Experiments and Simulation of pH-Responsive *N*-Isopropylacrylamide–Acrylic Acid Copolymer Hydrogels

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ABSTRACT: In this study, *N*-isopropylacrylamide–acrylic acid (NIPAAm–AAc) copolymer hydrogels were synthesized by radical polymerization. The equilibrium and dynamic water uptake of these copolymer hydrogels were investigated as a function of acrylic acid content of copolymer, pH, and temperature. The pH-dependent swelling ratio of the hydrogels was distinguishable between two pH-modulating methods. In addition, a modified thermodynamic simulation that is able to predict pH-dependent swelling of polyanionic gels was developed. In the simulation, the influence of ionic strength on dissociation of carboxyl groups was taken into consideration. Also a new relation between Debye length and volume change of gels was derived from the approximation used in derivation of ionic osmotic pressure. The predictions from this modified equation were reasonably good compared with experiments. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 101: 323–330, 2006

Key words: copolymerization; thermodynamics; hydrogels; poly(acrylic acid); poly(*N*-isopropylacrylamide)

INTRODUCTION

Hydrogels are an essential stimuli-responsive or smart polymeric systems that have been widely used in different biological applications, such as the delivery of therapeutics, cell culture, tissue engineering, bioseperations, sensors or actuator systems.[1–6] These polymers respond to small external stimuli with large changes in their properties. The external stimuli may be temperature, pH, electric field, chemicals, or ionic strength and the responses are large changes in the properties such as shape, surface characteristics, solubility, or homogeneous solution phase to gel phase transition.

Poly(*N*-isopropylacrylamide) (polyNIPAAm) hydrogels are temperature-sensitive and they undergo a discrete phase transition at their lower critical solution temperature (LCST) of 32°C.[7,8] Below this temperature, the polymer is hydrophilic and soluble, and above LCST it is hydrophobic and becomes collapsed. Because of the good compatibility with bio-issues, polyNIPAAm hydrogel has been investigated thoroughly. However, for some purposes, hydrogel systems are required to have a combination of two or more stimuli-responsive abilities. Temperature- and pH-responsive polymers have been prepared by copolymerization of the temperature-sensitive monomer NIPAAm with hydrophilic comonomers containing ionizable groups such as acrylic acid (AAc). Therefore,

the NIPAAm–AAc copolymer has both temperature- and pH-sensitivity. Addition of AAc comonomer also results in an increase in LCST.[9]

Several models have been suggested to describe the relationships between structure and properties for polyelectrolyte hydrogels. For characterizing the charge interaction in the chain by means of the Debye–Huckel theory, Katchalsky and Lifson proposed a random coil model[10] for titration curve[11] and swelling equilibria[12] of polyelectrolyte gels in salt solutions. Hasa et al. modified the kinetic theory of rubber-like elasticity by including changes of electrostatic interaction energy with deformation and attempted to predict the stress–strain, swelling, and potentiometric behavior of ionized poly(methacrylic acid) gels.[13,14] Konak and Bansil[15] introduced the idea of electrostatic persistence length, suggested first by Odijk, to conformational changes of polymer chains, and they derived equations for the swelling equilibria of polyelectrolyte gels. The swelling behavior of ionized poly(methacrylic acid) hydrogels in the absence of salt was described reasonably well by these relations.[15]

In this study, dynamic and equilibrium swelling of NIPAAm–AAc copolymer hydrogels is investigated against pH and temperature. A modified model is presented in the attempt to predict the pH-responsive swelling behavior of polyanionic hydrogels.

EXPERIMENTAL

Materials and reagents

AAc monomer was purified by distillation under reduced pressure to remove hydroquinone inhibitor.

TABLE I
Monomer Fractions for the Preparation of Copolymer Gels and Repeat Unit Fractions in the Resulting Gels

Sample code	Feed composition (mmol)		Monomer fraction (mol %)		Fraction in gel[a] (mol %)	
	NIPAAm	AAc	NIPAAm	AAc	NIPAAm	AAc
G100	0	100	0	100	0	100
G75	25	75	25	75	26.1	73.9
G50	50	50	50	50	48.3	51.7
G25	75	25	75	25	76.5	23.5

NIPAAm (N-isopropylacrylamide), AAc (acrylic acid).
[a] Determined by elemental analysis using vacuum-dried samples.

NIPAAm monomer (Acros Organics, Shanghai Agent) was used without further treatment. Methylenebisacrylamide (Bis) (Acros Organics) was used as crosslinker and ammonium persulfate (AP) and N,N,N',N'-tetramethyl ethylene diamine (TEMED) (Merck AG, Shanghai Agent) were used as initiator and accelerator, respectively.

Gel preparation

Poly(acrylic acid-co-N-isopropylacrylamide) hydrogels were prepared by radical polymerization in distilled water under 30°C, Bis (1% molar ratio to total monomer) was used as crosslinker, AP (2.1×10^{-3} mol/L) and TEMED (2.1×10^{-3} mol/L) were used as initiator and accelerator, respectively. For preparation, different molar ratios of AAc and NIPAAm monomer (100/0, 75/25, 50/50, and 25/75) were employed. The so-prepared hydrogels are called g100, g75, g50, and g25 in the following. The total concentration of AAc and NIPAAm was 100 g/L. The polymerization was carried out in glass tubes (15 cm long and 1 cm diameter). The glass tubes were immersed in a toluene solution of dichlorodimethylsilane (2 vol %) for 2 min before use.[16] Gelation occurred in the tubes within 30 min, and the gels were kept in them for 24 h to ensure completion of the reaction. After removal from the tubes, the gel samples were sliced into discs (about 5 mm thick) and soaked for about 7 days in distilled water, which was replaced every 24 h to remove the impurities.

Measurements

The fraction of AAc units in the copolymer gels was determined by an elemental nitrogen analysis of the dried gels (Model 24 Elemental Analyzer, Perkin–Elmer). The swelling ratio of the gel samples was characterized by the ratio M/M_0, where M is the mass of the gel sample swollen in aqueous solution and M_0 is the mass of the dry gel. During the washing of samples in pure water as described earlier, the gels finally approached equilibrium state with water. The approach to swelling equilibrium was monitored in

that the mass of gel samples cease to change at equilibrium and required typically about a week. A series of aqueous solutions of different pH values was also prepared with HCl and NaOH, respectively, and gel samples were also swollen in it to study the influence of pH value on swelling equilibrium.

Dynamic swelling studies were undertaken to elucidate the mechanism of water diffusion into the hydrogel matrix as determined by the dynamic portion of the gravimetric curve. The water uptake, M_t, was monitored as a function of time until equilibrium was attained (M_∞), to provide the data for dynamic and equilibrium time frames. The hydrogel discs were placed in 100 mL of buffered solution, which was maintained at 25, 30, and 33°C. The polymer samples were periodically removed from the solution, patted dry, and weighed.

RESULTS AND DISCUSSION

The NIPAAm and AAc fractions in the gels were calculated from the C/N ratio obtained from the results of elemental analysis of the vaccum-dried samples (Table I) The unit fraction in the gels was in good agreement with the monomer fraction used for the synthesis of porous gels. Under radical polymerization, random copolymerization between the NIPAAm and the AAc took place under the LSCT.

Swelling kinetics in water or buffered solution

The following equation was used to determine the nature of the dynamic swelling process

$$M_t/M_\infty = kt^n$$

where M_t and M_∞ designate the amounts of the solvent diffused into the gel matrix at time t and at equilibrium, respectively; k is the gel characteristic constant; and swelling exponent n describes the type of diffusion. For cylindrical gels, $n = 0.45$–0.5 corresponds to a Fickian diffusion process and $0.5 < n < 1$ indicates non-Fickian diffusion. This equation is applicable to the initial stage of swelling, and a plot of

$\log (M_t/M_\infty) - \log (t)$ gives a straight line up to almost a 60% increase in the mass of the gel.

The hydrogel system under investigation consists of two structural components: NIPAAm (temperature-sensitive) and AAc (pH-sensitive). Therefore, this gel is supposed to function via a coupled mechanism involving pH- and thermosensitive swelling. In a low pH medium, the hydrogel exhibits minimum swelling because of the formation of inter- and intramolecular hydrogen bonds among undissociated acrylic acid units and amide groups of NIPAAm,[17,18] whereas at elevated temperatures, it would undergo deswelling due to the hydrophobic phase separation among NIPAAm units. Pure PAAc hydrogels show a typical positive swelling with temperature (upper critical solution temperature [UCST] behavior) and their swelling variation is gentle and no phase transition occurs. PolyNIPAAm hydrogels display negative swelling with temperature (LCST behavior) and undergo a phase transition at their LCST; they are water soluble below the LCST and become insoluble above LCST. The thermodynamic driving force for the phase transition of nonionic polyNIPAAm has been concluded to be mainly entropic due to the release of bound water molecules from the hydrophobic polymer chains.

The swelling kinetics of the hydrogels was probed against pH and temperature. The gel discs were put into neutral solution (pH ≈ 6.5) and basic solution (pH 8.7), and the temperature was set at 25, 30, and 33°C. The swelling and weighing was performed until the weight of gel discs ceases to change. The lower the temperature, the longer time it would take to approach equilibria. The swelling kinetics in neutral solution and basic solution are plotted in Figures 1 and 2, respectively. It can be seen from Figures 1 and 2 that the equilibrium swelling ratio significantly decreases with the increasing NIPAAm content and increasing temperature. In neutral medium of pH ≈ 6.5, the carboxylic groups attached along polymer chains are in an almost unionized state, thus imparting a non-polyelectrolyte character to the gel. As a result, the ionic osmotic pressure, which depends on the concentration of pendent ionized groups, is nearly ineffective. Moreover, the existence of hydrogen-bonding interactions between —COOH groups in the polymer matrix results in additional crosslinking sites within the network, and so the movements of polymer segments are restricted. This accounts for the minimum swelling ratio and small swelling rate, i.e., it takes a long time to reach the equilibrium. Swelling kinetics at 33°C shows that the equilibrium swelling ratio significantly decreases due to the hydrophobic phase separation of NIPAAm units. But when the temperature increases, the time to equilibrium is actually shortened. From the initial linear plots, the swelling exponent in neutral medium, n, is evaluated as 0.89, 0.76,
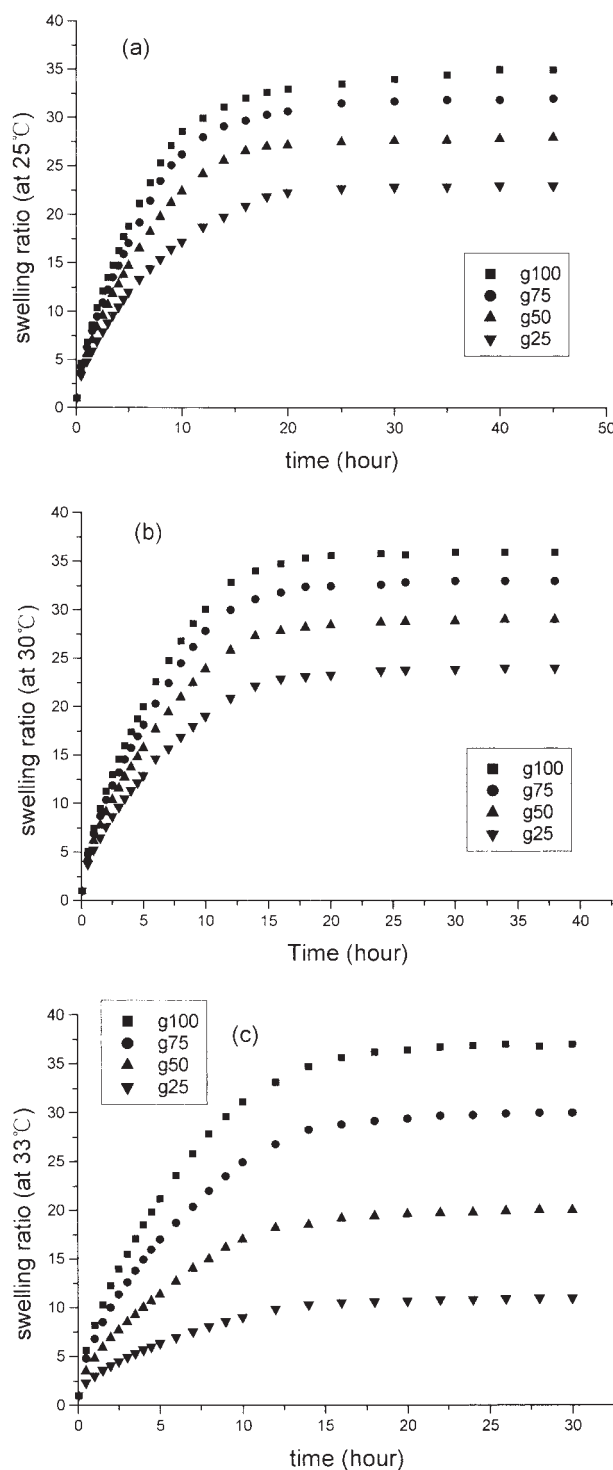

Figure 1 Swelling kinetics of AAc–NIPAAm copolymer hydrogels in pure water.

and 0.62 for swelling kinetics at 25, 30, and 33°C respectively. This indicates that at lower temperatures the swelling was governed more by a chain-relaxation-controlled mechanism.

As shown in Figure 2, in basic solution of pH 8.7, the almost complete ionization of —COOH groups
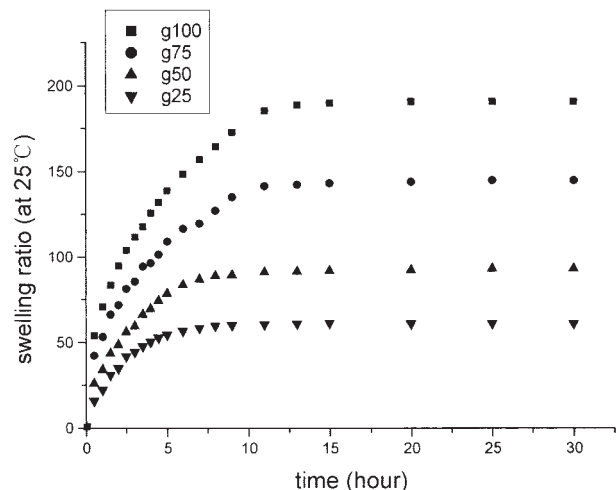
Figure 2 Swelling kinetics of AAc–NIPAAm copolymer hydrogels in basic solution of pH 8.7 at 25°C.

present within the polymer network takes place not only providing ionic osmotic swelling pressure to a great extent but also enhancing the relaxation of polymer segments because of the elimination of hydrogen-bonding and electrostatic repulsion between similarly charged —COO⁻ groups. These factors result in a greater water uptake rate. The swelling exponent, n, determined from initial swelling moment, was found to be about 0.41. This value clearly suggests anomalous transition from Fickian swelling behavior, because the electrorepulsion provides additional swelling force.

Two methods of modulating the pH

For the pH-dependent swelling experiments of NIPAAm–AAc copolymer hydrogels, two pH-modulating methods, which was possibly not considered by other authors, are considered in this study. The first method is by using hydrochloric acid and sodium hydroxide to prepare a series of aqueous solutions of different pH; the experimental data of pH-dependent swelling degree of gel samples are shown in Figure 3(a). The second method is by using hydrochloric acid to prepare a solution of pH = 3 at first, and dipping gel sample in it to swelling equilibrium, then modulating the pH by gradually adding in 0.493N NaOH, thus increasing the pH step by step; the experimental data are shown in Figure 3(b). It is necessary to distinguish these two methods because of several reasons. First, the electroneutralization should be kept in gel phase, so that in the absence of foreign acid or alkali, the hydrogen cation from the dissociation of carboxyl group will be arbitrarily retained in the gel phase, thus resulting in the different pH in gel and surrounding solution.[19] But in general, the equilibrium pH refers to that of surrounding aqueous solu-

tion, foreign acid must be added to modulate the pH of surrounding solution to a desired value that inevitably changes the environment in gel and influences the dissociation of pendent —COOH groups. In addition, Donnan distribution of the mobile ion species will be in a distinct way and will affect to the dissociation of carboxyl groups, and the ionic strength in the gel phase would vary significantly.

It can be seen from Figure 3 that the different pH dependence of swelling behavior is exhibited in the vicinity of pH = 7. For the first modulating method, below pH 7, the only mobile cation in the system is hydrogen ion; the dissociation of —COOH was more restrained with the decrease of pH value, and the ionization degree of —COOH was kept at a very low level. Because the electrostatic repulsion between ionic —COO⁻ residuals has a significant positive effect on swelling, the swelling degree of gel samples are low
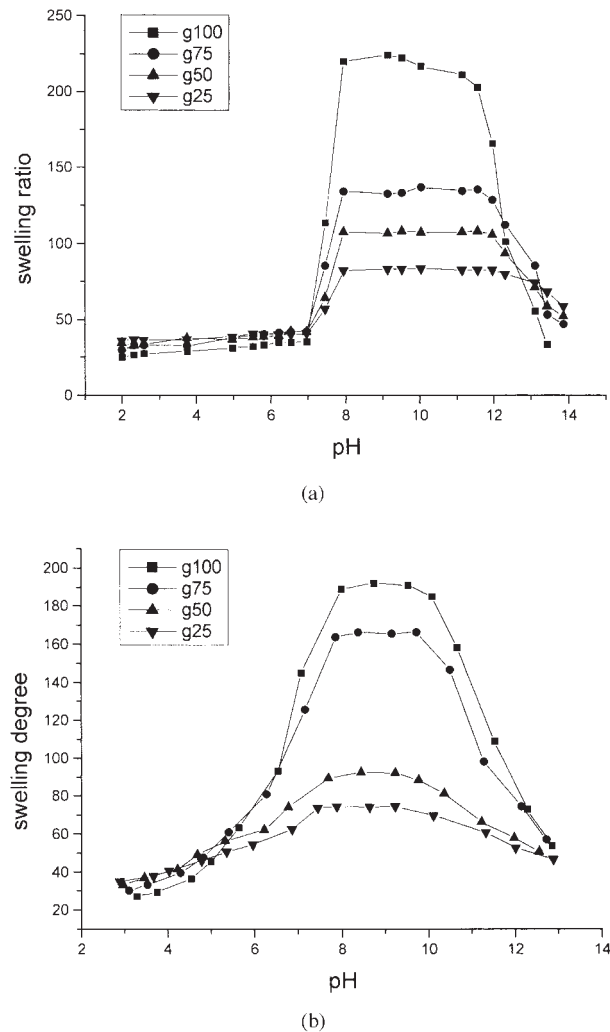

(a)

(b)

Figure 3 pH dependence of swelling ratio of AAc–NIPAAm copolymer hydrogels at 25°C. (a) The pH was modulated by using HCl and NaOH, respectively; (b) the pH was modulated by gradually adding in 0.493N NaOH aqueous solution.

and exhibit slight variation with pH. Above pH 7, there are two types of mobile cations in the system: hydrogen ions and base cations. One can consider an initial state where the base cations exist only in the external solution. Because there are no base cations in the gel, the base cations will diffuse into the gel phase and try to establish their own equilibrium. As the pH increases, the concentration of base cations in the outer solution will also increase. Those cations will diffuse into the gel and will replace the mobile H^+ ions. The gel of course acts as an ion exchanger. New H^+ ions will be supplied by the yet undissociated acrylic acid. The supply of H^+ ions is, however, limited. Eventually, all the acrylic acid will be dissociated. Calculation shows that the complete dissociation of acrylic acid will be accomplished when the pH reaches a value of 8.

To account for the large swelling in the pH = 7–8 range, Ricka and Tanaka[19] considered the aspect of Donnan contribution in which the concentration of mobile ions in the gel would increase more rapidly than in the outer solution, and the ion swelling pressure would increase. This means the Donnan ratio K would reach the maximum in this pH range and any further increase of pH would decrease the Donnan ratio K. However, it is similarly reasonable to attribute the large swelling of gels in this pH range to the electrostatic repulsion between dissociated acrylic acid.[15]

The second pH modulating method is predominantly different from the first method in that the swelling ratio of the gel sample begins to significantly increase well before pH 7; in addition, the maximum swelling ratio is lower. One can find the answer from analyzing the existing mobile ion species and their Donnan distribution in and out of the gels. In the first method, there is only one species of mobile cation, H^+, combining with the requirement of electroneutralization in the gel phase, resulting in that in the range pH < 7, the pH in the gel phase is much lower than that in outer solution, the more closer to pH 7, the more difference in pH. When the pH reaches about 7 in the outer solution, one can calculate from the dissociation reaction of acrylic acid ($pK_a \sim 4.28$) that pH ~ 3 in the gel phase and as a result, the ionization degree of acrylic acid is kept very low. This leads to a low electrostatic repulsion pressure and low Donnan ratio of mobile ion species. So in the first pH modulating method, the swelling ratio of gels are low below pH 7. For the second pH modulating method, the base cation is present in the system and it will establish its own Donnan distribution between the gel and the outer solution. The presence of base cation can level the pH difference and make the pH in and out of the gel nearly equal. In this case, the dissociation of acrylic acid is promoted with increasing pH, the more closer to pH 7, the more the ionization degree, leading to a

considerably large electrostatic repulsion and Donnan ratio, and this results in a gradual increase of swelling ratio with pH.

The swelling ratio begins to decrease at high pH range. This is due to the electrostatic screening of concentrated base, which makes the Donnan ratio and the electrostatic repulsion weakened.

Thermodynamic simulation of pH-responsive swelling

The treatment in this article is restricted to an idealized network of geometrical chains crosslinked by fixed junctions. During swelling, the gel sample is subjected to the swelling pressure ϕ. ϕ is determined by the sum of contributions due to the mixing of polymer segments with the solvent (ϕ_1), mixing of ions with the solvent (ϕ_2), conformational elasticity of the polymer network (ϕ_3), and the electrostatic interaction of charges in the chains (ϕ_4). The pressure ϕ_1, according to the Flory-Huggin's equation, can be expressed as

$$\Phi_1 = -RT/V_1[ln(1 - v_2) + v_2 + xv_2^2] \quad (1)$$

where V_1 is the molar volume of the solvent, v_2 is the volume fraction of polymer in swollen gel, and x is the polymer–solvent interaction parameter. The osmotic pressure due to the difference of concentration of mobile ion species between the gel and the surrounding solution can be expressed as

$$\Phi_2 = RTi\rho v_2/M_0 \quad (2)$$

The contribution ϕ_3 has been calculated from finite extensibility of chains, including an intrinsic Gaussian part that would characterize the chain in the absence of charge interactions, and a non-Gaussian part, which is the effect of the electrostatic persistence length.

$$\Phi_3 = -RTv_d\left(\langle\alpha_0^2\rangle v_2^{1/3} - \frac{v_2}{2}\right)$$

$$-RT\left\{\begin{array}{l} \dfrac{3}{5}\langle\alpha_0^2\rangle^2 v_2^{-1/3}n^{-1}\left(1 + \dfrac{3L_c}{4L_t}\right) \\[2mm] +\dfrac{99}{175}\langle\alpha_0^2\rangle^3 v_2^{-1}n^{-2}\left(1 + \dfrac{L_c}{L_t}\right) \\[2mm] +\dfrac{513}{875}\langle\alpha_0^2\rangle^4 v^{-5/3}n^{-3}\left(1 + \dfrac{9L_c}{8L_t}\right) + \cdots \end{array}\right\} \quad (3)$$

where v_d is the number of chains in the dry state. The contribution ϕ_4 is obtained from the change in the free energy of electrostatic interaction during swelling, $\phi_4 = \Delta F_{el}/\Delta V$, given by Katchalsky as

$$\Phi_4 = -\left(\frac{\partial F_c}{\partial V}\right)_{T,H_1} = -\frac{v_c}{V_0}\frac{N_A Z^2 i^2 e^2 v_2^{4/3}}{3Dh_0}$$

$$\times\left(\frac{2.5A}{1+A} - \log(1+A)\right) \quad (4)$$

where

$$A = \frac{6(V/V_0)^{1/3}}{\kappa h_0} = \frac{6}{\kappa h_0}v_2^{-1/3},$$

if calculated from a pair-wide summation of the screened Coulomb potential between charges separated by distance $B = b/i$ arranged on a rod, resulting in

$$\Phi_4 = -RT\frac{Q\rho i v_2}{M_0}\frac{\kappa e^{-kB}}{1-e^{-kB}} \quad (5)$$

where κ is the inverse of the debye radius of the ionic atmosphere,

$$\kappa = \left(\frac{4\pi e^2 N_A \sum c_i}{DkT \times 1000}\right)^{1/2} \quad (6)$$

at atmosphere pressure for swelling equilibrium, the total swelling pressure ϕ should satisfy

$$\Phi = \Phi_1 + \Phi_2 + \Phi_3 + \Phi_4 = 0$$

The dissociation of carboxyl group can be expressed as[20]

$$\text{pH} = \text{p}K_a - n\log\left(\frac{\alpha}{1-\alpha}\right) \quad (7)$$

The above equation is commonly used to describe the titration curves of polyacids, since ionization becomes increasingly difficult as the concentration of dissociated —COOH increases. The dissociation of carboxyl group would also be influenced by several other factors. Firstly, the dissociated anionic groups would be reversibly bound with the small cations in solution,[6] as in the following equation

$$[\text{—COO}^-]_h = [\text{—COO}^-]_{\text{total}} \times \left(\frac{K_a}{K_a + c_i}\right) \quad (8)$$

where c_i is the concentration of i species counterion (hydrogen ion or sodium ion in this article) reversibly bound to the polymer chains. This binding equilibrium, not only is thermocontrolled and obeys simple mass-action law, but also becomes serious at high degree of ionization. Secondly, according to theory of counterion condensation, where the linear charge den-

sity of polymer chain is above a certain value (0.365 in the case that only monovalent counterion is available in the solution, 0.183 for divalent counterion), the counterions in solution will be captured and bound to the pendent ionic groups in the chain by strong local electrostatic field to decrease the linear charge density on the polymer chains, this process is energetically favored. In this article only 1–1 strong acid or alkali will be used to modulate the pH, so that the effective uncompensated ionization degree of pendent ionizable group could not exceed 0.365. Only the uncompensated ionic carboxyl groups will work to produce electrostatic repulsive force for the swelling.

For numerical simulation for pH-dependent swelling of polyionic gel, poly(acrylic acid) hydrogel is chosen as the model. The parameters used for crosslinked poly(acrylic acid) hydrogels are: $x = 0.45$, $\rho = 1.517$ g/cm^3, $b = 2.55 \times 10^{-8}$ cm for vinyl polymer, crosslinking density is 5×10^{-5} mol/cm^3, and concentration of —COOH in dry PAAc, $c_2 = 36.5 \times 10^{-3}$ mol/cm^3. Equations (1)–(3) were generally used in all simulations, for ϕ_4 eqs. (4) and (5) were used to give a comparison. Using eqs. (1)–(5), the simulation results are shown in Figure 4. Simulation result in Figure 4(b) takes into consideration the influence of ionic strength on dissociation of carboxyl groups.

In this article, we derive a new equation for the electrorepulsive swelling pressure, based on the electrostatic free energy, F_{el}, given by Katchalsky as following

$$F_{\text{el}} = \frac{v_c}{V_0}\frac{Z^2 i^2 e^2}{Dh_0(V/V_0)^{1/3}}\log\left(1 + \frac{6(V/V_0)^{1/3}}{\kappa h_0}\right) + B \quad (9)$$

where Z is the number of ionizable pendent groups on the chain (for poly(acrylic acid) Z is also the number of repeat units in the chain), i is the ionization degree, $(h_0)^2$ is the mean square end-to-end distance of chain in the reference state, which can be given as $h_0 = Z(s_0 + is_i)b^2$, $s_0 = 9$ and $s_i = 24$. The electrostatic swelling pressure can be expressed as

$$\Phi_4 = -\left(\frac{\partial F_{\text{el}}}{\partial V}\right)_\kappa - \left(\frac{\partial F_{\text{el}}}{\partial \kappa}\right)_v\frac{d\kappa}{dV} \quad (10)$$

The swelling pressure ϕ_4 is directly formulated from eq. (10). The Debye length, κ, representing the electrostatic screening of pendent ionized groups resulting from mobile ions, is proportional to the concentration of mobile ions in the gel phase. As the concentrations of H$^+$, OH$^-$, and the co-ions of acid/base are controlled by pH, they not related with volume change of gel. However, it is just the concentration of pendent ionic residual that depends on the volume change. In calculation of difference between
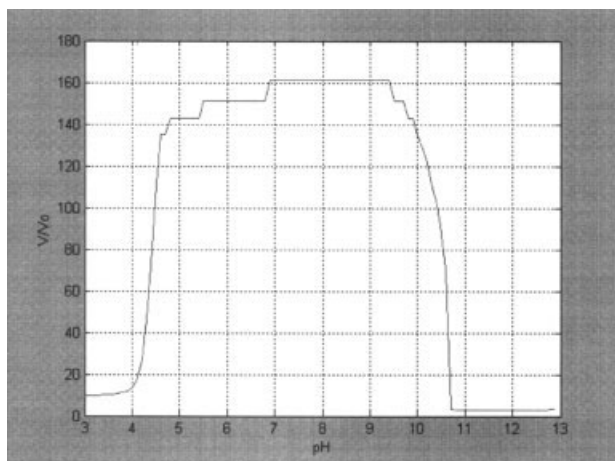
(a)
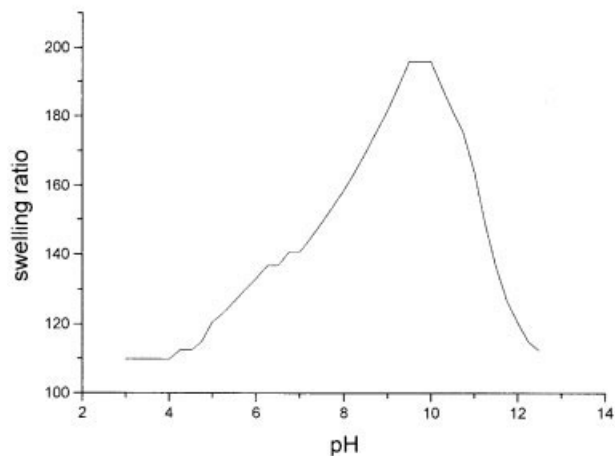
(b)

Figure 4 Dependence of the swelling ratio ($1/v_2$) of the gel on pH calculated (a) from eqs. (1)–(4) and (b) from eqs. (1)–(3) and (5).

the osmotic pressure in the gel containing mobile ions and in the surrounding solution, an approximation that the concentration difference of mobile ions is equal to the concentration of pendent ionic residual on the chain was adapted. So we attempt this approximation in evaluating the concentration change of mobile ions in the gel related to volume change. So we get

$$\frac{d\kappa}{dV} = \frac{\kappa}{2\sum c_i v_2^2 V_0} \frac{K_a c_2}{[H^+] + K_a} \qquad (11)$$

Substituting eq. (11) into eq. (10), and the other terms in eq. (10) were derived based on eq. (9), thus getting formulation of ϕ_4. Combined with eqs. (1)–(3), the simulation results obtained by using our derivation, shown in Figure 5, reasonably well describe the characteristic of pH-dependent swelling behavior. The influence of ionic strength on dissociation of —COOH
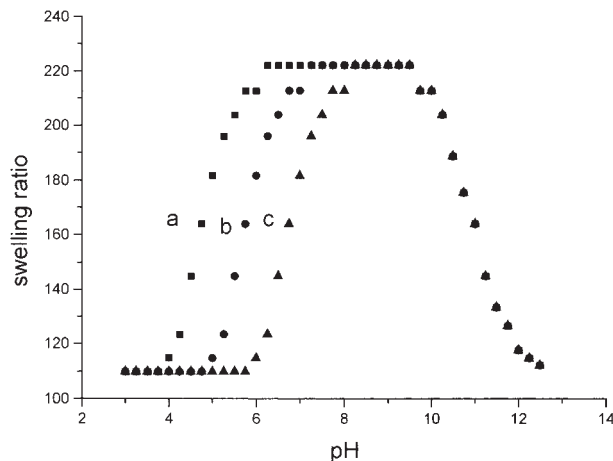

Figure 5 Dependence of the swelling ratio ($1/v_2$) of the gel on pH calculated from our modified equations. (a), (b), and (c): pK_a = 4.8, 5.8, and 6.8, respectively.

[eq. (7)] is not taken into account. All plots show sharp increases in swelling over narrow pH range, as observed in experimental results (also in refs. 19 and 21), and the narrow pH range moves with changes in pK_a values. It also can be seen that in Figure 5 plot c (pK_a = 6.8) is the best that reflects the experimental swelling data, implying that the dissociation constant of polyacid was lower than that of acid monomer. Figure 6 is the simulation result based on our formulation with the influence of ionic strength on dissociation of —COOH [eq. (7)] taken into account. pK_a = 6.8 was used.

CONCLUSIONS

NIPAAm–AAc copolymer hydrogels were synthesized. The dynamic swelling behavior of these gels is significantly influenced by pH of medium. At low pH, because of the intra- and intermolecule hydrogen
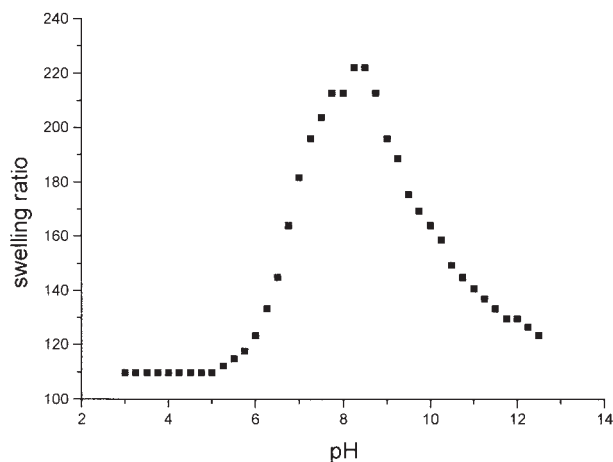

Figure 6 Dependence of the swelling ratio of the gel on pH.

bonding formed among acrylic acid groups and amine groups, the water diffusing is a segment-relaxation controlled process; at high pH, because of the elimination of hydrogen bonding and electrostatic repulsion in the gels, the swelling rate is far accelerated. The equilibrium swelling ratio is predominated by the composition of gels, and the gels undergo phase transition at LCST. The pH-modulating methods significantly influence the pH-responsive swelling behavior, which can be interpreted from the presented mobile ion species and their Donnan contribution. In thermodynamic simulation, a new derivation for swelling pressure of electrostatic repulsion and dependence of Debye length on volume change of swollen gel is presented, based on similar assumption used in derivation of ionic osmotic pressure. The simulation results give a reasonably good explanation for pH-responsive swelling behavior.

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