

Molecular tailoring of thermoreversible copolymer gels: Some new mechanistic insights

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We earlier reported the role of hydrophobic and hydrogen bonding interactions on the transition temperatures of thermoreversible copolymer gels. We show here that the chemical structure of the hydrophobe and its concentration determine the transition temperatures [lower critical solution temperature (LCST)] and the heat of transition of new hydrophobically modified poly(N-isopropyl acrylamide) [PNIPAm] copolymer gels. The gels, prepared by copolymerizing NIPAm monomer with hydrophobic comonomers containing increasing lengths of alkyl side groups and a terminal carboxyl acid group, showed lower LCST and lower heat of transition when compared to pure PNIPAm gel. The experimental results were also compared with theoretical calculations based on a lattice-fluid-hydrogen-bond [LFHB] model. We show experimentally and theoretically that a linear correlation exists between the transition temperature and length of the hydrophobic alkyl side group. Also, in apparent contradiction to previous work, we found a reduction in the heat of transition with increasing hydrophobicity. We propose that the presence of the terminal carboxyl acid group on the hydrophobic side chain of the comonomer prevents the association of water molecules around the hydrophobe, thereby causing a reduction in the heat of transition. The LFHB model supports this argument. © 1998 American Institute of Physics. [S0021-9606(98)50827-6]

INTRODUCTION

Polymeric hydrogels such as poly(N-isopropylacrylamide) [PNIPAm]¹ and poly(vinyl methyl ether) [PVME]² are attracting increasing attention lately because of their characteristic temperature driven volume transition near the lower critical solution temperature (LCST).³ The thermoreversible swelling-collapse transitions of gels have opened up a multitude of innovative applications in the areas of controlled drug delivery,^{4,5} bioseparations,⁶ robotics,⁷ biomedical,⁸ and even consumer products, as summarized recently by Dagani.⁹

The LCST-type volume transitions of nonionic gels such as PNIPAm can not be predicted by the Flory theory of polymeric networks since they do not consider specific energetic interactions such as hydrogen bonding, which are predominantly present in hydrogels. Our previous work using the lattice-fluid-hydrogen-bond (LFHB) theory clearly showed¹⁰ that the discontinuous volume transition of PNIPAm gel in water is caused by a large increase in the interpolymer hydrogen bonds at the transition temperature and by the temperature dependent effective hydrophobicity of the polymer. Ours is the first theoretical prediction, which has pointed out clearly the role of both hydrogen bonding and hydrophobic interactions. In a series of recent papers we have used the LFHB model to successfully predict reentrant volume transition of PNIPAm gel in ethanol-water mixture¹¹ and to

show how the hydrophilic and hydrophobic interactions could be used to control the transition temperatures of gels.¹²

The ability to control volume transition temperatures has significance in synthesizing tailored gels for specific applications such as novel separation processes. Predictions of our LFHB model have shown that large changes in the transition temperatures of thermoreversible gels can be induced by a small change in the hydrophobic nature of the monomer. This has been experimentally validated by a “pin-point variation” of methyl to ethyl groups in *L*-alanine ester side chains in hydrogels containing methacryloyl backbone.¹³ On the other hand, we have also shown that the transition temperatures can be controlled by incorporating hydrophobic comonomers which reduce the LCST, and hydrophilic comonomers which increase the LCST.

The effect of comonomers has been investigated by various groups. Mumick and McCormick¹⁴ reported that copolymerizing NIPAm with acrylamide (AAm) resulted in higher transition temperatures than pure PNIPAm gel. Similarly, Shibayama *et al.*¹⁵ found that copolymerizing NIPAm with increasing acrylic acid (AAc) or dimethylacrylamide (DMAAm) content gives gels with increasing LCSTs. They also found that the heat of demixing associated with the volume transition, which was experimentally measured by the area under the endothermic peak in differential scanning calorimetry (DSC) scans, decreased with the addition of AAc and DMAAm. Feil *et al.*¹⁶ found that copolymerization of hydrophilic comonomers such as AAm, AAc, and (diethylamino)ethyl methacrylate (DEAEMA) increased the LCST of poly(NIPAm-co-butyl methacrylate-co-*X*) terpolymer

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gels, while the copolymerization of hydrophobic butyl methacrylate with the terpolymer decreased the LCST of the gels. Moreover, the heat of the transition decreased with the addition of the hydrophilic comonomers and increased with the addition of the hydrophobic comonomer. It has also been recently reported that the copolymerization of hydrophilic AAm with hydrophobic *N,N*-dimethylamino ethyl methacrylate (DMAEMA) results in lower LCSTs than pure DMAEMA gels.¹⁷

The heat of volume transition ΔH is considered to be associated with the breakage of hydration layers of water molecules surrounding the hydrophobic groups on the polymer network. Feil *et al.*¹⁶ proposed that the presence of hydrophilic comonomers reduces the concentration of the hydrophobic groups and consequently the hydrating water layers, hence decreasing the ΔH . The opposite is true for the presence of hydrophobic comonomers in gels. Inomata *et al.*¹⁸ have shown that *n*-propylacrylamide (NPAm) gel has a lower LCST, a higher ΔH , and a larger magnitude of the transition than NIPAm and cyclopropylacrylamide (CPAm) gels. The authors propose that the larger "contact area" of the *n*-propyl group as compared to isopropyl and cyclopropyl groups enables the structuring of hydrated water molecules to a greater extent, which results in lowering of LCST and increase of ΔH for the NPAm gels.

It is clear from the foregoing that the balance of hydrophobic and hydrophilic groups in the copolymer gels plays a vital role in determining the LCST. However, it is not yet fully understood as to how various factors such as the chemical structure, the bulkiness, and the contact area of the hydrophobe affect the LCST of copolymer gels. In this paper we will investigate the role of the chemical structure of the hydrophobic comonomer on the volume phase transition and heat of demixing in PNIPAm gel. We show that, while our experimental results are in agreement with our earlier theoretical predictions,¹² they also provide new insights into the subtle effects of hydrophobic interactions on volume transitions.

We have synthesized three comonomers with increasing alkyl chain lengths using 4-aminobutyric acid, 6-aminocaproic acid, and 11- ω , aminoundecanoic acid. The above compounds were condensed with acryloyl chloride in the presence of alkali to get monomers, which were copolymerized with NIPAm to give new hydrophobically modified copolymer gels. The structures of the copolymer gels were elucidated by using ¹³C cross polarization-magic angle sample spinning (CP-MASS) nuclear magnetic resonance (NMR) spectroscopy. We observe a reduction in the LCST as well as a decrease in the heat of demixing of the copolymer gels by increasing the hydrophobic alkyl chain length in the comonomer or by increasing the content of the hydrophobic comonomer in the copolymer. A linear relation was observed between the length of the alkyl chain and the transition temperature. The reduction in the heat of demixing with increasing hydrophobicity was surprising. However, experimental results and theoretical calculations using the LFHB model suggest that while the LCSTs depend on the overall hydrophobicity of the gel, the heat of demixing depends on the extent of hydration of water around the hydrophobes,

which is crucially determined by its chemical structure. This result provides a deeper mechanistic insight into the nature of volume transition phenomenon in gels.

THEORY

We will briefly describe the extended LFHB model as applicable for the binary system of a copolymer gel and water. The total free energy of the system is the sum of free energies of mixing polymer segments with water molecules and the elastic energy of affine network deformation. The free energy of mixing is given by the LFHB theory of Panayiotou and Sanchez,¹⁹ while the elastic free energy ΔG_{el} is given by the theory of rubber elasticity as

$$\Delta G_{\text{el}} = \frac{3}{2} \left(\frac{\nu_e}{V_0} \right) \left\{ \left(\frac{V}{V_0} \right)^{2/3} - 1 - \frac{1}{3} \ln \left(\frac{V}{V_0} \right) \right\}, \quad (1)$$

where ν_e/V_0 is the number density of elastically active chains in as-synthesized gels of volume V_0 , and V is the volume of the gel at given temperature and pressure.

The free energy of mixing is calculated from a mean-field assumption in which the mers of the two components 1 and 2 are randomly placed on a lattice. For the mixture of n_1 molecules of component 1 and n_2 molecules of component 2 ($N = n_1 + n_2$), the mer length (r), the characteristic mer volume (ν^*), and the characteristic mean-field mer-mer interaction energy (ε^*) are given by

$$\frac{1}{r} = \frac{\phi_1}{r_1} + \frac{\phi_2}{r_2}, \quad (2)$$

$$\nu^* = \phi_1 \nu_1^* + \phi_2 \nu_2^*, \quad (3)$$

$$\varepsilon^* = \phi_1^2 \varepsilon_1^* + \phi_2^2 \varepsilon_2^* + 2 \phi_1 \phi_2 \zeta_{12} (\varepsilon_1^* \varepsilon_2^*)^{0.5}, \quad (4)$$

where subscripts 1 and 2 represent the components water (1) and polymer (2), respectively. ϕ is the volume fraction, r_i is the number of lattice sites occupied by a molecule of component i , ν_i^* is the characteristic mer volume of component i , and ε_i^* is the characteristic mer-mer interaction energy for component i . A pure component i is thus characterized by three parameters r_i , ν_i^* , and ε_i^* . ζ_{12} is the binary interaction parameter between components 1 and 2.

The characteristic parameters of the pure copolymer are obtained from Eqs. (2) to (4) by assuming that the copolymer can be considered as a random mixture of the two homopolymers *A* and *B*, which form the copolymer *A-B*, and that the binary interaction parameter between the two polymers ζ_{AB} is unity. In using Eqs. (2) to (4) for the copolymer, the subscripts 1 and 2 are replaced by *A* and *B* representing the two homopolymers. Thus the theory is essentially applicable only for a random copolymer *A-B*. The volume fractions of the mers of two homopolymers are calculated as

$$\phi_i = \frac{w_i / \rho_i^*}{\sum_i w_i / \rho_i^*}, \quad (5)$$

where w_i is the weight of the component i ($i = A, B$) and ρ_i^* is its characteristic density.

In a mixture of the copolymer (component 2) and the water (component 1), the binary interaction parameter ζ_{12} is calculated as

$$\zeta_{12} = \zeta_{1A}\phi_A + \zeta_{1B}\phi_B, \quad (6)$$

where the binary interaction parameters between water and the two homopolymers *A* and *B* are in general given as

$$\zeta_{1i} = a_i T + b_i; \quad i = A, B. \quad (7)$$

The binary interaction parameter between the copolymer and the water can be considered as simulating the "hydrophobicity" of the copolymer since the hydrophilic part of the interactions is considered separately in the hydrogen bonding terms in the mean-field framework of the LFHB theory as summarized below.

Let there be *i* (*i* = 1, *m*) types of proton donors and *j* (*j* = 1, *n*) types of proton acceptors in the system of gel and solvent. The total number of donors and acceptors is given by

$$N_d^i = \sum_k d_i^k n_k \quad \text{and} \quad N_a^j = \sum_k a_j^k n_k, \quad (8)$$

where d_i^k and a_j^k are the number of donors of type *i* and acceptors of type *j* in component *k*. If N_{ij} is the total number of hydrogen bonds formed between an *i*-*j* donor-acceptor pair, then the number of undonated protons of type *i* and unaccepted protons of type *j* are given by

$$N_{io} = N_d^i - \sum_j N_{ij} \quad \text{and} \quad N_{0j} = N_a^j - \sum_i N_{ij}. \quad (9)$$

If E_{ij}^0 , S_{ij}^0 , and V_{ij}^0 are the changes in the energy, entropy, and volume due to the formation of an *i*-*j* hydrogen bond, then the fraction of such *i*-*j* bonds formed is given by

$$\nu_{ij} = \left[\nu_d^i - \sum_k \nu_{ik} \right] \left[\nu_a^j - \sum_k \nu_{kj} \right] \exp(-G_{ij}^0/RT), \quad (10)$$

where,

$$\nu_{ij} = \frac{N_{ij}}{rN}; \quad \nu_d^i = \frac{N_d^i}{rN}; \quad \nu_a^j = \frac{N_a^j}{rN};$$

$$G_{ij}^0 = E_{ij}^0 + PV_{ij}^0 - TS_{ij}^0. \quad (11)$$

The free energy of mixing in the LFHB model can be calculated from the mixing rules given by Eqs. (2)–(4) and the hydrogen bonding fractions given by Eq. (10). The details of the free energy of mixing terms are described in Lele *et al.*¹⁰ From the free energy of mixing and the elastic free energy of Eq. (1), the chemical potential of water in the gel phase can be calculated as

$$\frac{\mu_1^G}{RT} = \ln(\phi_1/\omega_1) + \left(1 - \frac{r_1}{r_2}\right) \phi_2 + r_1 \tilde{\rho} \phi_2^2 X_{12}$$

$$+ r_1 \left\{ -\frac{\tilde{\rho}}{\tilde{T}_1} + \frac{\tilde{P}_1 \tilde{\nu}}{\tilde{T}_1} + (\tilde{\nu} - 1) \ln(1 - \tilde{\rho}) + \frac{1}{r_1} \ln \tilde{\rho} \right\}$$

$$+ r_1 \sum_i^m \sum_j^n \nu_{ij} - \sum_i^m d_i^1 \ln \frac{\nu_d^i}{\nu_{io}} - \sum_j^n a_j^1 \ln \frac{\nu_a^j}{\nu_{0j}}$$

$$+ \left\{ r_1 \left(\frac{\nu_e}{V_0} \right) \nu_1^* \tilde{\nu} \left[\left(\frac{V_0}{V} \right)^{1/3} - \frac{1}{2} \left(\frac{V_0}{V} \right) \right] \right\}, \quad (12)$$

where,

$$X_{12} = \frac{\varepsilon_1^* + \varepsilon_2^* - 2\zeta_{12}(\varepsilon_1^* \varepsilon_2^*)^{1/2}}{RT} \quad (13)$$

and $\tilde{\rho}$ is the reduced density of the mixture which is related to the reduced pressure $\tilde{P} = P/P^*$ and reduced temperature $\tilde{T} = T/T^*$ by the equation of state

$$\tilde{\rho}^2 + \tilde{P} + \tilde{T} \left\{ \ln(1 - \tilde{\rho}) + \tilde{\rho} \left[1 - \left(\frac{1}{r} - \sum_i^m \sum_j^n \nu_{ij} \right) \right] \right\}$$

$$+ \frac{\nu_e}{V_0} \tilde{T} \nu^* \left[\left(\frac{V_0}{V} \right)^{1/3} - \frac{1}{2} \left(\frac{V_0}{V} \right) \right] = 0. \quad (14)$$

In the first line of Eq. (12), the first two terms are the combinatorial entropy contribution, the third term is the energetic (effective hydrophobic) contribution, and the fourth term in brackets represents the effect of the pure component properties. The terms in the second line represent the hydrogen bonding contribution and the bracketed term in the third line represents the elastic energy contribution.

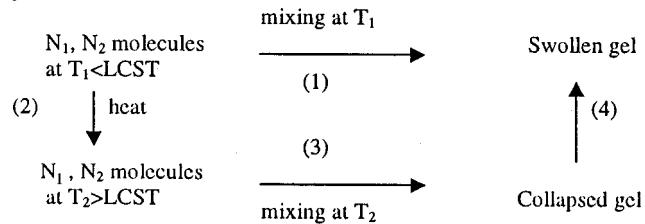
The equilibrium swelling capacity of the gel, $q = 1/\phi_2$, can be calculated from the condition that the swelling pressure of the gel at equilibrium is equal to zero. Thus,

$$\pi = \mu_1^G - \mu_1^O = 0, \quad (15)$$

where μ_1^O is the chemical potential of pure water outside the gel. Equation (15) can be solved by simultaneously solving Eqs. (10), (12), and (14). These are the main equations constituting the model.

The model parameters for a binary mixture include six pure component parameters (three for each component), one binary interaction parameter (ζ_{12}), three hydrogen bonding parameters ($E_{ij}^0, S_{ij}^0, V_{ij}^0$) for each *i*-*j* type of H bond, and the crosslink density (ν_e/V_0). Parametric values are discussed in the Results and Discussions section.

The collapse of the gel at the transition temperature occurs by demixing of polymer and water molecules, which is accompanied by a heat of demixing. This heat of demixing per gram of dry polymer gel, which is observed as an endothermic peak in a DSC experiment, can be calculated from the LFHB model by using the following thermodynamic cycle:



From the above cycle, the heats associated with steps 1 and 3 are responsible for the peak in the DSC endotherm. Therefore,

$$\Delta H_4 = -\Delta H_1 + \Delta H_3, \quad (16)$$

where ΔH_1 and ΔH_3 are the enthalpies of mixing and can be calculated from the LFHB theory on a per gram dry polymer basis by the following equation:

$$\Delta H_{\text{mix}} = \frac{r}{x_2 M W_2} \left\{ -\tilde{\rho} \varepsilon^* + \sum \tilde{\rho}_k \phi_k \varepsilon_k^* + \sum_i^m \sum_j^n E_{ij}^0 \left[\nu_{ij} - \sum_k \nu_{ij}^k \right] \right\}, \quad (17)$$

where $M W_2$ is the molecular weight of the polymer, $\tilde{\rho}_k$ is the reduced density of pure component k , and ν_{ij}^k is the number of hydrogen bonds between an $i-j$ pair in pure component k .

In the following section, we show that the extended LFHB model can quantitatively fit the experimental swelling measurements of the copolymer gels, and also qualitatively predict the experimentally observed trends in the heat of demixing of the copolymer gels.

EXPERIMENT

Materials

Acrylic acid, 4-aminobutyric acid, 6-aminocaproic acid, 11, ω -aminoundecanoic acid, ethylene glycol dimethacrylate (EGDMA), and methylene bis-acryl-amide (Bis-A) were all obtained from Aldrich Chemical Company Inc. *N*-isopropylacrylamide (NIPAm) was purchased from Poly-Sciences Inc. (Warrington, PA) and was used without further purification. AR grade 1,4-dioxane was obtained from J. T. Baker Chemical Co., Phillipsburg, NJ. Thionyl chloride was procured from S. D. Fine Chemicals, Mumbai, India and purified by distillation. The initiator azo bisobutyronitrile (AIBN) was purchased from SAS Chemical Co., Mumbai, India, and was purified by recrystallization in ethanol. The deionized distilled water was prepared in the laboratory using standard procedures.

Synthesis of monomers

Acryloyl chloride

Acryloyl chloride was synthesized by the reaction between acrylic acid and thionyl chloride. Thus, acrylic acid (20.5 ml, 0.3 M) along with dimethyl formamide (2 ml) and hydroquinone (3 g) was taken in a round bottomed flask. Freshly prepared thionyl chloride (23 ml, 0.3 M) was added dropwise over a period of 1–2 h. After complete addition of thionyl chloride, the reaction mixture was heated at 60 °C for 6 h with continuous stirring. The flask was then kept overnight at room temperature. Another 3 g of hydroquinone was added and pure acryloyl chloride was distilled out from the flask at 70–71 °C under normal conditions. The hydrophobic monomers were synthesized by the reaction between acryloyl chloride and corresponding aminoacids as per the reaction scheme shown in Fig. 1. The hydrophobic comonomers are coded on the basis of length of the alkyl chain (X).

Acryloyl-4-aminobutyric acid [X3]

In a 100 ml beaker equipped with a pH electrode, 2.25 g of 4-aminobutyric acid (0.02 M), 15 ml distilled water, and 0.8 g sodium hydroxide were placed to give a clear solution. The solution was stirred with a magnetic needle at 5–10 °C (ice-water bath). To this solution, 1.7 ml acryloyl chloride

(0.02 M) in 2 ml of dichloromethane was added dropwise over a period of 1–2 h. After addition of half of the acid chloride, pH of the reaction mixture dropped to 7.5 and it was maintained between 7.5 and 7.8 by the addition of sodium hydroxide solution. Unreacted acryloyl chloride and dichloromethane were removed by extraction with ethyl acetate. The clear aqueous layer was acidified to pH 5.0–5.5 with dilute hydrochloric acid and extracted with ethyl acetate. The product in the ethyl acetate layer was dried with anhydrous sodium sulfate and concentrated in rotavapor. On cooling the concentrate, solid monomer was precipitated. It was further purified by redissolving in ethyl acetate and reprecipitating in petroleum ether (white powder, yield—49%, melting point (m.p.) 90.1 °C).

IR (Nujol). 3278 (-NH and -OH stretching), 2950 and 2957 (-CH stretching), 1701 (-CO stretching of -COOH), 1643 (-CO stretching of -CONH₂), 1540 cm⁻¹ (-NH bending).

¹H NMR (D₂O, ppm). δ 2.3 (-CH₂COO), δ 1.8 (-CH₂-), δ 3.3 (-CH₂-N), δ 4.8 (HOD), δ 5.8 (CH₂=CH), δ 6.2 (CH₂=CH).

Acryloyl-6-aminocaproic acid [X5]

X5 was synthesized by the reaction between acryloyl chloride and 6-aminocaproic acid using the same procedure used for the preparation of X3 mentioned above. Stoichiometric amounts of reactants were used for the reaction (white powder, yield—55%, mp 77.4 °C).

IR (Nujol). 3284 (-NH and -OH stretching), 2978 and 2852 (-CH stretching), 1697 (-CO stretching of -COOH), 1650 (-CO stretching of -CONH₂), 1622 (-C=C stretching), 1546 cm⁻¹ (-NH bending).

¹H NMR (CDCl₃, ppm). δ 2.3 (CH₂COO), δ 1.7 (-CH₂-)₂, δ 1.4 ((-CH₂)₂-CH₂), δ 3.3 (-N-CH₂), δ 5.6 (CH₂=CH), δ 6.2 (CH₂=CH).

Acryloyl-11, ω -aminoundecanoic acid [X10]

X10 monomer was synthesized by the reaction between acryloyl chloride and 11, ω -aminoundecanoic acid, using the same procedure with the stoichiometric amounts of reactants. The dissolution of 11, ω -aminoundecanoic acid in aqueous alkali, however, was carried out at room temperature (28 °C) instead of 5–10 °C because of its precipitation at low temperature (white powder, yield—53%, mp 237 °C).

IR (Nujol). 3304 (-NH, -OH stretching), 2924 and 2854 (-CH stretching), 1693 (-C=O stretching of -COOH), 1652 (-C=O stretching of -CONH₂), 1623 and (-C=C stretching), 1540 cm⁻¹ (-NH bending).

¹H NMR (CDCl₃, ppm). δ 2.3 (CH₂-COO), δ 1.6 ((CH₂)₂-CH₂-COO), δ 1.3 ((-CH₂)₆), δ 3.3 (NH-CH₂), δ 5.7 (CH₂=CH₂), δ 6.25 (CH₂=CH-).

Synthesis of copolymer gels

We synthesized the gels by copolymerizing X3, X5, and X10 monomers with *N*-isopropylacrylamide as per the feed composition given in Table I. The copolymerization was carried out in 1,4-dioxane using EGDMA as a cross linker and AIBN as a free radical initiator. The reaction scheme is

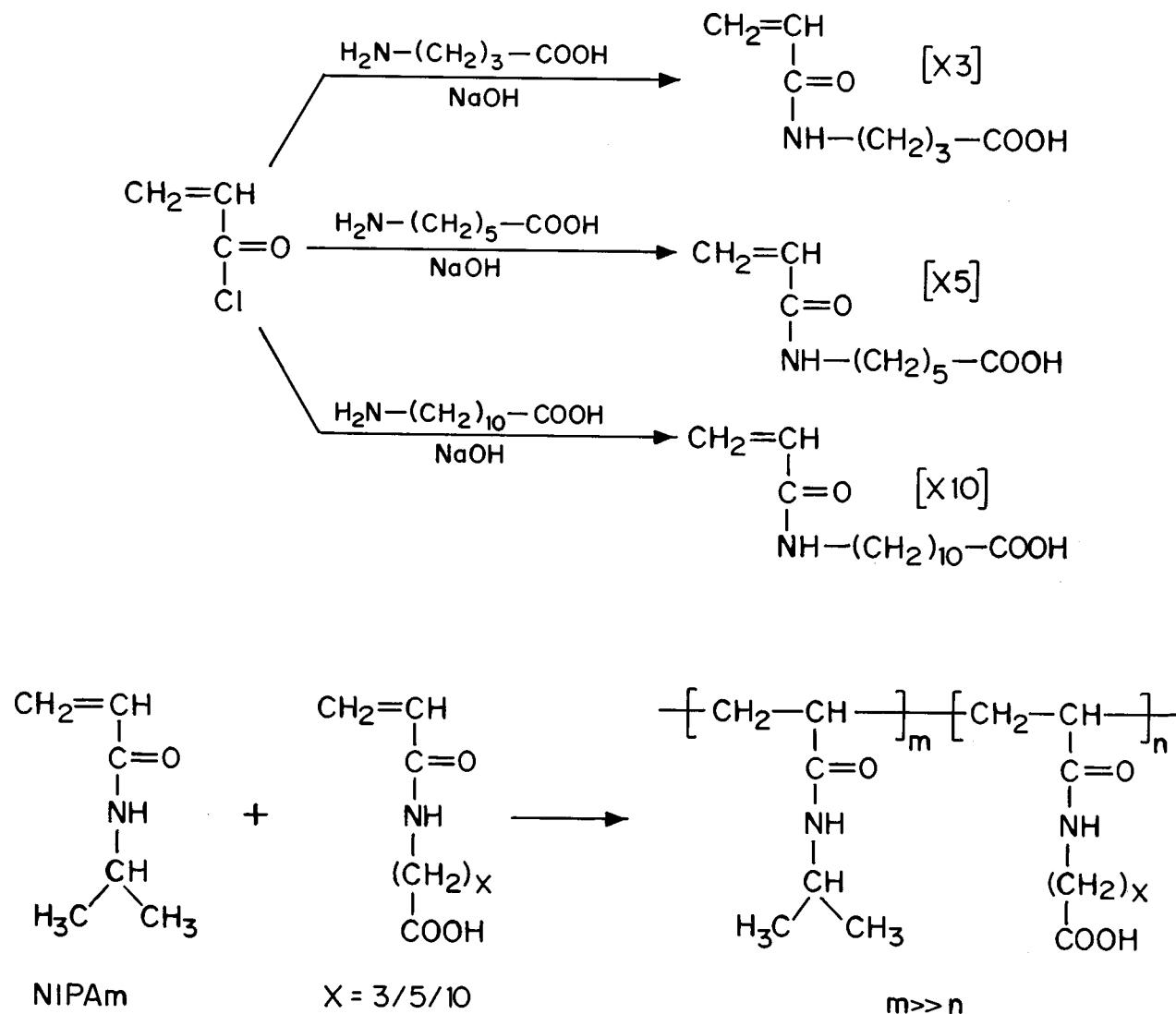


FIG. 1. Reaction scheme for the synthesis of hydrophobic monomers and the copolymer gels.

TABLE I. Feed compositions of copolymer gels.

Sample code	Mole ratio = 1/0.1 (moles)	Cross linker (moles)	Initiator (moles)	Solvent (ml)
X3-1	NIPAm/X3 (0.0177/0.00177)	EGDMA (1.5×10^{-3})	AIBN (4.87×10^{-4})	1,4-Dioxane (20 ml)
X5-1	NIPAm/X5 (0.0177/0.00177)	EGDMA (1.5×10^{-3})	AIBN (4.87×10^{-4})	1,4-Dioxane (20 ml)
X10-1	NIPAm/X10 (0.0177/0.00177)	EGDMA (1.5×10^{-3})	AIBN (4.87×10^{-4})	1,4-Dioxane (20 ml)
X5-3	NIPAm/X5 (0.0177/0.00531)	EGDMA (1.5×10^{-3})	AIBN (4.87×10^{-4})	1,4-Dioxane (20 ml)
X5-5	NIPAm/X5 (0.0177/0.0885)	EGDMA (1.5×10^{-3})	AIBN (4.87×10^{-4})	1,4-Dioxane (20 ml)
NIPAm	<i>N</i> -isopropylacrylamide			
EGDMA	Ethylene glycol dimethacrylate			
AIBN	Azo-bis-isobutyronitrile			
X3	Acryloyl-4-aminobutyric acid			
X5	Acryloyl-6-aminohexanoic acid			
X10	Acryloyl-11- ω -aminoundecanoic acid			

shown in Fig. 1. The required amounts of monomers (with defined mole ratios), crosslinking agent, and initiator were taken in a beaker and dissolved in 1,4-dioxane with constant stirring and N_2 bubbling. The reaction mixture was poured into test tubes and sealed. The polymerization was carried out at 70 °C for 24 h. The gels obtained in a cylindrical form were washed with water and ethanol for one day and dried in an oven at 40 °C till the constant weight was obtained. Copolymer gels of NIPAm and monomer X5 were prepared with three different compositions corresponding to a NIPAm/X5 mol ratio of 1/0.1 (X5-1), 1/0.3 (X5-3), and 1/0.5 (X5-5).

Characterization of gels

The gels were characterized for their molecular structure by ^{13}C MASS spectroscopy. All ^{13}C -NMR spectra were obtained on a Bruker MSL-300 FT NMR spectrometer operating at a carbon frequency of 75.47 MHz. For the CP-MASS experiments, cross polarization was established using matched Hertmann-Han conditions at 50 kHz using an adamantane as a standard. ^{13}C CP-MASS spectra of each sample were taken at two different speeds to identify the center band and side bands. The spectra were recorded at a probe temperature of 25 °C.

The thermal characterization of the gels was done using a DSC (Model 2920, TA Instruments) at a heating scan rate of 3 °C/min. Thoroughly sealed samples were equilibrated at 5 °C and then heating scans were recorded from 5 to 50 °C.

Swelling measurements were carried out by immersing 4×5 mm cylindrical dry gel samples in excess water, which was maintained at a controlled temperature within ± 0.5 °C. The gels were allowed to equilibrate for 72 h during which constant weight was reached, after which they were quickly removed and weighed. The surface water was carefully wiped off before weighing. Swelling capacity was recorded gravimetrically as

$$q = \frac{\text{wt. equilibrated gel}}{\text{wt. of dry gel}}$$

RESULTS AND DISCUSSIONS

Copolymer structure

We show in Fig. 2 the ^{13}C spectra of X3-1, X5-1, and X10-1 copolymer gels and compare them with the spectra of two homopolymer gels PNIPAm and X10. In the PNIPAm homopolymer spectrum, the $-\text{CH}_3$ peaks appear at 24.8 ppm, carbonyl of $-\text{CONH}_2$ appear at 174.7 ppm. The backbone $-\text{CH}$ and $-\text{CH}_2$ peaks resonate at the broad range of 40–50 ppm. The incorporation of hydrophobic monomer in the copolymer is confirmed by careful analysis of all the spectra. The ^{13}C spectrum of homopolymer of acryloyl-11,ω-aminoundecanoic acid shows a characteristic peak of hydrophobic side chain $-\text{CH}_2$ group at 29.6 ppm which is totally absent in the ^{13}C spectrum of PNIPAm homopolymer. However, this peak is progressively distinct in copolymer gels X3-1, X5-1, and X10-1 as the chain length of $-\text{CH}_2$ increases. This clearly indicates the incorporation of hydrophobic comonomer in the copolymer gels. It is difficult to

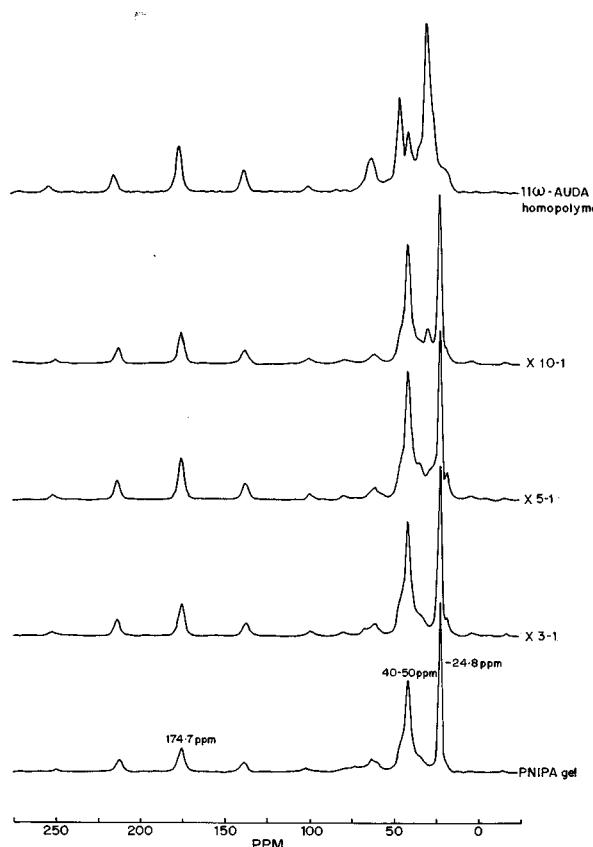


FIG. 2. Comparison of ^{13}C NMR spectra of homopolymer and copolymer gels.

distinguish between the $-\text{CO}$ signals arising due to $-\text{CONH}_2$ and $-\text{COOH}$ of copolymer gels because of their very small chemical shift differences. The quantitative estimation of the copolymer composition is extremely difficult due to uncertainties in the integration of the ^{13}C signals of copolymer gels. Moreover, the mole ratio of hydrophobically modified monomer to NIPAm monomer used for copolymerization is very low to get well resolved ^{13}C signals from comonomer structure.

We assume that since the concentration of comonomer in the gel is very small and the monomers are completely soluble in the solvent used for synthesis (1,4-dioxane), the copolymers thus formed are random copolymers.

Swelling behavior and LCST

The effect of the presence of hydrophobic comonomers on the swelling of PNIPAm based gels is shown in Fig. 3. PNIPAm homopolymer gel was found to undergo a nondiscontinuous but a steep LCST-type deswelling as the temperature was raised between 27 and 30 °C. The nature of the transition and the LCST of the gel was also confirmed from the DSC results shown in Fig. 4. As seen from the DSC heating scans, the volume transition is accompanied by a heat of demixing which appears as an endothermic peak. The broadness of the endotherm indicates that the volume transition is not completely discontinuous, which is in agreement with the swelling measurements. Also, the peak temperature of 28.5 °C corresponds closely to the midway temperature of

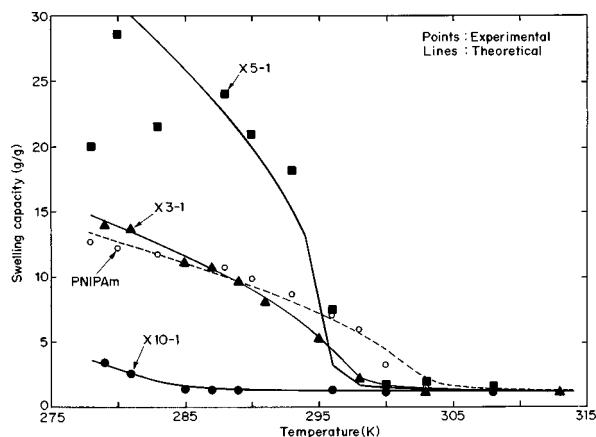


FIG. 3. Effect of alkyl chain length on swelling behavior of copolymer gels. Experimental data: (○) PNIPAm; (▲) X3-1; (■) X5-1; (●) X10-1. Lines are theoretical fits.

the range in which deswelling occurs. Therefore, we will report here the peak temperatures as the LCSTs for all gels.

X3-1 gel was found to have a lower equilibrium swelling capacity than the PNIPAm gel. The LCST of the gel as measured from swelling measurements and DSC was 24.9 °C which is lower than that of PNIPAm gel. X5-1 has a higher swelling capacity than PNIPAm, as seen from Fig. 3. However, the LCST of 21.3 °C for X5-1 is lower than PNIPAm and X3-1 gels. The higher swelling capacity of X5-1 could be due to a lower crosslink density of the gel. X10-1 has the smallest equilibrium swelling capacity and the lowest capacity LCST (10 °C) of all the copolymer gels. It was not possible to observe the endotherm for the gel in the DSC because of the low temperatures at which the LCST transition occurs for this gel. The equilibration to baseline from the initiation of the scan occurred from 5 to about 10 °C. Since the volume transition for the X10-1 gel occurred in this range, it was not possible to record its endotherm in DSC. Hence we report the LCST for this gel from the swelling measurements alone.

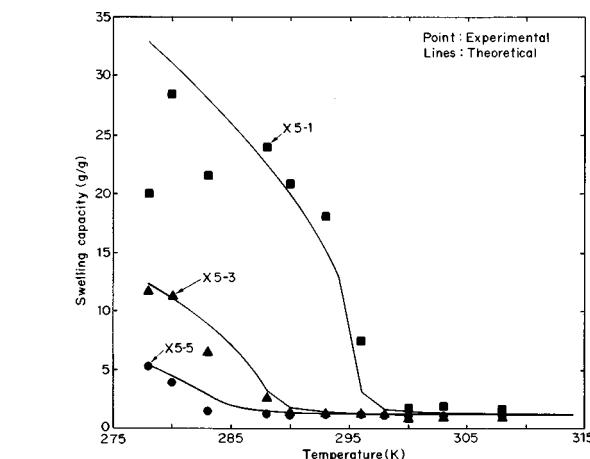


FIG. 5. Effect of concentration of hydrophobic comonomer on swelling behavior of copolymer gels. Experimental data: (■) X5-1; (▲) X5-3; (●) X5-5. Lines are theoretical fits.

The effect of increase in the concentration of the hydrophobic comonomer X5 on the swelling ratio is shown in Fig. 5. Copolymer gels X5-1, X5-3, and X5-5, which contain increasing concentrations of X5, show a decrease in LCSTs and reduced equilibrium swelling capacities. The corresponding DSC endotherms for these gels are shown in Fig. 4. X5-3 shows an LCST of 13.5 compared to 21.3 °C for X5-1. The scan for X5-5 does not show any endotherm for the same reasons as for X10-1 described above.

It can be seen from the above results that the main effect of copolymerizing NIPAm with hydrophobic comonomers is to lower the LCST of the gel. The higher the concentration of the hydrophobic comonomer and the longer the hydrophobic alkyl chain length, the lower is the LCST of the gel. Thus, increasing the concentration of the X5 comonomer reduces the LCST significantly, and increasing the chain length of the hydrophobe from X3 to X5 to X10 also reduces the LCST of the gel. These effects can be understood more quantitatively by fitting the experimental data to the extended LFHB theory as described below.

The lines through the experimental data points in Figs. 3 and 5 are the calculations of the extended LFHB theory. The various model parameters used for obtaining the theoretical fits are listed in Tables II to IV and are discussed below. Following our earlier successful work,¹⁰⁻¹² we have assumed that the pure component parameters of PNIPAm are the same as those of PMMA, given by Sanchez and Lacombe.^{20,21} We have shown that these parameters can quantitatively fit the

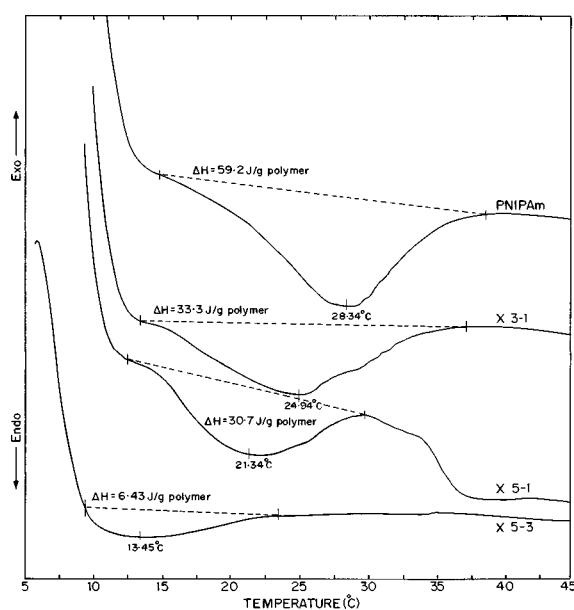


FIG. 4. DSC heating scans of copolymer gels.

TABLE II. Molecular parameters.

Component	P^* (MPa)	T^* (K)	ρ^* (kg/cm ³)	MW (g/mol)
PNIPAM	503	699	1269	10 000
Homopolymers of hydrophobic monomers	431	627	1125	10 000
Water	475	578	853	18

TABLE III. Hydrogen bonding parameters.

H bonding parameters	Donors→ acceptors ↓	—NH $d_1^2 = 80$	—OH $d_2^1 = 2$	—COOH $d_3^2 = 8, 24, 40^a$
E_{ij}^0 (J/gmol)		-3.24×10^3	-16.0×10^3	-3.24×10^3
S_{ij}^0 (J/gmolK)	—C=O	-9.9	-25.8	-10.0
V_{ij}^0 (cm ³ /gmol)	$a_1^2 = 80$	-0.85	-0.85	-0.85
E_{ij}^0 (J/gmol)		-12.5×10^3	-16.595×10^3	-12.5×10^3
S_{ij}^0 (J/gmolK)	—OH	-17.8	-26.6	-17.8
V_{ij}^0 (cm ³ /gmol)	$a_2^1 = 2$	-0.85	-4.2	-0.85
E_{ij}^0 (J/gmol)		-12.5×10^3	-16.0×10^3	-12.5×10^3
S_{ij}^0 (J/gmolK)	—COOH	-7.8	-16.6	-7.8
V_{ij}^0 (cm ³ /gmol)	$a_3^2 = 8, 24, 40^a$	-0.85	-0.85	-0.85

^a $a_3^2 = d_3^2 = 8$ for X3-1, X5-1 and X10-1. $a_3^2 = d_3^2 = 24$ for X5-3. $a_3^2 = d_3^2 = 40$ for X5-5.

swelling behavior of PNIPAm gel.¹⁰ For the copolymers of NIPAm and the hydrophobic comonomers, the extended LFHB model requires pure component properties of the homopolymer of the hydrophobic monomer. In the absence of any data for the pure component properties of these homopolymers, we have assumed, in a manner similar to the case of PNIPAm, the values for pure component properties of poly(*n*-butyl methacrylate) as being applicable for these homopolymers. These values have been reported by Sanchez and Lacombe.²² The rationale for the choice of poly(*n*-butyl methacrylate) is that it is more hydrophobic than poly(*m*-ethyl methacrylate) and that it has a similar hydrophobic side chain as that for the comonomers in our case. Table II gives the pure component properties assumed for PNIPAm and the homopolymer of the hydrophobic comonomers.

The calculations of the hydrogen bonding terms in the chemical potential require solving nine simultaneous equations represented by Eq. (10) for three pairs of donors and acceptors, which are listed in Table III. The number of donors and acceptors, and their hydrogen bonding energies, entropies, and volume changes are also listed in Table III. The hydrogen bonding parameters for the PNIPAm–water system are the same as those reported in our earlier work.¹⁰ The parameters corresponding to the hydrogen bonding between the terminal carboxyl (—COOH) group on the hydrophobic comonomer and the other donors and acceptors in the

mixture are assumed to be such that the hydrogen bonds formed are slightly stronger than those for the amide groups.

The effective hydrophobicity of the copolymer gel is represented by the binary interaction parameter ζ_{12} given by Eqs. (6) and (7). The binary interaction parameters for homopolymer PNIPAm (ζ_{1A}) and homopolymer of the comonomer (ζ_{1B}) which are required for fitting the experimental swelling data are listed in Table IV. A lower value of ζ indicates greater hydrophobicity. It is seen from the values of ζ that the effective hydrophobicity of all gels is temperature dependent and that the value of ζ at any temperature decreases for increasing chain length of the hydrophobic group. Figure 6 shows a correlation between the experimental LCST ζ , and X for the copolymer gels. The almost linear correlation between the LCST and X suggests that the LCST is reduced by about 2 °C for every additional —CH₂ group on the terminal side chain of the hydrophobe. The correlation between X and ζ at any given temperature is also almost linear. These correlations can be useful not only in quick “designing” of gels, but could also provide insights into the mechanism of volume transition of gels. It is also important to note that in fitting the swelling behavior of X5-1, X5-3, and X5-5 gels, we have not changed the interaction

TABLE IV. Binary interaction parameters and crosslink density.

Gel	Components	ζ	(ν_e / ν_0) (g/mol/cm ³)
PNIPAM	NIPAm	$1.5 - 1.56 \times 10^{-3}T$	90
X3-1	NIPAm	$1.5 - 1.56 \times 10^{-3}T$	65
	X3	$1.5 - 1.78 \times 10^{-3}T$	
X5-1	NIPAm	$1.5 - 1.56 \times 10^{-3}T$	20
	X5	$1.5 - 1.82 \times 10^{-3}T$	
X10-1	NIPAm	$1.5 - 1.56 \times 10^{-3}T$	250
	X10	$1.5 - 2.1 \times 10^{-3}T$	
X5-3	NIPAm	$1.5 - 1.56 \times 10^{-3}T$	55
	X5	$1.5 - 1.82 \times 10^{-3}T$	
X5-5	NIPAm	$1.5 - 1.56 \times 10^{-3}T$	135
	X5	$1.5 - 1.82 \times 10^{-3}T$	

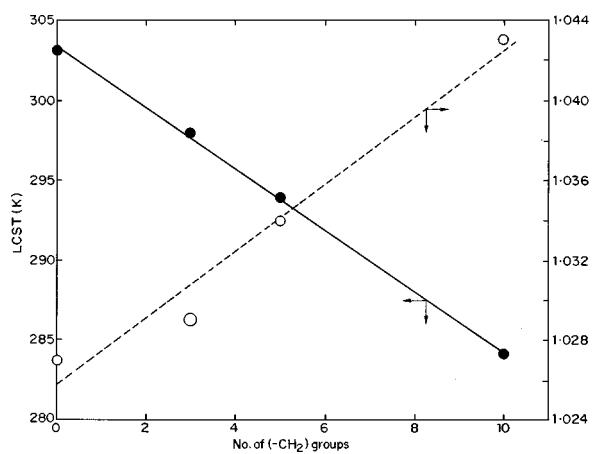
FIG. 6. Correlation between LCSTs, ζ , and length of alkyl group (X) of the comonomer.

TABLE V. Comparison between experimentally measured heat of demixing (DSC) and theoretical predictions from Eq. (17).

Length of hydrophobe (No. of $-\text{CH}_2$ groups, X)	Experimental (J/g dry polymer) (area under DSC endotherm)	Theoretical (J/g dry polymer) (Eq. 17)
0	59.2	53.90
3	33.3	50.04
5	30.7	48.30
10	...	29.94

parameter ζ_{1B} of the hydrophobic homopolymer. Since the value of ζ determines the transition temperature of the gels, the predicted lowering of the LCSTs with increasing composition of $X5$ validates our assumption of a "random" copolymer in the model and proves the strength of the model.

The values of crosslink density of the gels required for quantitatively fitting the experimental swelling data are reported in Table IV. It is seen that $X3-1$ and $X5-1$ required a lower value of crosslink density than PNIPAm gel; however, the $X10-1$ gel required a very high value of crosslink density. Similarly, the $X5-3$ and $X5-5$ gels, which contain increasing concentrations of $X5$ comonomer, required increasing values of the crosslink densities. Our synthesis procedure for copolymer gels does not provide any control over the crosslink density, hence it is possible that the copolymer gels $X3-1$ and $X5-1$ have lower crosslink densities than the PNIPAm gel. However, it is also possible that the effective crosslink density of the copolymer gels could increase as a result of additional "physical" crosslinks such as hydrophobic interactions or chain entanglements of the long hydrophobic side groups of the comonomers. This effect will increase with an increase in the chain length of the side group and with increasing contents of the hydrophobe in the copolymer gels. This could be the reason for the higher crosslink density values for the $X10-1$, $X5-3$, and $X5-5$ gels.

The DSC heating scans in Fig. 4 show the endothermic heat associated with the volume transitions of the gel. It is believed that this externally supplied heat is used to break the hydration layers around the hydrophobic groups. The exposed hydrophobes then associate, causing the gel to collapse. The temperature at which the hydrophobic hydration breaks down would decrease with an increase in the hydrophobicity of the gel. Indeed, in our copolymer gels, we find a decrease in the transition temperature with increasing hydrophobic nature (increasing X) and content (composition of the comonomer). The LFHB model also shows that a decrease in the transition temperature is caused by an increase in hydrophobicity (lower ζ) of the gel.

Besides the transition temperature, the heat associated with the volume transition will also depend on the hydrophobicity of the gel. If the heat of transition is used for breaking the hydration layers around the hydrophobic groups, then greater is the extent of hydration, and the larger will be the heat associated with the transition. Therefore it might appear that increasing the hydrophobic alkyl chain length would facilitate the formation of a larger hydration layer, and therefore would result in an increased heat of transition. This has

been discussed in the Introduction section. However, our hydrophobically modified copolymer gels showed a lower heat of transition when compared to PNIPAm homopolymer gels. Table V shows a comparison between the heat of mixing calculated from Eq. (17) for the transitions between 5 to 40 °C for all gels and the endotherms of the DSC. All the model parameters given in Tables II to IV have been used for calculating the heat of mixing. The calculations thus become completely predictive. The comparison is only qualitative, probably because of errors in the baseline fitting of heating scans and perhaps also because of the transient nature of the DSC experiment. However, it is important to note that the trends are in agreement: namely, the heat of demixing decreases with an increase in the hydrophobicity of the copolymer gels.

The above observations suggest that the water molecules are unable to structure around the hydrophobic groups in our copolymer gels. This can probably be attributed to the presence of the terminal hydrophilic carboxyl group, which hinders the formation of hydrophobic hydration around the $-\text{CH}_2$ groups of the alkyl chain. Thus, our comonomers increase the overall hydrophobicity of the copolymer gels compared to PNIPAm gel and thereby reduce the LCSTs. However, the comonomers do not allow structuring of water molecules around them and therefore do not increase the heat of demixing. The LFHB model also supports this rationale. Being an essentially mean-field theory, the model does not account specifically for structuring of water molecules around hydrophobic groups. Therefore it can not predict an increase in the heat of demixing caused by breaking down of hydration layers around the hydrophobes. On the contrary, it predicts a decrease in the ΔH due to decreased polymer–water interactions caused by the increased hydrophobicity of the copolymer (as indicated by reduced ζ). The experimental results match with the predictions, thus indicating that water does not hydrate the hydrophobic groups in our copolymers.

This shows that the subtleties of chemical structure of hydrophobes play an important role in determining the extent of hydration. We are currently investigating these effects by developing designed hydrophobic comonomers which can allow structuring of water molecules.

CONCLUSIONS

We have synthesized hydrophobic vinyl monomers containing varying lengths of alkyl groups X and copolymerized these monomers with *N*-isopropyl acrylamide monomer to give hydrophobically modified copolymer gels. These gels show lower LCST-type transition temperatures than that of pure PNIPAm gel. The reduction in the transition temperature was found to increase with the length of the alkyl group in the hydrophobic comonomers and also with an increase in the content of the comonomers. A linear correlation between the transition temperature and the number of alkyl groups was found to exist in these gels. Such a correlation could be a useful tool in designing gels having a specific transition temperature.

We have also shown that the extended LFHB theory can quantitatively fit the swelling data of the copolymer gels. The temperature dependent binary interaction parameter ζ ,

which simulates the effective hydrophobicity of the gels, was found to decrease with an increase in the alkyl chain length. The predictions of the transition temperatures of NIPAm-X5 gels containing increasing concentrations of the comonomer validate the assumption of a "random" copolymer in our model.

In apparent contradiction to previous work,^{16,17} our copolymer gels show that the heat associated with the volume transition decreases with an increase in the hydrophobic alkyl chain length. Our theoretical predictions of the heat of demixing are also in qualitative agreement with experimental observations. These results suggest that the hydrophobic groups used in our copolymer gels do not allow structuring of water around them, which is probably due to the presence of the strongly hydrophilic carboxyl terminal group. The lack of structured water reduces the heat of demixing; however, the increase in the overall hydrophobicity of the comonomer causes a reduction in LCSTs.

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