

# Swelling of pH-Sensitive Chitosan–Poly(vinyl alcohol) Hydrogels

Sundaram Gunasekaran,<sup>1</sup> Tao Wang,<sup>2</sup> Chunxiang Chai<sup>3</sup>

<sup>1</sup>Department of Biological Systems Engineering, University of Wisconsin–Madison, Madison, Wisconsin 53706

<sup>2</sup>Department of Food Science, University of Wisconsin–Madison, Madison, Wisconsin 53705

<sup>3</sup>Department of Food Science and Engineering, Tianjin University of Commerce, Tianjin, China 300134

Received 6 June 2006; accepted 22 May 2006

DOI 10.1002/app.24825

Published online in Wiley InterScience (www.interscience.wiley.com).

**ABSTRACT:** The swelling properties of different chitosan–poly(vinyl alcohol) (PVA) hydrogels were investigated as functions of the medium pH and salt concentration. The maximum swelling ability of the hydrogels was at a buffer pH of approximately 3, regardless of the PVA content in the hydrogels. The maximum mass of the swollen hydrogels was about 13 times that of their contracted counterparts. The cyclical swelling and contraction between pH 3 and pH 7 buffers and pH 3 and pH 3 buffers with salt confirmed the Donnan swelling mechanism of these hydrogels. The swelling mechanism was considered the transfer

of water molecules driven by a concentration gradient. This was represented by a simplified mass-balance model, which neglected the effect of the ionization reaction, for the initial swelling period. The effective mass-transfer coefficient of water molecules during swelling, estimated with this model, gradually decreased with increasing PVA content in the hydrogels. © 2006 Wiley Periodicals, Inc. *J Appl Polym Sci* 102: 4665–4671, 2006

**Key words:** diffusion; hydrogels; modeling; stimuli-sensitive polymers; swelling

## INTRODUCTION

Most pH-sensitive hydrogels have a high density of dissociable acidic or basic groups that can be ionized at a certain pH. The ionization of these groups causes a high concentration of ions inside the gel structure because of these fixed-charge groups and the migration of counterions from the surrounding medium. The high ion concentration encourages the transfer of water molecules into the gel network to reduce the concentration difference between the inside and outside of the hydrogels induced by the fixed-charge groups. As a result, a substantial volume change occurs, and it is known as the gel phase transition. This process is also described as the Donnan equilibrium, which regards swelling as the elimination of the osmotic pressure difference between the inside and outside of gels caused by the migration of charged ions. While taking up water, ionic gels usually expand or swell. The swelling of ionic gels in water or another polar solvent will eventually reach an equilibrium state, in which the gel expansion is balanced by a contractive force generated by the expanding networks. The hydrogels will maintain their three-dimensional structure, unless the crosslinked bonds are breached. The swelling equilibrium is very difficult to model mathematically

because of the network expansion and the electrostatic interactions along the chains. Nevertheless, there are a few existing models that deal with the swelling of ionic gels or the hydrogel phase transition.

For instance, Gregor's model considers the gel matrix as a network of elastic springs. When a gel swells under proper conditions, the network stretches and exerts a pressure on the internal pore liquid. The swelling pressure in the gel affects the swelling, sorption, and ion-exchange abilities of the gel.<sup>1,2</sup> However, this is purely a mechanical model based only on the swelling pressure of the gel network and does not consider the electrostatic interactions. A refinement of Gregor's model has been made under the assumption that electric surface charges are uniformly distributed on the adjacent parallel plates, repelling one another and stretching the interconnected elastic springs.<sup>3</sup> However, equations derived from this refined model are rather complex and difficult to evaluate.

Gregor's model is a macroscopic model because it does not involve single ions as discrete particles, and the ideal elasticity of the springs represents the matrix network structure. On the other hand, Rice and Nagasawa<sup>4</sup> proposed a model based on molecular-scale considerations. The elasticity of the matrix is not mechanical but instead is due to an increase in the entropy, which accompanies the configuration of coiling chains. Swelling equilibrium is attained when the free energy of the gel system is at its minimum. Equilibrium between an ionic gel and solutions can be described by means of rigorous thermodynamics.<sup>5</sup>

Correspondence to: S. Gunasekaran (guna@wisc.edu).

The swelling behavior of hydrogels is heavily dependent on the ionization of the gels as well as the ionic strength of the surrounding solution.<sup>6–11</sup> Many research groups have derived models for the swelling of ionic gels based on the Donnan theory.<sup>12–14</sup> Compared with other existing models, the Donnan theory is simpler because it does not involve parameters from the elastic free energy of the network. Other quantitative analyses of the charges and water content in microspheres as functions of the pH and salt concentration have also been obtained.<sup>15</sup> An attempt has also been made to relate gel swelling to the valence and concentration of ions present in the swelling medium.<sup>16</sup>

### Modeling water transfer

One characteristic phenomenon of pH-sensitive hydrogels is the dynamic swelling corresponding to different pHs of the surrounding medium. The transfer of water molecules from the surroundings into the hydrogels is the primary reason for swelling. Most applications of hydrogels in biotechnology and controlled-release systems are intimately related to water or solute mass-transport properties of gels. However, the existing swelling models are still either too complicated or too difficult to apply. Therefore, it is helpful to simplify the swelling model in an attempt to learn about the mass-transport mechanism of hydrogels.

For instance, the dimensional changes in pH-sensitive hydrogels take place because of ionization by acid or base transfer from the surrounding bulk solution. The acid or base character of the bulk solution causes the gels to swell or shrink.<sup>17</sup> In the case of swelling, water and solute molecules move from the bulk solution into the gel, and in the case of shrinkage, the reverse occurs. In either case, the gel normally keeps its overall geometry,<sup>18</sup> and the swelling/shrinkage facilitates water and solute transfer. Although the pH of the bulk solution and character of the hydrogel determine the direction of mass transfer, the mass-transfer process itself is governed by the physicochemical properties of the gel. Still, because of the comparatively high concentration (often in excess of 90%), water is the dominant factor contributing to gel properties.

Two mass-transfer modes can take place during swelling and contraction. Water and solute molecules travel within the gel by the osmotic pressure gradient (due to the water concentration gradient) between the inside and outside of the hydrogel. The mechanism of water transport could be diffusion, convection, or both. The same effect should also apply to solutes because of the partition effect between the solution and the gel. However, the solute diffusion effect may be less significant than that of the water molecules.

Our objectives were (1) to investigate the swelling behavior of chitosan (CS)–poly(vinyl alcohol) (PVA)

hydrogels as a function of the CS/PVA ratio and the pH and ionic strength of the swelling medium and (2) to develop a simplified model to describe the water transport through hydrogels during the initial swelling period and determine the corresponding mass-transfer coefficient ( $k_m$ ).

## EXPERIMENTAL

CS [weight-average molecular weight ( $M_w$ ) =  $6.1 \times 10^5$  Da, N-deacetylation degree = 72%] and PVA (hydrolysis > 99%,  $M_w$  = 89,000–98,000) were purchased from Aldrich Chemical, Inc. (Milwaukee, WI). Chemical-grade acetic acid, sodium acetate, dibasic and monobasic sodium phosphate, sodium hydroxide, and sodium chloride were used. A pH meter equipped with a Ag/AgCl combination electrode (Accumet Model 20, Fisher Scientific, Pittsburgh, PA) was used for pH measurements. A micrometer (Mitutoyo CD-6" BS, Mitutoyo Corp., Yamagata, Japan) was used to measure the dimensions of hydrogel beads.

### Formation of the hydrogel beads

CS was first dissolved in acetic acid (0.75% v/v) to prepare a 1% (w/v) solution. This solution was filtered and degassed before further use. PVA was added to the CS solution in the desired molar proportions (i.e., CS/PVA = 1 : 0, 1 : 4, 1 : 5, 1 : 7, 1 : 10, or 1 : 15 mol/mol), and the mixture was heated to 80°C and held for several minutes until the white PVA powder was completely dissolved and a clear and homogeneous blend with CS was formed. During the experiments, the CS–PVA solutions was covered by a commercial polyethylene film to prevent moisture loss through evaporation. Then, the mixed solution was cooled to room temperature (25°C). A solution of the crosslinking agent glutaraldehyde (25% v/v) was added slowly to the well-stirred CS–PVA mixture. The final crosslinker concentration in the gel bead was 33.3  $\mu$ M. All experiments were performed in an incubator (model 2005, VWR Scientific, Inc., West Chester, PA) to ensure proper temperature control during the experiments.

The CS–PVA beads were prepared by the slow dropping of the CS–PVA mixture solution into a plastic centrifuge tube filled with oleic acid immediately after the addition of the crosslinking agent with a small burette. The volume of each drop was controlled by the flow rate and the tip of the burette. The final number of beads in the 15-mL test tube was about 15–20. The test tubes were screw-covered tightly, horizontally placed on a VWR Scientific model 7637-01 rotator, and rotated for about 8 h at a speed of 12 rpm to prepare a spherical shape. The hydrogel beads were then recovered by the filtration of the oleic acid and stored in a refrigerator for fur-

ther experiments. The fatty acid film was removed right before further individual experiments via the rinsing of the beads in acetone for a very short time.

### Dynamic swelling and shrinkage

The masses and dimensions of the CS-PVA hydrogel beads were measured with an electronic balance with an accuracy of  $\pm 0.1$  mg (AG245, Mettler-Toledo, Worthington, OH). Several beads with similar masses and dimensions were chosen and allowed to swell in a pH 2 medium. Periodically, the hydrogel beads were removed from the swelling medium, wiped for excess surface moisture, and weighed. When the mass of the hydrogel beads reached a plateau value, they were transferred to a pH 10 medium. Subsequently, the shrunken gel beads were placed in a pH 2 buffer. This dynamic swelling and shrinking was repeated three times. Under each equilibrium condition, the swelling ratio ( $Q$ ) was calculated as follows:

$$Q = \frac{M_f}{M_i} \quad (1)$$

where  $M_f$  is the final equilibrium mass of the swollen or shrunken hydrogel and  $M_i$  is the initial mass of the hydrogel.

### Hydrogel swelling at different pHs

The hydrogel swelling properties at different pHs (from pH 1 to pH 10) were investigated by the placement of three hydrogel beads in each pH medium, which were prepared with either hydrochloric acid or a sodium hydroxide solution. The pH of the swelling media was monitored constantly during swelling with the pH meter. The final equilibrium mass of the hydrogel beads was measured, and the corresponding  $Q$  value was calculated.

To determine the maximum swelling properties of the CS-PVA hydrogel, the gel beads were equilibrated in solutions of different pHs. Then, they were subjected to a pH 7 buffer medium. The bead mass values between the initial condition (pre-equilibrium at different pHs) and the pH 7 equilibrium condition were used to calculate the maximum  $Q$  value; that is, the gel mass at pH 7 was used as  $M_i$  in eq. (1).

### Cyclical swelling and contraction of the CS-PVA hydrogel

The pH 3 and pH 7 buffers were used to study the cyclical swelling and contraction triggered by the pH. The pH 3 medium and pH 3 medium with salt (0.1M NaCl) were chosen to study the salt-triggered swelling and contraction cycles of the hydrogel.<sup>19</sup> First, six gel beads with similar masses and dimen-

sions were chosen and swollen in the pH 3 buffer until they reached the swelling plateau. Then, three swollen beads were placed in the pH 7 buffer and pH 3 buffer with 0.1M NaCl for deswelling. Later, the contracted beads were transferred back to the pH 3 buffer for swelling. The experiment was conducted likewise for several cycles. At the end of each equilibrium condition, the mass of the gel beads was recorded; the equilibrium mass of the control beads, those allowed to contract continuously in the pH 3/0.1M NaCl and pH 7 buffers, was also measured periodically. The average value of triplicates was used to calculate the  $Q$  values.

### Estimation of the effective $k_m$ value

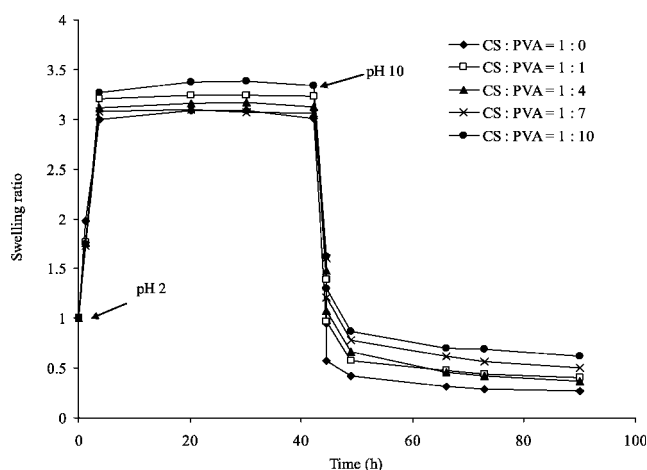
Experiments were conducted in bulk solutions with a pH 3 (acetic acid/sodium acetate) buffer at 25°C. The changes in the masses of the hydrogel beads were recorded periodically during the experiment with a precision balance, and the characteristic dimension changes were obtained by the measurement of the diameter of the spherical beads at two positions.

Equation (7) was programmed with MatLab (MathWorks, Inc., Natick, MA). A nonlinear optimization technique was used to minimize the sum of squares of the deviation between the observed and estimated data. Because over 95% of the water transfer occurred during the first 4 h (see Fig. 1), only data over the first 250 min of swelling were used for calculating the effective  $k_m$  value.

## RESULTS AND DISCUSSION

### Hydrogel swelling and deswelling

The Donnan theory states that the swelling ability is basically determined by the osmotic pressure gradi-

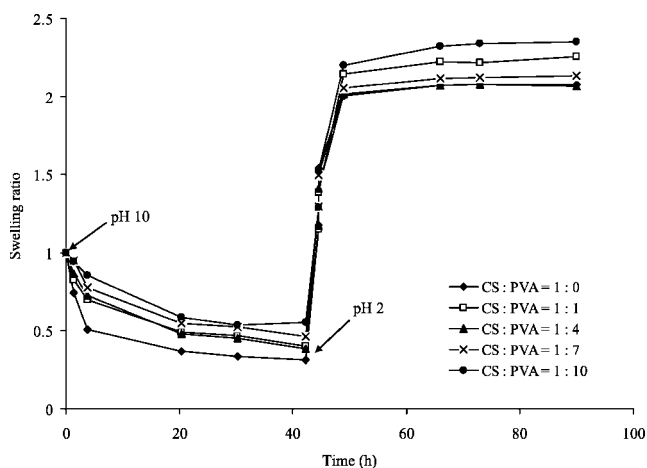


**Figure 1** Swelling and contraction transition of CS-PVA hydrogels with different CS/PVA molar ratios.

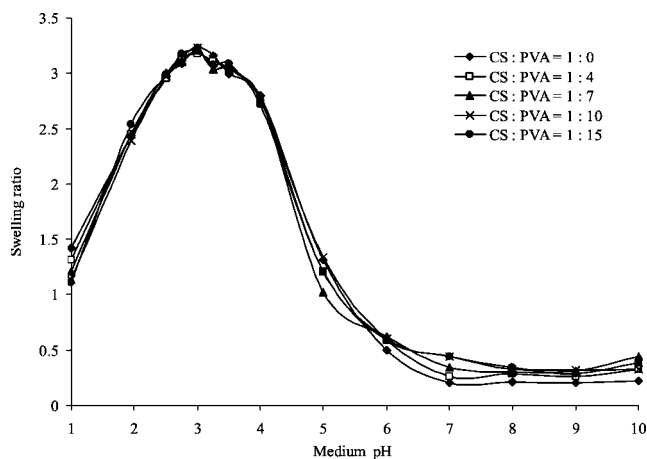
ent between the inside and outside of a gel. The osmotic pressure gradient here could also be represented as the ion concentration gradient between the inside and outside of the hydrogel. Because of the presence of a high density of fixed-charge groups inside the hydrogel, the counterion concentration is always higher inside the hydrogel. Therefore, the hydrogel is like a highly concentrated solution of both ions and has a tendency to dilute itself by taking up additional solvent (water). Therefore, from a macroscopic point of view, the swelling phenomenon appears to be a balance of the osmotic pressure gradient or concentration gradient between the interior of the hydrogel and the external solution.

In addition to the osmotic pressure, an electrostatic repulsion force provided by charged groups contributes to the expansion of the gel network, that is, the swelling of the hydrogel. If this swelling is triggered by proton ionization, such a hydrogel is pH-sensitive. As the hydrogel swells and packed polymer coils expand, the osmotic pressure decreases, whereas the elastic contraction forces provided by the crosslinked network increases. They eventually balance each other; that is, the swelling equilibrium is reached.

The swelling of the CS-PVA hydrogel in a buffer with a pH below its  $pK_a$  and the contraction of the hydrogel in a buffer with a pH higher than its  $pK_a$  are shown in Figures 1 and 2. A low buffer pH ( $<pK_a = 6.3$ ) of CS is essential for the ionization of primary amine groups. As  $-NH_2$  groups of the hydrogel are ionized, positively charged  $-NH_3^+$  groups are distributed in the hydrogel network. This attracts and creates a higher concentration of counterions ( $Ac^-$ ) inside the hydrogel and results in a net osmotic pressure difference between the inside and outside of the hydrogel. These positive charges also provide electrostatic repulsion forces, which contribute to the expansion of the gel network. When the buffer pH is above



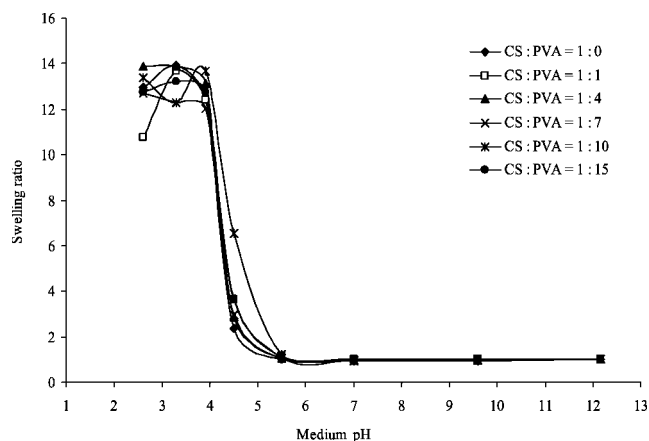
**Figure 2** Contraction and swelling transition of CS-PVA hydrogels with different CS/PVA molar ratios.



**Figure 3** Effect of the medium pH on the swelling behavior of CS-PVA hydrogels with different CS/PVA molar ratios in the equilibrium state.

$pK_a$  of CS, the exact opposite happens. The optimal swelling medium pH for the hydrogel is between 2.8 and 3.5, regardless of the PVA content in the hydrogel (Fig. 3). At  $pH \sim 3$ , the concentration of  $H^+$  ions is high enough to provide sufficient  $H^+$  for  $-NH_2$  ionization. The counterions ( $Ac^-$ ) can easily couple with the  $-NH_3^+$  groups at this pH, which maximizes the total ion number concentration in the gel matrix and enhances the associating ability with water molecules by the formation of more solvation shells.<sup>20</sup> As a result, the hydrogel reaches its maximum swelling ability. When the  $H^+$  concentration in the solution further increases, it lowers the effective  $Ac^-$  concentration because of the  $Ac^-$ -HAc buffering properties and increases the shield effect caused by excess  $Cl^-$  ions. Furthermore, because of the presence of an excess amount of  $H^+$ , it reduces the osmotic pressure difference and therefore reduces its swelling ability. For swelling media with pH values higher than  $pK_a$  of CS, originally ionized groups in the gel matrix gradually lose their charges and thus lose their attraction for counterions; that is, they eliminate the osmotic pressure difference. Consequently, to balance the osmotic pressure inside and outside of the hydrogel, the gel matrix contracts.

The effect of the pH and PVA content on the swelling or contraction capacity is also shown in Figures 1–3. The PVA content of the hydrogel shows no effect on  $Q$  or the time needed to reach swelling or contraction equilibrium. This is because PVA does not have any ionizable groups in its molecular structure at any buffer pH value. Also, the presence of PVA in the CS-PVA hydrogel matrix may be just a simple physical entanglement that cannot exert any significant contractive force on the expanding network. The maximum swelling ability of the CS-PVA hydrogel is shown in Figure 4. The maximum mass difference between the swollen state (at pH 3) and

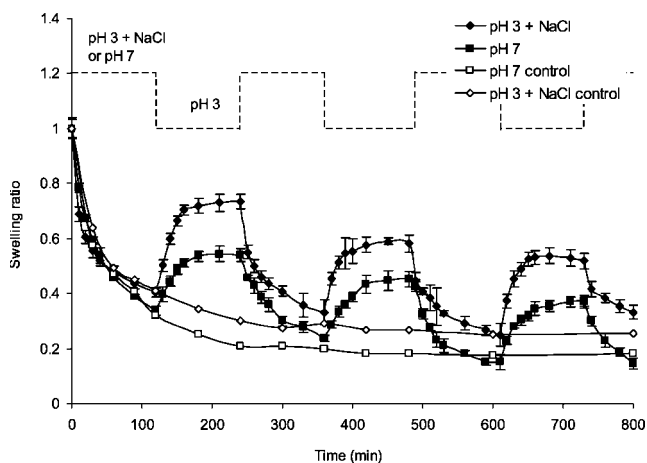


**Figure 4** Maximum contraction ratio (based on the contracted state) of CS-PVA hydrogels with different CS/PVA molar ratios.

contracted state (at pH 7) of the hydrogel is about 13 times, independent of the PVA content.

Cyclical swelling and deswelling patterns are shown in Figure 5. The gradually lowering swelling profile at each subsequent cycle is due to the nonequilibrium during the deswelling of gel beads, which are shown by the profiles of their controls. The swelling ability can be restored to the previous swollen state if the deswelling profiles of the control counterparts are deducted.

The solution pH has a pronounced influence on the swelling of the hydrogel. The CS-PVA hydrogel carries a high density of ionic groups,  $-\text{NH}_3^+$  and  $\text{Ac}^-$ , at low pHs, such as  $\text{pH} \sim 3$ . The positive  $-\text{NH}_3^+$  groups inside the hydrogel can be shielded by a high concentration of a strong electrolyte such as NaCl. As  $-\text{NH}_3^+$  is shielded by counterion  $\text{Cl}^-$ , two changes occur. First, the net effectively positive charge decreases, as well as the electrostatic repulsion. As a



**Figure 5** Cyclical swelling and contraction profile of CS-PVA hydrogels in pH 3 and pH 7 buffer systems and a pH 3/0.1M NaCl buffer system.

result, the ability to attract counterions is impaired by these electrolyte ions. Second, the net osmotic pressure difference (swelling drive force) between the inside and outside of the hydrogel diminishes because of increasing ion concentration in the swelling buffer, and this results in a decreased swelling ability, shown in the pH 3 buffer with 0.1M NaCl salt deswelling of the gel (Fig. 5). When the high salt concentration around the hydrogel is removed, for instance, by the replacement of the beads in the unsalted pH 3 buffer with a very low ionic strength, the shielding effect is gradually removed by the dialysis of salt from the hydrogel. The CS-PVA hydrogel regains its swelling ability, as shown by the reswelling of the gel in a pH 3 buffer (Fig. 5).

### Simplified mass-transport model

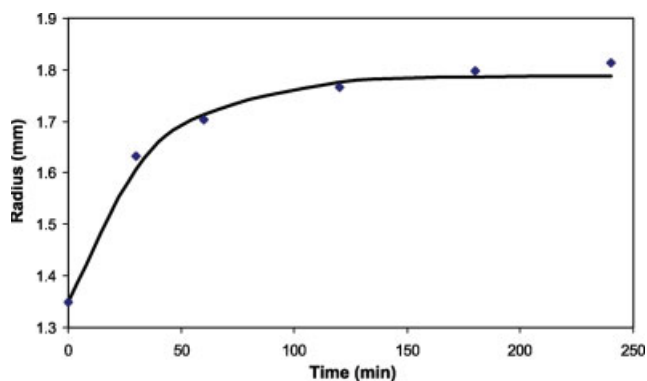
Water transport in the gel structure can be set up on the basis of the overall mass balance of water, with the effect of ionization neglected, under the following assumptions:

1. Water transport occurs mainly under the moisture concentration gradient between the surface layer of the hydrogel and the interior of the gel.
2.  $k_m$  is constant and independent of the concentration.
3. The hydrogel beads remain spherical for the duration of the swelling.

For a spherical hydrogel bead, we can write the following mass-balance equation:

$$k_m A (C_e - C) = V \frac{dC}{dt} \quad (2)$$

where  $C$  is the water concentration of the hydrogel at time  $t$  ( $\text{mg}/\text{mm}^3$ ),  $C_e$  is the water concentration of the hydrogel at equilibrium ( $\text{mg}/\text{mm}^3$ ),  $A$  is the surface area of the hydrogel ( $\text{mm}^2$ ),  $V$  is the volume of the hydrogel ( $\text{mm}^3$ ), and  $t$  is the time (min).



**Figure 6** Change in the gel bead radius with time according to eq. (3). [Color figure can be viewed in the online issue, which is available at [www.interscience.wiley.com](http://www.interscience.wiley.com).]

**TABLE I**  
Parameters  $m$ ,  $a$ , and  $b$  from Eq. (3) Used To Describe Changes in the Hydrogel Bead Radius as a Function of Time and  $R^2$  for the Model Fit

CS/PVA molar ratio	1 : 0	1 : 5	1 : 10	1 : 20
$R^2$	0.9972	0.9887	0.9843	0.9958
$m$	-0.5023	-0.6144	-0.5974	-0.4403
$a$	0.0262	0.0196	0.0162	0.0296
$b$	1.7206	1.9011	2.0207	1.7886

As the hydrogel bead imbibes water and swells,  $V$  increases. The concomitant increase in its radius can be modeled with the following empirical equation:

$$r = m \cdot \exp(-at) + b \quad (3)$$

where  $r$  is the hydrogel radius at time  $t$  (mm) and  $m$ ,  $a$ , and  $b$  are constants.

Integrating eq. (2), we obtain

$$\int_0^t \frac{k_m A}{V} dt = \int_{C_0}^{C_t} \frac{dC}{(C - C_e)} \quad (4)$$

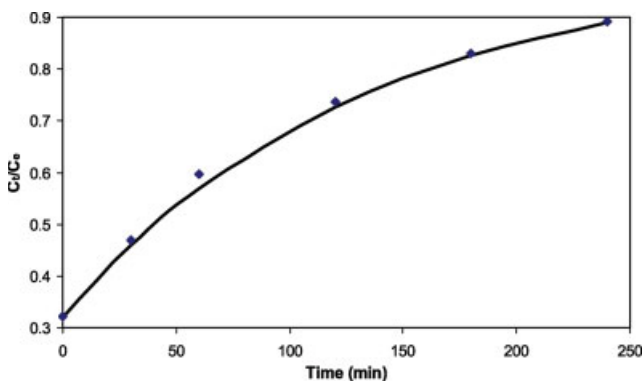
$$\int_0^t \frac{3k_m}{r} dt = \int_{C_0}^{C_t} \frac{dC}{(C - C_e)} \quad (5)$$

Combining eq. (3) with eq. (5) we get

$$\int_0^t \frac{3k_m}{m \cdot \exp(-at) + b} dt = \int_{C_0}^{C_t} \frac{dC}{(C - C_e)} \quad (6)$$

Integrating eq. (6), we obtain the following model:

$$\frac{C_t}{C_e} = 1 - \left(1 - \frac{C_0}{C_e}\right) \exp\left(\frac{-3tk_m}{b}\right) \left(\frac{m \cdot \exp(-at) + b}{m + b}\right)^{\frac{3k_m}{ab}} \quad (7)$$



**Figure 7** Experimental data and model fit for the swelling profile of the CS-PVA hydrogel (at a CS/PVA molar ratio of 1:20). [Color figure can be viewed in the online issue, which is available at [www.interscience.wiley.com](http://www.interscience.wiley.com).]

**TABLE II**  
Values of  $k_m$  Estimated with the Simplified Model [Eq. (7)] and  $R^2$  for the Model Fit

	CS/PVA molar ratio			
	1 : 0	1 : 5	1 : 10	1 : 20
$k_m$ (mm/min)	0.0073	0.0065	0.0058	0.0045
$R^2$	0.9855	0.9881	0.9973	0.9982

The fit of eq. (3) to the change in the hydrogel bead radius with time is shown in Figure 6 for a CS/PVA molar ratio of 1 : 20. The model fits very well [coefficient of determination ( $R^2$ ) = 0.9958]. The model parameters and  $R^2$  values for other hydrogel compositions are listed in Table I.

The fit of our simplified mass-balance model to describe water transport into the hydrogel is very good, as shown in Figure 7 for a CS/PVA molar ratio of 1 : 20. Hydrogels made with different CS/PVA ratios exhibit similarly good fits. The summary of  $R^2$  for the model fit and the effective  $k_m$  values calculated are listed in Table II. The experimental data for all the hydrogels conform to the predictions of our model over the first 250 min of swelling ( $R^2 > 0.985$ ), during which more than 95% of the water transfer takes place.

The effective  $k_m$  values exhibit a clear trend of gradually decreasing with increasing PVA content in the hydrogel. This suggests that increasing the PVA content leads to higher network density and increased hindrance for water transport through the gel matrix. Therefore, the relative amount of PVA in the CS/PVA hydrogel could be used to control to some extent the rate of water transport in the hydrogel.

## CONCLUSIONS

The swelling of a CS-PVA hydrogel can be well explained by Donnan swelling equilibrium, which is governed by the osmotic pressure gradient between the inside and outside of the hydrogel due to the electrostatic charges and counterion concentration built up inside the hydrogel. The swelling and contraction of the hydrogel in solutions with different pHs and salt concentrations have confirmed this type of swelling. The swollen state and contracted state of the hydrogel have a maximum mass difference of about 13 times, and the optimal swelling ability of the hydrogel is around pH 3, regardless of the PVA content in the hydrogel. A simplified mass-transfer model, neglecting the effect of ionization, gives a good correlation between the experimental data. The effective  $k_m$  value of the water molecules decreases with increasing PVA content in the gel.

## References

1. Gregor, H. P. *J Am Chem Soc* 1948, 70, 1293.
2. Gregor, H. P. *J Am Chem Soc* 1951, 73, 642.
3. Lazare, L.; Sundheim, B. R.; Gregor, H. P. *J Phys Chem* 1956, 60, 641.
4. Rice, S. A.; Nagasawa, M. In *Polyelectrolyte Solutions: A Theoretical Introduction*; Academic: New York, 1961; p 461.
5. Horkay, F.; Tasaki, I.; Bassar, P. J. *Biomacromolecules* 2001, 2, 195.
6. Hasa, J.; Ilavsky, M.; Dusek, K. *J Polym Sci Polym Phys Ed* 1975, 13, 263.
7. Ilavsky, M.; Dusek, K.; Vacik, J.; Kopecek, J. *J Appl Polym Sci* 1979, 23, 2073.
8. Kienzle-Sterzer, C. A.; Rodriguez-Sanchez, D.; Karalekas, D.; Rha, C. K. *Macromolecules* 1982, 15, 631.
9. Brannon-Peppas, L.; Peppas, N. A. *Polym Bull* 1988, 20, 285.
10. Oppermann, W. *Angew Makromol Chem* 1984, 123, 229.
11. Brannon-Peppas, L.; Peppas, N. A. *Chem Eng Sci* 1991, 3, 46.
12. Baker, J. P.; Hang, L. H.; Blanch, H. W.; Prausnitz, J. M.; Siegel, R. A. *Polym Prepr (Am Chem Soc Div Polym Chem)* 1993, 3, 974.
13. Ricka, J.; Tanaka, T. *Macromolecules* 1984, 17, 2916.
14. Tanaka, T. *Sci Am* 1981, 124, 138.
15. Eichenbaum, G. M.; Kiser, P. F. Simon, S. A.; Needham, D. *Macromolecules* 1998, 31, 5084.
16. Firestone, B. A.; Siegel, R. A. *J Biomater Sci Polym Ed* 1994, 5, 433.
17. Gehrke, S. H.; Cussler, E. L. *Chem Eng Sci* 1989, 44.
18. Park, H.; Park, K. American Chemical Society: Washington, DC, 1996.
19. Nishi, S.; Kotaka, T. *Polym J (Tokyo)* 1989, 21, 393.
20. Guan, Y. L.; Shao, L.; Liu, J.; Yao, K. D. *J Appl Polym Sci* 1996, 62, 1253.