Preferential Adsorption and Co-nonsolvency of Thermoresponsive Polymers in Mixed Solvents of Water/Methanol
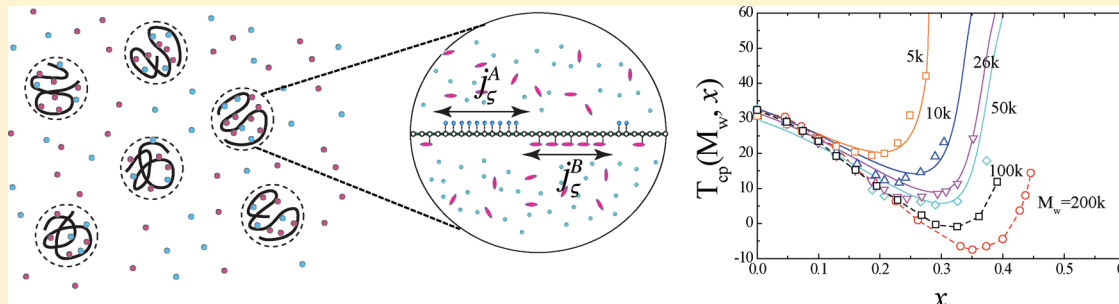
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ABSTRACT:

If two good solvents become poor for a polymer when mixed, the solvent pair is called a co-nonsolvent pair for the polymer. The sharp depression of the LCST by the co-nonsolvency in solutions of poly(N-isopropylacrylamide) in the mixed solvent of water and methanol is shown to be caused by the competitive hydrogen bonding of water and methanol molecules onto the polymer chains. On the basis of a new statistical-mechanical model for competitive hydrogen bonds, the degree of hydration $\theta^{(w)}$ and of methanol binding $\theta^{(m)}$, excess degree $\Delta\theta^E$ of solvent binding, preferential adsorption coefficients Γ, LCST spinodal lines, and cloud-point depression ΔT_{cl} are theoretically calculated and compared with the experimental results. The optimal composition $x_m(M)$ of methanol at which LCST takes the minimum value is studied as a function of the polymer molecular weight M. In the high molecular weight limit, it takes $x_m \simeq 0.35$. The solution recovers a uniform state in the region of higher methanol composition. Such a peculiar phase separation is caused by the dehydration of the polymer chains by the mixed methanol molecules in a cooperative way.

1. INTRODUCTION

The behavior of polymers in mixed solvents has been attracting the interest of many researchers ever since the concept of preferential adsorption was introduced by Ewart et al.,[1] Stockmayer,[2] Read,[3] and Dondos-Benoit.[4,5] There are several important cases depending on the nature of the solvent components.

The first one is the combination of the solvent A and B, which are both poor for the polymer but become good when mixed (cosolvency).

The second one is the opposite: the combination of solvent A and B, which are both good for the polymer but become poor when mixed (co-nonsolvency).[6−8] In particular, co-nonsolvency in aqueous solutions of temperature-sensitive polymers is practically important and has been experimentally explored over the past decades.[9−11]

The third one is the critical region of nearly incompatible mixture A and B, where the polymer chain collapses due to the concentration fluctuation of the solvent mixture, followed by the reswelling to the ideal state in the extreme vicinity of the critical point.[12−14]

In all of these cases, the treatment of the classical literature[15] on the basis of the effective interaction parameter

$$\chi_{eff} = \chi_{AP}\phi_A + \chi_{BP}\phi_B - \chi_{AB}\phi_A\phi_B \qquad (1.1)$$

breaks down because one of the components (assumed to be A) is preferentially adsorbed into the polymer coil region. The solvent composition inside the polymer coil region may be completely different from the composition in the bulk due to the interaction between the polymer and solvents.

Let θ_A be the number of A molecules attracted in the coil region (divided by the total number n of monomers (statistical units)). If these A molecules are bound in the coil region but still mobile inside it, they are called *space-bound* molecules. In contrast, if they are directly bound to the polymer chains, as seen in hydrogen-bonding (H-bonding) solvents such as water and methanol, they are called *site-bound* molecules. In either case, the degree θ_A of binding is defined by the number of A molecules bound in the coil region per monomer unit of the polymer chain. The coefficient of preferential adsorption Γ is then defined by the change of the degree of binding θ_A due to the infinitesimal increment of the composition of B molecules in the mixed solvent under a fixed temperature and pressure

$$\Gamma \equiv \left(\frac{\partial\theta_A}{\partial\phi_B}\right)_{p,T,\phi} \qquad (1.2)$$

where ϕ is the volume fraction of the polymer and ϕ_B the volume fraction of the second solvent. A small change in ϕ_B may cause a large effect on the fraction θ_A of the adsorbed molecules.

The preferential adsorption coefficient was first introduced by Ewart et al.[1] by the definition $\alpha \equiv -(dm_B/dm)_{p,T,\mu_B}$ to determine the polymer molecular weight in mixed solvents by light scattering, where m and m_A, m_B are the molarity of the polymer, the primary and secondary solvent and μ_B is the chemical potential of the second solvent. Later, a more general theory of concentration fluctuations in relation to light scattering intensity in multicomponent systems was developed by Stockmayer,[2] in which the adsorption coefficient was shown to be proportional to $(\partial\mu_B/\partial m)_{m_B}/(\partial\mu_B/\partial m_B)_m$. In order to see the sensitivity of the bound A molecules to mixed B solvent more directly, we study here the preferential adsorption by introducing the coefficient Γ under a fixed finite polymer concentration, which is related to the reduction of the bound A molecules to the infinitesimal increment of the B composition in the mixed solvent. This coefficient may be applied to both space-bound case and site-bound case equally well. Condensation of counterions near the polymer chains fall on the former category. The bound molecules, or ions, move with the polyelectrolyte polymer chains, so that the mixing entropy is substantially reduced.

The statistical-thermodynamics of preferential adsorption in mixed solvents was attempted by Yamamoto et al.[16] by introducing a *coating monolayer* into the conventional Flory—Huggins theory of polymer solutions within quasi-chemical approximation. The idea was later applied to the chain conformation in mixed solvents.[17] Though the idea hit the central concept of preferential adsorption, this theory unfortunately remained too complicate to reach specific results regarding the problems described above.

The problem of the chain dimensions in critical solvent mixtures was first studied by de Gennes[12] on the basis of preferential adsorption for the case where A and B are both good and for the case where A is good but B is poor. It was found that the polymer chain collapses in the critical region due to the attractive interaction between the polymer segments.[12] The source of this effect is indirect long-range interaction between monomers; one monomer creates a cloud of preferential solvation in its vicinity, and a second monomer is then attracted by this cloud. The interaction range is decided by the correlation length ξ of the A/B mixture, which can be large near the critical point. The result was later refined by including the shift of the critical temperature inside the coil region when the polymer collapses.[13] The drastic shift of the coexistence line of A/B solvent mixture near the critical point induced by adding small quantity of polymers was experimentally confirmed by Dondos and Izumi.[14] There have been recently renewed interest in the problem of polymer conformation in critical solvent mixtures. For instance, Grabowski et al.[18] experimentally confirmed contraction and reswelling of poly(acrylic acid)in a critical 2,6-lutidine/water mixture by the measurement of the diffusion constant. Refinement of the theory by field theoretical calculation of the polymer dimensions in critical solvent mixtures was also attempted.[19]

Polymers in aqueous media in contrast exhibit a more dramatic behavior due to the direct H-bonding of water molecules when the second solvent is mixed. For instance, poly(N-isopropylacrylamide) (PNIPAM) exhibits peculiar conformational changes in water upon mixing of a second water-miscible solvent such as methanol, tetrahydrofuran, or dioxane. Although the second solvent is a good solvent for the polymer, the polymer

chain collapses in certain compositions of the mixed solvent, followed by the reswelling under majority of the second solvent.[20]

The tendency for phase separation is also strongly enhanced by the presence of the second solvent. For instance, the LCST of aqueous PNIPAM solutions shifts to lower temperature when methanol is added.[9−11] The temperature drop is the largest, from 31.5 °C down to −7 °C, for the specific molar fraction $x_m = 0.35$ of methanol. This enhanced phase separation in mixed good solvents is known as *co-nonsolvency*.[9] Cross-linked PNIPAM gels are also known to collapse sharply in water in the presence of methanol, at around $x_m = 0.3$, and gradually recover their swollen state with increasing methanol content.[21−23]

There have been efforts to understand co-nonsolvency by the combination of three χ-parameters[9] and also by the formation of stoichiometric compounds between the solvent molecules.[20] Without considering direct hydrogen bonds between polymer and solvents, however, it is difficult to explain sharp LCST behavior and sensitivity to the molecular weight of the polymers.

We recently showed that, in solutions of PNIPAM in a mixed solvent of water and methanol, the competition in forming PNIPAM—water (p—w) H-bonds and PNIPAM—methanol (p—m) H-bonds (*competitive adsorption*) results in co-nonsolvency.[24,25] In such a case, the second solvent molecules are also site-bound. The bound methanol molecules block the formation of continuous trains of bound water molecules caused by the cooperativity of hydration. Small difference in the composition of the mixed solvent is greatly amplified, and, as a result, the composition of the bound molecules along the chain deviates substantially from that in the bulk (*nonlinear amplification*). The total coverage $\theta = \theta_A + \theta_B$ of the chain by bound molecules exhibits a minimum at the composition where the competition is strongest; hence, the chain collapses around this composition by hydrophobic aggregation of the dehydrated chain segments.

In this paper, we apply our model of cooperative hydration to the preferential adsorption and phase separation of PNIPAM in a mixed solvent of water and methanol. We calculate the fraction of bound water, the preferential adsorption coefficient, spinodal line, etc., as a function of the composition of the mixed solvent and report that the phase transition becomes sharper with increasing cooperativitiy, and hence the effect of co-nonsolvency is enhanced.

2. THE MODEL OF PREFERENTIAL ADSORPTION IN HYDROGEN-BONDING MIXED SOLVENTS

The model we consider is a polymer solution in which the number N of polymer chains with degree of polymerization (referred to as DP) n are dissolved in the number N_A of A solvent molecules and the number N_B of B solvent molecules. The polymer chains are H-bonded with both solvents A and B (Figure 1). We are specifically interested in PNIPAM dissolved in water (w) as the primary solvent A, and methanol (m) as the secondary solvent B. But the model is general enough to be applied to other polymer solutions with both site- and space-bound solvents.

The solvents A and B are assumed to be mutually miscible, and they are capable of forming H-bonds with the polymer chains (site-binding case). Therefore, there is a competition in forming p—A and p—B H-bonds.

We are based on the lattice-theoretical picture of polymer solutions and divide the system volume V into cells of size a, each of which can accommodate a statistical repeat unit of the polymer. The volume of the solvent molecule is assumed to be
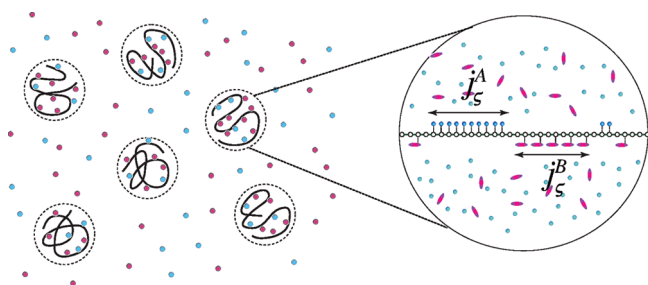
Figure 1. Model solution of hydrogen-bonded polymers in a mixed solvent. Both solvents A and B are assumed to be capable of forming hydrogen bonds with the polymers, so that there is a competition in forming p−A and p−B hydrogen bonds.

n_A for A and n_B for B in the unit of the cell volume. We assume incompressibility of the solution, so that we have $\Omega = nN + n_A N_A + n_B N_B$, where $\Omega \equiv V/a^3$ is the total number of cells.

To describe the H-bonds of A and B with the polymer chains, let (l, m) be the type of the polymer chains which carry the number l of bound A molecules and m of bound B molecules and let $N_{l,m}$ be the number of polymers of the type (l, m) in the solution. The total number of A molecules on a chain is $\Sigma l N_{l,m}$, and B molecules is $\Sigma m N_{l,m}$. Let N_{fA} be the number of free A molecules, and let N_{fB} be that of free B molecules.

We then have the material conservation laws

$$N = \sum_{l,m} N_{l,m} \tag{2.1a}$$

$$N_A = N_{fA} + \sum_{l,m} l N_{l,m} \tag{2.1b}$$

$$N_B = N_{fB} + \sum_{l,m} m N_{l,m} \tag{2.1c}$$

and

$$\Omega = \sum_{l,m} (n + n_A l + n_B m) N_{l,m} + n_A N_{fA} + n_B N_{fB} \tag{2.2}$$

The free energy we consider is

$$\beta \Delta F = \sum_{l,m} N_{l,m} \ln \phi_{l,m} + N_{fA} \ln \phi_{fA} + N_{fB} \ln \phi_{fB}$$
$$+ \sum_{l,m} \Delta_{l,m} N_{l,m} + \Omega g(\{\phi\}) \tag{2.3}$$

where $\beta \equiv 1/k_B T$, and

$$\phi_{l,m} \equiv (n + n_A l + n_B m) N_{l,m}/\Omega \tag{2.4}$$

is the volume fraction of the (l, m) polymers, and

$$\phi_{f\alpha} \equiv n_\alpha N_{fa}/\Omega \quad (\alpha = A, B) \tag{2.5}$$

are the volume fractions of the free solvent molecules. The number density of the complex molecules of the type (l, m) is

$$\nu_{l,m} = N_{l,m}/\Omega \tag{2.6}$$

The free energy

$$\Delta_{l,m} \equiv \beta \Delta A_{l,m} \tag{2.7}$$

for the formation of a complex of the type (l, m) depends on the details of the H-bonds, which will be specified when we calculate the solution properties.

The molecular interaction is included in the last term of eq 2.3 in the form

$$g(\{\phi\}) \equiv (\chi_A \phi_A + \chi_B \phi_B)\phi + \chi_{AB}\phi_A \phi_B \tag{2.8}$$

where χ_A, χ_B, and χ_{AB} are Flory's interaction parameters between polymer and A-solvent (p/A), polymer and B-solvent (p/B), and A-solvent and B-solvent (A/B). They are based on the van der Waals interaction in the background and functions of the temperature only. (We do not assume ternary interaction term $\chi_T \phi \phi_A \phi_B$ in the free energy because its molecular origin is not clear.)

By differentiation with respect to $N_{l,m}$, N_{fA}, and N_{fB}, we find the chemical potentials

$$\frac{\beta \Delta \mu_{l,m}}{n + n_A l + n_B m} = \frac{1 + \Delta_{l,m} + \ln \phi_{l,m}}{n + n_A l + n_B m} - \nu^S + g_{l,m} \tag{2.9}$$

for the polymer of (l, m) type, and

$$\beta \Delta \mu_{fA}/n_A = (1 + \ln \phi_{fA})/n_A - \nu^S + g_{fA} \tag{2.10a}$$

$$\beta \Delta \mu_{fB}/n_B = (1 + \ln \phi_{fB})/n_B - \nu^S + g_{fB} \tag{2.10b}$$

for the free solvent molecules, where

$$\nu^S \equiv \sum_{l,m} \nu_{l,m} + \frac{\phi_{fA}}{n_A} + \frac{\phi_{fB}}{n_B} \tag{2.11}$$

is the total number of translational degree of freedom in the solution, and

$$g_{fA} \equiv -g + \chi_A \phi + \chi_{AB} \phi_B \tag{2.12a}$$

$$g_{fB} \equiv -g + \chi_B \phi + \chi_{AB} \phi_A \tag{2.12b}$$

have appeared from the interaction terms. Also, we have

$$g_{l,m} \equiv \frac{n g_{0,0} + n_A l g_{fA} + n_B m g_{fB}}{n + n_A l + n_B m} \tag{2.13}$$

for the (l, m) complexes, where

$$g_{0,0} \equiv -g + \chi_A \phi_A + \chi_B \phi_B \tag{2.14}$$

By imposing the association equilibrium conditions

$$\Delta \mu_{l,m} = \Delta \mu_{0,0} + l \Delta \mu_{fA} + m \Delta \mu_{fB} \tag{2.15}$$

we find

$$\phi_{l,m} = K_{l,m} \phi_{0,0} \phi_{fA}{}^l \phi_{fB}{}^m \tag{2.16}$$

where

$$K_{l,m} = \exp(l + m - \Delta_{l,m}) \tag{2.17}$$

is the equilibrium constant. Let us write as $x \equiv \phi_{0,0}$ and $y_\alpha \equiv \phi_{f\alpha}$ ($\alpha = A, B$) for the bare polymer chains and the free solvent molecules. We then have

$$\phi = nxp(y_A, y_B) \tag{2.18a}$$

$$\phi_A = y_A + n_A \phi \theta_A(y_A, y_B) \tag{2.18b}$$

$$\phi_B = y_B + n_B \phi \theta_B(y_A, y_B) \tag{2.18c}$$

by the material conservation laws (2.1a) to (2.1c), where the function $p(y_A, y_B)$ is defined by

$$p(y_A, y_B) \equiv \sum_{l,m} b_{l,m} y_A^l y_B^m \tag{2.19}$$

($b_{l,m} \equiv K_{l,m}/(n + n_A l + n_B m)$). This function is called *binding polynomial* in the literature. It is equivalent to the grand partition function of a H-bonding chain in the mixed solvent.

The degree of binding for each component is defined by the average number of bound molecules per binding site on the polymer chain and derived from the binding polynomial by differentiation

$$\theta_\alpha(y_A, y_B) \equiv \frac{1}{n} \frac{\partial \ln p}{\partial \ln y_\alpha} \quad (\alpha = A, B) \tag{2.20}$$

In summary, we have found

$$\beta \Delta \mu_{0,0} = 1 + \ln x - nv^S + ng_{0,0} \tag{2.21a}$$

$$\beta \Delta \mu_{fA} = 1 + \ln y_A - n_A v^S + n_A g_{fA} \tag{2.21b}$$

$$\beta \Delta \mu_{fB} = 1 + \ln y_B - n_B v^S + n_B g_{fB} \tag{2.21c}$$

with

$$v^S = \phi/n + y_A/n_A + y_B/n_B \tag{2.22}$$

Substituting the equilibrium distribution function (2.16) back into the original free energy, we find

$$\beta \Delta F/\Omega = \mathscr{F}_{FH} + \mathscr{F}_{AS} \tag{2.23}$$

where

$$\mathscr{F}_{FH} = \frac{\phi}{n} \ln \phi + \frac{\phi_A}{n_A} \ln \phi_A + \frac{\phi_B}{n_B} \ln \phi_B + g(\{\phi\}) \tag{2.24}$$

is the conventional Flory–Huggins free energy, and

$$\mathscr{F}_{AS} = \frac{\phi}{n} \ln \frac{x}{\phi} + \frac{\phi_A}{n_A} \ln \frac{y_A}{\phi_A} + \frac{\phi_B}{n_B} \ln \frac{y_B}{\phi_B} + (\theta_A + \theta_B)\phi \tag{2.25}$$

is the free energy due to the molecular association.

3. PREFERENTIAL ADSORPTION BY POLYMERS IN MIXED SOLVENTS

The total degree of binding is

$$\theta \equiv \theta_A + \theta_B \tag{3.1}$$

If there is no interaction between the bound molecules, the total is given by the simple mixing law

$$\theta^\circ \equiv \theta_A^\circ x_A + \theta_B^\circ x_B \tag{3.2}$$

where θ_α° is the degree of binding in each pure solvent, and

$$x_\alpha \equiv N_\alpha/(N_A + N_B) \quad (\alpha = A, B) \tag{3.3}$$

are the mole fractions of the solvent. The excess binding is then defined by

$$\Delta \theta^E \equiv \theta - \theta^\circ = \theta_A - \theta_A^\circ x_A + \theta_B - \theta_B^\circ x_B \tag{3.4}$$

For cosolvency, the excess is positive, while for co-nonsolvency it is negative. There is a possibility that the excess binding changes its sign at a certain composition of the mixed solvent. The mole fraction of the bound molecules at such a particular concentration takes exactly the same value as the mole fraction of the solvent in the bulk outside the coil region. Such a particular point is called *azeotropic* binding.[26]

In what follows we focus on co-nonsolvency, and derive Gibbs matrix for the study of phase separation. As for the composition of the solvent mixture, we use its volume fraction

$$v_\alpha \equiv n_\alpha N_\alpha/(n_A N_A + n_B N_B) \quad (\alpha = A, B) \tag{3.5}$$

as well as the mole fraction. We then have

$$\phi_A = (1 - \phi)v_A, \quad \phi_B = (1 - \phi)v_B \tag{3.6}$$

We regard the volume fraction v_B of the second solvent as the controlling parameter, and write it as $v_B \equiv \xi$. We then have $v_A = 1 - \xi$.

3.1. Transition Matrix. Let us first relate the variation of the volume fraction y_A and y_B of the free solvents by the variation of the independent variable ϕ_A and ϕ_B (solvent composition) which are controlled variables in the experiments. We first define a matrix $J_{\alpha,\beta}$ by the equation

$$d \ln y_\alpha = \sum_\beta J_{\alpha,\beta} d\phi_\beta \tag{3.7}$$

Or, in the matrix form

$$\begin{bmatrix} d \ln y_A \\ d \ln y_B \end{bmatrix} = \begin{bmatrix} J_{A,A} & J_{A,B} \\ J_{B,A} & J_{B,B} \end{bmatrix} \begin{bmatrix} d\phi_A \\ d\phi_B \end{bmatrix} \tag{3.8}$$

By taking the derivatives of the material conservation laws (2.18a) to (2.18c), we have

$$p \, dx + \phi(\theta_A \, d \ln y_A + \theta_B \, d \ln y_B) = -(d\phi_A + d\phi_B)/n$$

$$(y_A + n_A \phi \theta_A K_{A,A}) \, d \ln y_A + n_A \phi_A \theta_A K_{A,B} \, d \ln y_B$$
$$= (1 + n_A \theta_A) \, d\phi_A + n_A \theta_A \, d\phi_B$$

$$n_B \phi \theta_B K_{B,A} \, d \ln y_B + (y_B + n_B \phi \theta_B K_{B,B}) \, d \ln y_B$$
$$= n_B \theta_B \, d\phi_A + (1 + n_B \theta_B) \, d\phi_B \tag{3.9}$$

where the matrix $K_{\alpha,\beta}$ is defined by

$$K_{\alpha,\beta} \equiv \frac{\partial \ln \theta_\alpha}{\partial \ln y_\beta} \tag{3.10}$$

Solving these equations for $d \ln y_\alpha$, we find

$$J_{A,A} = \{(1 - \phi_B - y_A)[y_B + (\phi_B - y_B)K_{B,B}] - (\phi_A - y_A)(\phi_B - y_B)K_{A,B}\}/\phi\Phi$$

$$J_{A,B} = (\phi_A - y_A)[y_B - \phi K_{A,B} + (\phi_B - y_B)(K_{B,B} - K_{A,B})]/\phi\Phi$$

$$J_{B,A} = (\phi_B - y_B)[y_A - \phi K_{B,A} + (\phi_A - y_A)(K_{A,A} - K_{B,A})]/\phi\Phi$$

$$J_{B,B} = \{(1 - \phi_A - y_B)[y_A + (\phi_A - y_A)K_{A,A}] - (\phi_B - y_B)(\phi_A - y_A)K_{B,A}\}/\phi\Phi \tag{3.11}$$

where

$$\Phi(y_A, y_B) \equiv y_A y_B + (\phi_A - y_A)y_B K_{A,A} + (\phi_B - y_B)y_A K_{B,B} + (\phi_A - y_A)(\phi_B - y_B)K \tag{3.12}$$

and

$$K \equiv K_{A,A} K_{B,B} - K_{A,B} K_{B,A} \tag{3.13}$$

is the determinant of the matrix $\hat{K}$.

3.2. Preferential Adsorption Coefficients. The preferential adsorption coefficient $\Gamma_{\alpha,\beta}$ is defined by the change $d \ln \theta_\alpha$ of the adsorbed α-component by an infinitesimal increment $d\phi_\beta$ of the β-component solvent. By multiplication of K matrix to the transition J matrix, we find

$$
\begin{bmatrix} d \ln \theta_A \\ d \ln \theta_B \end{bmatrix} = \begin{bmatrix} K_{A,A} & K_{A,B} \\ K_{B,A} & K_{B,B} \end{bmatrix} \begin{bmatrix} J_{A,A} & J_{A,B} \\ J_{B,A} & J_{B,B} \end{bmatrix} \begin{bmatrix} d\phi_A \\ d\phi_B \end{bmatrix}
$$

$$
= \begin{bmatrix} \Gamma_{A,A} & \Gamma_{A,B} \\ \Gamma_{B,A} & \Gamma_{B,B} \end{bmatrix} \begin{bmatrix} d\phi_A \\ d\phi_B \end{bmatrix} \tag{3.14}
$$

where

$$
\begin{aligned}
\Gamma_{A,A} = \{ &(1 - \phi_B - y_A)[y_B K_{A,A} + (\phi_B - y_B)K] \\
&+ (\phi_B - y_B)y_A K_{A,B}\}/\phi\Phi
\end{aligned}
$$

$$
\begin{aligned}
\Gamma_{A,B} = \{ &(1 - \phi_A - y_B)y_A K_{A,B} + (\phi_A - y_A)y_B K_{A,A} \\
&+ (\phi_A - y_A)(\phi_B - y_B)K\}/\phi\Phi
\end{aligned}
$$

$$
\begin{aligned}
\Gamma_{B,A} = \{ &(1 - \phi_B - y_A)y_B K_{B,A} + (\phi_B - y_B)y_A K_{B,B} \\
&+ (\phi_A - y_A)(\phi_B - y_B)K\}/\phi\Phi
\end{aligned}
$$

$$
\begin{aligned}
\Gamma_{B,B} = \{ &(1 - \phi_A - y_B)[y_A K_{B,B} + (\phi_A - y_A)K] \\
&+ (\phi_A - y_A)y_B K_{B,A}\}/\phi\Phi
\end{aligned} \tag{3.15}
$$

If the volume fraction ϕ of the polymer is fixed, $d\phi_A$ and $d\phi_B$ are not independent, but related by

$$
d\phi_A = -(1 - \phi)d\xi \tag{3.16a}
$$

$$
d\phi_B = (1 - \phi)d\xi \tag{3.16b}
$$

and hence the preferential adsorption coefficient is

$$
\Gamma \equiv \frac{\partial \theta_A}{\partial \xi}
$$

$$
= \frac{(1 - \phi)\theta_A}{\phi\Phi(y_A, y_B)}[(-y_B K_{A,A} + y_A K_{A,B})\phi - (\phi_B - y_B)\phi K] \tag{3.17}
$$

Here y_A and y_B are the solutions of the coupled equations

$$
y_A + n_A\phi\theta_A(y_A, y_B) = (1 - \phi)(1 - \xi) \tag{3.18a}
$$

$$
y_B + n_B\phi\theta_B(y_A, y_B) = (1 - \phi)\xi \tag{3.18b}
$$

4. PHASE SEPARATION IN MIXED SOLVENTS

Although we are ready to find the binodals by using the chemical potentials, we are involved in many technical difficulties for numerical calculations of three-component systems, in particular in the presence of the cooperativity in the H-binding. Therefore, we attempt to find spinodal lines only by the calculation of Gibbs matrix.

4.1. Construction of the Gibbs Matrix. In tertiary systems, two of the three chemical potentials are independent due to the Gibbs–Dühem relation. Here we use the chemical potentials of the free solvent molecules. The Gibbs matrix is then defined by

$$
G_{\alpha,\beta} \equiv \frac{\partial \Delta\mu_{f\alpha}}{\partial \phi_\beta} \tag{4.1}
$$

Because we have

$$
dv^S \equiv v_A\, d\phi_A + v_B\, d\phi_B \tag{4.2}
$$

for the variation of v^S, where

$$
v_A \equiv -\frac{1}{n} + \frac{y_A}{n_A}J_{A,A} + \frac{y_B}{n_B}J_{B,A} \tag{4.3a}
$$

$$
v_B \equiv -\frac{1}{n} + \frac{y_A}{n_A}J_{A,B} + \frac{y_B}{n_B}J_{B,B} \tag{4.3b}
$$

and also

$$
\begin{bmatrix} dg_{fA} \\ dg_{fB} \end{bmatrix} = \begin{bmatrix} g_{A,A} & g_{A,B} \\ g_{B,A} & g_{B,B} \end{bmatrix} \begin{bmatrix} d\phi_A \\ d\phi_B \end{bmatrix} \tag{4.4}
$$

for the variation of the interaction, we find

$$
\begin{bmatrix} d\Delta\mu_{fA} \\ d\Delta\mu_{fB} \end{bmatrix} =
$$

$$
\begin{bmatrix} J_{A,A} - n_A v_A + n_A g_{A,A} & J_{A,B} - n_A v_B + n_A g_{A,B} \\ J_{B,A} - n_B v_A + n_B g_{B,A} & J_{B,B} - n_B v_B + n_B g_{B,B} \end{bmatrix} \begin{bmatrix} d\phi_A \\ d\phi_B \end{bmatrix} \tag{4.5}
$$

for the variation of the chemical potentials, where

$$
g_{A,A} \equiv -2\chi_A\phi - (\chi_A - \chi_B + \chi_{AB})\phi_B \tag{4.6a}
$$

$$
g_{A,B} \equiv -\chi_B(\phi - \phi_B) - (\chi_A - \chi_{AB})(1 - \phi_A) \tag{4.6b}
$$

$$
g_{B,A} \equiv -\chi_A(\phi - \phi_A) - (\chi_B - \chi_{AB})(1 - \phi_B) \tag{4.6c}
$$

$$
g_{B,B} \equiv -2\chi_B\phi + (\chi_A - \chi_B - \chi_{AB})\phi_A \tag{4.6d}
$$

The Gibbs matrix is

$$
\hat{G} = \begin{bmatrix} J_{A,A} - n_A v_A + n_A g_{A,A} & J_{A,B} - n_A v_B + n_A g_{A,B} \\ J_{B,A} - n_B v_A + n_B g_{B,A} & J_{B,B} - n_B v_B + n_B g_{B,B} \end{bmatrix} \tag{4.7}
$$

4.2. Spinodal Condition. The spinodal condition is given by $|\hat{G}| = 0$. After lengthy calculation, we finally find

$$
\begin{aligned}
& -nn_A n_B \tilde{\chi}\phi\Phi - 2n_A n_B \chi_{AB}(\Phi + n\Psi) - 2n(\chi_A\Phi_A + \chi_B\Phi_B) \\
& + \Psi_A + \Psi_B + n(1 + n_A\theta_A + n_B\theta_B)^2\phi = 0 \tag{4.8}
\end{aligned}
$$

where Φ is defined by eq 3.12. The rests are

$$
\begin{aligned}
\Psi \equiv\; & y_B\theta_A(\phi_A - y_A) + y_A\theta_B(\phi_B - y_B) \\
& + \frac{1}{2}\phi^2(\theta_A K_{A,B} + \theta_B K_{B,A}) + (\phi_A - y_A)(\phi_B - y_B)[\theta_A(K_{B,B} - K_{A,B}) \\
& + \theta_B(K_{A,A} - K_{B,A})] \tag{4.9}
\end{aligned}
$$

and

$$
\Psi_A \equiv n_A y_A + (\phi_A - y_A)(n_A K_{A,A} + n_B K_{A,B}) \tag{4.10a}
$$

$$
\Psi_B \equiv n_B y_B + (\phi_B - y_B)(n_B K_{B,B} + n_A K_{B,A}) \tag{4.10b}
$$

$$\Phi_A \equiv \Psi_A \phi + (\phi_A - y_A)(\phi_B - y_B)[n_A(K_{B,A} - K_{A,A}) \\ - n_B(K_{A,B} - K_{B,B})] \tag{4.10c}$$

$$\Phi_B \equiv \Psi_B \phi + (\phi_A - y_A)(\phi_B - y_B)[n_B(K_{A,B} - K_{B,B}) \\ - n_A(K_{B,A} - K_{A,A})] \tag{4.10d}$$

The effective interaction parameter $\tilde{\chi}$ is defined by

$$\tilde{\chi} \equiv \chi_A{}^2 + \chi_B{}^2 + \chi_{AB}{}^2 - 2\chi_A\chi_B - 2\chi_A\chi_{AB} - 2\chi_B\chi_{AB} \tag{4.11}$$

5. RANDOM HYDRATION

For random hydration, the coefficient $b_{l,m}$ in eq 2.19 is proportional to the number of different ways to place l of A molecules and m of B molecules on the total cites n, and hence $b_{l,m} \sim n!/l!m!(n-l-m)!$. Let $\lambda_\alpha(T) \equiv \exp(-f_\alpha/k_B T)$ be the association constant of the H-bonding of α molecule. (f_α is the binding free energy of a single H-bond.) We then find as usual Langmuir type competitive adsorption of molecules. The binding polynomial is

$$p(y_A, y_B) = t^{-n} \tag{5.1}$$

where

$$t \equiv 1/(1 + \lambda_A y_A + \lambda_B y_B) \tag{5.2}$$

We then have

$$\theta_A = \lambda_A y_A t \tag{5.3a}$$

$$\theta_B = \lambda_B y_B t \tag{5.3b}$$

From the materials conservation law (2.1a) to (2.1c), the volume fractions of the free solvents are written as

$$y_A = \phi_A/(1 + n_A\lambda_A\phi t) \tag{5.4a}$$

$$y_B = \phi_A/(1 + n_B\lambda_B\phi t) \tag{5.4b}$$

Substituting into eq 5.2, we find that the equation to decide t as a function of the total volume fractions of the solvents is given by

$$n_A n_B \lambda_A \lambda_B \phi^2 t^3 + [\lambda_A \lambda_B (n_B \phi_A + n_A \phi_B) + n_A \lambda_A + n_B \lambda_B \\ - n_A n_B \lambda_A \lambda_B \phi] \phi t^2 + (\lambda_A \phi_A + \lambda_B \phi_B) t - 1 = 0 \tag{5.5}$$

The $\hat{K}$ matrix takes the form

$$\hat{K} = \begin{bmatrix} 1 - \theta_A, & -\theta_B \\ -\theta_A, & 1 - \theta_B \end{bmatrix} \tag{5.6}$$

Its determinant is

$$K = 1 - \theta \tag{5.7}$$

where $\theta = \theta_A + \theta_B$ is the total degree of binding, and Φ reduces to

$$\Phi = \phi_A \phi_B (1 - \theta) + y_A \theta_A \phi_B + y_B \theta_B \phi_A \tag{5.8}$$

The preferential adsorption coefficient is

$$\Gamma = -\frac{(1 - \phi)\theta_A}{\phi \Phi}\{[y_B(1 - \theta_A) + y_A \theta_B]\phi \\ + (\phi_B - y_B)(1 + \phi_A - \phi_B - 2y_A)(1 - \theta)\} \tag{5.9}$$

The spinodal condition is given by eq 4.8, where we have

specifically

$$\Psi = \phi_A \phi_B - \Phi \tag{5.10a}$$

$$\Psi_A = n_A y_A + [n_A(1 - \theta_A) - n_B \theta_B](\phi_A - y_A) \tag{5.10b}$$

$$\Psi_B = n_B y_B + [n_B(1 - \theta_B) - n_A \theta_A](\phi_B - y_B) \tag{5.10c}$$

$$\Phi_A = [n_A \phi_A - (n_A \theta_A + n_B \theta_B)(\phi_A - y_A)]\phi \\ - (n_A - n_B)(\phi_A - y_A)(\phi_B - y_B) \tag{5.10d}$$

$$\Phi_B = [n_B \phi_B - (n_A \theta_A + n_B \theta_B)(\phi_B - y_B)]\phi \\ - (n_B - n_A)(\phi_B - y_B)(\phi_A - y_A) \tag{5.10e}$$

Obviously, there is no excess binding $\Delta\theta^E = 0$.

For numerical calculation of the phase diagrams, we fix the necessary parameters in the following way. We first assume the conventional Shultz−Flory form

$$n_A \chi_A(T) = n_B \chi_B(T) = 1/2 - \psi\tau \tag{5.11}$$

for the χ-parameters,[27] where $\tau = 1 - \Theta_0/T$ is the reduced temperature deviation measured from the reference theta temperature Θ_0 satisfying $\chi(\Theta_0) = 1/2$, and ψ is a material parameter of order unity. At the temperature Θ_0, the second virial coefficient of a hypothetical Flory−Huggins solution without hydrogen-bonding interaction vanishes. The reference temperature Θ_0 is not the true theta temperature Θ at which the second virial coefficient of the osmotic pressure vanishes. The latter lies far below Θ_0. As for A/B interaction, we assume the athermal mixture $\chi_{AB} = 0$ because the mixed solvent is completely miscible.

The association constant is then expressed as $\lambda_A(T) = \lambda_{A0} \exp(|\varepsilon|/k_B T) = \lambda_{A0} \exp[\gamma_A(1 - \tau)]$, where λ_{A0} gives the entropy part of the binding free energy, and $\gamma_A \equiv |\varepsilon|/k_B\Theta_0$ gives the binding energy of a water molecule measured relative to the thermal energy at the reference theta temperature. Throughout the present numerical calculation, we fix ψ at $\psi = 1.0$, and other parameters are $n = 100$, $n_A = n_B = 1$, $\lambda_{A0} = 0.002$, $\gamma_A = 3.5$, and $\sigma_A = 1.0$.

Figure 2a shows how the phase diagram shifts by mixing the fictitious second solvent, which is assumed to be symmetric to water, but with slightly different H-bonding amplitude $\lambda_{B0} = 0.003$. The volume fraction of the second solvent is varied from curve to curve. The miscibility loop monotonically shrinks with the volume fraction ξ. The bottom part of the miscibility loop corresponds to the LCST phase separation.

Figure 2b shows the spinodal temperature plotted against the volume fraction ξ of the second solvent. The amplitude λ_{B0} of the H-bond of the second solvent is varied from curve to curve. For small values of λ_{B0}, the LCST decreases (the miscibility gap expands) with the composition of the second solvent, while for large values of λ_{B0}, it goes up (the miscibility gap shrinks).

Figure 3a shows the binding isotherms of the completely symmetric solvent pair A and B at the polymer concentration $\phi = 0.1$ plotted against the solvent composition. The temperature is fixed at $\tau = -1.0$. The amplitude of the H-bond is fixed at $\lambda_{A0} = \lambda_{B0} = 0.002$. Because the adsorption takes place independently, θ_A decreases in proportion to the composition (Raoult's law), while θ_B increases in proportion to the composition (Henry's law). The composition of the adsorbed molecules is the same as
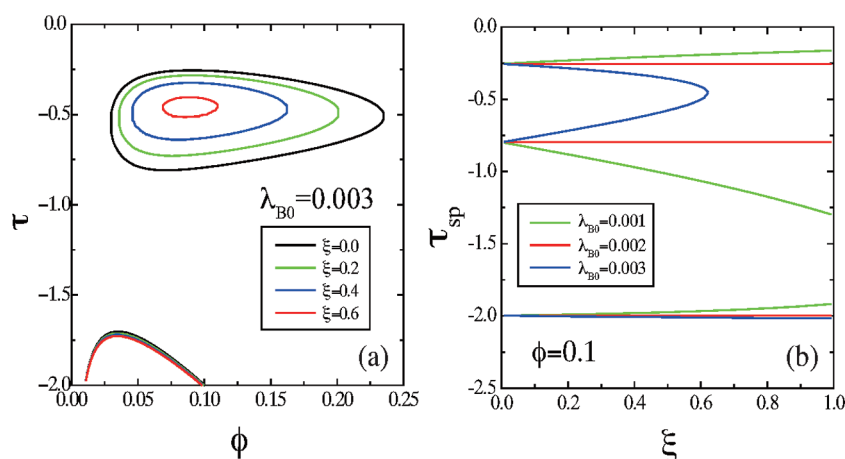
Figure 2. (a) Phase diagrams on the (ϕ,τ) plane for random binding. The solvent composition ξ is changed from curve to curve. (b) Shift of LCST line by mixing the second solvent for the polymer volume fraction $\phi = 0.1$. The strength $\tilde\lambda_{B0}$ is changed, while $\gamma = 3.5$ is fixed.
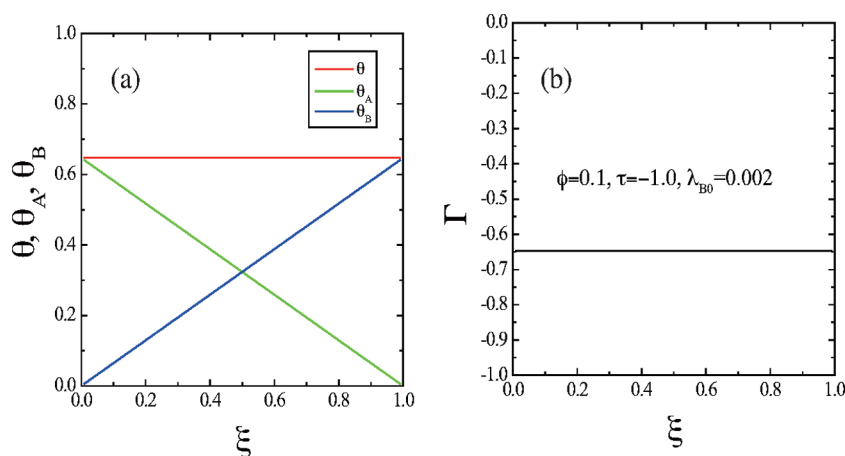

Figure 3. (a) Binding isotherm for random adsorption. The degree of binding for each solvent component and the total degree of binding are plotted against the solvent composition ξ in the symmetric case $n_A = n_B = 1$ and $\lambda_A(T) = \lambda_B(T) = 0.002$. (b) Preferential adsorption coefficient Γ plotted against ξ.

that in the bulk. The total degree of adsorption $\theta = \theta_A + \theta_B$ is therefore independent of the solvent composition.

Figure 3b shows the preferential adsorption coefficient plotted against the solvent composition. It is negative and independent of the solvent composition. It gives the initial slope of θ_A in Figure 3a if we put $\xi = 0$.

6. COOPERATIVE HYDRATION

If there is attractive interaction between the adjacent bound molecules of the same species, H-bonding is not random but cooperative. Each chain carries continuous H-bonding sequences of A and of B (Figure 1). Let j_ζ^A be the number of the A-sequences that consist of a number ζ of contiguous bound A molecules, and let j_ζ^B be that of the B-sequences. The H-bonded state of a chain is specified by the indices $\mathbf{j}^A \equiv \{j_1^A, j_2^A,...\}$ and $\mathbf{j}^B \equiv \{j_1^B, j_2^B,...\}$. We then find necessary relations simply by replacing $l \rightarrow \Sigma\zeta j_\zeta^A$ and $m \rightarrow \Sigma\zeta j_\zeta^B$.

The equilibrium constant (2.17) is given by[25]

$$K(\mathbf{j}^A, \mathbf{j}^B) = \omega(\mathbf{j}^A, \mathbf{j}^B) \prod_\zeta (\eta_\zeta^A)^{j_\zeta^A}(\eta_\zeta^B)^{j_\zeta^B} \quad (6.1)$$

The combinatorial factor ω is the number of different ways to find the distribution of sequences specified by $(\mathbf{j}^A, \mathbf{j}^B)$ and is given by

$$\omega(\mathbf{j}^A, \mathbf{j}^B) = \frac{[n - \sum \zeta(n_A j_\zeta^A + n_B j_\zeta^B)]!}{\prod j_\zeta^A! \prod j_\zeta^B![n - \sum[(n_A\zeta + 1)j_\zeta^A + n_B\zeta + 1)j_\zeta^B]]!} \quad (6.2)$$

The statistical weights η_ζ^α for $\alpha = A, B$ are found by considering the detailed structure of molecular binding. If the free energies $\Delta f_\alpha (\alpha = A,B)$ of the attractive interactions between the adjacent bound molecules of the same species are strong, we can assume that they are given by the Zimm–Bragg form[24,28-30]

$$\eta_\zeta^\alpha = \sigma_\alpha \lambda_\alpha(T)^\zeta \quad (6.3)$$

to include cooperativity within the same species, where $\lambda_\alpha(T) \equiv \exp[-(f_\alpha + \Delta f_\alpha)/k_B T]$ is the association constant for the H-bonding of a solvent molecule of α species onto the repeat unit of the polymer chain, and $\sigma_\alpha \equiv \exp(-|\Delta f_\alpha|/k_B T)$ is the cooperativity parameter due to the interaction free energy Δf_α

between the nearest-neighboring bound water molecules. Smaller σ_α gives a stronger cooperativity.

6.1. One-Mode Approximation. Because it is difficult to take the sum over all possible H-bonding types $(j_\zeta{}^A, j_\zeta{}^B)$, let us find the most probable distribution (referred to as mpd) that minimizes the free energy $\mathscr{F}_{AS}$ eq 2.25 by imposing the conditions

$$\frac{\partial \mathscr{F}_{AS}}{\partial j_\zeta{}^A} = \frac{\partial \mathscr{F}_{AS}}{\partial j_\zeta{}^B} = 0 \qquad (6.4)$$

Simple calculation leads to the result

$$j_\zeta{}^\alpha / n = (1 - \tilde{\theta}) t \eta_\zeta{}^\alpha q_\alpha{}^\zeta \quad (\alpha = A, B) \qquad (6.5)$$

for mpd, where

$$\tilde{\theta} \equiv n_A \theta_A + n_B \theta_B, \quad v \equiv v_A + v_B \qquad (6.6)$$

$$q_\alpha \equiv y_\alpha t^{n_\alpha} \quad (\alpha = A, B) \qquad (6.7)$$

and

$$t \equiv 1 - v/(1 - \tilde{\theta}) \qquad (6.8)$$

Substituting these results into the definitions, we find

$$\theta_\alpha \equiv \frac{1}{n} \sum_\zeta \zeta j_\zeta{}^\alpha = (1 - \tilde{\theta}) t V_1{}^\alpha(q_\alpha) \qquad (6.9)$$

for the degree of H-bonding, and

$$v_\alpha \equiv \frac{1}{n} \sum_\zeta j_\zeta{}^\alpha = (1 - \tilde{\theta}) t V_0{}^\alpha(q_\alpha) \qquad (6.10)$$

for the average number of H-bonded sequences, where

$$V_k{}^\alpha(q_\alpha) = \sum_{\zeta=1}^{n_\alpha^*} \zeta^k \eta_\zeta{}^\alpha q_\alpha{}^\zeta \quad (k = 0, 1, 2, \ldots) \qquad (6.11)$$

(n_α^* is the maximum integer smaller than or equal to n/n_α.)

From the definition of t, we then find

$$t(q_A, q_B) = 1/[1 + V_0{}^A(q_A) + V_0{}^B(q_B)] \qquad (6.12)$$

and

$$\theta_\alpha = V_1{}^\alpha(q_\alpha)/[1 + V_{01}{}^A(q_A) + V_{01}{}^B(q_B)] \quad (\alpha = A, B) \qquad (6.13)$$

with $V_{01}{}^\alpha$ defined by

$$V_{01}{}^\alpha(q_\alpha) \equiv V_0{}^\alpha(q_\alpha) + n_\alpha V_1{}^\alpha(q_\alpha)$$

$$= \sum_{\zeta=1}^{n_\alpha^*} (1 + n_\alpha \zeta) \eta_\zeta{}^\alpha q_\zeta{}^\alpha \qquad (6.14)$$

The coupled equations to find y_α in terms of ϕ_α are

$$y_A = \phi_A - n_A \phi \theta_A(q_A, q_B) \qquad (6.15a)$$

$$y_B = \phi_B - n_B \phi \theta_B(q_A, q_B) \qquad (6.15b)$$

Eliminating y_α by the substitution of these relations into (6.7), we find the coupled equations for q_A and q_B as

$$q_A = [\phi_A - n_A \phi \theta_A(q_A, q_B)] t(q_A, q_B)^{n_A} \qquad (6.16a)$$

$$q_B = [\phi_B - n_B \phi \theta_B(q_A, q_B)] t(q_A, q_B)^{n_B} \qquad (6.16b)$$

6.2. Transition Matrix in One-Mode Approximation. From the form (6.13) for θ_A, its infinitesimal variation is given by

$$d \ln \theta_A = \left[\frac{V_2{}^A(q_A)}{V_1{}^A(q_A)} - \frac{V_{12}{}^A(q_A)}{1 + V_{01}{}^A(q_A) + V_{01}{}^B(q_B)} \right] d \ln q_A$$

$$- \frac{V_{12}{}^B(q_B)}{1 + V_{01}{}^A(q_A) + V_{01}{}^B(q_B)} d \ln q_B$$

$$= [\zeta_A - (1 + n_A \zeta_A) \theta_A] d \ln q_A - (1 + n_B \zeta_B) \theta_B d \ln q_B \qquad (6.17)$$

where

$$\zeta_\alpha \equiv V_2{}^\alpha(q_\alpha)/V_1{}^\alpha(q_\alpha) \qquad (6.18)$$

is the average sequence length of the α component. Hence we have

$$\begin{bmatrix} d \ln \theta_A \\ d \ln \theta_B \end{bmatrix} =$$

$$\begin{bmatrix} \zeta_A - (1 + n_A \zeta_A) \theta_A, & -(1 + n_B \zeta_B) \theta_B \\ -(1 + n_A \zeta_A) \theta_A, & \zeta_B - (1 + n_B \zeta_B) \theta_B \end{bmatrix} \begin{bmatrix} d \ln q_A \\ d \ln q_B \end{bmatrix} \qquad (6.19)$$

Similarly, by taking the derivatives of the coupled eqs 6.15a and 6.15b for q_A and q_B, we find after lengthy calculation

$$\begin{bmatrix} d \ln y_A \\ d \ln y_B \end{bmatrix} =$$

$$\begin{bmatrix} 1 + n_A \theta_A/(1 - \tilde{\theta}), \, n_A \theta_B/(1 - \tilde{\theta}) \\ n_B \theta_A/(1 - \tilde{\theta}), \, 1 + n_B \theta_B/(1 - \tilde{\theta}) \end{bmatrix} \begin{bmatrix} d \ln q_A \\ d \ln q_B \end{bmatrix} \qquad (6.20)$$

Solving these equations for $d \ln q_A$ and $d \ln q_B$ and substituting the results into eq 6.19, we find for the transition matrix in the form

$$K_{AA} = [\zeta_A - (1 + n_A \zeta_A) \theta_A](1 - n_A \theta_A) + (1 + n_B \zeta_B) n_B \theta_A \theta_B \qquad (6.21a)$$

$$K_{AB} = -[\zeta_A - (1 + n_A \zeta_A) \theta_A] n_A \theta_B$$
$$\qquad\qquad - (1 + n_B \zeta_B) \theta_B (1 - n_B \theta_B) \qquad (6.21b)$$

$$K_{BA} = -[\zeta_B - (1 + n_B \zeta_B) \theta_B] n_B \theta_A$$
$$\qquad\qquad - (1 + n_A \zeta_A) \theta_A (1 - n_A \theta_A) \qquad (6.21c)$$

$$K_{BB} = [\zeta_B - (1 + n_B \zeta_B) \theta_B](1 - n_B \theta_B) + (1 + n_A \zeta_A) n_A \theta_A \theta_B \qquad (6.21d)$$

The determinant of the transition matrix $\hat{K}$ is

$$|\hat{K}| = (1 - \tilde{\theta})[\zeta_A \zeta_B - \zeta_A (1 + n_B \zeta_B) \theta_B - \zeta_B (1 + n_A \zeta_A) \theta_A] \qquad (6.22)$$

In summary, our strategy is as follows. We first solve the coupled eqs 6.16a and 6.16b for q_A and q_B for the given temperature and ternary composition ϕ, ϕ_A, ϕ_B. Then we substitute the result
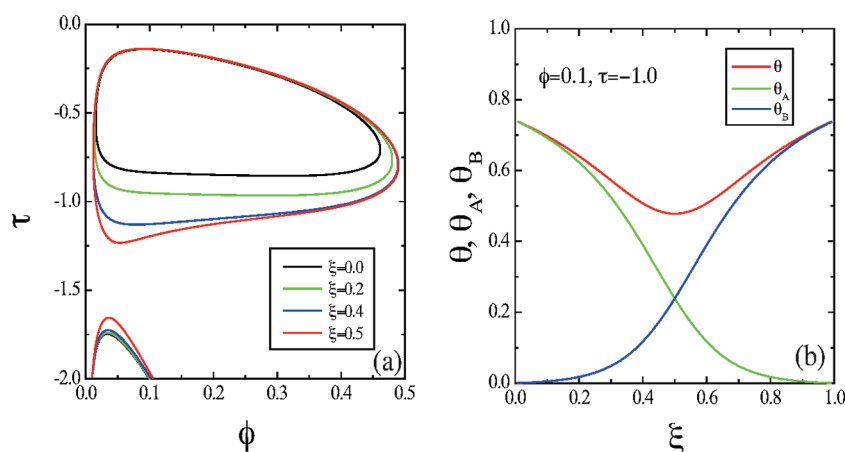
Figure 4. (a) Phase diagrams on (ϕ, τ) plane for the cooperative binding in the case of a completely symmetric mixed solvent. The solvent composition is changed from curve to curve for $n = 100$, $\gamma = 3.5$, $\lambda = 0.002$, $\sigma = 0.3$. (b) Binding isotherm for the cooperative binding. The degree of binding θ_α for each solvent component and the total degree of binding θ plotted against the volume fraction ξ of the B-component.

into θ_α, $\Gamma_{\alpha,\beta}$, and the spinodal condition (4.8) to find the preferential adsorption coefficients and LCST spinodal lines.

Specifically, we use ZB form (6.3) for the statistical weight of the ζ sequences. Then, we have

$$V_0^A(q_A) = \sigma_A w_0^A(\lambda_A q_A) \tag{6.23a}$$

$$V_{01}^A(q_A) = \sigma_A w_{01}^A(\lambda_A q_A) \tag{6.23b}$$

etc., where

$$w_k^\alpha(q) \equiv \sum_{\zeta=1}^{n_\alpha^*} \zeta^k q^\zeta \tag{6.24a}$$

$$w_{01}^\alpha(q) \equiv w_0^\alpha(q) + n_\alpha w_1^\alpha(q) \tag{6.24b}$$

etc. Rewriting $\lambda_\alpha q_\alpha$ as q_ω, we have

$$t = 1/[1 + \sigma_A w_0^A(q_A) + \sigma_B w_0^B(q_B)] \tag{6.25a}$$

$$\theta_A = \sigma_A w_1^A(q_A)/[1 + \sigma_A w_{01}^A(q_A) + \sigma_B w_{01}^B(q_B)] \tag{6.25b}$$

$$\theta_B = \sigma_B w_1^B(q_B)/[1 + \sigma_A w_{01}^A(q_A) + \sigma_B w_{01}^B(q_B)] \tag{6.25c}$$

$$\zeta_A = w_2^A(q_A)/w_1^A(q_A) \tag{6.25d}$$

$$\zeta_B = w_2^B(q_B)/w_1^B(q_B) \tag{6.25e}$$

6.3. Phase Diagrams and the Nature of Preferential Adsorption. Let us study the phase diagrams of polymers in mixed solvents. To find the characteristics of H-bonding mixed solvents, the association constants are described by the form $\lambda_\alpha(T)$ $= \lambda_{\alpha,0} \exp(|\varepsilon_\alpha + \Delta\varepsilon_\alpha|/k_B T) = \lambda_{\alpha,0} \exp[\gamma_\alpha(1 - \tau)]$, where $\lambda_{\alpha,0}$ gives the entropy part of the binding free energy, and $\gamma_\alpha \equiv |\varepsilon_\alpha + \Delta\varepsilon_\alpha|/k_B \Theta_0$ gives the binding energy of a water molecule measured relative to the thermal energy at the reference theta temperature. The cooperativity parameters are $\sigma_\alpha = \exp(-|\Delta f_\alpha|/k_B T)$. In the following calculation, we assume σ_α are independent of the temperature for the reason that cooperativity originates in the conformation entropy of the hydrophobic groups on the side chains.

We first consider the simplest case of symmetric solvent mixture for which $n_A = n_B$, $\chi_A(T) = \chi_B(T) = 1/2 - \psi\tau$ and $\chi_{AB} = 0$ holds. The cooperativity of the solvents is also assumed to be the same $\sigma_A = \sigma_B \equiv \sigma$.

Figure 4a shows how the phase diagram is modified by mixing second solvent. As for the H-bonding associating constant, we assume $\gamma_A = \gamma_B \equiv \gamma$. The miscibility loop expands, while the miscibility dome at low temperature goes up with the volume fraction ξ of the second solvent. Although the bottom part of the miscibility loop is very flat in pure A solvent, the lower critical solution point (the minimum in LCST) becomes evident when B solvent is mixed. In this figure, it is located at $\phi \simeq 0.05$.

Figure 4b shows how the bound A molecules are replaced by B molecules with the solvent composition for the completely symmetric solvent mixture. The polymer volume fraction and the temperature are fixed at $\phi = 0.1$, $\tau = -1.0$. They deviate from Henry's (Raoult's) law, and the total degree of binding has a minimum at the center $\xi = 0.5$ due to the cooperativity. The binding isotherms take a so-called sigmoidal shape.

Figure 5a shows the excess degree of binding. It is negative definite due to the cooperativity of H-bonding. Its initial slope is finite. The components A and B are mutually exclusive on the polymer chain. They repel each other and avoid forming mixed sequences. As a result, the total degree of adsorption is reduced by the competition in forming bonds. The corresponding selective adsorption coefficient is plotted in Figure 5b. It shows how sharply the A component is dissociated by mixing the B component in the solution. At the composition where this coefficient takes the minimum value (maximum in the absolute value), the bound A molecules are most sensitively dissociated by B molecules. This composition (0.42 in this figure) takes place before the total degree of adsorption becomes minimum.

Figure 6a shows more about the phase diagram for the symmetric mixture with slightly smaller binding energy $\gamma_A = \gamma_B = 3.1$. The LCST and UCST merge in the phase diagram by mixing the second solvent, so that the miscibility gap takes an hourglass shape. When mapped onto the temperature−solvent composition plane, its cross section takes the shape shown in Figure 6b. There is a continuous phase separation region in the central part of the composition. The polymer is completely immiscible in this region. The upper UCST is independent of the solvent composition, while the LCST is very sensitive to the
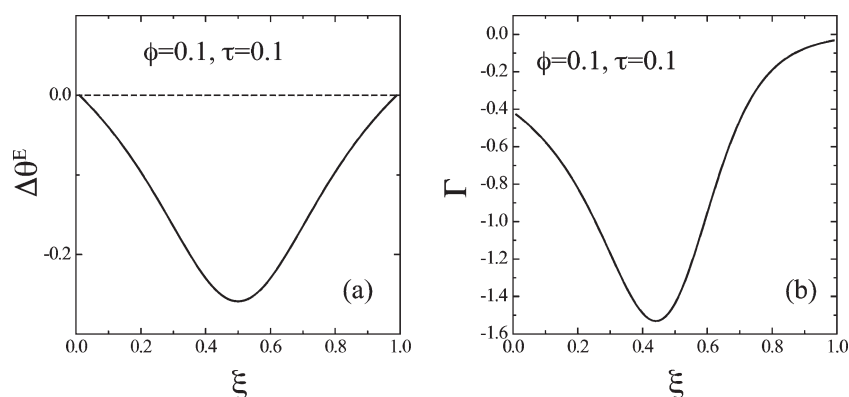
Figure 5. (a) Excess binding $\Delta\theta^E$ plotted against ξ for the symmetric mixture with the cooperative parameter $\sigma = 0.3$. (b) Its preferential adsorption coefficient Γ plotted against ξ. The minimum, where the degree of binding θ_A drops most sharply, takes place below 0.5.
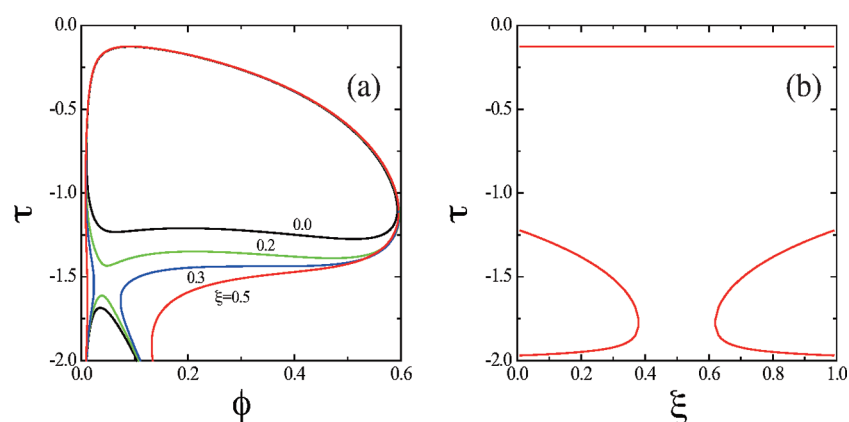

Figure 6. (a) Hourglass type of the phase diagrams on (ϕ,τ) plane for cooperative binding in symmetric solvent mixture. The solvent composition is changed from curve to curve ($n = 100$, $\gamma = 3.1$, $\lambda = 0.002$, $\sigma = 0.3$). (b) Cross section of the phase diagram at polymer volume fraction $\phi = 0.1$.

solvent composition. In fact, such an hourglass-type co-nonsolvency phase diagrams have been observed for ethanol, propanol, etc., as the second solvent[31] although the shape of the miscibility gap is asymmetric.

In order to see how the loop and dome merge in detail, we show in Figure 7 the shift of LCST and UCST by changing γ from 3.1 to 3.5. The point at which LCST and UCST merge is called double critical point (DCP). We have here a DCP on the temperature–solvent composition plane occurring at the critical value of $\gamma = 3.244$. The ternary solution exhibits an interesting critical behavior characteristic to the DCP, but its study is beyond the scope of this paper.

6.4. Comparison with the Experiments. So far, we have been confined to the model calculations mainly of the symmetric solvent mixture. We now break the symmetry and attempt to describe the mixture of water and methanol. The volume fraction ξ of methanol introduced in eq 3.6 is related to the mole fraction x through

$$\xi = n_B x / [n_A(1 - x) + n_B x] \qquad (6.26)$$

We first introduce a couple of new quantities which characterize the LCST cloud point (CP) temperature $T_{cl}(x)$ as a function of the methanol composition (mole fraction) x. We regard the main A component as water and the secondary B component as methanol. Let $T_{min} \equiv T_{cl}(x_{min})$ be the minimum temperature of the CP curve which takes place at the mole fraction x_{min} and
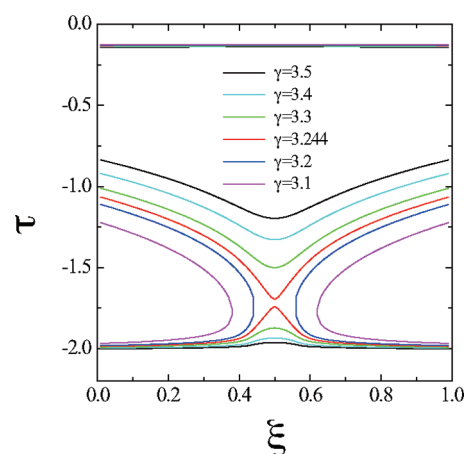

Figure 7. Double critical point appearing at a certain value of H-bonding energy ($\gamma = 3.1$ in this figure) on the temperature–solvent composition plane. For simplicity, solvents are assumed to be symmetric.

introduce the temperature difference

$$\Delta T_{min} \equiv T_{cl}(0) - T_{cl}(x_{min}) \qquad (6.27)$$

between CP in pure water and its value at methanol composition x_{min}. Figure 8 shows the graphical counterparts of these definitions.

We prepared the samples by mixing the solutions of PNIPAM (1.0 g L^{-1}) in water and PNIPAM (1.0 g L^{-1}) in methanol. The amount of the solutions was measured by weight. Cloud points were determined by the detection of changes in turbidity of solutions heated at a constant rate $(0.2 \text{ °C min}^{-1}$ for most samples, 0.5 °C min^{-1} for several samples with a very wide phase transition temperature scale). Turbidity was measured with UV spectrometer. Both the inflection points in the absorbance–temperature plots and the 90% transmittance points in the transmittance–temperature plots were chosen as the LCST and plotted as a function of the methanol volume fraction. Details of the experimental part will be reported in our forthcoming paper.[32]

The inflection points in the absorbance–temperature plots for polymers of different molecular weights are plotted in Figure 9a. The data (symbols) show a systematic shift to deeper minimum and larger methanol fraction with increase in the molecular weight. The fitting the LCST data by theoretical calculation (solid lines) of the spinodal curve for cooperative H-bonding is also shown. The concentration of the polymer is fixed at 1 g L^{-1} in the experiment, while the molecular weight is changed from curve to curve. The parameters used are $n_A = 1$, $n_B = 2$, $\sigma_A = 0.30$, $\sigma_B = 0.42$, $\gamma_A = \gamma_B = 3.5$, $\lambda_{A0} = 0.002$, and $\lambda_{B0} = 0.004$. The interaction parameters are eq 5.11 and $\chi_B = 0.34$, $\chi_{AB} = 0$.

We have neglected the H-bonding between water and methanol and assumed $\chi_{AB} = 0$ because water and methanol are completely miscible. Although this is a crude treatment of the

water/methanol mixture, it seems that p–w and p–m H-bonds play the dominant role for the molecular weight dependence of co-nonsolvency. However, the effect of water–methanol clustering remains an open question.

Because we know from the literature[33] that the spinodal line deviates upwards substantially from the cloud point curve in the very dilute region, we have fixed the volume fraction of the polymer at the value $\phi = 0.1$, larger than the actual experiment. In the region between $\phi = 0.001$ and $\phi = 0.2$, LCST in pure water is almost independent of the polymer concentration, but the polymer concentration may cause a profound effect, such as merging of LCST and UCST as seen in Figure 6a, and should be studied in detail.

For high molecular polymers $(M_w = 200 \text{ kg mol}^{-1})$ deviation of the LCST from the spinodal is large due to the predicted DCP formation as shown in in Figure 9b. Therefore, we have not tried the fitting in Figure 9a. The appearance of a DCP, followed by formation of an hourglass phase separation region, has not been observed in water/methanol mixture, but the phase separation regions identifiable to be hourglass are reported for water/ethanol and water/propanol mixtures.[31]

The cloud point depression and the minimum composition are plotted against the reciprocal molecular weight in Figure 9b. For the molecular weights below 50 kg mol^{-1}, $\Delta T_{\min}$ falls on a straight line, although the data for larger molecular weight deviate from this line. The large positive deviation indicates that the cloud point temperature goes down lower than that expected by simple extrapolation due to the DCP formation. The UCST co-nonsolvency accelerates the downward shift of the LCST.

7. CONCLUSIONS AND DISCUSSION

We have developed a new theoretical framework capable of studying polymers in mixed solvents in which polymer and solvents strongly interact. The special case of competitive H-bonding between the polymer and the two solvents is studied in detail, and the results were applied to the co-nonsolvency phenomena observed in aqueous polymer solutions with methanol as the second solvent. These are typical cases of preferential adsorption by the direct site-binding. If H-bonding is cooperative, the composition of the bound water molecules along the polymer chain is not proportional to the composition in the bulk but shows a large deviation from linearity (nonlinear amplification). Also, a slight bias in the overall solvent composition from the stoichiometric one is largely amplified on the chain due to the interaction
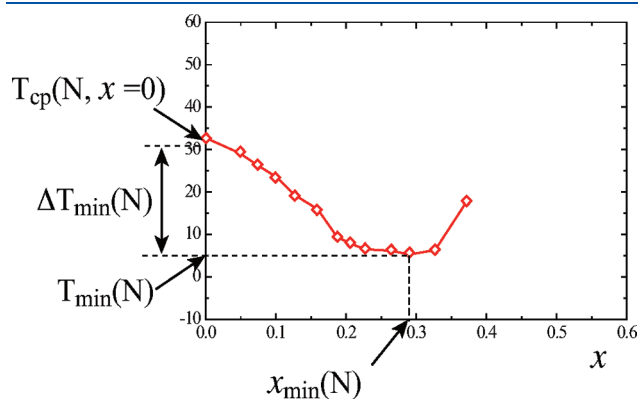

Figure 8. Definitions of the cloud point depression $\Delta T_{\min}$ and the composition x_m the lowest cloud temperature.
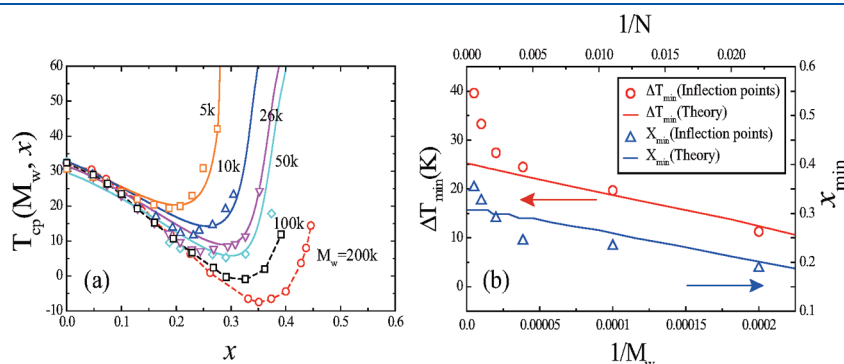

Figure 9. (a) Cloud point curves plotted against the methanol mole fraction. The polymer molecular weight is varied from curve to curve. Experimental data (symbols) are compared with the theoretical calculation (solid lines) on the basis of the cooperative H-bonding. (b) Cloud point depression $\Delta T_{\min}$ and the methanol mole fraction $x_{\min}$ plotted against the reciprocal of the polymer molecular weight. In the limit of high molecular weight, theoretical curve (solid line) largely deviate from the data (symbols) due to the DCP formation.

between the bound molecules (majority rule). The co-nonsolvency is one manifestation of such interesting nonlinear effects whose molecular origin lies in the cooperativity of H-bonds in polymeric systems.

There have been several theoretical studies to elucidate the mysterious co-nonsolvency phenomena of PNIPAM in mixed solvent of water and methanol. The first one postulates that the main cause of this phenomenon is the formation of a H-bonding network (clustering) between water and methanol molecules (w—m).[20] According to this theory, the solvent composition at the minimum cloud point temperature must stay independent of the polymer molecular weight. The observed sensitivity of the LCST line to the polymer molecular weight is difficult to explain based on this interpretation. Moreover, the observed hourglass-type co-nonsolvency[31] in the combination of water and ethanol, propanol is also difficult to explain because no specific structures in these mixtures have been reported in the literature.

The second interpretation stresses the importance of the composition fluctuation in the solvent mixture.[34] The preferential adsorption of one component near the polymer chains induces attractive interaction between the chain segments, as in the critical solvent mixture as described in the Introduction. Composition fluctuations may be important for the solvent pairs with partial miscibility, such as water and tetrahydrofuran (THF), which was shown to reveal LCST phase separation at the 0.2 mole fraction of THF and $T = 40$ °C. For a completely miscible pair, such as water and methanol, however, the correlation length ξ of the concentration fluctuations stays much smaller than the average radius R_g of gyration of a chain, so that a significant fluctuation effect is unlikely to occur.

The third interpretation is the selective adsorption by competitive H-bonding. There are mainly two cases of the competition: (1) the primary solvent A (water) competes with the secondary solvent B (methanol) in forming H-bonds on the polymer chain, and (2) the secondary solvent B competes with the polymer in forming A—B and p—A H-bonds. The first case is what we have studied here. The second case occurs when the secondary solvent molecules take the bound water molecules away from the polymer chains. The LCST depression observed in aqueous PNIPAM solutions by added salts falls in this category, although the second component is not a solvent but hydrated ions. We have successfully described the observed co-nonsolvency phenomena from the viewpoint of the type (1) competitive H-bonding. The theoretical model developed here on the basis of the assumption (1) has however strict limitations in its application range because other possibilities such as composition fluctuation, structure formation of the mixed solvents, the type (2) of competitive H-bonding, etc., have not been examined.

Finally, we discuss potential application of our theoretical model to co-nonsolvency (reentrant volume phase transition) of cross-linked PNIPAM gels.[23] If the average sequence length $\bar{\zeta}$ of the bound water molecules is shorter than the length $n_\times$ of the subchain connecting the cross-links, the cooperativity in hydration is not affected by the cross-links, and hence sharp collapse by temperature change is expected.[35] Under such conditions, bound water molecules are blocked by H-bonding of methanol molecules onto the polymer chains when they are mixed below the collapse transition temperature, so that dehydration, followed by the collapse, takes place sharply. If H-bonds of methanol has also cooperativity, the recovery to the swollen state also takes place sharply with increase in the methanol composition. Studies of the

co-nonsolvency in cross-linked gels along this line will soon be reported in our forthcoming paper.[36]

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