

Swelling and Deswelling Transition of Water-Soluble Poly(N-isopropylacrylamide) by a Method of Blob Rescaling

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Abstract—The transition behavior of swelling and deswelling of water-soluble poly(N-isopropylacrylamide) was calculated by a *decorated UNIQUAC model* with blob concept. The deswelling behavior of hydrogels at high temperatures was also reported with shrinking volumes during the transition. Polymer chains were scaled within a directly interacting size as blobs, which are composed of a segmentalized polymer chain and solvent molecules and counted blobs of hypothetical components or segments. The interaction parameters of bulks, UNIQUAC interaction parameters, were approximated with temperature-independent site interaction energies following the blob renormalization transformation. The swelling gel transition volume at each given temperature was calculated with the decorated UNIQUAC model. The blob rescaling model successfully described the first order transition of swelling-deswelling behaviors.

Key words: Swelling Transition, Poly(N-isopropylacrylamide), Blob Rescaling, *Decorated UNIQUAC*

INTRODUCTION

Temperature-sensitive hydrogels have received considerable attention because of their technical importance and scientific interest. There sometimes occurs a reversible, discontinuous change of phases in environmental conditions such as solvent composition, pH, ionic composition, and temperature [Bae et al., 1990; Chun and Kim, 1996; Dong and Hoffman, 1991; Gehrke et al., 1989; Kim and Kim, 1997; Kim et al., 1999; Kwon et al., 1991; Ohmine and Tanaka, 1982; Park and Hoffman, 1992; Peppas and Peppas, 1991; Shild, 1992; Tanaka, 1981].

Recently, poly(N-isopropylacrylamide) gels in water have been shown to exhibit a thermoshinking type of transition [Hirokawa and Tanaka, 1984], in which the collapse of gels occurs in response to an increase in temperature. Since swelling changes of gels enable one to regulate the solute diffusivity within gels, the on-off solute release or release rates may be controlled by swelling-shrinking changes induced in gels [Chun and Kim, 1996; Iwata et al., 1991]. The temperature-induced collapse transition of gels is analogous to the phase separation of polymer solutions with a lower critical solution temperature (LCST). Therefore, it cannot be explained by conventional polymer-solution theories such as the Flory-Huggins model [Flory, 1953] and by Tanaka's theory [Tanaka, 1981], but may depend largely on the interaction affinity between polymer chains and solvents, i.e., water. Aqueous solutions of poly(N-isopropylacrylamide) [p(NIPAAm)] exhibit a lower critical solution temperature (LCST) in the vicinity of 305 K [Bae et al., 1990; Shild, 1992], and the temperature-responsive behavior can be controlled by sim-

ply changing the temperature without altering the chemical structure.

For binary systems of polymer-solvent mixtures, the UCST's were explained in terms of the conformational entropy, but the LCST's were attributed to local molecular interactions between the specific orientation or to the free volume effect created by a thermal expansion of polymer molecules and solvent. This general phenomenon, in which two liquids that are completely miscible at a lower temperature form a two-phase system at higher temperatures [Kim and Kim, 1988], has been extensively studied. The models, which are normally used today to explain this phenomenon are based on the idea of Hirschfelder et al. [Hirschfelder et al., 1937]. They suggested that intermolecular potentials between two types of molecules forming solubility gap are strongly attractive (e.g., hydrogen bonds) in small regions and repulsive in large regions.

Here we are interested in the phase equilibria of water-soluble polymers in terms of the *decorated UNIQUAC model* by the blob rescaling [Ban et al., 1989; Kim and Kim, 1988]. It is known that solvents adsorbed on or near polymer chains may alter the chain properties and that the boundary layer structures of solvents near a chain would differ from their bulk structures as well. Therefore, the renormalized lattice of blobs was approximated by performing two-step renormalization of lattice [Kim and Kim, 1988; Kim et al., 1996].

DECORATED UNIQUAC MODEL WITH BLOB CONCEPT

1. Blob Solution Presentation

Let us imagine the solution structure of polymer in a good solvent. The orientational and configurational structures of a polymer chain in a solution fluctuate around a stable structure of having the minimum free energy mainly in the form of a thermal motion of a chain and its neighboring sites. In such a dynamic interaction of a polymer chain with a solvent or polymer, a contact scale between solvent and some finite dimensions of polymer segments, called a blob, is approximated as the most important part of interaction. The

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dimension of contact may not extend toward the entire dimension of a polymer chain, but localize within the dimension.

Within this picture, we observe first that a collision occurs within a finite contact area and a cross section of polymer segment (i.e., blob) relevant to a solvent molecule. In interactions on or through a chain that does not belong to the target sites, the impact of collision is of a higher order and negligible. Second, individual groups (i.e., blobs) are also assumed to have independent motions free from neighboring groups in a chain and behave like an independent molecule - as subdivided pseudocomponents. Any linkages between such blobs are not allowed despite the connectivity of chains, but are relaxed as in freely rotating joints. Third, such a blob, having a finite number of segments, is assumed to undergo no significant structural change internally during the course of an instantaneous collision. In these assumptions, polymer chains are fundamentally treated as chains of blobs (i.e., pseudocomponents), but the internal structure of blobs may depend only on a polymer itself and solvents. The internal structure of a blob thus remains unchanged, as it was at the concentration range of calculation.

For a polymer chain in a solution, let's take a random walk of N blobs on a periodic lattice and operate N successive steps from one end of a chain to the other. At each step of varying a step size g , the next jump of a blob may proceed toward any of its nearest-neighbor sites; the statistical weight is the same for all these possibilities. The length of a step in a chain is the size of a blob, whose distribution can be normalized by taking a proper distribution function. Here we face a problem of N/g independent variables, leading to Gaussian statistics provided that N/g is large and the mean-square end-to-end distance is linear in the number of blobs N ;

$$\langle r^2 \rangle = \frac{N}{g} \langle c^2 \rangle = N\xi^2 \quad (1)$$

where $\xi = (\langle c^2 \rangle / g)^{1/2}$ is now an effective length per blob. Then we can break up the chain into a series of blobs, each with an average size of ξ .

In addition to the size of blobs, the shape and molecular weight of blobs are also important factors accounting for interactions between blobs and solvents. Therefore, another structural factor of blob q , representing the ratio of surface areas, is introduced. The shape of blobs and the blob weight are closely related to the step size g and are averaged along with ξ . For convenience, volume and surface area parameters of blobs in polymers can be obtained from the van der Waals volume and area parameters $\Gamma_i^* = (V_{wi}/V_{ws})$ and $q_i^* = (A_{wi}/A_{ws})$ of species i can be determined by the standard method, where V_{wi} and A_{wi} are the van der Waals volumes and areas of a molecule given by Bondi [Bondi, 1968] and the subscript s represents the reference segment of methylene group.

2. Lattice and Group Renormalization

It is also known that solvents adsorbed on or near polymer chains may alter chain properties and that the boundary layer structures of solvents near a chain would differ from their bulk structures. Therefore, our third assumption follows that groups of polymer segments and solvents will form new groups of blobs. In fact, one of the simplest idealizations of these semi-flexible polymer chains or groups in a chain consists of such a successive renormalization of lattices or groups. A successive lattice transformation of mixtures occurs from their sub-lattice onto a lattice, and groups in a chain also are

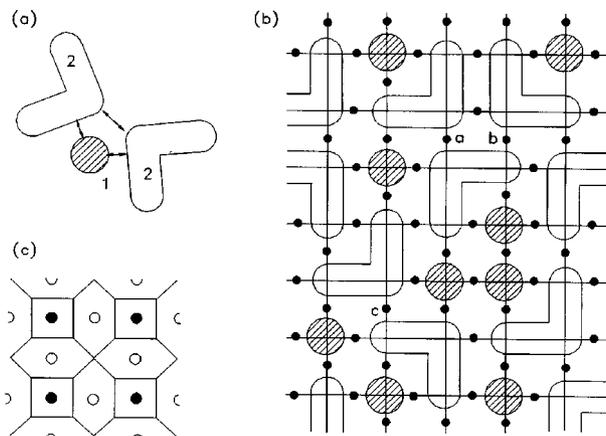


Fig. 1. Molecular interactions and decorated lattice representations.

(a) Various types of molecular interactions in the system consisting of the molecules of different sizes and shapes. (b) Two-dimensional lattice representation of interaction in (a); ● represents for the interaction sites. (c) Two-dimensional representation of interaction of decorated lattice containing the real (●) and the ghost (○) molecules. The ghost molecules introduced to consider the strong third body effect or the hydrogen bonding.

transformed into a wider range than that of their repeating unit scale. The transformations for both lattices and groups may be applied simultaneously or independently.

Fig. 1 shows a lattice representation of the blobwise interaction and spatial occupation. In Fig. 1(a), a schematic of two interacting molecules intervened by a third molecule and the decorated lattice model was approximated. In Fig. 1(b) and 1(c), a schematic mapping of blob picture onto a decorated lattice was illustrated. The renormalized lattice of blobs was approximated by incorporating a two-step renormalization of lattices. First, a primary lattice ζ for polymer molecules is normalized to a blob lattice ξ with the effective interaction energy of the lattice bond U_{ij} . Second, the blob lattice with bond ij is renormalized under local compositions to yield the excess free energy of systems.

EXPERIMENT

1. Preparation of p(NIPAAm) Hydrogel Spheres

N-isopropylacrylamide (NIPAAm) monomer was purchased from Tokyo Kasei Kogyo Co. (Japan) and used without further purification. N,N-methylene bisacrylamide (MBAAm) was purchased from Aldrich Chemical Co. (USA). Ammonium persulfate, and N,N,N',N'-tetramethylethylenediamine (TEMED) were all obtained from Sigma Chemical Co. (USA). Hydrogel spheres were synthesized by a surfactant-free inverse emulsion polymerization along with Tanaka et al. [Tanaka et al., 1985]. After sedimented particles were collected, hydrogel spheres were redispersed into methanol and washed with distilled water, and repeated twice.

In our swelling experiments, volume changes of hydrogels were measured by optical microscopy in the temperature range of 20–50 °C. Hydrogel spheres for determination of volume swelling ratio were prepared by an inverse emulsion polymerization. Hydrogel

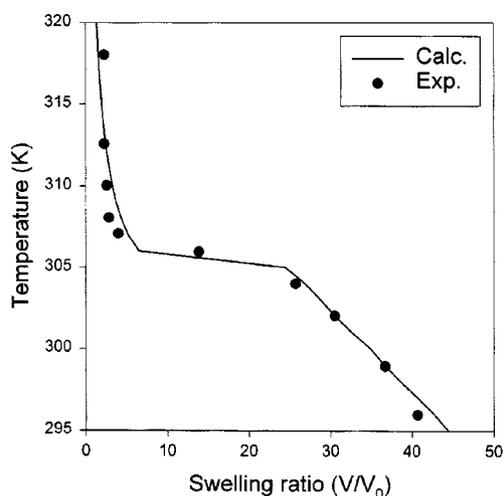


Fig. 2. Swelling behavior of poly(N-isopropylacrylamide) with varying temperatures. Parameters of decorated UNQUAC model for poly(N-isopropylacrylamide) gel-water system (unit: kcal/mole): $r=10$, $q=15$, $\phi_{11}=-2.72$, $\phi_{12}=-5.7$, $\epsilon_{12}=0.56$, $\epsilon_{22}=0.80$, component 1: water, component 2: poly(N-isopropylacrylamide).

spheres were inserted in a sealed glass cell containing water, and we observed the volume change by an optical microscope with a temperature controller. The mean diameter of prepared hydrogel spheres is 100 μm [Chun, 1995; Chun and Kim, 1996].

The poly(N-isopropylacrylamide) gel is swollen at lower temperatures and undergoes a sharp collapse at 32 $^{\circ}\text{C}$ [Bae et al., 1990] and the swelling has a discontinuous transition as shown in Fig. 2.

POLY(N-ISOPROPYLACRYLAMIDE) GEL SYSTEM

In normalizing blobs in polymer, the shape of blobs need not be invariant but is assumed to remain unchanged after this rescaling. Then the rescaled q_i of the a blob of species q_i can be written by,

$$q_i = q_i \left(\frac{l_i}{r_i} \right)^3 \quad (2)$$

where l is equal to 1 for cylindrical blobs and 2/3 for spherical blobs. Decorated UNQUAC model with the blob concept needs one structural parameter and 4 of temperature independent energy parameters.

In an isothermal and isobaric system containing a crosslinked polymer in equilibrium with pure solvent, swelling equilibria must fulfill the equilibrium condition.

$$\mu'_1 = \mu''_1 \quad (3)$$

where ' and '' denote the pure solvent phase and the gel phase, respectively, and subscript 1 refers to the solvent.

Swelling curves of poly(N-isopropylacrylamide) gel are discontinuous, containing a first-order transition in the swelling equilibrium (Fig. 2), many theories have been exercised to explain the LCST phenomenon in poly(N-isopropylacrylamide) single chains and gels. All of these gel theories basically contain four terms reflecting the changes in free energies of mixing, elasticity, osmotic effects, and specific interactions for a gel in aqueous media. Some efforts qualitatively summarized that both so-called hydrogen bonding [Prange

et al., 1989] and hydrophobic efforts [Shild, 1992] contribute to the driving force for the transition. With such diversity among theories, it appears clear that theoretical explanation of the LCST of poly(N-isopropylacrylamide), whether as a gel or as single chains, is far from complete.

According to Flory [Flory, 1953], the chemical potential of solvent in a gel phase coexisting with a pure solvent is given by

$$\mu_1 - \mu_1^o = \Delta\mu_1 = \Delta\mu_{1,mixing} + \Delta\mu_{1,elastic} \quad (4)$$

An expression for the contribution of mixing is obtained by the decorated UNQUAC equation with the blob concept [Ban et al., 1989; Kim et al., 1996] and an expression for the elastic forces to the chemical potential can be obtained from the theory of rubber elasticity. We use an expression given by Flory [Flory, 1953].

$$\Delta\mu_{1,mixing} = RT \left(\frac{\partial \Delta G_{mix}}{\partial n_1} \right) \quad (5)$$

$$\Delta\mu_{1,elastic} = \left[\frac{v_1}{v_u} \phi_2^o (\rho - \rho_f) \left\{ \left(\frac{\phi_2}{\phi_2^o} \right)^{1/3} - \frac{\phi_2}{2\phi_2^o} \right\} \right] \quad (6)$$

where v_1 is the molar volume of solvent, v_u , the molar volume of monomer unit, ϕ_2^o , the volume fraction of the gel in the standard state, ρ the fraction of monomer units that are connected via crosslinks, and ρ_f the fraction of chains in the network terminated by a crosslink only on one end, which do not contribute to the elasticity.

Fig. 2 shows the experimental and calculated swelling equilibria for the system water/poly(N-isopropylacrylamide) gel. The calculated curve is obtained by using Eqs. (4), (5), and (6), and the calculation procedures of the partition function of a decorated cell lattice are described in the Appendix. The gel composition parameters re-

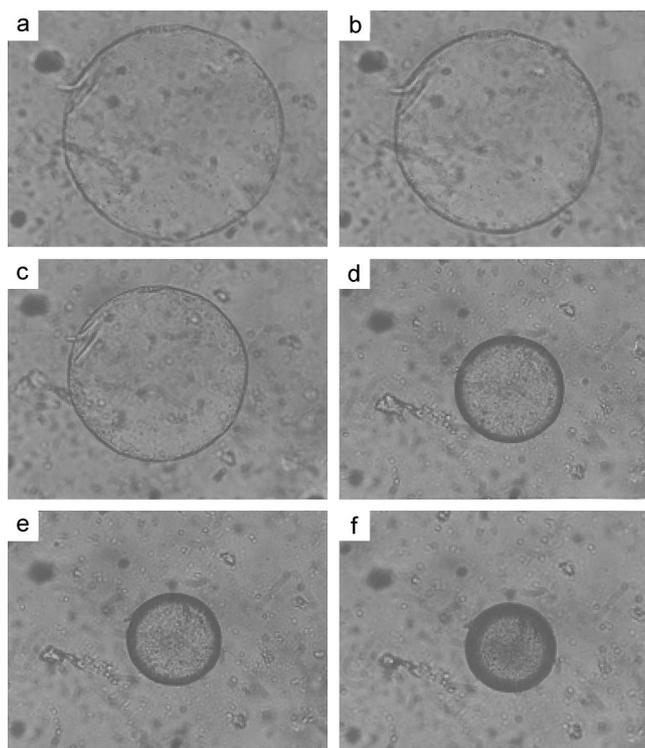


Fig. 3. Photographs of poly(N-isopropylacrylamide) hydrogel. (a) 26 $^{\circ}\text{C}$, (b) 29 $^{\circ}\text{C}$, (c) 33 $^{\circ}\text{C}$, (d) 34 $^{\circ}\text{C}$, (e) 40 $^{\circ}\text{C}$, (f) 45 $^{\circ}\text{C}$

quired in the Eq. (6) are obtained from conditions under which the gel is prepared ($\rho=0.018$, $\phi_2^*=0.07$); the value of ρ_i is estimated to be 0.0001 [Prange et al., 1989].

The poly(N-isopropylacrylamide) gel undergoes a sharp collapse at 32 °C and a discontinuous transition in Figs. 2 and 3. The semi-quantitative agreement of the predicted swelling equilibria with experiment is encouraging. The model can predict the existence of lower critical solution temperatures that are caused by the order-disorder transition without using temperature-dependent parameters. For binary closed-loop diagrams of polyethyleneglycol-water mixtures having strongly interacting groups [Ban et al., 1989], in previous works, calculated equilibrium concentrations of polymer solutions incorporated the blob configurations of polymers and strong interactions like hydrogen bonding toward one or more directions with a *decorated UNIQUAC model* [Kim and Kim, 1988].

The *decorated UNIQUAC model* with the blob concept can be used to calculate the phase equilibria for aqueous solutions of hydrophilic polymers or gels.

CONCLUSIONS

The transition behavior of swelling and deswelling of water-soluble poly(N-isopropylacrylamide) was calculated by a *decorated UNIQUAC model* with blob concept and the volume changes were determined by a photographic method. In modeling, polymer chains were scaled within a directly interacting size as blobs, which were composed of a segmentalized polymer chain and solvent molecules and counted blobs of hypothetical components or segments. In calculation, the interaction parameters of bulks, UNIQUAC interaction parameters, were approximated with temperature-independent site interaction energies following the blob renormalization transformation. The blob rescaling model for a polymer solution successfully described the first order transition of swelling and gel of poly(N-isopropylacrylamide) by a computer simulation.

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APPENDIX

A. Degeneracies and interaction energies for the construction of the decorated cell partition function depending on the configuration of a ghost molecule in the decorated cell is listed below.

$$Q_{ikj} = \sum_{\sigma} g(\sigma, \kappa) \exp[-E(\sigma, \kappa)/RT]$$

σ	κ	$g(\sigma, \kappa)$	$E(\sigma, \kappa)$
1	i	1	$\phi_{ki} + \phi_{kj} + \epsilon_{ki} + \epsilon_{kj}$
	ii	$\omega_1^* - 1$	$\phi_{ki} + \epsilon_{ki} + \epsilon_{kj}$
	iii	$\omega_1^* - 1$	$\phi_{ki} + \epsilon_{ki} + \epsilon_{ki}$
	iv	$\omega_1 \omega_1^*/2 - 2(\omega_1^* - 1) - 1$	$\epsilon_{kj} + \epsilon_{kj}$
2	i	1	$\phi_{ki} + \epsilon_{ki} + \epsilon_{kj}$
	ii	1	$\phi_{kj} + \epsilon_{ki} + \epsilon_{kj}$
	iii	$\omega_1^* - 1$	$\epsilon_{ki} + \epsilon_{kj}$

B. The decorated cell partition function, Q_{ikj} .

Q_{ikj}	$\sum_{\sigma} g(\sigma, \kappa) \exp[-E(\sigma, \kappa)/RT]$
Q_{111}	$[\eta_1^2 + 2(\omega_1^* - 1)\eta_1 + \omega_1 \omega_1^*/2 - 2(\omega_1^* - 1) - 1]\eta_1^2$
Q_{112}	$[\eta_1 \eta_2 + (\omega_1^* - 1)(\eta_1 + \eta_2) + \omega_1 \omega_1^*/2 - 2(\omega_1^* - 1) - 1]\eta_1 \eta_2$
Q_{122}	$[\eta_2 + (\omega_2 - 1)\eta_6]\eta_4 \eta_5$
Q_{212}	$[\eta_2^2 + 2(\omega_1^* - 1)\eta_2 + \omega_1 \omega_1^*/2 - 2(\omega_1^* - 1) - 1]\eta_2^2$
Q_{121}	$[\eta_2 + (\omega_2 - 1) - 1]\eta_5^2$
Q_{222}	$[2\eta_6 + (\omega_2 - 1) - 1]\eta_4^2$

$$\eta_1 = \exp(-\phi_{11}/RT) \quad \eta_2 = \exp(-\phi_{12}/RT) \quad \eta_3 = \exp(-\epsilon_{11}/RT)$$

$$\eta_4 = \exp(-\epsilon_{22}/RT) \quad \eta_5 = \exp(-\epsilon_{12}/RT) \quad \eta_6 = \exp(-\phi_{22}/RT)$$

$$\omega_1^* = \omega_1 \sin \phi \sqrt{\frac{\omega_1 \pi}{2}}$$

solve for ζ

$$1 = \zeta \cdot \left(\frac{w_1}{w_2}\right) \cdot \left(\frac{Q_{121} + \zeta Q_{111}}{Q_{222} + \zeta Q_{212}}\right)^3$$

$$Q_{ij} = Q_{i2j} + \zeta Q_{i1j}$$

$$\tau_{12} = \frac{Q_{22}}{Q_{12}} \quad \tau_{21} = \frac{Q_{11}}{Q_{12}}$$

where Q_{ij} is partition function of the bond, Q_{ikj} is the partition function for k (ghost molecule in the second cell), ζ is fugacity ratio, and ϕ_{ij} is directional interaction and ϵ_{ij} is nondirectional interaction.

REFERENCES

- Bae, Y. H., Okano, T. and Kim, S. W., "Temperature Dependence of Swelling of Crosslinked Poly(N,N-alkyl Substituted Acrylamide) in Water," *J. Polym. Sci., Polym. Phys.*, **28**, 923 (1990).
- Ban, Y. B., Kim, Y. C. and Kim, J. D., "Blob Calculation Method for the LLE of Polymer Solutions," *Fluid Phase Equilibria*, **53**, 331 (1989).
- Bondi, A. (eds.), "Physical Properties of Molecular Crystals, Liquid and Glasses," Sheel Development Co. (1968).
- Chun, S. W., "Thermoresponsive Characteristics of Complex Membrane of Poly(N-Isopropyl Acrylamide) Hydrogel Embedded in Polymer Matrix," PhD Dissertation, KAIST (1995).
- Chun, S. W. and Kim, J. D., "A Novel Hydrogel Dispersed Composite Membrane of Poly(N-Isopropylacrylamide) in a Gelatin Matrix and its Thermally Actuated Permeation of 4-Acetamidophen," *J. Controlled Release*, **38**, 39 (1996).
- Dong, L. C. and Hoffman, A. S., "A Novel Approach for Preparation of pH Sensitive Hydrogels for Enteric Drug Delivery," *J. Controlled Release*, **15**, 141 (1991).
- Flory, P. J. (eds.), "Principles of Polymer Chemistry," Cornell University Press, Ithaca, NY (1953).
- Gehrke, S. and Cussler, E. L., "Mass Transfer in pH-Sensitive Hydrogels," *Chem. Eng. Sci.*, **44**, 559 (1989).
- Hirshfelder, J., Stevenson, D. and Eyring, H., "A Theory of Liquid Structure," *J. Chem. Phys.*, **5**, 896 (1937).
- Hirokawa, Y. and Tanaka, T., "Volume Phase Transition in a Nonionic Gel," *J. Chem. Phys.*, **81**, 6379 (1984).
- Iwata, H., Oodate, M., Uyama, Y., Amemiya, H. and Ikada, Y., "Preparation of Temperature-Sensitive Membrane by Graft Polymeriza-

- tion onto a Porous Membrane," *J. Membrane Sci.*, **55**, 119 (1991).
- Kim, J. C. and Kim, J. D., "Temperature Sensitivity of Liposomal Lipid Bilayers Coated with Poly(N-Isopropylacrylamide-co-acrylic Acid)," *J. Biochemistry*, **121**, 15 (1997).
- Kim, J. C., Kim, M. S. and Kim, J. D., "Temperature Sensitive Release from Liposomes Containing Hydrophobically Modified Poly(N-Isopropylacrylamide)," *Korean J. Chem. Eng.*, **16**, 56 (1999).
- Kim, Y. C. and Kim, J. D., "Decorated Lattice Model for Closed Loop Liquid-Liquid Equilibria and its Applications to Pyridine Derivatives-Water Mixtures," *Korean J. Chem. Eng.*, **3**, 99 (1986).
- Kim, Y. C. and Kim, J. D., "New Calculation Method for Asymmetric Closed-Loop Liquid-Liquid Equilibria by Lattice Decoration," *Fluid Phase Equilibria*, **41**, 339 (1988).
- Kim, Y. C., Kim, J. D. and Kim, H. Y., "Ternary Liquid-Liquid Phase Behavior by Decorated-UNIQUAC," *Korean J. Chem. Eng.*, **13**, 439 (1996).
- Kwon, I. C., Bae, Y. H., Okano, T. and Kim, S. W., "Drug Release from Electric Current Sensitive Polymers," *J. Controlled Release*, **17**, 149 (1991).
- Ohmine, I. and Tanaka, T., "Salt Effects on the Phase Transition of Ionic Gels," *J. Chem. Phys.*, **77**, 5725 (1982).
- Park, T. G. and Hoffman, A. S., "Synthesis and Characterization of pH and/or Temperature Sensitive Hydrogels," *J. Appl. Polym. Sci.*, **46**, 659 (1992).
- Peppas, L. B. and Peppas, N. A., "Equilibrium Swelling Behavior of pH Sensitive Hydrogels," *Chem. Eng. Sci.*, **46**, 715 (1991).
- Prange, M. M., Hooper, H. H. and Prausnitz, J. M., "Thermodynamics of Aqueous Systems Containing Hydrophilic Polymer or Gels," *AIChE J.*, **35**, 803 (1989).
- Shild, H. G., "Poly(N-Isopropylacrylamide): Experiment, Theory, and Application," *Prog. Polym. Sci.*, **17**, 163 (1992).
- Tanaka, T., "Gels," *Sci. Amer.*, **224**, 124 (1981).
- Tanaka, T., Sato, E., Hirokawa, Y., Hirotsu, S. and Peetermans, J., "Critical Kinetics of Volume Phase Transition of Gels," *Phys. Rev. Lett.*, **55**, 2455 (1985).