Soft Matter

Accepted Manuscript

ROYAL SOCIETY
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www.rsc.org/softmatter

Journal Name RSCPublishing

ARTICLE

Cosolvency Effect on Tunable Thermosensitive Core-Shell Nanoparticle Gels

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

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The influence of co-solvents on the swelling behavior of tunable thermosensitive core-shell nanoparticle gels was investigated. The poly(methyl methacrylate) (PMMA) core and poly(2-hydroxyethyl methacrylate) (PHEMA) shell network in 1-propanol reacted differently upon the addition of three co-solvents (cyclohexane (CHX), 1,3-propanediol (PDO), and water), resulting in highly controllable swelling properties of the core-shell gels. In particular, a strong enhanced solvation effect, named the cosolvency phenomenon, occurred even with a very small amount of water (1-3 wt%). To examine the tunability, thermo-optical analysis (TOA) and photon correlation spectroscopy (PCS) were employed. The results show that a small addition of CHX, PDO, or water induced the "lower/upper," "even/upper," and "lower/lower" volume transition temperatures (VTTs) of the core/shell networks, respectively. For theoretical treatment, a multi-component lattice theory of mixing was combined with the Flory-Rehner (F-R) chain model to calculate the net free energy of mixing. Required interaction parameters were obtained from the binary and ternary phase diagrams of the linear polymer solutions and were applied directly to swelling calculation of the cross-linked core-shell network solutions. The calculated results corresponded well with the experimental swelling data without further adjustment.

1. Introduction

Networks composed of thermoresponsive polymers have been intensely researched over the past few years due to their potential applications in numerous fields.[1-3] These polymer networks can undergo a reversible volume change near the critical solution temperature of the polymer. Their unique characteristic is the ability to swell but not dissolve in thermodynamically good solvents due to the physically or chemically cross-linked network. However, polymer gel networks are also sensitive to surrounding conditions such as pH[4] and ionic strength.[5]

The responsive characteristics have been modified by either co-polymerization or an advanced polymer architecture, where nano-sized particle gels with core-shell or core-corona structures are of particular interest.[6,7] Such advanced polymer architectures can lead to materials with superior properties since the two domains, core and shell, are mutually influenced.[8-10] Lyon and co-workers[6,11] introduced a multiresponsive core-shell structure consisting of a PNIPAM core and a PNIPAM-*co*-acrylic acid (AAc) shell with both temperature and pH sensitivity. Xia and co-workers[12] developed "yolk/shell" structured particles to impart a physical separation between the core and shell. Richtering and co-workers[10,13] introduced LCST-type multiple-temperature-sensitive core-shell nanoparticle gels by arranging two different thermosensitive polymers. Recently, Lee and Bae[14] designed UCST-type temperature-responsive core-shell nanoparticle gels in organic solvents composed of a PMMA core/PHEMA shell structure using a two-step swelling process upon heating. The enhanced properties and unique behaviors of the polymer structures have stimulated interest in multiple fields such as chemical sensing,[15] separations,[16] catalysis,[17] and drug delivery systems.[18,19]

Adding a co-solvent is a powerful tool to control the responsive property of polymer network gels where inter-solvent interactions sometimes give rise to unexpected swelling behaviors. After the pioneering work of Tanaka and co-workers,[20] the re-entrant volume transition (swelling-to-collapsing-to-swelling) of PNIPAM gels in mixed solvents has been intensively researched.[21-23] Also, some investigations concerning the opposite phenomenon known as the re-collapsing volume transition (collapsing-to-swelling-to-collapsing) of PMMA networks have been published in recent years.[14,24] However, there are only a few reports regarding the influence of mixed solvents on the swelling behavior of core-shell nanoparticle gels,[25] and there are no reports of controlling the thermosensitivity of core-shell nanoparticle gels with the addition of a co-solvent. Moreover, a quantitative approach to core-shell swelling in a mixed solvent using a thermodynamic model has not previously been attempted.

Since the pioneering work of Flory,[26] many researchers have applied thermodynamic models to the swelling behaviors of gels in many different ways, although most of them only concern the swelling behavior of homogeneous gel networks. The core-shell network structure, however, is fundamentally different from a homogeneous structure. Core and shell networks are physically constrained by each other, and thus, neither is able to swell in a homogeneous and isotropic state. Furthermore, each network has different sensitivities to surrounding conditions, resulting in a mutual influence on the swelling kinetics. An early theoretical approach to the inhomogeneous gel structure was attempted by Sekimoto and Kawasaki,[27] but their general field theory is too complex for practical applications. Suo and co-workers[28] derived a field theory in the same tradition and employed a finite element method to analyze the dynamics of the volume transition of hydrogels under the constraint of hard materials. Gernandt and co-workers[29] combined Suo's work with the conventional Flory-Huggins[26] theory and suggested the first general thermodynamic model for calculating the internal structure of core-shell gels. Recently, based on Lian's[30] simple geometrical approach, Lee and Bae[14] introduced a conceptually simple and precise thermodynamic model for thermosensitive core-shell gels. Although a noticeable improvement in representation of the swelling behavior of core-shell gels has been achieved, these models are limited to core-shell gels in a mono-solvent system, with no systematic methodology for determining model parameters.

Herein, we analyzed the swelling behavior of PMMA/PHEMA doubly thermosensitive core-shell nanoparticles in three different 1-propanol/co-solvent mixtures (1,3-propanediol (PDO), cyclohexane (CHX), and water). We confirmed by means of a thermo-optical analysis (TOA) technique that the thermosensitivity of the two polymers can be conveniently controlled by adding a small amount of a co-solvent. The photon correlation spectroscopy (PCS) measurements indicate that the influence of the co-solvents was identically appeared in the core-shell nanoparticle gel solutions, with the core-shell gels exhibiting tunable thermosensitivity depending on the co-solvents, as shown in Fig. 1. For quantitative representation, we calculated the total free energy (ΔG_{net}) of the core-shell gel solutions by combining the modified double lattice temperature-optimized (MDL-T) model for the free energy of mixing (ΔG_{mix}) and the classical Flory-Rehner (F-R) chain model for the elastic free energy (ΔG_{el}). Required interaction parameters ($\tilde{\varepsilon}_{ij}$) were obtained from the phase diagrams of linear polymer solutions, and polymer network parameters (ϕ_{g0} and k_c) were determined from the mono-solvent gel solution system. By directly applying these model parameters, we successfully described the influence of co-solvents on the core-shell swelling in mixed-solvents without further adjustment.

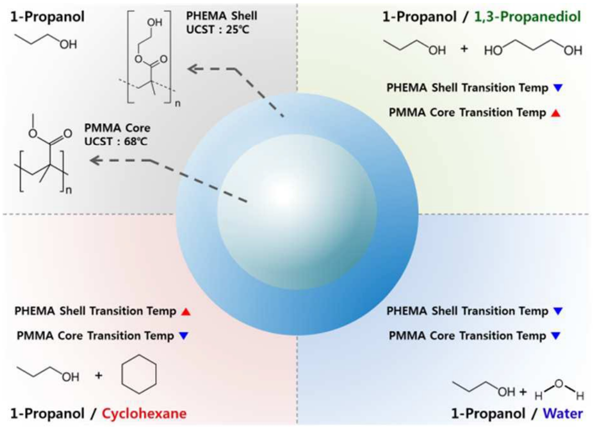

Fig. 1 Schematic depiction of the core-shell structure composed of PMMA core and PHEMA shell, and the influence of the three co-solvents on the volume transition temperature of the core-shell structure in 1-propanol solution.

2. Experimental Details

2.1 Chemicals

PMMA (M_w=15,000), PHEMA (M_w=20,000), 1-propanol, cyclohexane, and 1,3-propanediol were used as received from Aldrich. Methyl methacrylate (MMA) and 2-hydroxyethyl methacrylate (HEMA), ammonium persulfate (APS), and N-N'-methylenebisacrylamide (BIS, M_w=154.17) were used as the core and shell monomers, initiator, and cross-linker, respectively.

2.2 Preparation of homo-polymer nanoparticles

The PMMA and PHEMA nanoparticles were prepared via precipitation polymerization. The detailed synthesis protocol was adopted from the literature.[31,32] Briefly, PMMA nanoparticles were synthesized by mixing 50 ml of a water-acetone mixture (35 vol% acetone), MMA monomer (1 g), and N,N'-methylenebis (acrylamide) (BIS) cross-linker (1 mol% monomer) in a three-neck round-bottom flask equipped with a reflux condenser. The mixture was heated to 70°C under continuous stirring using a mechanical stirrer. After approximately 30 min of equilibration, 1 ml of an ammonium persulfate (APS, initiator) aqueous solution (1 wt%) was added. After 4 h of reaction time under a nitrogen stream, the acetone was evaporated at 55°C for 3 h, and the solution was filtered using a 0.45 μm syringe filter. To prepare PHEMA nanoparticles, 0.65 g of HEMA monomer and BIS cross-linker (2 mol% monomer) were mixed with 50 ml of water in the same three-neck flask above, and the mixture was heated to 90°C and pre-mixed for 30 min. After stirring, 1.2 ml of an aqueous APS solution (1 wt%) was added to the flask, and the mixture was polymerized for 4 h. The synthesized solution was filtered using a 0.45 μm syringe filter.

2.3 Preparation of core-shell nanoparticles

The core-shell nanoparticles were prepared using a seed and feed synthesis process.[11,13] The detailed procedure is described in our previous work.[14] In brief, the PMMA nanoparticles served as nuclei for the subsequent polymerization of the PHEMA shell. A mixture of HEMA monomer (0.65 g) and BIS cross-linker (2 mol% shell monomer) in water (50 ml) was added to the prepared PMMA core solution (50 ml), and the polymerization was initiated with 1 ml of an APS aqueous solution after heating the mixture to 80 °C. The core particles synthesized by the APS initiator contained a small number of charged groups on the surface that stabilized the core particles in the next step where the PHEMA shell is polymerized on the core surface.[33,34] After 4 h of reaction, the product was filtered using the method applied to the homo-polymer gel solutions.

2.4 Thermo-optical Analysis (TOA)

To determine the phase transition temperature of the polymer solution, we adopted the TOA method suggested by Prausnitz and co-workers.[35] The intensity of transmitted light was measured while varying the temperature. The cloud point was determined as the point where the first phase separation occurred, as this corresponds to the temperature of the abrupt transition of luminosity, as shown in Fig. 2. We used a sufficiently low scan rate of 0.5°C/min to accurately determine the transition temperature. A detailed description of the apparatus has been addressed elsewhere.[35]

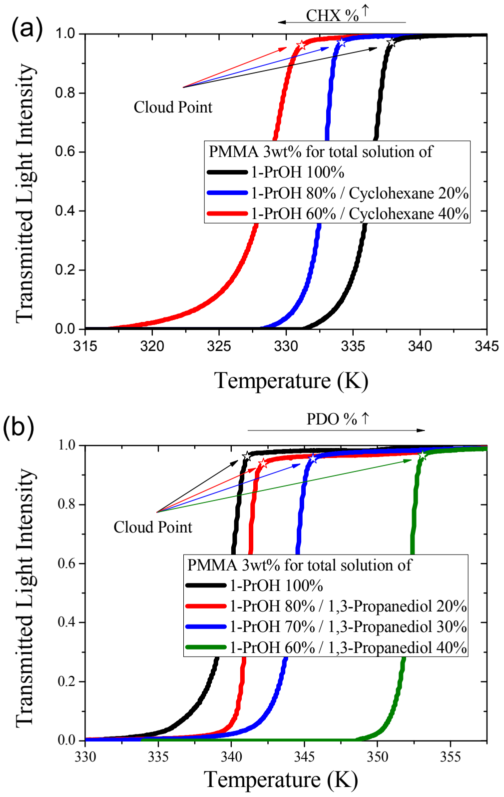

Fig. 2 Cloud point results obtained using the TOA method. The UCST-type phase transition temperature change of the PMMA (M_w=15,000)/1-propanol solution with the addition of (a) CHX and (b) PDO co-solvents. The PMMA content for each sample was maintained at 3 wt% of the total solution.

2.5 Photon Correlation Spectroscopy (PCS)

The diameters of the homo-polymer and core-shell nanoparticle gels were determined using the PCS technique with highly diluted samples to prevent multiple scattering. The measurements were carried out using a Zetasizer Nano ZS (Malvern Instruments, UK) equipped with a He-Ne laser (λ = 633 nm) at an angle of 173° and were evaluated using Malvern Zetasizer Software ver. 5.10. The diameter was determined as the average of three measurements for each temperature with an equilibrium time of 20 min. The polydispersity index (PDI) value for each set of conditions was less than 0.1, indicating uniform size distribution of the particles. Fig. 3 shows the PCS measurement results for the PMMA core and PMMA/PHEMA core-shell nanoparticles at three different temperatures. From the results, we confirmed that the PHEMA shell was successfully polymerized on the core surface. If the separated PHEMA particles were synthesized, the PCS result of the core-shell may show double or multiple peaks and high PDI value. However, as shown in Fig. 3(b), the PDI values were less than 0.08 for each set of conditions, indicating no separated PHEMA particles in the dispersion. In addition, at the collapsing state (5°C), the core-shell particles had a larger diameter of about 30 nm than that of the PMMA core particles, indicating that the PHEMA shell was coated on the core surface. At 40°C (higher than the UCST of PHEMA), the diameters of the PMMA core particles did not change, while the core-shell particles were swollen due to shell swelling.

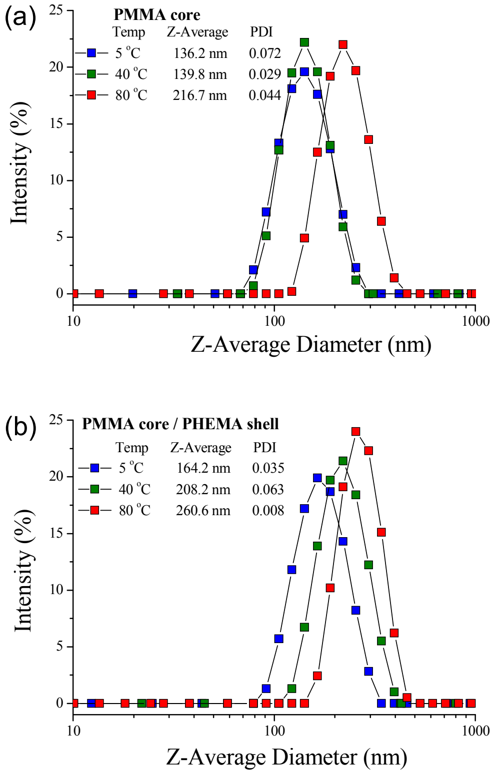

Fig. 3 Particle size measurement results obtained using the PCS technique. The diameters of the (a) PMMA homo-polymer gels and (b) PMMA/PHEMA core-shell gels were measured at three different temperatures in 1-propanol: the reference state (5°C), shell swelling state (40°C), and core swelling state (80°C).

3. Model development

3.1 Free energy of mixing

A multi-component lattice model is a conceptually simple and convenient mathematical tool for calculating the phase behaviors of linear polymer solutions. Based on the classical theory of Flory, Freed and co-workers[36] developed an exact but complicated mean field theory referred to as the lattice cluster theory (LCT). Bae and co-workers[37] revised the LCT model into the simple modified double-lattice (MDL) model. Herein, we adopted the MDL theory to calculate the Gibbs energy of mixing for incompressible linear polymer solutions, which can be expressed as follows:

$$\frac{\Delta G_{mix}}{N_r kT} = \sum_{i=1}^{K}\sum_{j=1}^{K}\frac{\tilde{\varepsilon}_{ij}}{2}\left(2-\left(\frac{\phi_i}{r_i}+\frac{\phi_j}{r_j}\right)+\left(\frac{1}{r_i}+\frac{1}{r_j}\right)\right)\phi_i\phi_j \qquad (1)$$
$$-(\sum_{i=1}^{K}\sum_{j=1}^{K}\tilde{\varepsilon}_{ij}\phi_i\phi_j\sqrt{C_\gamma/4})^2-\sum_{i=1}^{K}\frac{\phi_i}{r_i}\ln\phi_i+\frac{C_\beta}{2}\sum_{i=1}^{K}\sum_{j=1}^{K}\phi_i\phi_j\left(\frac{1}{r_i}-\frac{1}{r_j}\right)^2$$

where N_i is the number of molecules of the ith component, $N_r(=\sum_{i=1}^{K} N_i r_i)$ is the total number of sites composed of K components, r_i is the relative size parameter, k is the Boltzmann constant, $\phi_i(=N_i r_i/N_i)$ is the volume fraction of component i, C_γ and C_β are universal constants ($C_\gamma = 1.7986$ and $C_\beta = 0.1415$) determined from the Monte Carlo simulation data,[37] and $\tilde{\varepsilon}_{ij}$ is the reduced interaction parameter between the i and j components. The size parameter (r_i) is determined using the relative size of each component to the reference molecule. In this work, water is the reference molecule (r_{water} = 1) because it is the smallest component. The size parameters of the components were calculated as follows:

$$r_i = \frac{v_{w,i}}{v_{w,water}}\ (Simple\ molecule)$$

$$r_i = \frac{v_{w,i(ru)}}{v_{w,water}} \frac{Mw_i}{Mw_{i(ru)}}\ (Polymer) \tag{2}$$

where v_w is the Bondi's van der Waals volume[38] of a component, Mw is the molecular weight, and the subscript ru is the repeating unit of the polymer. For cross-linked polymer networks, the size parameters are considered to be infinite. To determine the phase equilibrium conditions, the chemical potential of each component is required and can be calculated using the following equation.

$$\frac{\Delta\mu_i}{kT} = \left[\frac{\partial(\Delta G_{mix}/kT)}{\partial N_i}\right]_{T,V,N_{j\neq 1}} \tag{3}$$

In addition, a coexistence curve can be generated when $\Delta\mu_i^\alpha = \Delta\mu_i^\beta$, where the superscripts α and β denote the two phases at equilibrium.

3.2 Swelling Equilibrium of Polymer Gel Solution

According to the classical formalism suggested by Flory and Rehner,[39,40] the swelling behavior of a polymer gel solution can be determined via two separate contributions as the following sum:

$$\Delta G_{net} = \Delta G_{mix} + \Delta G_{el} \tag{4}$$

where ΔG_{mix} is the mixing free energy, and ΔG_{el} is the elastic free energy of a cross-linked polymer network. The equation of elastic contribution proposed by Flory and Rehner[39,40] was revised by Moerkerke and co-workers[41] into a lattice-based formula as follows:

$$\frac{\Delta G_{el}}{N_r kT} = \left(\frac{3A\phi_{g0}^{2/3}}{2m_c}\right)\left(\phi_g^{1/3} - \phi_g\right) + \left(\frac{B}{m_c}\right)\phi_g \ln\phi_g \tag{5}$$

$$A = \frac{f-2}{f} + \frac{2\phi_g}{f}, B = \frac{2\phi_g}{f} \tag{6}$$

where m_c is the number of lattice sites occupied by a network chain, f is the functionality of the cross-links (we assumed a perfect tetra-functional network, f = 4), ϕ_g is the volume fraction of the polymer network, and the subscript 0 refers to the *reference state*.

The swelling ratio of nanoparticle gels is generally determined from the volume ratio of the gels while assuming negligible surface effects as follows:[42,43]

$$Swelling\ Ratio = \frac{\phi_{g0}}{\phi_g} = \frac{V}{V_0} = \left(\frac{d}{d_0}\right)^3 \tag{7}$$

where d is the average diameter of the particles, and V is the volume of gel in the equilibrium state. Determination of the swelling ratio of core-shell gels needs to consider the structure of the networks and can be calculated using the simple geometrical approach suggested by Lian and co-workers[30] as follows:

$$Swelling\ Ratio = \frac{\mathrm{V}}{\mathrm{V_0}} = \left(\frac{\mathrm{d_{total}}}{\mathrm{d_{0,total}}}\right)^3$$

$$= \left(1 - \left(\frac{\mathrm{d_{0,core}}}{\mathrm{d_{0,total}}}\right)^3\right)\frac{\phi_{\mathrm{g0,shell}}}{\phi_{\mathrm{g,shell}}} + \left(\frac{\mathrm{d_{0,core}}}{\mathrm{d_{0,total}}}\right)^3 \frac{\phi_{\mathrm{g0,core}}}{\phi_{\mathrm{g,core}}} \tag{8}$$

where d_{total} is the total diameter of the core-shell particle, d_{core} is the core diameter in the core-shell structure, and $d_{0,core}$ / $d_{0,total}$ is obtained from the PCS results at the reference state, 5°C in Fig. 3. In lattice-based models, the cross-linking density parameter (m_c) is defined as the average number of lattice sites between two crosslinking points of gel network,[41] which can be determined from experimental conditions as follows:

$$m_c = \frac{1}{2} \times \frac{moles\ of\ monomer}{moles\ of\ crosslinker} \times \frac{lattice\ size\ of\ monomer}{reference\ lattice\ size} = \frac{1}{2\phi_j} \times r_m \tag{9}$$

where ϕ_j is the mole fraction of cross-linker to the total monomer, and r_m is the relative lattice size of the monomer. The model parameters discussed above are listed in Table 1.

Table 1. The MDL-T model parameters for the components including the size and structural properties of the gel networks.

Size Parameter	Water	1-PrOH	PDO
r_i	1	3.68	4.08
	CHX	PMMA (Mw=15,000)	PHEMA (Mw=20,000)
	5.26	711.6	978.7
Network Parameter	PMMA Gel		PHEMA Gel
m_c	303.9		168.5
ϕ_{g0}	0.38		0.41
Core-Shell Parameter	$k_{c,core}$	$k_{c,shell}$	$d_{0,core}$ / $d_{0,total}$
	1.24	2.81	0.83

The chemical potential of each component can be derived in a way similar to eqn (3), and the swelling equilibrium condition is given by $\Delta\mu_i^{in} = \Delta\mu_i^{out}$, where the superscripts "in" and "out" denote the inside and outside phases of the polymer network system, respectively. For the core-shell gel system, the chemical potential of a solvent inside the core ($\Delta\mu_i^{in,core}$) and shell ($\Delta\mu_i^{in,shell}$) networks should be equal to that outside the network ($\Delta\mu_i^{out}$).

3.3 Temperature dependency of intermolecular energy

Discussions of the phase behaviors of polymer solutions are usually couched in terms of the inter-segment exchange energy parameters. In the classical theory of Flory and Huggins (F-H),[26] the energy parameter, χ, is simply inversely proportional to temperature; however, this simple form fails to represent various types of thermal behavior including specific interactions such as hydrogen bonding and strong dipole-dipole interactions. To overcome this shortcoming, researchers have suggested a number of corrected forms of χ and achieved significant practical improvements.[36,37,44-46]

However, these previous studies were confined to a narrow temperature range, and the thermal behavior of the exchange energy above the UCST and below the LCST were out of their scope. This gives rise to significant deviation when applying the parameters directly to cross-linked polymer gel systems over a wider temperature range. Thus, we recently suggested a new expression of $\tilde{\varepsilon}_{\mathrm{ij}}$ optimized for the overall temperature range as follows:[14]

$$\tilde{\varepsilon}_{\mathrm{ij}} = \tilde{\varepsilon}_{\mathrm{ij},weak} + \frac{\delta\tilde{\varepsilon}_{\mathrm{ij}}}{1 + \kappa\,(\delta\tilde{\varepsilon}_{\mathrm{ij}})^2} \tag{10}$$

where $\tilde{\varepsilon}_{weak}(= \varepsilon/kT)$ and $\delta\tilde{\varepsilon}\ (= \delta\varepsilon/kT)$ are the ordinary and specific interaction parameters, respectively, and κ is a degeneracy parameter. To consider enthalpic and entropic contributions, the ε and $\delta\varepsilon$ terms are replaced with $\varepsilon^H - \varepsilon^S T$ and $\delta\varepsilon^H - \delta\varepsilon^S T$, respectively.

Fig. 4 shows the thermal behavior of the reduced interchange energy parameter between PHEMA and 1-propanol calculated from experimental data (for the detailed calculation procedure, see the supplementary material of ref. 14) and its model calculations using the F-H,[26] corrected F-H,[45] MDL,[37] and MDL-T theories.[14] Below the UCST of PHEMA (298K), the last three models exhibit good agreement with the data both for linear and cross-linked PHEMA. Above the UCST, however, only the MDL-T model corresponds well with the data, while the other three models deviate somewhat from the appropriate thermal behavior. The mathematical forms of the temperature-dependent interaction parameter for the four models are listed in Table 2.

Table 2. Functional forms of the interaction parameters (χ_{ij} and $\tilde{\varepsilon}_{\mathrm{ij}}$) of four lattice-based models.

Model	Interaction Parameter	Functional Form
F-H[26]	$\chi_{\mathrm{ij}}(T)$	$\dfrac{z \cdot \Delta w_{\mathrm{ij}}}{k\mathrm{T}}$
Corrected F-H[45]	$\chi_{\mathrm{ij}}(\phi, T)$	$\alpha + (\beta_{00} + \beta_{01}/\mathrm{T})(1-\gamma\phi)^{-1}$
MDL[37]	$\tilde{\varepsilon}_{\mathrm{ij}}(T)$	$\dfrac{\varepsilon_{\mathrm{ij}}}{k\mathrm{T}} - \dfrac{2}{z}\left[\eta\ln + (1-\eta)\ln(1-\eta) + \dfrac{zC_a\delta\varepsilon_{\mathrm{ij}}kT(1-\eta)\eta}{1 + C_a\delta\varepsilon_{\mathrm{ij}}kT(1-\eta)\eta}\right]$
MDL-T[14]	$\tilde{\varepsilon}_{\mathrm{ij}}(T)$	$\tilde{\varepsilon}_{\mathrm{ij},weak}\,\dfrac{\varepsilon^H_{\mathrm{ij},weak} - \varepsilon^S_{\mathrm{ij},weak}\,\mathrm{T}}{k\mathrm{T}} + \dfrac{\delta\varepsilon^H_{\mathrm{ij}}/kT - \delta\varepsilon^S_{\mathrm{ij}}/kT}{1 + \kappa\,(\delta\varepsilon^H_{\mathrm{ij}}/kT - \delta\varepsilon^S_{\mathrm{ij}}/kT)^2}$

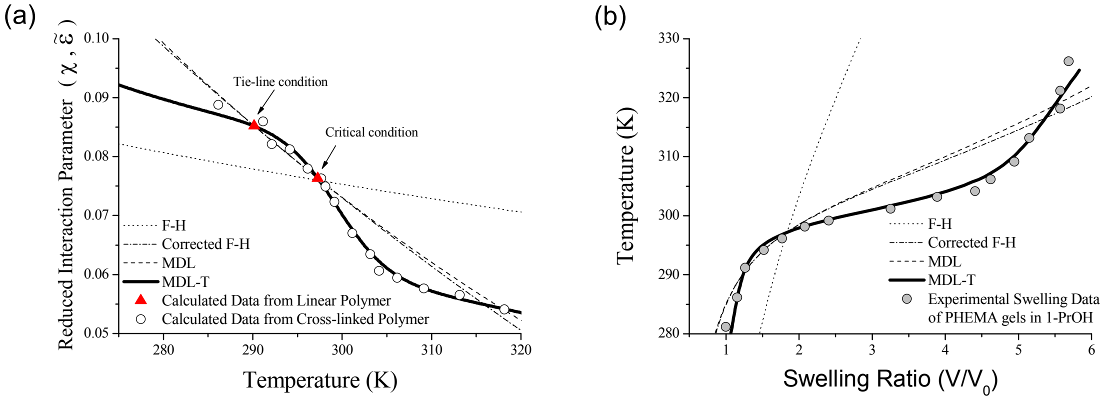

Fig. 4 (a) Thermal behavior of the interaction parameters (χ_{ij} and $\tilde{\varepsilon}_{\mathrm{ij}}$) between PHEMA and 1-propanol calculated using experimental data and four different models. (b) Experimental swelling data of PHEMA gels in 1-propanol and comparison of the models.

4. Results and discussion

4.1 The UCST-type doubly thermosensitive core-shell

PMMA/PHEMA core-shell nanoparticle gels were prepared via two-stage seed polymerization and characterized by the PCS technique. Fig. 5 shows the influence of temperature on the diameters of the PMMA core/PHEMA shell nanoparticle gels and the parent PMMA core for comparison. As described previously, the introduction of the shell to the core particles should be accompanied by an increase in diameter at both low and high temperatures. This effect is evidenced by the results of the PCS measurements shown in Fig. 5. The collapsed diameters of the core-shell samples are larger than those of the parent cores by ~30 nm, and the swollen diameters are ~60 nm larger. From the thermosensitivity point of view, the core-shell nanoparticles exhibit two distinct volume transitions upon heating near 68°C and 25°C, which are the intrinsic UCST values of the parent polymers in 1-propanol.[32,47] Specifically, at the reference state (5°C), which is sufficiently below the UCSTs of the core and shell polymers, the core-shell gels are fully collapsed because of a lack of affinity between the polymer networks and solvent molecules. Above the

UCST of the shell polymer (T > 25°C), the shell network begins to pull the solvent into the network, leading to the first volume transition, although the solvent molecules still cannot penetrate the core network. When the temperature is higher than the UCST of the core polymer (T > 68°C), the solvent becomes a good solvent for the PMMA core networks, resulting in the second swelling process. These results indicate that the thermosensitivity of the PMMA and PHEMA homo-polymer networks are maintained even though they are arranged in a core-shell nanostructure.

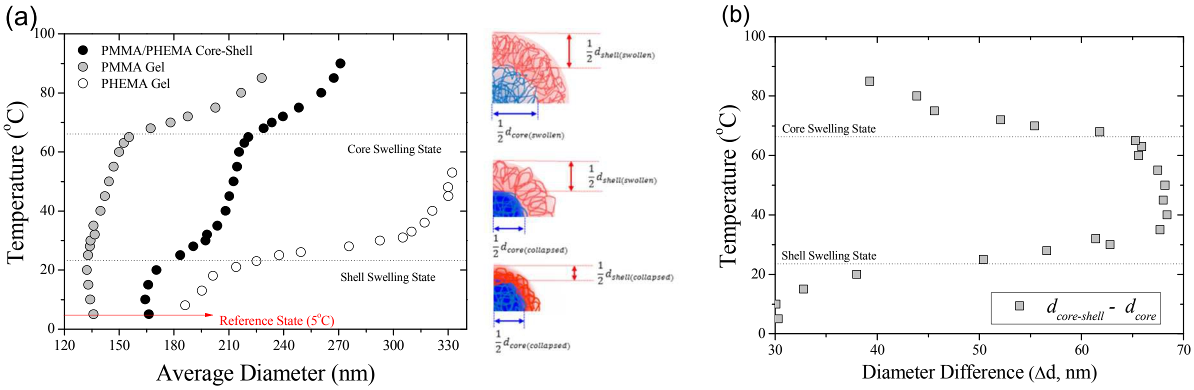

Fig. 5 (a) Average diameters of the PMMA and PHEMA homo-polymer gels and the PMMA/PHEMA core-shell gels as a function of temperature measured by the PCS technique under equilibrium conditions in 1-propanol. The cross-linker content of PMMA is 1 mol%, and that of the PHEMA is 2 mol%. (b) Diameter difference between the PMMA core and the PMMA/PHEMA core-shell particles as function of temperature.

4.2 Tunable Thermosensitivity of the core-shell by addition of co-solvents

There is great interest in the fabrication of easily accessible polymeric products with predictable and fine-tunable stimulus sensitivity in organic solvents. The tunability of thermosensitive polymers can be conveniently achieved by adding a wide variety of co-solvents. Specifically, in a multi-compartment structure composed of at least two polymers, the addition of co-solvent produces different responses for each polymer, giving the structure further versatility. Furthermore, in some cases, synergism of a mixed solvent caused by specific interactions often leads to unexpected phase behaviors of polymers such as cononsolvency and cosolvency. Here, we suggest a simple and convenient method to control the volume transition temperature (VTT) of PMMA/PHEMA core-shell nanoparticle gels in a 1-propanol solution by making use of the different effects of three added co-solvents (PDO, CHX, and water) in each polymer network.

Fig. 6 shows the results when altering the VTTs of PMMA/PHEMA doubly thermosensitive core-shell nanoparticle gels with the three co-solvents. The PCS data in Fig. 6(a) suggests that the small addition of PDO (5 wt%) reduces the PHEMA shell transition temperature by ~5°C, while the added content has practically no impact on the PMMA core transition temperature. On the other hand, the CHX co-solvent noticeably influences both the core and shell networks in opposite directions, as shown in Fig. 6(b). 10 wt% CHX in 1-propanol causes the shell transition temperature to increase by 10°C, while the core transition temperature is lowered by 5°C in the mixture. In the case of water, however, an unexpected effect on the transition temperature was observed. As is widely known, water is a non-solvent for PMMA and PHEMA over the entire temperature range. Thus, an increased VTT might be expected for the PMMA/PHEMA core-shell gels. However, in the experimental results shown in Fig. 6c, the VTT values of the core and shell networks decreased by 6°C and 8°C, respectively, with the addition of only 1 wt% water, indicating a significant increase in solubility of PMMA and PHEMA in the 1-propanol solution. The strong enhanced solvation effect (often named cosolvency) of the 1-propanol/water mixture for PMMA and PHEMA can be explained by the solvent-solvent cluster model, which is the most plausible and widely employed theory.[48,49] Briefly, the 1-propanol/water cluster is linked by hydrogen bonding and can be regarded as a new compound that functions as a good solvent for the polymers. The dramatic influence of water on the volume transition of the core-shell gels indicates the promising potential of these gels either for water detection purposes or for the identification of water generated or removed by a reaction.

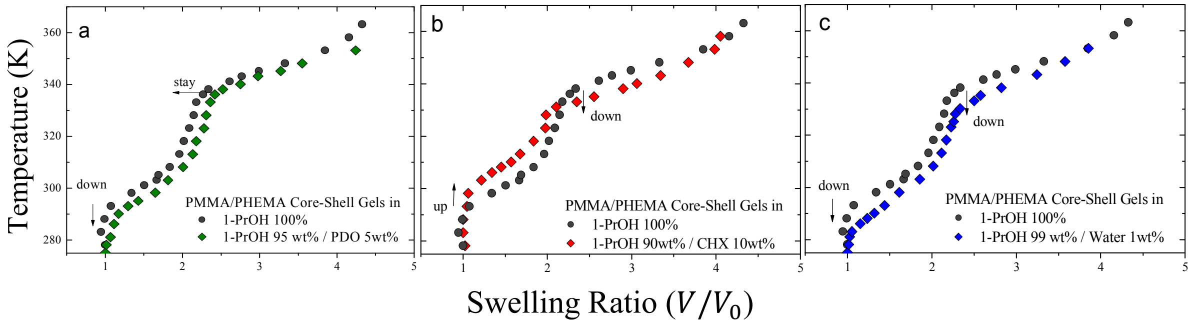

Fig. 6 Swelling ratio of the PMMA/PHEMA core-shell nanoparticle gels as a function of temperature in 1-propanol and three co-solvent mixtures: (a) 5 wt% PDO, (b) 10 wt% CHX, and (c) 1 wt% water. Each co-solvent induces different effects on the VTT of the core and shell networks.

4.3 Thermodynamic Modeling

Quantitative representation of the swelling behaviors of a gel network is required in a number of fine chemical processes, and lattice-based thermodynamic models offer a simple mathematical concept to achieve this. In this work, we suggest a systematic process to quantify the swelling behavior of doubly thermosensitive core-shell nanoparticle gels and describe the influence of co-solvents on the core-shell swelling with no arbitrary adjustment.

As we confirmed experimentally, there is a close relationship between the linear and cross-linked polymer networks, especially in terms of the thermal-dependent interactions with solvent molecules. Furthermore, in lattice-based models, it is reasonable to consider that the interaction energy between a polymer and solvent should be the same regardless of the polymer structure. Thus, we determined the interaction parameters ($\tilde{\varepsilon}_{\mathrm{ij}}$) from the phase behavior of linear polymer solutions and applied them directly to the swelling calculation of cross-linked polymer networks. Fig. 7(a) shows the UCST-type temperature-composition phase diagrams of binary PMMA/1-propanol and PHEMA/1-propanol systems. By correlating eqns (1) and (3) with the experimental data, the binary interaction parameters were obtained, and the parameters were applied to the swelling calculation of each homo-polymer gel solution. However, as shown in Fig. 7(b), the modeling results deviated significantly from the experimental swelling data when we assumed that the polymer network was perfectly dried at the reference state ($\phi_{g0} = 1$). By adjusting the parameters to the experimental data, reasonable values of ϕ_{g0} were obtained for the PMMA and PHEMA homo-polymer gels (Table 1). In Fig. 7(c), the interaction and network parameters were directly applied to the PMMA/PHEMA core-shell swelling calculations. Although the model successfully represented the two-step swelling process upon heating, it again showed a large deviation in the degree of swelling, indicating the necessity to consider the structural characteristics of the core-shell. Inherent structural properties, which hinder the swelling ability of the core-shell network, have been investigated by Ballauf and Lyon, who demonstrated the fixation of a shell network on the core surface and the shell restriction on the core swelling.[8,33] Thus, in our recent work,[14] constraint parameters ($k_{c,core}$ and $k_{c,shell}$) were incorporated within the elastic term (eqn (5)) as follows:

$$\frac{\Delta G_{el,core}}{NRT} = k_{c,core}\left(\frac{3A\phi_{g0,core}^{2/3}}{2m_{c,core}}\right)\left(\phi_{g,core}^{1/3}-\phi_{g,core}\right) + k_{c,core}\left(\frac{B}{m_{c,core}}\right)\phi_{g,core}ln\phi_{g,core} \tag{11}$$

$$\frac{\Delta G_{el,shell}}{NRT} = k_{c,shell}\left(\frac{3A\phi_{g0,shell}^{2/3}}{2m_{c,shell}}\right)\left(\phi_{g,shell}^{1/3}-\phi_{g,shell}\right) + k_{c,shell}\left(\frac{B}{m_{c,shell}}\right)\phi_{g,shell}ln\phi_{g,shell} \tag{12}$$

where k_{core} and $k_{shell} \geq 1$, indicating the increased stiffness of the core and shell networks, respectively. Fig. 7(c) shows that the corrected model represents the experimental core-shell swelling data with great accuracy, and the constraint parameters are listed in Table 1.

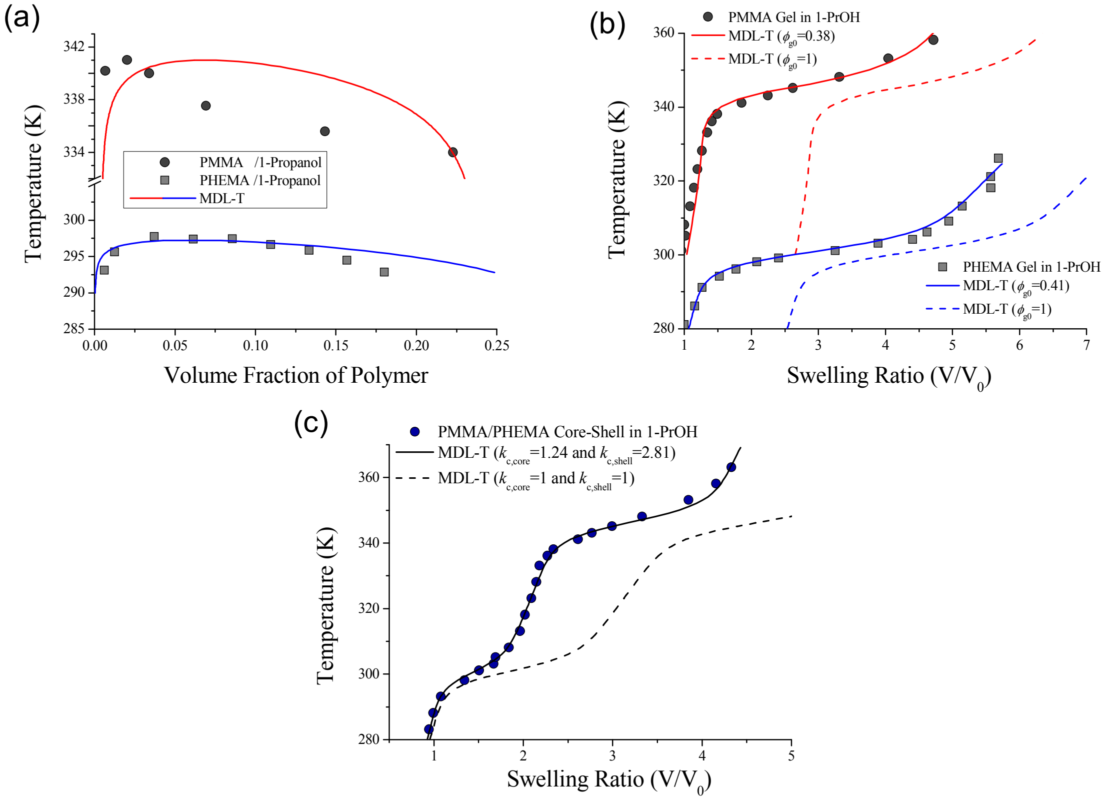

Fig. 7 The procedure used to obtain model parameters. (a) Interaction parameters are obtained from correlating eqns (1) and (3) with the phase diagrams of linear polymer solutions. (b) Using the interaction parameters, the swelling behaviors of homo-polymer gels are calculated by assuming $\phi_{g0} = 1$ (perfect dryness in the reference state) and subsequently adjusting ϕ_{g0} based

on the swelling data. (c) Using the parameters, the swelling behavior of the core-shell gel is calculated by assuming no constraint effects ($k_c = 1$) in the core-shell structure and then adjusting k_c to agree with the experimental data.

To model the influence of co-solvents on the swelling behavior of the core-shell gel, the required interaction parameters were obtained from ternary phase diagrams of the linear polymer solutions. Fig. 8 shows the procedure used for the model calculation of the core-shell swelling in the 1-PrOH/CHX mixed solvent. In Fig. 8(a) and 8(b), the binary interaction parameters of PMMA/CHX, PHEMA/CHX, and 1-PrOH/CHX were obtained by correlating eqns (1) and (3) with the experimental data. Given the interaction parameters, we first confirmed that the MDL-T model successfully represents the swelling behavior of each homo-polymer networks in the CHX/1-PrOH mixed solvent (Fig. 8(c)) with no additional parameters. Subsequently, the model parameters were directly applied to the core-shell swelling calculation in the CHX/1-PrOH mixed-solvent. As shown in Fig. 9(d), the MDL-T model successfully describes the influence of CHX on the PMMA/PHEMA core-shell gels by representing the decreased/increased core/shell VTTs without further adjustment.

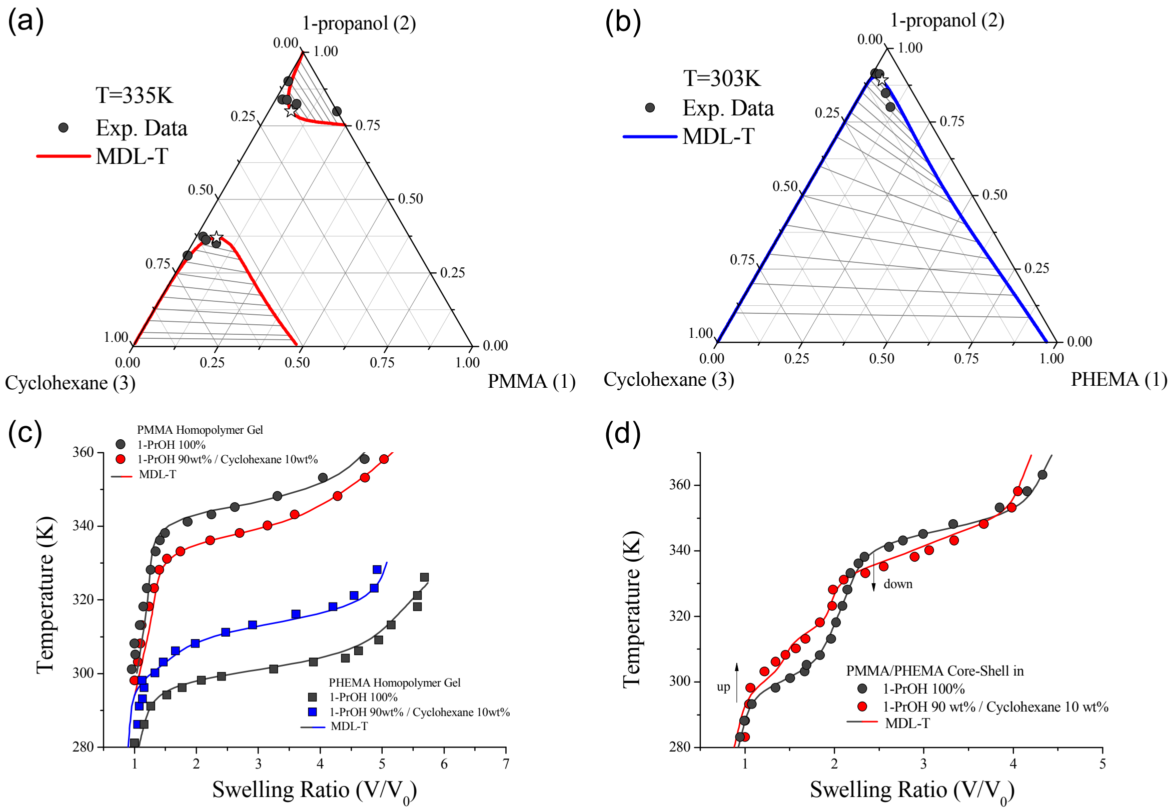

Fig. 8 Ternary phase diagrams of (a) PMMA/1-PrOH/CHX and (b) PHEMA/1-PrOH/CHX based on volume fraction. The symbols correspond to the experimental data, and the lines are the results of the MDL-T model. The open star (☆) is the calculated critical point, and the gray lines are the tie lines. (c) Swelling data of PMMA and PHEMA homo-polymer networks and (d) PMMA/PHEMA core-shell gels in the pure 1-PrOH solvent and CHX 10 wt% mixed solvent. The lines are the results of the MDL-T model.

Table 3. Interaction parameters of the MDL-T model obtained from linear polymer solutions.

$\tilde{\varepsilon}_{ij}$	$\varepsilon_{ij}^{H}/k\,(K)$	$\varepsilon_{ij}^{S}/k\,(K)$	$\delta\varepsilon_{ij}^{H}/k\,(K)$	$\delta\varepsilon_{ij}^{S}/k\,(K)$	κ
PMMA / 1-PrOH	2.90×10^1	0.011	1.44×10^2	0.42	5.29×10^3
PMMA / CHX	2.32×10^2	0.66	1.47×10^3	4.36	3.17×10^1
PMMA / PDO	5.08×10^1	-0.003	5.18×10^2	1.45	5.79×10^2
PMMA / Water	-7.05×10^2	-2.78	1.17×10^3	3.87	3.86

PHEMA /1-PrOH	5.27×10^1	0.11	1.55×10^2	0.52	3.74×10^3
PHEMA / CHX	3.42	-0.17	7.34×10^2	2.33	3.67×10^2
PHEMA / PDO	-4.00×10^2	0.89	-5.29×10^3	-22.45	4.66×10^{-2}
PHEMA / Water	-2.21×10^2	-1.10	-2.01×10^3	-6.90	1.25×10^2
1-PrOH / CHX	-1.58×10^3	-4.87	1.62×10^3	4.87	1.05×10^{-3}
1-PrOH / PDO	-3.97×10^2	-1.37	4.43×10^2	1.38	1.28×10^{-1}
1-PrOH / Water	-3.77×10^3	-12.31	3.94×10^3	12.34	5.32×10^{-3}
$\tilde{\varepsilon}_{co,PMMA}$	2.21×10^3	0.94	2.47×10^3	7.70	5.42
$\tilde{\varepsilon}_{co,PHEMA}$	-1.48×10^3	-4.59	2.14×10^4	74.33	2.83×10^{-1}

We applied the same calculation procedure to other co-solvent systems to confirm the validity of this approach and the applicability of the MDL-T model. Fig. 9 shows the experimental data and modeling results of the swelling behavior of PMMA/PHEMA core-shell gels in 1-PrOH/PDO and 1-PrOH /water mixed solvents. The required interaction parameters were determined from ternary phase diagrams of linear polymer solutions (Fig. S2). In Fig. 9(a), although the model result slightly overestimates the shell swelling data, the core swelling transition is successfully predicted, and the overall tendency of the calculated results correspond well with the experimental data. Fig. 9(b) exhibits the effect of water on the PMMA/PHEMA core-shell gels in a 1-propanol solution. As discussed previously, water molecules create a strong synergy effect with 1-propanol, resulting in an enhanced solvation effect of PMMA and PHEMA. With a very small water content, the mixed solvent results in a large decrease in the VTT of the core-shell gels. Thus, a slight modification of the model was required to consider the abnormal synergism between water and 1-propanol. We adopted the simple concept of the cosolvency parameter ($\tilde{\varepsilon}_{co}$) suggested by Lee and Bae,[24] modifying the interaction parameter between polymer and solvents ($\tilde{\varepsilon}_{ps}$) to $\tilde{\varepsilon}_{ps,\mathrm{eff}} = \tilde{\varepsilon}_{ps} + \tilde{\varepsilon}_{co}\phi_{s1}\phi_{s2}$, where $\tilde{\varepsilon}_{ps,\mathrm{eff}}$ is an effective interaction parameter considering the enhanced solvation effect. The modification seems physically acceptable since the added cosolvency term becomes zero in a pure solvent ($\phi_{s1}\phi_{s2} = 0$) and has a maximum value when the amounts of the two solvents are equal. Fig. 9(b) shows that the corrected model (solid line) produces a much better result compared to the original model (dashed line), and the parameters are listed in Table 3.

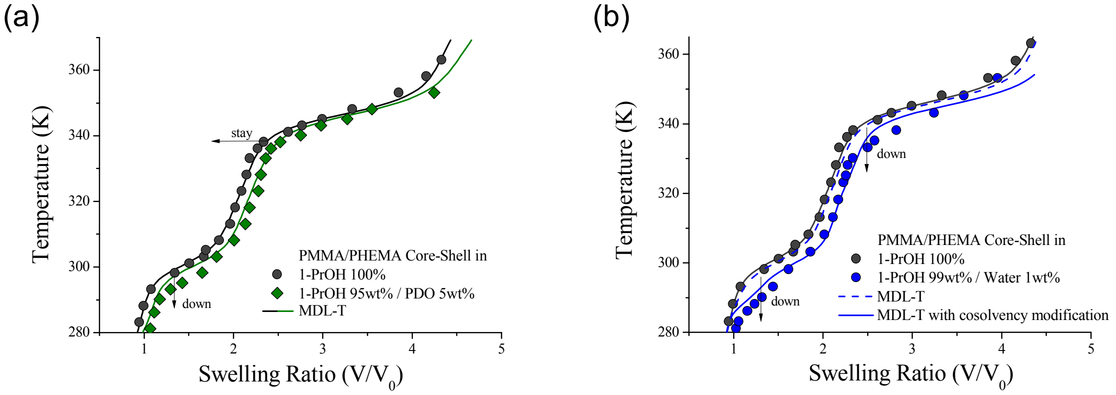

Fig. 9 Experimental swelling data and model calculations of the PMMA/PHEMA core-shell nanoparticle gels in (a) 1-PrOH/PDO and (b) 1-PrOH/water mixed solvents. In panel b, the dashed line was calculated without consideration of the cosolvency effect, and the solid line (blue) was calculated by incorporating the cosolvency modification ($\tilde{\varepsilon}_{co}$).

5. Conclusions

UCST-type doubly thermosensitive core-shell nanoparticle gels with tunable thermal swelling behavior were prepared via seed and feed precipitation polymerization. Photon correlation spectroscopy measurements show that the thermosensitivity of the PMMA core and PHEMA shell networks are differently influenced by the addition of three co-solvents where the CHX, PDO, and water co-solvents respectively induce “lower/upper,” “even/lower,” and “lower/lower” VTTs of the core/shell networks. Specifically, it was unexpected that the addition of a small amount of the water co-solvent, which is a non-solvent of PMMA and PHEMA, created a strong enhanced solvation effect for both polymers, resulting in large decreases in the VTTs. The tunability of the core-shell gels was quantitatively represented by a combination of the MDL-T model, optimizing the thermal behavior of interactions between components, and the Flory-Rehner chain model. Required interaction parameters ($\tilde{\varepsilon}_{\rm ij}$) were obtained from the binary and ternary phase diagrams of linear polymer solutions, and the network parameters (ϕ_{g0} and k_c) were determined from the 1-propanol mono-solvent gel solution. Using the model parameters, the swelling behaviors of core-shell gels in mixed solvents were successfully described without further adjustment. It is expected that this simple and convenient method to tune the thermal sensitivity of core-shell nanoparticle gels and its quantitative model will promote the use of core-shell gels in thermally controlled drug delivery and release, chemical separation platform, and water treatment applications.

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Acknowledgements

This research was respectfully supported by Engineering Development Research Center (EDRC) funded by the Ministry of Trade, Industry & Energy (MOTIE). (No. N0000990)

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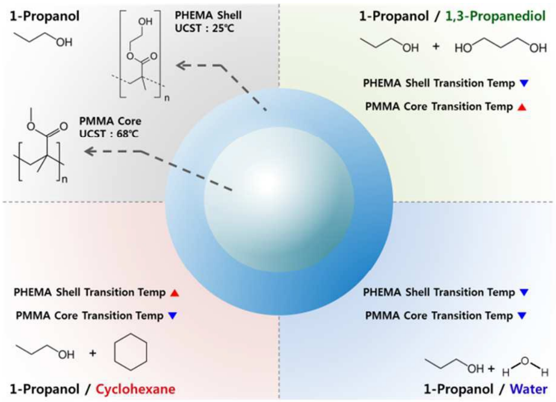
Cosolvency Effect on Tunable Thermosensitive Core-Shell Nanoparticle Gels

Sang Min Lee and Young Chan Bae*



Texture abstract

Schematic depiction of a core-shell structure composed of PMMA core and PHEMA shell, and the influence of three co-solvents on the volume transition temperature of the core-shell gels in 1-propanol solution.