zeng, F.; Tong, Z. *J. South China Univ. Technol.* (in Chinese) **1998**, *26* (3), 64.
(14) Zeng, F.; Tong, Z.; Sato, T. *Sci. China (B)* **1999**, *42*, 290.
(15) Tsuyumoto, M.; Einaga, Y.; Fujita, H. *Polym. J.* **1984**, *16*, 229.
(16) Zeng, F. Doctoral Dissertation, South China University of Technology, 1998.
(17) Flory, P. J.; Orwoll, R. A.; Vrij, A. *J. Am. Chem. Soc.* **1964**, *86*, 3507.
(18) Flory, P. J. *J. Am. Chem. Soc.* **1965**, *87*, 1833.
(19) Orwoll, R. A.; Flory, P. J. *J. Am. Chem. Soc.* **1967**, *89*, 6814.
(20) Tobitani, A.; Ross-Murphy, S. B. *Macromolecules* **1997**, *30*, 4845.
(21) Nemethy, G.; Scheraga, H. A. *J. Chem. Phys.* **1962**, *36*, 3382.
(22) Nemethy, G.; Scheraga, H. A. *J. Chem. Phys.* **1962**, *36*, 3401.
(23) Nemethy, G.; Scheraga, H. A. *J. Phys. Chem.* **1962**, *66*, 1773.
(24) Urry, D. W. *J. Phys. Chem. B* **1997**, *101*, 11007.
(25) Matsumoto, T.; Inoue, H. *J. Chem. Soc., Faraday Trans.* **1991**, *87*, 3385.
(26) Zeng, F.; Tong, Z.; Feng, H. *Polymer* **1997**, *38*, 5539.
(27) Zeng, F.; Zheng, X.; Tong, Z. *Polymer* **1998**, *39*, 1249.

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