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Equilibrium swelling of thermo-responsive copolymer microgels†

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Thermo-responsive (TR) hydrogels with a lower critical solution temperature swell strongly at temperatures below their volume phase transition temperature T_c and collapse above T_c. Biomedical application of these materials requires tuning the critical temperature in a rather wide interval. A facile method for modulation of T_c is to polymerize the basic monomers with hydrophilic or hydrophobic comonomers. Although the effectiveness of this method has been confirmed by experimental data, molar fractions of comonomers necessary for fine tuning of T_c in macroscopic gels and microgels are unknown. A simple model is developed for the equilibrium swelling of TR copolymer gels. Its adjustable parameters are found by fitting swelling diagrams on several macro- and microgels with *N*-isopropylacrylamide as a basic monomer. Good agreement is demonstrated between the experimental swelling curves and results of numerical analysis. An explicit expression is derived for the volume phase transition temperature as a function of molar fraction of comonomers. The ability of this relation to predict the critical temperature is confirmed by comparison with observations.

1 Introduction

Thermo-responsive (TR) gels form a special class of hydrogels whose equilibrium degree of swelling is strongly affected by temperature. TR gels of the LCST (lower critical solution temperature)-type swell pronouncedly at temperatures T below their volume phase transition temperature T_c and collapse when T exceeds T_c. Preparation of TR gels and analysis of their properties have recently attracted substantial attention due to a wide range of biomedical and biotechnological applications of these materials.[1,2] Covalently cross-linked poly(*N*-isopropylacrylamide) (PNIPAm) gel is the most extensively studied TR gel.[3,4] It exhibits a sharp volume phase transition at $T_c = 32$ °C and demonstrates good mechanical properties below and above T_c.

As swelling of a gel is driven by diffusion of water molecules, the rate of its response to external stimuli is determined by the characteristic size: the smaller a sample is, the faster it swells or collapses. Equilibrium and transient swelling of TR microgels (spherical particles with radii ranging from 10 to 1000 nm) has become a hot topic in the past decade.[5] This interest is driven by applications of these materials as carriers for targeted delivery of drugs and genes,[6] scaffolds for tissue regeneration,[7] systems for biosensing and bioimaging,[8] and nanoreactors with high catalytic activity,[9] to mention a few.

Biomedical applications of microgels (for electrophoretic separation of DNA and proteins,[10] targeted delivery of drugs and genes,[11] storage and transportation of vaccines,[12] and as temperature-triggered actuators[13]) require modulation of their volume phase transition temperature T_c in a rather wide interval.[1] Several methods for tuning T_c of TR gels have been proposed.[14–17] It is found that (i) T_c is practically unaffected by molar fractions of monomers and cross-linkers, as well as by the polymerization temperature and solvent for synthesis, (ii) it is weakly affected by the presence of polymer chains immersed into a pre-gel solution to prepare gels with inter-penetrating networks, and (iii) T_c changes significantly when TR monomers are polymerized with neutral or ionic comonomers whose hydrophilicity differs from that of the basic monomers. Although the trend in alteration of T_c is clear: the volume phase transition temperature decreases due to the presence of hydrophobic comonomers and increases when hydrophilic comonomers are incorporated, no explicit relations have been developed for the quantitative prediction of these changes.

Macroscopic TR gels are conventionally prepared by free-radical cross-linking polymerization of an aqueous solution of monomers and cross-linker at temperatures T below T_c.[18] On the contrary, TR microgels are synthesized by precipitation or emulsion polymerization (with or without surfactants) under stirring at temperatures far above their volume phase transition temperature.[19] As the mechanical response of TR gels is strongly affected by polymerization conditions,[20–22] equilibrium swelling diagrams of macro- and microgels distinguish substantially.[23]

The objective of this work is three-fold: (i) to develop a model for the equilibrium swelling of TR macro- and microgels with

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a relatively small number of material constants, (ii) to determine adjustable parameters by fitting experimental swelling diagram on copolymer gels with NIPAm as basic monomers and non-ionic comonomers whose hydrophilicity is lower and higher than that of NIPAm, (iii) to derive a analytical formula that expresses the volume phase transition temperature of a copolymer gel T_c by means of the molar fraction of comonomers in a pre-gel solution c_{co} and to examine its ability to predict observations.

The novelty of this study consists in the following. (I) The polymer network in a TR gel is treated as a superposition of two networks: the first is formed under preparation when chains are covalently cross-linked, and the other is developed at $T > T_c$ when new physical bonds between chains are formed due to aggregation of hydrophobic segments. This approach allows us to describe a strong increase in the elastic modulus of TR gels above their volume-phase transition temperature T_c, on the one hand, and to avoid introduction of nonlinear dependencies of the Flory–Huggins parameter on volume fraction of polymer network, on the other. (II) A simple equation (see eqn (27) below) is derived that connects the volume phase transition temperature of a copolymer gel with the molar fraction of comonomers. The ability of this relation to predict T_c is confirmed by comparison with experimental data. It is shown, in particular, that eqn (27) predicts accurately T_c of microgels when its only coefficient a is found by matching experimental data on macroscopic gels, and *vise versa*. (III) A phenomenological relation (32) is established between the modified Flory–Huggins parameter of comonomers and their Hildebrand solubility parameter. Based on this approach, the volume phase transition temperature of copolymer gels is predicted for several copolymer gels and a reasonable agreement is demonstrated between results of numerical analysis and experimental data.

2 Model

2.1 Swelling of homopolymer gels

A TR gel is modeled as a two-phase medium composed of solid (an equivalent polymer network) and fluid (water) constituents. The solid and fluid phases are treated as immiscible interpenetrating continua.

The initial state of a gel coincides with that of an undeformed dry specimen at some temperature $T_0 < T_c$. According to the affinity hypothesis, deformation of the gel coincides with deformation of its polymer network. Transformation of the initial state into the actual state at temperature T is described by the deformation gradient $\mathbf{F}$. We disregard thermally induced volume expansion and write the molecular incompressibility condition in the form

$$\det \mathbf{F} = 1 + Cv, \tag{1}$$

where C denotes concentration of water (number of molecules per unit volume in the initial state), and v is the characteristic volume of a molecule. Eqn (1) means that volume deformation of a gel is driven by changes in water content only.

To describe abrupt changes in the equilibrium degree of swelling of TR gels above their volume phase transition temperature T_c, we follow the approach proposed in ref. 24 and 25, see also recent reviews.[26,27] Polymer chains in a network are presumed to consist of hydrophilic and hydrophobic segments. At temperatures $T < T_c$, each hydrophobic segment is surrounded by a cage-like structure formed by water molecules bridged by hydrogen bonds. An increase in temperature results in the growth of intensity of thermal fluctuations that destabilize these bonds. Breakage of cage-like structures surrounding hydrophobic segments induces their agglomeration and formation of aggregates from which water molecules are expelled. At temperatures above T_c, all cage-like structures are broken, and a gel consists of a number of deswollen hydrophobic aggregates bridged by hydrophilic segments and separated by nano-channels in which water molecules are located.[28]

According to this scenario, the polymer network in a TR gel involves two components. The first network with covalent bonds is formed under cross-linking polymerization of a pre-gel solution. The other network is built at temperatures $T > T_c$ due to aggregation of hydrophobic segments into clusters that serve as physical bonds between chains. For simplicity, both networks are treated as permanent. This picture is confirmed by observations on TR macroscopic gels[29,30] and microgels[31] that show a pronounced (by an order of magnitude) increase in their elastic moduli when temperature T exceeds T_c.

The deformation gradient for macro-deformation $\mathbf{F}$ is connected with the deformation gradient for elastic deformation of the mth network $\mathbf{F}_e^{(m)}$ by the multiplicative decomposition formula

$$\mathbf{F} = \mathbf{F}_e^{(m)} \cdot \mathbf{f}_m \ (m = 1, 2), \tag{2}$$

where $\mathbf{f}_m$ denotes deformation gradient for transition from the initial to the reference (stress-free) state of the mth network, and the dot stands for inner product.

Homogeneous transformation of the initial configuration into the reference configuration of a covalently cross-linked network is described by the deformation gradient

$$\mathbf{f}_1 = (1 + Q_0)^{\frac{1}{3}} \mathbf{I}, \tag{3}$$

where $\mathbf{I}$ is the unit tensor, $Q_0 = C_0 v$ is the degree of swelling, and C_0 stands for the concentration of water molecules in the reference state.

Keeping in mind that all water molecules are expelled from hydrophobic aggregates, we presume the reference state of the network with physical bonds to coincide with the initial (dry) state of the gel,

$$\mathbf{f}_2 = \mathbf{I}. \tag{4}$$

The Helmholtz free energy of the gel (per unit volume in the initial state) Ψ equals the sum of the specific energies of fluid and solid components not interacting with each other and the energy of their interaction,

$$\Psi = \Psi_1 + \Psi_2 + \Psi_{\text{int}}, \tag{5}$$

where Ψ_1 is the specific energy of water molecules not interacting with segments of chains, Ψ_2 is the specific energy of polymer chains not interacting with water, and Ψ_{int} is the specific energy of mixing of water molecules with segments of chains.

The specific energy of water molecules is given by

$$\Psi_1 = \mu^0 C, \tag{6}$$

where μ^0 denotes chemical potential of water molecules not interacting with the polymer network.

The specific energy of the network (consisting of two parts with chemical and physical bonds) reads

$$\Psi_2 = \sum_{m=1}^{2} W_m\left(I_{\text{e}1}{}^{(m)}, I_{\text{e}2}{}^{(m)}, I_{\text{e}3}{}^{(m)}\right). \tag{7}$$

The specific mechanical energy W_m stored in chains of the mth network depends on the principal invariants $I_{\text{e}1}{}^{(m)}$, $I_{\text{e}2}{}^{(m)}$, $I_{\text{e}3}{}^{(m)}$ of the corresponding Cauchy–Green tensor for elastic deformation

$$\mathbf{B}_{\text{e}}{}^{(m)} = \mathbf{F}_{\text{e}}{}^{(m)} \cdot \mathbf{F}_{\text{e}}{}^{(m)\top}, \tag{8}$$

where $\top$ stands for transpose. For definiteness, the neo-Hookean formulas are accepted for the strain energy densities of polymer networks with covalent and physical bonds,

$$W_m = \frac{1}{2} G_m\left[\left(I_{\text{e}1}{}^{(m)} - 3\right) - \ln I_{\text{e}3}{}^{(m)}\right], \quad (m = 1, 2), \tag{9}$$

where G_1 and G_2 stand for the shear moduli. The physical meaning of eqn (9) was discussed in ref. 32, where this relation was re-derived within the concept of entropic elasticity. More sophisticated expressions for the functions W_m were developed and verified by comparison with observations in ref. 33 and 34.

We disregard the effect of temperature on the elastic modulus of the covalently cross-linked network and treat G_1 as a constant. The modulus G_2 of the network with physical bonds vanishes below T_{c} and grows with the difference $T - T_{\text{c}}$ above the volume phase transition temperature. The following expression is adopted for this function:

$$G_2(T) = 0, \quad (T < T_{\text{c}}),\ G_2(T) = \overline{G}_2\left[1 - \exp\left(-\beta\sqrt{T - T_{\text{c}}}\right)\right], \quad (T \geq T_{\text{c}}), \tag{10}$$

where $\bar{G}_2$ and β are adjustable parameters. The ability of eqn (10) to describe experimental data on PNIPAm gels with a sharp volume phase transition was verified in ref. 35. The temperature-induced growth of G_2 in copolymer gels with wider regions of volume phase transition are determined by an analog of eqn (10) with the square root replaced with some power of the temperature increment $T - T_{\text{c}}$.

The specific energy of mixing of water molecules with segments of chains is adopted in the conventional form[36]

$$\Psi_{\text{int}} = k_{\text{B}} T_0 (C \ln \phi_{\text{w}} + \chi C \phi_{\text{n}}), \tag{11}$$

where k_{B} is the Boltzmann constant, χ is the Flory–Huggins (FH) parameter, and

$$\phi_{\text{w}} = \frac{Cv}{1 + Cv},\ \phi_{\text{n}} = \frac{1}{1 + Cv} \tag{12}$$

are volume fractions of water (w) and polymer network (n) in the actual state. The first term in eqn (11) characterizes the entropy and the other term describes the enthalpy of mixing of water molecules and segments of chains. In a narrow interval of temperatures near T_{c}, the actual temperature T is replaced with the initial temperature T_0 in the thermodynamic factor $k_{\text{B}}T$.

Unlike the conventional approach to the analysis of swelling of TR gels,[37,38] we treat the FH parameter as a function of temperature T only. The following expression is accepted for χ:

$$\begin{aligned} \chi &= \chi_0 + \chi_1 T \quad (T < T_{\text{c}}), \\ \chi &= \chi_{\max} \quad (T \geq T_{\text{c}}), \end{aligned} \tag{13}$$

where T and T_{c} are measured in celsius, and the coefficients χ_0, χ_1, $\chi_{\max}$ obey the continuity condition

$$\chi_{\max} = \chi_0 + \chi_1 T_{\text{c}}. \tag{14}$$

Eqn (13) means that breakage of cage-like structures formed by water molecules around hydrophobic segments induces the growth of the effective hydrophobicity of chains (characterized by χ) at temperatures T below T_{c}. When T exceeds T_{c}, the increase in χ is prohibited due to formation of aggregates of hydrophobic segments. This condition ensures that material parameters do not accept anomalously high values mentioned in ref. 39. It has been demonstrated in ref. 40 that replacement of the first equality in eqn (13) with a nonlinear dependence of χ on temperature does not improve the quality of fitting (as T varies in a rather narrow interval between 0 °C and T_{c}).

Under unconstrained equilibrium swelling of a TR gel at an arbitrary temperature T, its degree of swelling

$$Q = Cv \tag{15}$$

obeys the nonlinear equation

$$\begin{aligned} &\ln \frac{Q}{1+Q} + \frac{1}{1+Q} + \frac{\chi}{(1+Q)^2} + \frac{g_1}{1+Q}\left[\left(\frac{1+Q}{1+Q_0}\right)^{\frac{2}{3}} - 1\right] \\ &+ \frac{g_2}{1+Q}\left[(1+Q)^{\frac{2}{3}} - 1\right] \\ &= 0, \end{aligned} \tag{16}$$

where

$$g_m = \frac{G_m v}{k_{\text{B}} T_0} \quad (m = 1, 2) \tag{17}$$

are dimensionless elastic moduli. A detailed derivation of eqn (16) is given in ESI.†

Eqn (16) together with eqn (13) for the FH parameter χ and eqn (10) and (17) for the dimensionless moduli provide governing equations for the equilibrium degree of swelling Q. These relations involve 7 adjustable parameters: (i) coefficients χ_0 and χ_1 describe how hydrophilicity of chains is affected by temperature below the critical temperature T_{c}, (ii) parameter

χ_{max} characterizes their hydrophilicity above the volume phase transition temperature, (iii) g_1 and Q_0 stand for the dimensionless shear modulus of the covalently cross-linked network and its degree of swelling in the reference state, and (iv) coefficients $\bar{g}_2$ and β describe an increase in the dimensionless shear modulus of the network with physical bonds above T_c. Given χ_0, χ_1 and χ_{max}, the volume phase transition temperature T_c is calculated from eqn (14).

Unlike macroscopic gels, whose degrees of swelling in the as-prepared and fully swollen states can be measured directly, the equilibrium degree of swelling of microgels Q is recalculated from their hydrodynamic radii r_h, which, in turn, are found from observations in dynamic light scattering, small-angle X-ray scattering or small-angle neutron scattering tests on diluted microgel colloids.[41] Under homogeneous swelling of a microgel, $Q(T)$ is connected with the hydrodynamic radius $r_h(T)$ by the equation

$$\frac{1+Q(T)}{1+Q(T_*)} = \left(\frac{r_h(T)}{r_h(T_*)}\right)^3, \tag{18}$$

where T_* stands for some temperature. Observations in equilibrium water uptake tests on PNIPAm macroscopic gels[42,43] and microgels[39,44] show that $Q(T_*)$ is very close to 1/2 when T_* exceeds strongly the critical temperature T_c. With reference to these data, we set

$$Q(T_*) = \frac{1}{2}, \tag{19}$$

where T_* is the maximum temperature at which measurements are performed, and determine $Q(T)$ from eqn (18) and (19). Given an experimental diagram $r_h(T)$, the only extra parameter in the model, radius R of a microgel particle in the initial state, is found from the equation

$$r_h(T) = (1+Q(T))^{\frac{1}{3}} R, \tag{20}$$

where Q is a solution of eqn (16).

2.2 Swelling of copolymer gels

We consider equilibrium swelling of binary copolymer gels prepared by cross-linking polymerization of thermo-responsive monomers (NIPAm) with non-ionic temperature-insensitive comonomers. Although some comonomers used in the analysis of experimental data demonstrate weak sensitivity to changes in temperature,[45] this effect is disregarded. Molar fraction of comonomers equals c_{co}, and molar fraction of NIPAm monomers equals $1 - c_{co}$, where c_{co} is presumed to be small compared with unity.

Eqn (10), (13) and (16) describe equilibrium swelling of homopolymer and copolymer gels. Our aim is to establish correlations between material constants of PNIPAm gel and its copolymer gels to be confirmed by fitting observations in Sect. 3.

The coefficients β and $\bar{g}_2 = \bar{G}_2 \nu/(k_B T_0)$ are presumed to be independent of c_{co}. These parameters describe the kinetics of aggregation of hydrophobic segments of NIPAm monomers above the volume phase transition temperature T_c. We suppose that the presence of comonomers does not affect the aggregation process when $c_{co} \ll 1$.

With reference to the conventional scaling rules for hydrogels,[46] we presume g_1 to be independent of c_{co}, as this quantity characterizes concentration of cross-links in a gel. It will be shown in what follows that this assumption is fulfilled for macroscopic gels, but it can be violated for microgels with strongly hydrophobic comonomers (these entities aggregate into hydrophobic clusters that serve as extra permanent cross-links between chains even at temperatures T below T_c). At small c_{co}, changes in g_1 with molar fraction of comonomers are described by the linear equation

$$g_1 = g_1^0(1 - c_{co}) + {g_1}^1 c_{co}, \tag{21}$$

where g_1^0 is the dimensionless elastic modulus of a homopolymer PNIPAm gel, and ${g_1}^1$ is proportional to concentration of bonds between polymer chains formed by clusters of hydrophobic comonomers.

The volume fraction of polymer network in the reference (stress-free) state ϕ_{n0} (this quantity is determined by eqn (12) where C is replaced with C_0) obeys the equation

$$\phi_{n0} = \phi_{n0}^0(1 - c_{co}) + {\phi_{n0}}^1 c_{co}, \tag{22}$$

where ϕ_{n0}^0 characterizes the reference state of a homopolymer PNIPAm gel, and ${\phi_{n0}}^1$ accounts for evolution of this state induced by the presence of comonomers.

As an analog of eqn (21) and (22) for the FH parameter of a copolymer gel (the so-called two-parameter model[47]) is overly simplified to describe equilibrium swelling diagrams, we use the three-parameter model,[48,49]

$$\chi = \chi_{PNIPAm}(1 - c_{co}) + \chi_{co} c_{co} - \chi_{int} c_{co}(1 - c_{co}), \tag{23}$$

where χ_{PNIPAm} and χ_{co} are the FH parameters describing interactions of water molecules with NIPAm monomers and comonomers, respectively, and the coefficient χ_{int} characterizes binary interactions between NIPAm monomers and comonomers. When molar fraction of comonomers is small compared with unity, eqn (23) is transformed into the two-parameter relation

$$\chi = \chi_{PNIPAm}(1 - c_{co}) + \tilde{\chi}_{co} c_{co}, \tag{24}$$

where χ_{PNIPAm} is given by eqn (13), and

$$\tilde{\chi}_{co} = \chi_{co} - \chi_{int}$$

stands for the modified FH parameter of comonomers (that accounts for their interactions with NIPAm monomers and water molecules simultaneously). Bearing in mind that comonomers are temperature-insensitive, we presume $\tilde{\chi}_{co}$ to be independent of temperature and arrive at the analog of eqn (13) for TR copolymer gels below their volume phase transition temperature

$$\chi = [\chi_0(1 - c_{co}) + \tilde{\chi}_{co} c_{co}] + \chi_1(1 - c_{co})T \ (T < T_c). \tag{25}$$

Above the critical temperature T_c, the FH parameter of the copolymer network obeys eqn (13) with χ_{max} independent of concentration of comonomers,

$$\chi = \chi_{\max}\ (T \geq T_c). \tag{26}$$

Eqn (26) means that the presence of a small molar fraction of comonomers in the pre-gel solution does not affect aggregation of hydrophobic segments of PNIPAm chains.

Substitution of eqn (25) and (26) into continuity condition (14) results in the formula for the volume phase transition of a copolymer gel

$$T_c = T_{c\ \mathrm{PNIPAm}} \frac{1 + a c_{co}}{1 - c_{co}}, \tag{27}$$

where

$$T_{c\ \mathrm{PNIPAm}} = \frac{\chi_{\max} - \chi_0}{\chi_1} \tag{28}$$

stands for the critical temperature of a homopolymer PNIPAm gel, and

$$a = \frac{\chi_0 + \tilde{\chi}_{co}}{\chi_{\max} - \chi_0}. \tag{29}$$

Given $T_{c\ \mathrm{PNIPAm}}$, eqn (27) involves the only material constant a that characterizes interactions of comonomers with NIPAm monomers and water molecules. It follows from eqn (27) that T_c increases with c_{co} when $a > -1(\tilde{\chi}_{co} > -\chi_{\max})$, decreases when $a < -1(\tilde{\chi}_{co} < -\chi_{\max})$, and remains unchanged when $a = -1$. These inequalities can serve as explicit conditions of hydrophilicity and hydrophobicity of comonomers.

To reduce the number of material constants in the model, we treat the coefficients χ_0 and χ_1 as universal (which means that their values are independent of preparation conditions and molar fraction of a cross-linker, and are determined by properties of NIPAm monomers exclusively). These parameters were found in ref. 50 by approximation of observations on PNIPAm gel prepared by irradiation cross-linking of an aqueous solution of PNIPAm chains,[51]

$$\chi_0 = -2.0980,\ \chi_1 = 7.908 \times 10^{-2}. \tag{30}$$

Given χ_0 and χ_1, the coefficient $\chi_{\max}$ (this quantity is weakly affected by preparation conditions for a copolymer gel) is calculated from eqn (28). The coefficient a in eqn (27) is determined by fitting an experimental dependence of T_c on c_{co}. Finally, the coefficient $\tilde{\chi}_{co}$ is found from eqn (29).

3 Comparison with experimental data

Our aim now is threefold: (i) to examine the ability of the model (10), (16), (25) and (26) to describe experimental swelling diagrams on PNIPAm microgels synthesized with various comonomers, (ii) to verify its ability to predict the influence of comonomers on the volume phase transition temperature, and (iii) to assess a difference between the thermo-mechanical responses of microgels and their macroscopic analogs.

When the coefficients χ_0 and χ_1 are given by eqn (30) and the coefficient $\chi_{\max}$ is determined from eqn (28), the governing equations for a copolymer gel involve only five adjustable parameters. This number is substantially (by twice) lower than that in conventional models for copolymer gels.[52,53] For each set of observations, three coefficients (g_1, Q_0, $\tilde{\chi}_{co}$) are found by fitting experimental data below T_c, and the remaining two coefficients ($\bar{g}_2$, β) are determined by matching observations above T_c. Adjustable parameters are calculated by the nonlinear regression method to minimize the expression

$$\sum (Q_{\exp} - Q_{\mathrm{sim}})^2,$$

where summation is performed over all temperatures T under consideration, $Q_{\exp}$ stands for the degree of swelling measured in a test, and Q_{sim} is determined by eqn (16), which is solved by the Newton–Raphson algorithm.

3.1 P(NIPAm–tBA) microgels

We begin with the study of swelling diagrams on poly(*N*-isopropylacrylamide-*co-tert*-butyl acrylate) (P(NIPAm–tBA)) microgels prepared by surfactant-free radical emulsion polymerization (6 h at 70 °C) of an aqueous solution of NIPAm (82.7 mM) and tBA (various amounts) monomers by using *N*,*N*′-methylene-bis(acrylamide) (BIS, 5.6 mol% with respect to NIPAm monomers) as a cross-linker and ammonium persulfate (APS) as an initiator.[54] Experimental data on microgels with $c_{co} = 0$ and 0.28 are reported in Fig. 1A and those on microgels with $c_{co} = 0.11$, 0.16 and 0.21 are presented in Fig. S-1A–C.† In these figures, the hydrodynamic radius r_h is plotted *versus* temperature T together with results of numerical simulation with the material parameters listed in Table S-1.†

Observations on homopolymer PNIPAm microgel (Fig. 1A) are fitted by using the following algorithm. Given a set of experimental data $r_h(T)$, the swelling curve $Q(T)$ is calculated from eqn (18) and (19), and the dependence $\chi(T)$ (below T_c) is found from eqn (16) with $g_2 = 0$. For χ_0 and χ_1 given by eqn (30), this dependence is matched by eqn (13), and parameters g_1 and Q_0 are found from the best-fit condition. The coefficients $\bar{g}_2$ and β are determined by fitting the swelling diagram $Q(T)$ above T_c. Parameters $\chi_{\max}$ and $\tilde{\chi}_{co}$ are found by fitting the experimental dependence of T_c on molar fraction of comonomers c_{co} (Fig. 1B) by means of eqn (27)–(29). After finding all material parameters, radius of a microgel particle in the initial state R is calculated by approximating the dependence $r_h(T)$ with the help of eqn (20).

Observations show that parameters g_1, Q_0, $\bar{g}_2$ and β are unaffected by c_{co}. The effect of molar fraction of comonomers on radius of microgel particles R is illustrated in Fig. 1C, where the data are approximated by the linear equation

$$R = R^0(1 - c_{co}) + R^1 c_{co} \tag{31}$$

with the coefficients calculated by the least-squares method. Fig. 1C shows that R decreases pronouncedly with c_{co} due to the strong hydrophobic nature of tBA.

To validate our results, we use observations of macroscopic P(NIPAm–tBA) gels prepared by means of a two-step process.[55] First, tBA monomers were dissolved in an aqueous solution of sodium dodecyl sulfate (SDS) at 80 °C. Afterwards, cross-linking polymerization was performed at room temperature of NIPAm monomers in an emulsion of tBA by using BIS as a cross-linker,

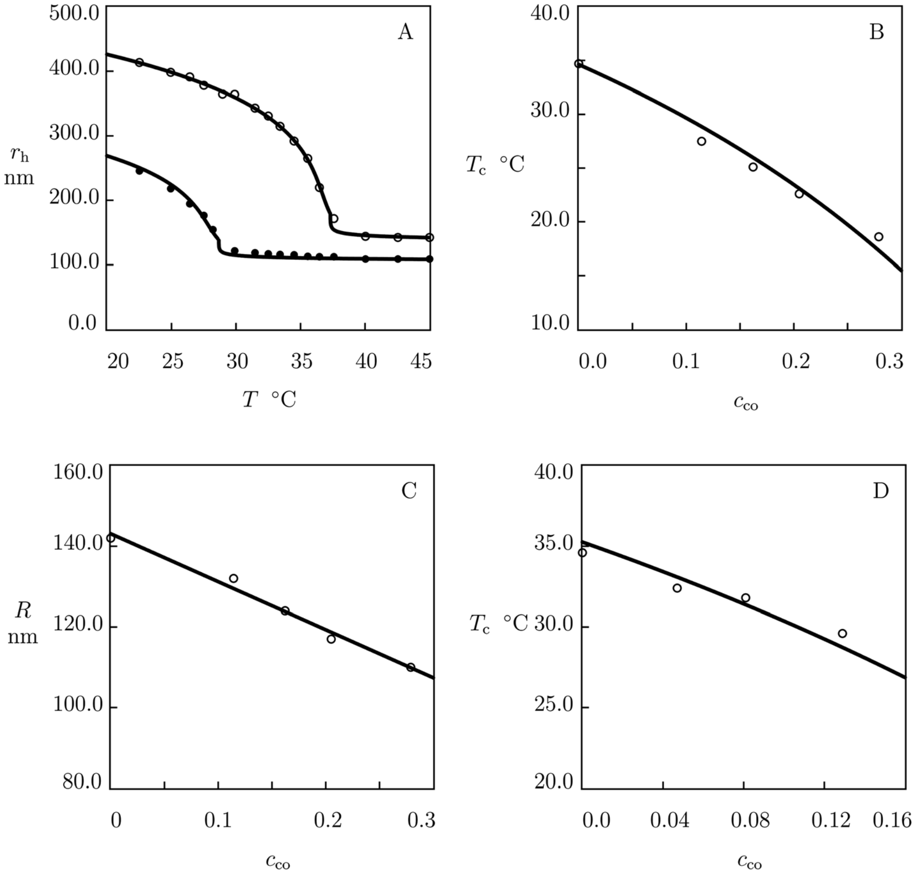

Fig. 1 (A) Hydrodynamic radius r_h of microgel particles *versus* temperature T. Symbols: experimental data[54] on P(NIPAm–tBA) microgels with molar fractions of comonomers $c_{co} = 0$ (○) and $c_{co} = 0.28$ (●). Solid lines: results of simulation. (B) Volume phase transition temperature T_c *versus* molar fraction of comonomers c_{co}. Circles: experimental data. Solid line: results of simulation. (C) Radius R of microgel particles *versus* molar fraction of comonomers c_{co}. Circles: treatment of observations. Solid line: results of simulation. (D) Volume phase transition temperature T_c *versus* molar fraction of comonomers c_{co}. Circles: experimental data[55] on P(NIPAm–tBA) gels. Solid line: predictions of the model.

APS as an initiator and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TEMED) as an accelerator. The effect of molar fraction of comonomers c_{co} on the volume phase transition temperature T_c is illustrated in Fig. 1D, where experimental data are plotted together with predictions of eqn (27) and (29) (without fitting parameters).

3.2 P(NIPAm–NtBAm) microgels

We analyze observations on poly(*N*-isopropylacrylamide-*co*-*N*-*tert*-butylacrylamide) (P(NIPAm–NtBAm)) microgels synthesized by surfactant-free radical emulsion polymerization (4 h at 70 °C) of an aqueous solution of NIPAm and NtBAm monomers by using BIS (5 mol% with respect to monomers) as a cross-linker and potassium peroxodisulfate (KPS) as an initiator.[56] Experimental swelling curves on microgels with $c_{co} = 0$ and 0.15 are reported in Fig. 2A and those on microgels with $c_{co} = 0.05$ and 0.10 are depicted in Fig. S-2A and B† together with results of simulation with the material constants collected in Table S-1.†

Adjustable parameters are determined by the same method that was applied to fit observations in Fig. 1. The only difference is that the dimensionless modulus g_1 is presumed to be affected by molar fraction of comonomers. For each c_{co}, this quantity is calculated by matching the swelling diagram $Q(T)$ below the critical temperature T_c. The coefficient $\tilde{\chi}_{co}$ is found by fitting the experimental dependence $T_c(c_{co})$ reported in Fig. 2B.

The effect of molar fraction of comonomers on the elastic modulus g_1 and radius of microgel particles R is demonstrated in Fig. 2C, where the data are approximated by eqn (21) and (31). This figure shows that g_1 increases and R decreases with c_{co} for a strongly hydrophobic comonomer NtBAm.

To verify our findings, we use experimental data on P(NIPAm–NtBAm) microgels synthesized by precipitation polymerization (4 h at 70 °C) of an aqueous solution of NIPAm and NtBAm monomers by using BIS (molar fraction is not provided) as a cross-linker, APS as an initiator, and TWEEN-20 as a non-ionic surfactant.[57] The experimental dependence of the volume phase transition temperature T_c on molar fraction of comonomers c_{co} is reported in Fig. 2D together with predictions of the model.

3.3 P(NIPAm–HEMA) gels

We now approximate experimental swelling diagrams on poly(*N*-isopropylacrylamide-*co*-2-hydroxyethyl methacrylate) (P(NIPAm–HEMA)) hydrogels. The gels were prepared by free radical cross-linking polymerization (1 day at room

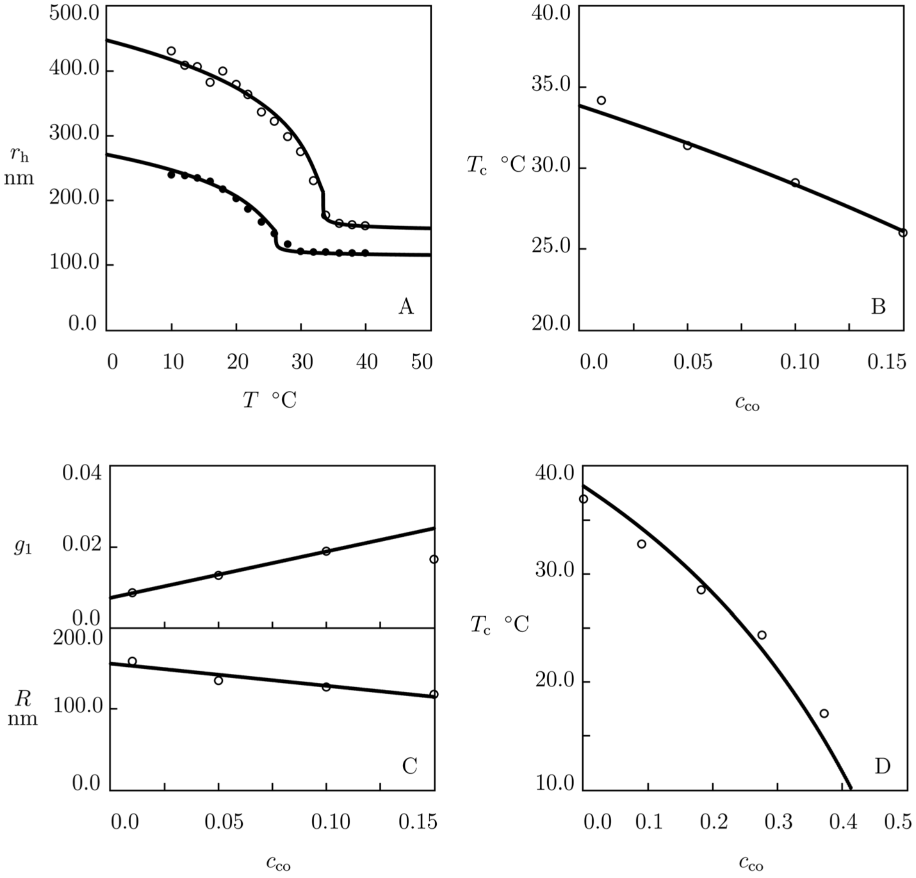

Fig. 2 (A) Hydrodynamic radius r_h of microgel particles *versus* temperature T. Symbols: experimental data[56] on P(NIPAm–NtBAm) microgels with molar fractions of comonomers $c_{co} = 0$ (○) and $c_{co} = 0.15$ (●). Solid lines: results of simulation. (B) Volume phase transition temperature T_c *versus* molar fraction of comonomers c_{co}. Circles: experimental data. Solid line: results of simulation. (C) Dimensionless modulus g_1 and radius R *versus* molar fraction of comonomers c_{co}. Circles: treatment of observations. Solid lines: results of simulation. (D) Volume phase transition temperature T_c *versus* molar fraction of comonomers c_{co}. Circles: experimental data[57] on P(NIPAm–NtBAm) microgels. Solid line: predictions of the model.

temperature) of a solution of NIPAm and HEMA monomers in 1 : 1 mixture of water and acetone by using BIS (3 mol% with respect to monomers) as a cross-linker, APS as an initiator, and TEMED as an accelerator.[58] Experimental swelling diagrams on gels with $c_{co} = 0$, 0.1 and 0.3 are presented in Fig. 3A together with results of simulation with the material parameters listed in Table S-1.† The effect of molar fraction of HEMA monomers c_{co} on the volume phase transition temperature T_c is illustrated in Fig. 3B, where the data are approximated by means of eqn (27)–(29).

Each swelling curve in Fig. 3A is fitted separately with the help of the only parameter: volume fraction of polymer network in the reference state ϕ_{n0}. This quantity is found by approximation of observations below T_c. Evolution of ϕ_{n0} with c_{co} is demonstrated in Fig. 3C, where the data are approximated by eqn (22).

To confirm that $\tilde{\chi}_{co}$ is determined correctly, we study observations on P(NIPAm–HEMA) microgels synthesized by surfactant-free radical polymerization (4 h at 90 °C) of an aqueous solution of NIPAm and NEMA monomers by using BIS (2 mol% with respect to NIPAm monomers) as a cross-linker and APS as an initiator.[59] The effect of comonomers on the volume phase transition temperature is reported in Fig. 3D, where experimental data are plotted together with predictions of the model.

To demonstrate that the value of $\tilde{\chi}_{co}$ found by matching experimental data in Fig. 3A can be used not only in prediction of T_c, but also in the analysis of swelling diagrams, we focus on observations on P(NIPAm–HEMA) gels prepared by free-radical cross-linking polymerization (1 day at 4 °C) in an aqueous solution of NIPAm and HEMA monomers (0.74 M) by using BIS (2.4 mol% with respect to monomers) as a cross-linker, KPS as an initiator, and TEMED as an accelerator.[60] Equilibrium swelling curves on the copolymer gels with c_{co} ranging from 0 to 0.47 immersed into phosphate buffer solution (with pH = 7 and ionic strength 0.1) are reported in Fig. S-3A† together with results of numerical analysis with the material parameters collected in Table S-1.† Each set of data in Fig. S-3A† is determined by the only parameter ϕ_{n0}. The effect of molar fraction of comonomers on this quantity is illustrated in Fig. S-3B,† where the data are approximated by eqn (22).

3.4 P(NIPAm–TREGMA) microgels

We match experimental data on poly(*N*-isopropylacrylamide-*co*-triethyleneglycol methacrylate) P(NIPAm–TREGMA) microgels prepared by surfactant-free precipitation polymerization (6 h at

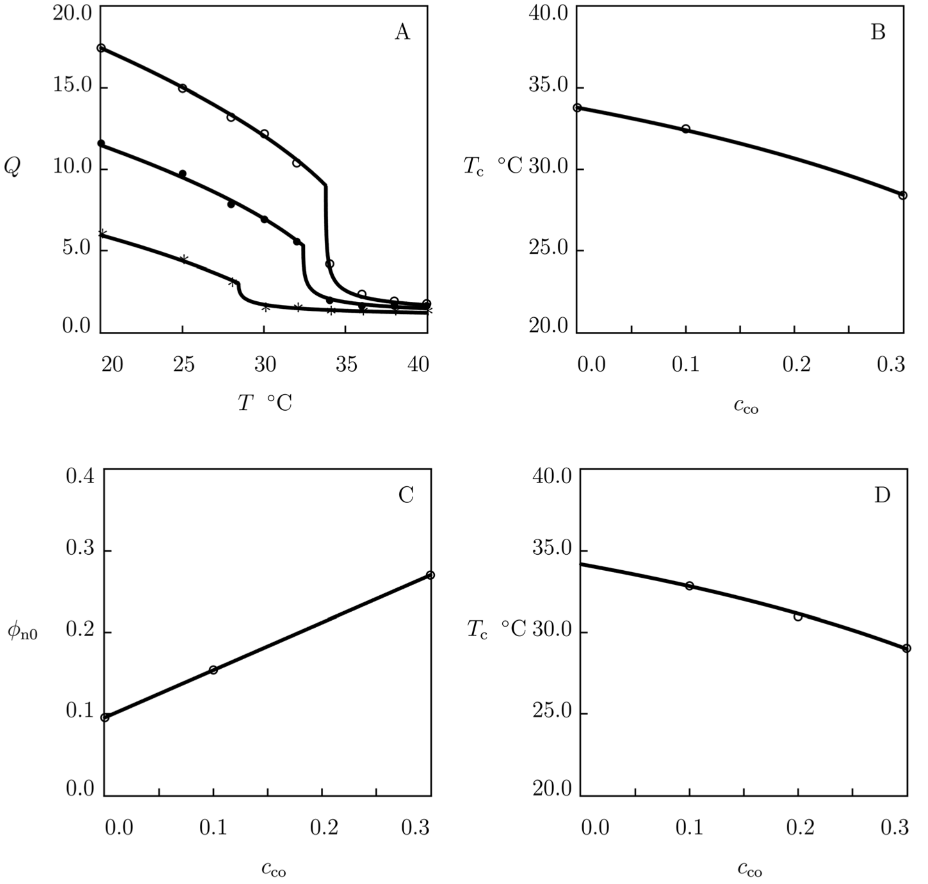

Fig. 3 (A) Degree of swelling Q *versus* temperature T. Symbols: experimental data[58] on P(NIPAm–HEMA) gels with molar fractions of comonomers $c_{co} = 0$ (○), $c_{co} = 0.1$ (●) and $c_{co} = 0.3$ (*). Solid lines: results of simulation. (B) Volume phase transition temperature T_c *versus* molar fraction of comonomers c_{co}. Circles: experimental data. Solid line: results of simulation. (C) Parameter ϕ_{n0} *versus* molar fraction of comonomers c_{co}. Circles: treatment of observations. Solid line: results of simulation. (D) Volume phase transition temperature T_c *versus* molar fraction of comonomers c_{co}. Circles: experimental data[59] on P(NIPAm–HEMA) microgels. Solid line: predictions of the model.

75 °C) of an aqueous solution on NIPAm and TREGMA monomers by using BIS (5 mol% with respect to monomers) as a cross-linker and KPS as an initiator.[61] Equilibrium swelling diagrams on microgels with $c_{co} = 0$ and 0.12 are reported in Fig. 4A and those on microgels with $c_{co} = 0.04$ and 0.08 are presented in Fig. S-4A and B† together with results of simulation with the materials constants collected in Table S-1.† The effect of molar fraction of TREGMA comonomers on the critical temperature T_c is illustrated in Fig. 4B, where the data are approximated by eqn (27)–(29).

Each swelling diagram in Fig. 4A and S-4† is fitted by means of two parameters: volume fraction of polymer network in the reference state ϕ_{n0} (this coefficient is determined by matching experimental data below T_c) and radius R of microgel particles in the initial state (this quantity is calculated by fitting the dependence $r_h(T)$ with the help of eqn (20)). Changes in ϕ_{n0} and R with c_{co} are demonstrated in Fig. 4C, where the data are approximated by eqn (22) and (31).

3.5 P(NIPAm–DMAAm) gels and microgels

We begin with fitting swelling diagrams on poly(*N*-isopropylacrylamide-*co*-*N*,*N*-dimethylacrylamide) (P(NIPAm–DMAAm)) gels prepared by free-radical polymerization (1 day at 55 °C) of a solution on NIPAm and DMAAm monomers in methanol by using BIS (3.3 mol% with respect to monomers) as a cross-linker and azobisisobutyronitrile (AIBN) as an initiator.[62] Experimental data in equilibrium water uptake tests on gels with molar fractions of comonomers $c_{co} = 0$ and 0.3 are reported in Fig. 5A, where degree of swelling Q is plotted *versus* temperature T together with results of simulation with the material parameters listed in Table S-1.† The effect of molar fraction of DMAAm comonomers on the volume phase transition temperature T_c is illustrated in Fig. 5B, where the data are approximated by eqn (27)–(29).

Each set of observations in Fig. 5A is determined by the only parameter ϕ_{n0}. Evolution of this quantity with c_{co} is shown in Fig. 5C, where the data are matched by means of eqn (22).

The modified FH parameter $\tilde{\chi}_{co}$ is calculated by using only two data points in Fig. 5B. To show that even a small number of observations ensures sufficient accuracy in determination of this parameter, we study experimental data on P(NIPAm–DMAAm) gels prepared by free-radical polymerization at room temperature of an aqueous solution of monomers (0.7 M) by using BIS (3.2 mol% with respect to monomers) as a cross-

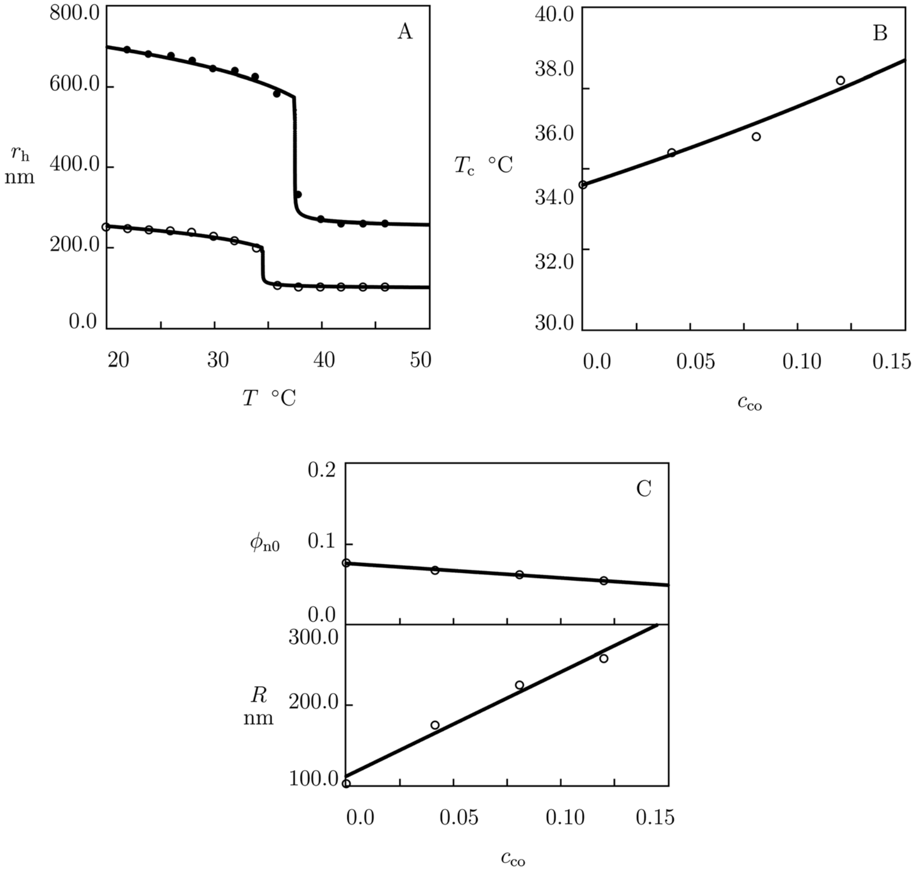

Fig. 4 (A) Hydrodynamic radius r_h of microgel particles *versus* temperature T. Symbols: experimental data[61] on P(NIPAm–TREGMA) microgels with molar fractions of comonomers $c_{co} = 0$ (○) and $c_{co} = 0.12$ (●). Solid lines: results of simulation. (B) Volume phase transition temperature T_c *versus* molar fraction of comonomers c_{co}. Circles: experimental data. Solid line: results of simulation. (C) Parameters ϕ_{n0} and R *versus* molar fraction of comonomers c_{co}. Circles: treatment of observations. Solid lines: results of simulation.

linker, APS as an initiator, and TEMED as an accelerator.[63] Fig. 5D demonstrates good agreement between predictions of the model and experimental volume phase transition temperatures T_c of copolymer gels with c_{co} ranging from 0.0 to 0.25.

To compare the thermo-mechanical responses of macroscopic gels and microgels, we analyze observations on P(NIPAm–DMAAm) microgels synthesized by free-radical polymerization (6 h at 75 °C) of an aqueous solution of NIPAm and DMAAm monomers (170 mM) by using BIS (1.4 mol% with respect to monomers) as a cross-linker, SDS (0.75 mol% with respect to monomers) as a surfactant, and KPS as an initiator.[64] Experimental data on microgels with $c_{co} = 0$ and 0.18 are plotted in Fig. 6A and those on microgels with $c_{co} = 0.06$, 0.10, 0.14 and 0.16 are depicted in Fig. S-5A–D.† In these figures, experimental dependencies of the hydrodynamic radius r_h on temperature T are reported together with results of simulation with the material parameters collected in Table S-1.†

The effect of molar fraction of comonomers on the volume phase transition temperature T_c is illustrated in Fig. 6B, where experimental data are reported together with predictions of the model (the parameter $\tilde{\chi}_{co}$ is found by fitting observations in Fig. 5B).

Each set of observations in Fig. 6A and S-5† is matched by means of two parameters: ϕ_{n0} (which is found by fitting swelling curves below T_c) and R (which is calculated by matching the experimental dependence $r_h(T)$ with the help of eqn (20)). The influence of c_{co} on ϕ_{n0} is illustrated in Fig. 5C, where the data are fitted by eqn (22). Changes in radius R with c_{co} are demonstrated in Fig. 6C, where the data are approximated by eqn (31).

To confirm that the volume phase transition temperature of P(NIPAm–DMAAm) microgels can be predicted correctly by using $\tilde{\chi}_{co}$ determined by fitting observations on macroscopic gels, we study experimental data on microgels synthesized by precipitation polymerization (4 h at 70 °C) of an aqueous solution of monomers by using BIS (4 mol% with respect to monomers) as a cross-linker, APS as an initiator, and TWEEN-20 as a non-ionic surfactant.[57] Fig. 6D reveals an acceptable agreement between predictions of the model and experimental data on microgels with c_{co} ranging from 0.0 to 0.22.

3.6 P(NIPAm–AAm) microgels

Finally, we analyze observations on poly(*N*-isopropylacrylamide-*co*-acrylamide) (P(NIPAm–AAm)) microgels prepared by precipitation polymerization (4.5 h at 70 °C) of an aqueous solution of monomers (0.12 M) by using BIS (1 mol% with respect to monomers) as a cross-linker, KPS as an initiator, and SDS (0.5 mol% with respect to monomers) as a surfactant.[65] The

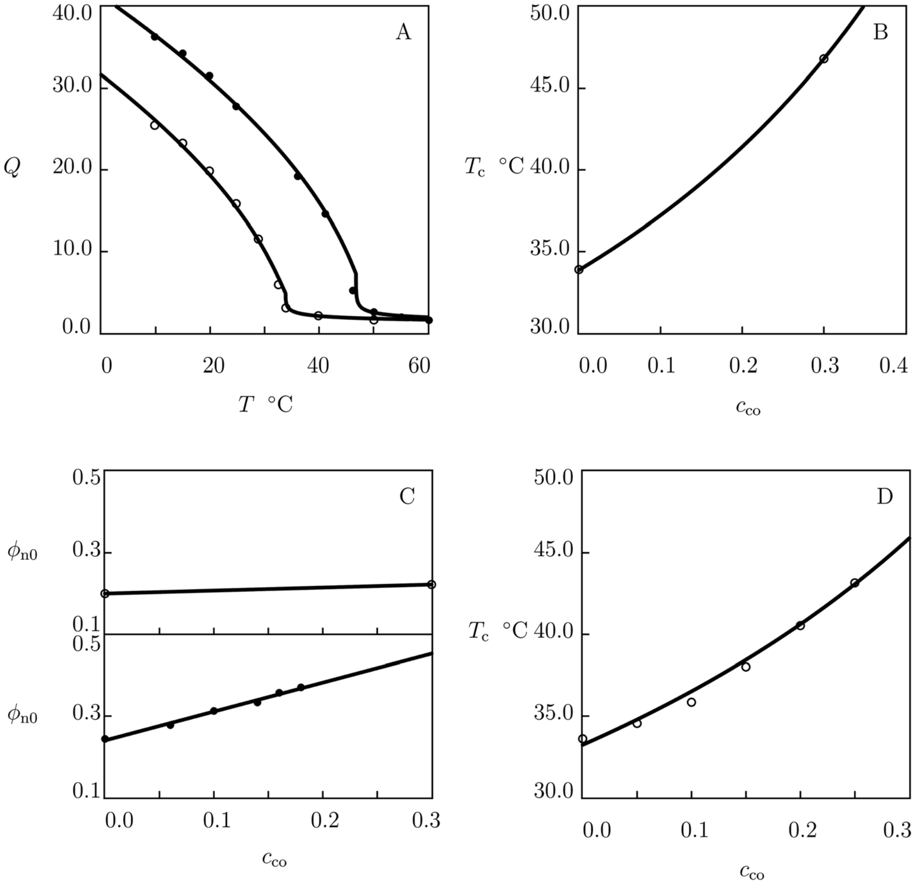

Fig. 5 (A) Degree of swelling Q *versus* temperature T. Symbols: experimental data[62] on P(NIPAm–DMAAm) gels with molar fractions of comonomers $c_{co} = 0$ (○) and $c_{co} = 0.3$ (●). Solid lines: results of simulation. (B) Volume phase transition temperature T_c *versus* molar fraction c_{co} of comonomers. Circles: experimental data. Solid line: results of simulation. (C) Parameter ϕ_{n0} *versus* molar fraction of comonomers c_{co}. Symbols: treatment of observations on P(NIPAm–DMAAm) gels (○) and microgels (●). Solid lines: results of simulation. (D) Volume phase transition temperature T_c *versus* molar fraction of DMAAm comonomers c_{co}. Circles: experimental data[63] on P(NIPAm–DMAAm) gels. Solid line: predictions of the model.

experimental dependencies of the hydrodynamic radius r_h on temperature T for microgels with $c_{co} = 0$ and 0.05 and 0.10 are reported in Fig. 7A together with results of simulation with the material parameters collected in Table S-1.† The effect of molar fraction of comonomers on the volume phase transition temperature T_c is demonstrated in Fig. 7B, where the data are approximated by eqn (27)–(29).

Each set of observations in Fig. 7A is determined by two parameters: volume fraction of polymer network in the reference state ϕ_{n0} (this coefficient is determined by matching experimental data below T_c) and radius R of microgel particles in the initial state (which is calculated by matching the dependence $r_h(T)$ by eqn (20)). Changes in ϕ_{n0} and R with c_{co} are illustrated in Fig. 7C, where the data are approximated by eqn (22) and (31). This figure shows that ϕ_{n0} and R remain practically independent of c_{co}.

To examine the ability of the model to predict the volume phase transition temperature of P(NIPAm–AAm) macroscopic gels based on observations on microgels, we analyze observations on gels with interpenetrating polymer network (IPN) formed by poly(vinyl alcohol) (PVA) and P(NIPAm–AAm) chains.[66] The gels were prepared by polymerization of NIPAm and AAm monomers in a 15 wt% aqueous solution of PVA chains. First, PVA chains were cross-linked (6 h at room temperature) by using glutaraldehyde (GDA, 0.5 mol% with respect to PVA). Afterwards, cross-linking photo-polymerization (12 h at room temperature) of NIPAM and AAm monomers was conducted by using BIS (0.2 mol% with respect to monomers) as a cross-linker and 2-ketoglutaric acid (KGA) as an initiator. The growth of T_c with molar fraction of AAm comonomers c_{co} is demonstrated in Fig. 7D, where experimental data are presented together with predictions of the model.

4 Discussion

Fig. 1–7 confirm the ability of the model to describe experimental swelling diagrams on thermo-responsive copolymer microgels and macroscopic gels. The entire set of equilibrium swelling curves for gels with a particular comonomer is determined by one (Fig. 1, 3 and 6) or two (Fig. 2, 4, 5 and 7) adjustable parameters. The effect of molar fraction of comonomers on these quantities is described by eqn (21), (22) and (31).

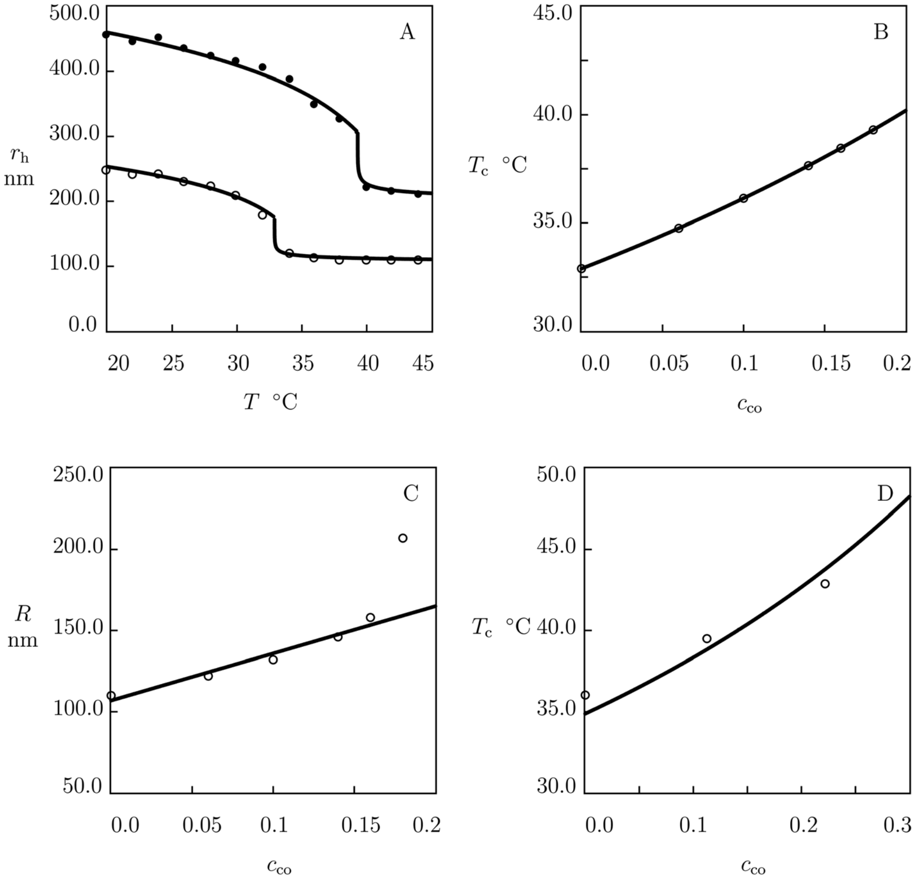

Fig. 6 (A) Hydrodynamic radius r_h of microgel particles *versus* temperature T. Symbols: experimental data[64] on P(NIPAm–DMAAm) microgels with molar fractions of comonomers $c_{co} = 0$ (○) and $c_{co} = 0.18$ (●). Solid lines: results of simulation. (B) Volume phase transition temperature T_c *versus* molar fraction of comonomers c_{co}. Circles: experimental data. Solid line: predictions of the model. (C) Radius R *versus* molar fraction of comonomers c_{co}. Circles: treatment of observations. Solid line: results of simulation. (D) Volume phase transition temperature T_c *versus* molar fraction of comonomers c_{co}. Circles: experimental data[57] on P(NIPAm–DMAAm) microgels. Solid line: predictions of the model.

The influence of comonomers on the volume phase transition temperature T_c is determined by eqn (27) and (29). These relations involve the only adjustable parameter $\tilde{\chi}_{co}$. Fig. 1–7 reveal that the coefficient $\tilde{\chi}_{co}$ is practically independent of preparation conditions and concentrations of monomers and cross-linker. This allows the effect of molar fraction of comonomers on the critical temperature of microgels to be predicted when this effect is known for macroscopic gels (Fig. 1 and 7) and *vice versa* (Fig. 3, 5 and 6).

Comparison of material parameters in Table S-1† demonstrates that g_1, $\bar{g}_2$, $\chi_{\max}$ and β adopt similar values that are weakly affected by the size (micro- *versus* macro-) and conditions of synthesis for the gels. In particular, $\chi_{\max}$ (this quantity characterizes the volume phase transition temperature for homopolymer PNIPAm gels) varies in a narrow interval between 0.51 and 0.64, which corresponds to small (about 4 K) variations in T_c driven by the temperature and solvent used in preparation of hydrogels. Changes in Q_0 induced the presence of comonomers are more pronounced: from 0.1 for strongly hydrophobic comonomers (tBA and NtBAm) up to more than 10 for hydrophilic comonomers (AAm). It is worth noting that these changes are not caused by molar fractions of monomers in pre-gel solutions: for all microgels under consideration, these fractions vary in the interval between 0.08 and 0.17 M.

Comonomers can be roughly split into two groups: (i) more hydrophobic than NIPAm (tBA, NIBAm, HEMA; their incorporation causes a reduction in the volume phase transition temperature) and (ii) more hydrophilic than NIPAm (PREGMA, DMAAm, AAm; copolymerization with these moieties leads to an increase in T_c). Fig. 1–7 show that the presence of hydrophobic comonomers results in a decrease in radius R (that characterizes the size of microgels in the dry state), while incorporation of hydrophilic monomers induces an increase in R.[67] Evolution of the volume fraction of polymer network in the reference (stress-free) state ϕ_{n0} obeys more sophisticated dependencies, as this parameter is strongly affected by hydrogen bonds between segments of chains. Concentration of these bonds depends not only on the hydrophilicity of comonomers, but on the presence of surfactant, temperature of polymerization, and composition of solvents used in preparation.[68]

Bearing in mind that the critical temperature T_c is determined uniquely by the modified FH parameter $\tilde{\chi}_{co}$, see eqn (27) and (29), which, in turn, serves as a measure of hydrophilicity of chains, it is tempting to connect this quantity with the Hildebrand solubility parameter of comonomers δ_H. Several attempts have previously been undertaken to establish correlations between the FH parameter of homopolymer and copolymer gels

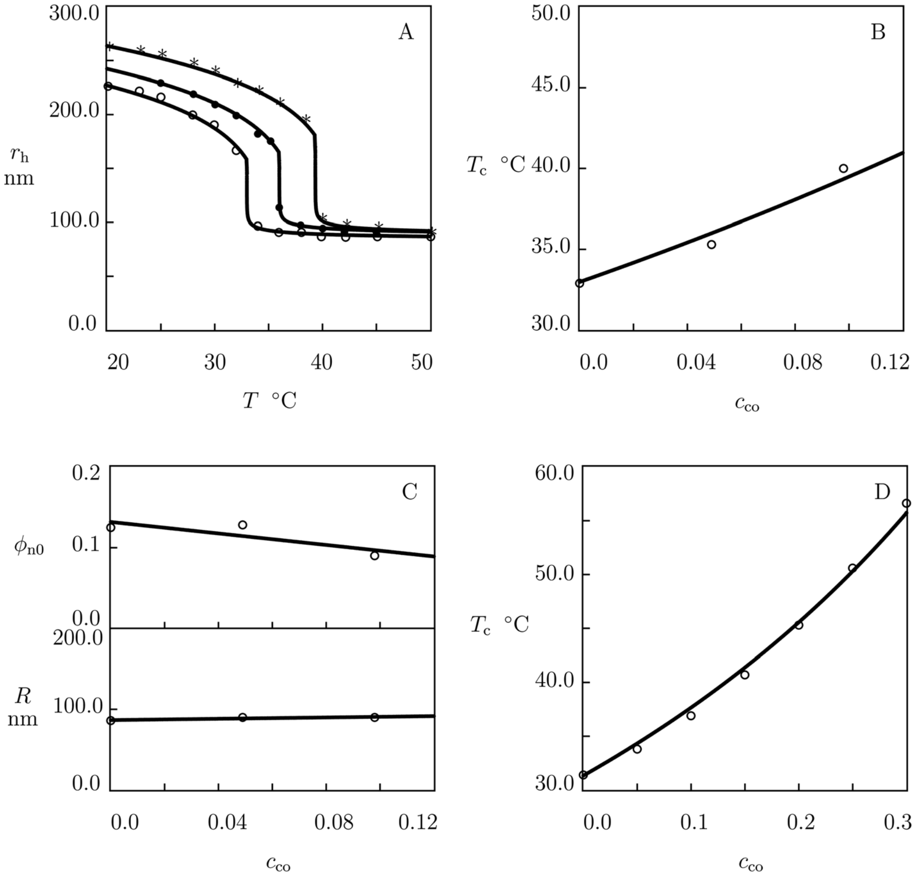

Fig. 7 (A) Hydrodynamic radius r_h of microgel particles *versus* temperature T. Symbols: experimental data[65] on P(NIPAm–AAm) microgels with molar fractions of comonomers $c_{co} = 0$ (○), $c_{co} = 0.05$ (●) and $c_{co} = 0.10$ (*). Solid lines: results of simulation. (B) Volume phase transition temperature T_c *versus* molar fraction of comonomers c_{co}. Circles: experimental data. Solid line: results of simulation. (C) Parameters ϕ_{n0} and R *versus* molar fraction of comonomers c_{co}. Circles: treatment of observations. Solid lines: results of simulation. (D) Volume phase transition temperature T_c *versus* molar fraction of comonomers c_{co}. Circles: experimental data[66] on PVA/P(NIPAm–AAm) gels with interpenetrating network. Solid line: predictions of the model.

with the Hildebrand and Hansen solubility parameters, see ref. 69–72, to mention a few. An advantage of this approach is that the Hildebrand solubility parameter of comonomers can be evaluated straightforwardly by means of the group contribution method,[73] whereas the accuracy of this method for calculation of the FH parameter (by using the UNIQUAC equation or its modifications[74,75]) is rather modest.[76–78] Possible reasons for such an inaccuracy are discussed in ref. 79. The most important of them is that the group contribution method estimates the energy contribution to the FH parameter, but it disregards the contribution of entropy.

For the comonomers used in the analysis of swelling of macro- and microgels, the modified FH parameter $\tilde{\chi}_{co}$ is reported in Table S-2† together with the Hildebrand solubility parameter δ_H calculated by means of the Hoftyzer–van Krevelen method (Table 7.10 in ref. 73). Table S-2† shows that $\tilde{\chi}_{co}$ is reduced with δ_H. The data are reported in Fig. 8A, where they are approximated by the linear equation

$$\tilde{\chi}_{co} = c_0 - c_1\delta_H \tag{32}$$

with the coefficients $c_0 = 18.606$ and $c_1 = 0.8740$ determined by the least-squares algorithm.

Fig. 8A reveals an acceptable agreement between the data and their description by eqn (32) for all comonomers except for NtBAm and HEMA (for which noticeable deviations are observed between results of simulation and predictions of eqn (32)). These deviations for P(NIPAm–NtBAm) microgels can be ascribed to built-up of aggregates formed by NtBAm monomers and hydrophobic segments of NIPAm monomers under preparation conditions. The fact that these aggregates remain sufficiently stable and they are not broken when temperature decreases below T_c is confirmed by Fig. 2C, which shows an increase in g_1 with c_{co}. For P(NIPAm–HEMA) gels, these deviations are ascribed to formation of hydrogen bonds between water molecules and HEMA segments,[80] which cause an "unusual" thermo-mechanical behavior of these gels.[81]

To demonstrate the ability of eqn (27), (29) and (32) to predict the effect of molar fraction of comonomers on the volume phase transition temperature T_c, we study two sets of observations on copolymer gels not included into Table S-2.†

We begin with the analysis of poly(*N*-isopropylacrylamide-*co*-ethylacrylate) (P(NIPAm–EA)) microgels prepared by precipitation polymerization (4 h at 90 °C) of an aqueous solution of PNIPAm and EA monomers (0.32 M) by using BIS (2 mol% with respect

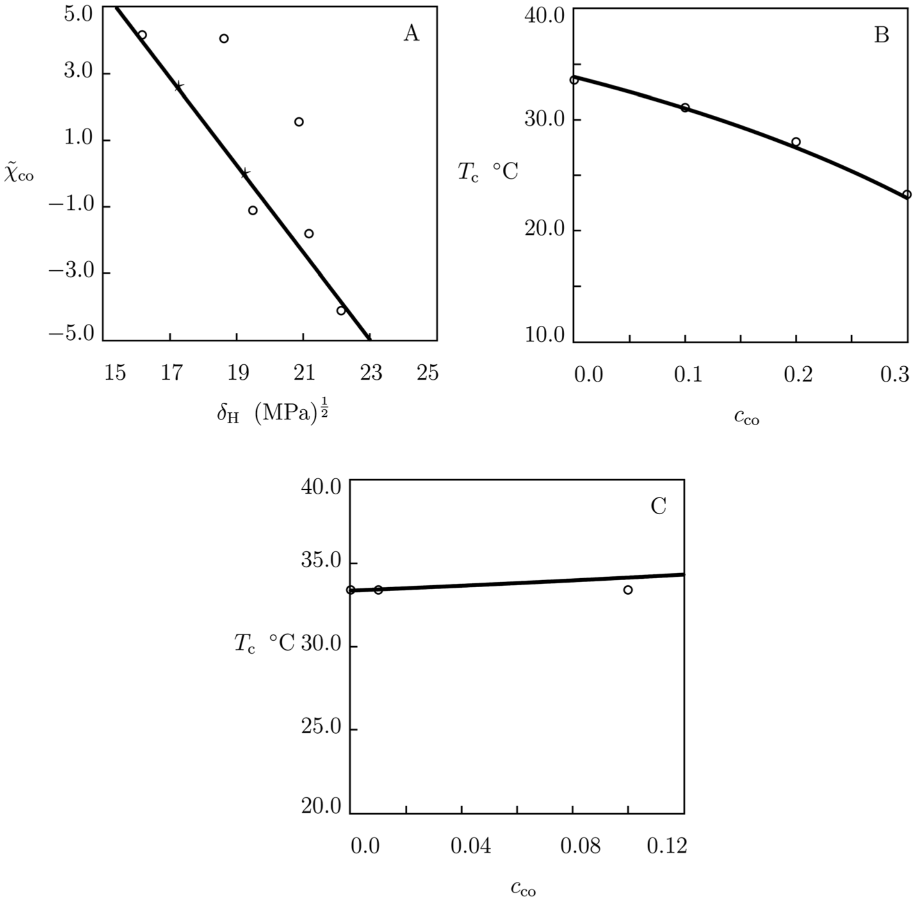

Fig. 8 (A) The modified Flory–Huggins parameter $\tilde{\chi}_{co}$ *versus* the Hildebrand solubility of comonomers δ_H. Circles: treatment of observations. Solid line: results of simulation. Stars: predictions for EA and AAc comonomers. (B and C) Volume phase transition temperature T_c *versus* molar fraction of comonomers c_{co}. Circles: experimental data on P(NIPAm–EA) microgels[59] (B) and P(NIPAm–AAc) gels in water with pH = 1 (ref. 82) (C). Solid lines: predictions of the model.

to monomers) as a cross-linker and APS as an initiator.[59] In simulation, we find $\delta_H = 18.32$ (MPa)$^{1/2}$ by means of the Hoftyzer–van Krevelen method for EA, determine $\tilde{\chi}_{co} = 2.595$ from eqn (32) and Fig. 8A, calculate the dependence $T_c(c_{co})$ from eqn (27) and (29), and present results of numerical analysis in Fig. 8B together with experimental values of T_c for microgels with $c_{co} = 0.1$, 0.2 and 0.3.

We proceed with prediction of the volume phase transition temperature for poly(*N*-isopropylacrylamide-*co*-acrylic acid) (P(NIPAm–AAc)) gels synthesized by free-radical cross-linking copolymerization (6 h at 25 °C) of an aqueous solution of NIPAm (1.55 M) and AAc monomers by using BIS (0.5 mol% with respect to monomers) as a cross-linker, APS as an initiator, and TEMED as an accelerator.[82] Following the above procedure, we find $\delta_H = 21.31$ (MPa)$^{1/2}$ by the Hoftyzer–van Krevelen method for AAc, determine $\tilde{\chi}_{co} = -0.0183$ from eqn (32) and Fig. 8A, and calculate the dependence $T_c(c_{co})$ from eqn (27) and (29). Bearing in mind that AAc is an ionic monomer with pK_a close to 4.2, we report results of simulation in Fig. 8C together with experimental values of T_c for gels with $c_{co} = 0.01$ and 0.1 in water with pH = 1 (under this condition, ionization of comonomers can be disregarded).

Fig. 8B and C show an acceptable agreement between the observations on T_c and predictions of the model. This implies that eqn (27), (29) and (32) can be used for "quick-and-dirty" evaluation of the effect of molar fraction of comonomers on the volume phase transition temperature of macro- and microgels.

5 Conclusions

A model is developed for equilibrium swelling of thermo-responsive copolymer gels. Following,[25,27] we presume chains in the polymer network to involve hydrophilic and hydrophobic segments. Below the volume phase transition temperature T_c, each hydrophobic segment is surrounded by a cage-like structure formed by water molecules bridged by hydrogen bonds. An increase in temperature induces breakage of these structures driven by thermal fluctuations. This process is accompanied by aggregation of hydrophobic segments and formation of clusters from which water molecules are expelled. These clusters serve as extra physical bonds between chains in the collapsed state of a gel. This scenario allows a pronounced increase in the elastic modulus of macroscopic gels[30] and microgels[31] above T_c to be described, on the one hand, and unrealistic values of the Flory–Huggins parameter[39] to be excluded from consideration, on the other.

Unlike the conventional approach grounded on the Flory–Rehner concept,[36] where the FH parameter χ is modeled as a nonlinear function of temperature and volume fraction of the polymer network, we treat χ as a linear function of temperature T only. Presuming the volume phase transition to occur in a homopolymer gel when χ reaches its maximum value $\chi_{\max}$, a simple relation, eqn (14), is derived for the critical temperature T_c. With the help of the three-parameter model for the FH parameter of copolymer gels,[47] this formula is extended to gels prepared by copolymerization of thermo-responsive and temperature-insensitive nonionic monomers, see eqn (27) and (29).

An advantage of the model is that it involves a relatively small number of material constant. According to eqn (30), for copolymer gels with NIPAm monomers as the main component of the network and an arbitrary molar fraction c_{co} of comonomers, the entire set of equilibrium swelling diagrams $Q(T)$ is described by six parameters with transparent physical meaning: g_1 and $\bar{g}_2$ are the dimensionless elastic moduli in the swollen and collapsed states, ϕ_{n0} denotes volume fraction of the polymer network in the stress-free state, $\chi_{\max}$ and $\tilde{\chi}_{co}$ stand for the FH parameters of NIPAm monomers and comonomers, and β characterizes the rate of aggregation of hydrophobic segments above T_c. To describe the equilibrium water uptake by a microgel (characterized by the dependence of its hydrodynamic radius r_h on temperature T), an extra parameter R (the radius of a microgel particle in the dry state) is added. Analysis of observations on copolymer gels and microgels reveals that only g_1, ϕ_{n0} and R may be affected by c_{co}. The other material parameters found by matching observations on homopolymer gels can be used for copolymer gels without modification.

The model is applied to fit experimental data on macroscopic gels and microgels prepared by copolymerization of NIPAm monomers with hydrophobic (tBA, NtBAm, HEMA) and hydrophilic (TREGMA, DMAAm, AAm) comonomers. The criteria of hydrophobicity and hydrophilicity of comonomers read $\tilde{\chi}_{co} > -\chi_{\max}$ and $\tilde{\chi}_{co} < -\chi_{\max}$, respectively. Fig. 1–7 demonstrate good agreement between observations and results of numerical simulation. An important conclusion of the analysis is that the effect of comonomers on the volume phase transition temperature T_c is independent of preparation conditions for macro- and microgels.

To establish correlations between the modified FH parameter of comonomers $\tilde{\chi}_{co}$ and their Hildebrand solubility parameter δ_H, phenomenological eqn (32) is suggested. This relation together with eqn (27) and (29) predicts changes in the critical temperature of copolymer gels by using an estimate of δ_H developed with the help of the group contribution method. Application of this method to P(NIPAm–EA) and P(NIPAm–AAc) copolymer gels reveals reasonable agreement between experimental data and results of simulation. This agreement confirms that the simplified approach can be used for a "quick-and-dirty" prediction of the volume phase transition temperature of copolymer gels.

Conflicts of interest

There are no conflicts of interest to declare.

Acknowledgements

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