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Osmotic properties of polyelectrolyte hydrogels in physiological salt solutions

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Abstract

The effect of cations on the osmotic properties of chemically cross-linked sodium polyacrylate hydrogels has been investigated. The variation of the osmotic swelling pressure, shear modulus and mixing pressure is measured when Na^+ ions are substituted by different monovalent and multivalent cations. The occurrence of a reversible volume transition induced by monovalent/divalent cation exchange is discussed. A hierarchy is established in the interaction strength according to the chemical group to which the ions belong. It is shown that a Flory-Huggins type expression provides a satisfactory description of the effect of divalent cations on the osmotic behavior of polyacrylate hydrogels both below and in the vicinity of the volume transition. Analysis of the osmotic data indicates a sharp increase in the third-order interaction parameter upon introduction of divalent cations while the second order interaction parameter

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only slightly increases. The swelling kinetics of polyacrylate hydrogels was investigated in NaCl solutions and in solutions containing both NaCl and CaCl₂. In NaCl solutions gel swelling is a single exponential type process described by a collective diffusion coefficient. In the presence of CaCl₂ the swelling/shrinking behavior becomes more complex. The diffusion of ions into the network, the ion-exchange and the coexistence of swollen and collapsed states in the gel have to be considered to describe gel swelling in solutions containing ions that interact with the polymer matrix.

Introduction

Polyelectrolytes are long-chain molecules with charged side-groups of either anionic or cationic character. Properties of polyelectrolyte solutions are very complex that cannot be understood as a simple superposition of polymer and electrolyte properties. The counterions are correlated with the polyions through long-range electrostatic (Coulomb) interaction. It is just at high ionic strength, i.e., when salt ions fully screen the electrostatic interactions between macroions and counterions, where polyelectrolytes are expected to behave like neutral polymers.

Polyelectrolyte gels are three-dimensional networks, which exhibit exceptional macroscopic properties that depend on external conditions and gel composition. During the last two decades remarkable progress has been made in understanding the thermodynamic properties of these systems [1-6]. First Tanaka observed a discrete volume transition in a partially ionized polyacrylamide gel in acetone/water mixed solvent [7]. It is now well established that polyelectrolyte gels are capable of undergoing a discrete volume transition when external conditions, such as ionic composition, solvent quality, temperature, etc. are changed incrementally. This volume transition is a result of a competitive balance between a repulsive force that acts to expand the polymer network and an attractive force that acts to shrink the network. The most important repulsive force is the electrostatic interaction between the charges of the same kind. The osmotic pressure by the counterions also adds to the expanding pressure. The attractive forces can be ion-ion interactions between opposite kinds of charges, van der Waals interaction, hydrogen bonds, and hydrophobic interaction. Under suitable experimental conditions two (or more) polymer phases can coexist in the swollen network: they differ in the conformation of the chains and the concentration of the polymer [8-10].

Certain aspects of the volume transition in polyelectrolyte gels have not been explored previously. Earlier studies have not addressed explicitly the thermodynamic conditions (i.e., pH, ionic composition, ionic strength, etc.) that are likely to occur in biological systems, and may play a crucial role in certain physiological processes. Monovalent-divalent cation-exchange is important in physiological processes such as nerve excitation and muscle contraction. Recent studies unambiguously indicate that swelling occurs in many physiological systems [11,12]. Viewing nerve excitation from a physico-chemical standpoint, Tasaki has shown that synthetic polyanionic gels (e.g., polyacrylic acid gels, polymethacrylic acid gels, polysulphonic acid gels) exhibit discontinuous volume changes by using a biologically plausible mechanism of monovalent-divalent cation-exchange [11-15].

These biomimetic studies raise several important questions: How do the mobile cations interact with the charged polymer chains? How reversible is the ion-exchange process? Does the reversibility of the volume transition depend on the type and ion

valence of the cations? What are the specific thermodynamic factors that govern the swelling behavior of anionic gels during monovalent-divalent cation-exchange? How are the components of the network free energy modified by different cations?

In order to address these questions systematic thermodynamic and mechanical measurements were performed on sodium polyacrylate hydrogels swollen in solutions containing the salts of alkali metal cations (Li^+ , Na^+ , K^+ , Rb^+ , Cs^+), alkaline earth metal cations (Ca^{2+} , Sr^{2+} , Ba^{2+}) and transition metal cations (Co^{2+} , Ni^{2+}). A procedure has been developed to separate the elastic, mixing and ionic contributions of the total free energy accompanied by swelling of the network. The swelling pressure, the elastic modulus and the equilibrium volume fraction were measured while the total salt concentration and the molar ratio of monovalent to divalent cations were varied systematically in the physiological range. The extent of monovalent/divalent cation exchange was monitored in the gel. Moreover, measurements of the swelling kinetics of gels were made to estimate the relative stability of various cation/polyanion associations.

In this article we review the work performed in our laboratory on polyelectrolyte gels during the last few years. First we briefly summarize the theoretical background, the gel preparation procedure and the experimental techniques. This is followed by the description of the main experimental findings and their evaluation for gels swollen in monovalent salt solutions. Then the behavior of similar gels in solutions containing both monovalent and multivalent cations is discussed. Based on the effect of the ions on the polymer-solvent interaction parameter and the effective cross-link density of the network a hierarchy is established in interaction strength according to the chemical group to which the ions belong. A summary of the results is given in the final part of the article.

Theory

Swelling of polyelectrolyte gels

Swelling equilibrium is attained when the change in the free energy, ΔF_{tot} , reaches a minimum. In the case of a nonionic network swollen in a one component liquid ΔF_{tot} is simply the sum of the free energy of elastic deformation of the network, ΔF_{el} , and the free energy of mixing of the network chains and solvent molecules, ΔF_{mix} [16-18]. In the case of polyelectrolytes there is an additional term, ΔF_{ion} , due to the presence of the counterions. Assuming that these terms are independent we can write [16]

$$\Delta F_{\text{tot}} = \Delta F_{\text{el}} + \Delta F_{\text{mix}} + \Delta F_{\text{ion}} \quad (1)$$

In an osmotic swelling experiment the measurable quantities involve derivatives of the free energy, i.e.,

$$\Pi_{\text{tot}} = -\partial(\Delta F_{\text{tot}}/V_1)/\partial n_1 = \Pi_{\text{el}} + \Pi_{\text{mix}} + \Pi_{\text{ion}} \quad (2)$$

where Π_{tot} is the swelling pressure of the gel, Π_{el} , Π_{mix} and Π_{ion} are the elastic, mixing and ionic contributions of Π_{tot} , respectively, V_1 is the molar volume of the solvent, and n_1 is the number of moles of solvent.

Several polyelectrolyte models have been proposed, differing in the treatment of the elastic, mixing and electrostatic free energy components. For networks made of flexible

chains the elastic pressure, Π_{el} , can be estimated from the theory of rubber elasticity [16,17]

$$\Pi_{el} = -ARTv \phi^{1/3} = -G \quad (3)$$

where v is the concentration of the elastic chains, ϕ is the volume fraction of the polymer, R is the gas constant, and T is the absolute temperature. The prefactor, A , depends on the functionality of the junctions. Π_{el} can be expressed by the shear modulus, G , of the gel.

The osmotic pressure, Π_{mix} , due to mixing of network chains and solvent molecules, can be given by the Flory-Huggins equation [16]

$$\Pi_{mix} = -RT[\ln(1-\phi) + \phi + \chi\phi^2] \quad (4)$$

where χ is the Flory-Huggins interaction parameter. In general, χ depends on polymer concentration, i.e., $\chi = \chi_0 + \chi_1\phi + \dots$

The Donnan theory predicts a difference in mobile ion concentrations inside and outside the polyelectrolyte gel [19]. This difference caused by the requirement to satisfy electroneutrality condition gives rise to an osmotic pressure difference between the gel and the equilibrium solution. A complete description of the effect of ions would also require to account for contributions due to mixing of ions with solvent molecules, and interactions between ions, polymer segments and solvent molecules [20]. Here we only consider the contribution given by the Donnan theory

$$\Pi_{ion} = RT \sum_{j=1}^N (c_j^{gel} - c_j^{sol}) \quad (5)$$

where c_j^{gel} and c_j^{sol} represent the concentrations of the ions in the gel and the equilibrium solution, respectively, and N is the number of mobile ions in the system.

For a monovalent salt (e.g., NaCl) we have

$$c_{Na^+}^{gel} c_{Cl^-}^{gel} = c_{Na^+}^{sol} c_{Cl^-}^{sol} \quad (6)$$

In the case of an anionic polyelectrolyte gel (e.g., sodium polyacrylate) the total amount of Na^+ ions in the gel equals to the sum of Cl^- that moved into the gel, and the amount of Na^+ needed to neutralize the charged groups

$$c_{Na^+}^{gel} = c_{Cl^-}^{gel} + i\phi/V_m \quad (7)$$

where i is the degree of ionization, and V_m is the molar volume of the monomer unit of the polymer. The concentration of the salt inside the swollen network can be obtained from the relation

$$c^{gel}/c^{sol} = c^{sol}/(c^{gel} + i\phi/V_m) \quad (8)$$

Polyelectrolyte behavior is governed by the ratio of the electrostatic energy between two neighboring charges on the chain to the thermal energy. In the classical Debye-Hückel theory of polyelectrolytes the effect of charged sites on the molecule is considered by an electrostatic free energy term [21]. In Manning's model some of the counterions remain bound to the chain [22]. Counterion condensation occurs when the distance between charges along the polymer chain is small compared to length scale set by the electrostatic interactions (Bjerrum length). As the density of charges on the polymer chains is increased, the relative importance of short-range attractive (van der Waals) interactions and long-range repulsive electrostatic interactions changes. The relevant characteristic length scale is defined by the Bjerrum length

$$\lambda = e^2/\epsilon kT \quad (9)$$

where e is the electron charge, ϵ is the permittivity of water, and k is the Boltzmann constant. When the distance, l , between neighboring charges is much larger than the Bjerrum length ($l/\lambda \gg 1$), counterions are uniformly distributed throughout the gel. Consequently, swelling is driven by their osmotic pressure. When ($l/\lambda < 1$), counterions are closely bound to the chains (counterion condensation).

Theoretical models [22-24] predict that counterions are bound to the polyelectrolyte chain when the charge density exceeds a critical threshold value, α , which can be estimated using the equation

$$\alpha = l/\lambda \quad (10)$$

where l is equal to the monomer length, i.e. 2.5 Å, and $\lambda = 7$ Å in water at 25 °C. This yields $\alpha = 0.36$.

Kinetics of gel swelling

The kinetic theory of gel swelling, based on the concept of cooperative diffusion of the network polymer in a continuous medium, was developed by Tanaka and Fillmore [25], and Li and Tanaka [26]. According to this theory

$$u(r, t)/u(r, \infty) = \sum_i B_i \exp[-t/\tau_i] \quad (11)$$

where $u(r, t)$ is the displacement vector, t is the swelling time, and τ_i is the relaxation time. The numerical factor B_i depends on the geometry of the gel and the ratio of the shear modulus G over the longitudinal osmotic modulus M_{os} . This theory views the swelling as a combination of pure diffusion and pure shear relaxation processes. The important role of the shear modulus is to keep the system in shape. Since during a shear relaxation process there is no relative motion and, consequently, no friction between the polymer and the solvent, the gel can instantaneously adjust its shape, thereby minimizing the nonisotropic deformation.

At large t the slowest term of eq.11 dominates. For spherical gels the theory predicts

$$d_t = d_{\infty} + [d_0 - d_{\infty}] B_1 \exp(-t/\tau_1) \quad (t > \tau_1) \quad (12)$$

where d_t is the diameter of the gel at time t , d_0 and d_∞ is the initial and final (equilibrium) diameter, respectively, and τ_1 is the relaxation time of the slowest mode in the swelling process.

Since gel swelling is a diffusion controlled process, the rate of swelling (or shrinking) depends on the size of the sample. The smaller the gel, the quicker the gel swells. The theory predicts that if the characteristic size of the gel is increased by a factor r , then the relaxation time increases by the factor r^2 . The collective diffusion coefficient D_c is given by

$$D_c = M_{os}/f = a^2/(\beta_1^2 \tau_1) \quad (13)$$

where f is the friction coefficient, a is the radius of the gel, and β_1 is the function of G/M_{os} . For typical polymer gels D_c is in the order of $10^{-6} - 10^{-7} \text{ cm}^2/\text{s}$.

Experimental

Gel preparation

Sodium polyacrylate gels were made by free-radical copolymerization of partially neutralized acrylic acid and N,N' -methylenebis(acrylamide) cross-linker in aqueous solution according to a procedure described previously [27]. The monomer concentration was 30% (w/w), and 35% of the monomers were neutralized by sodium hydroxide before polymerization. Dissolved oxygen was removed by bubbling nitrogen through the solution. Then ammonium persulfate (0.5 g/L) was added to initiate the polymerization reaction. Gelation was carried out at 80 °C.

Gel beads were made by polymerization in silicone oil (viscosity: 1000 cPs), that was previously degassed with nitrogen. Spherical droplets (diameter < 1 mm) of the mixture were injected into the silicone oil. After gelation gel samples were completely neutralized, and washed in deionized water to remove all extractable materials (e.g., sol fraction). Water was renewed every day for two weeks.

For the mechanical measurements cylindrical gel specimens (1 cm height, 1 cm diameter) were made in a special mold using the same cross-linking procedure. Gel cylinders were neutralized and washed for several weeks with deionized water before the experiments.

Osmotic deswelling measurements

Osmotic deswelling of polyacrylate gels was induced by aqueous solutions of poly(vinyl pyrrolidone) (PVP, molecular weight: 29 kDa). The osmotic pressure of the PVP is known from independent measurements [28,29]. The swollen network was separated from the solution by a semipermeable membrane, which prevented the penetration of the polymer molecules into the gel. At equilibrium, the swelling pressure of the gel inside the dialysis bag is equal to the osmotic pressure of the PVP solution outside. The size and the weight of the gel samples were measured when equilibrium was attained. The reversibility of the deswelling process was checked by transferring the deswollen gels into PVP solutions of different concentrations. No significant difference was found between swelling degrees obtained by decreasing or increasing the osmotic pressure of the equilibrium solution.

When gel beads were equilibrated with salt solutions it was assumed that the salt concentration in the liquid phase surrounding the gel sample was unchanged (infinite bath).

Swelling kinetics measurements

Gel beads prepared according to the procedure described above were put into a petri dish containing salt solution. The diameter of the gel was measured as a function of time under a Leica MZ 12 stereomicroscope using a calibrated scale. Photographs were captured using Polaroid Digital Microscope Camera, and analyzed using *National Institutes of Health Image Program* (version 1.62). Swelling kinetics measurements were carried out in 40 mM NaCl solutions containing different amounts of CaCl₂ at room temperature.

Elastic modulus measurements

Uniaxial compression measurements were performed on gel cylinders in equilibrium with salt solutions using a TA.XT2I HR Texture Analyser (Stable Micro Systems, UK). This apparatus measures the deformation (± 0.001 mm) as a function of the applied force (± 0.01 N). Measurements were performed at deformation ratios $0.7 < \Lambda < 1$. Typical sample sizes were: height 0.5 to 2 cm, diameter 0.5 to 2 cm. The elastic (shear) modulus, G , was calculated from the nominal stress, σ (force per unit undeformed cross-section), using the equation [17]

$$\sigma = G (\Lambda - \Lambda^{-2}) \quad (14)$$

Both swelling and mechanical measurements were carried out at 25 ± 0.1 °C.

Results and discussion

Swelling equilibrium in solutions of alkali metal salt solutions

Figure 1 shows the variation of the swelling degree of a sodium polyacrylate gel in solutions of alkali metal salts (LiCl, NaCl, KCl, RbCl, CsCl). (It should be noted that the gels used throughout this work were completely neutralized, i.e., prior to the swelling experiments all H⁺ ions of the carboxylate groups were exchanged for Na⁺. Thus, the total cation content in the system is the sum of the amounts of Na⁺ counterions from the gel and the cation from the added salt.)

The highest swelling degree is observed in pure water. In this case, counterions remain inside the gel to neutralize the fixed charges on the network chains. The driving force of the swelling is the presence of free (osmotically active) counterions. When salt is added to the surrounding solution free ions diffuse from the solution into the network. The overall concentration of free ions in the gel is now higher than before, but the difference between ion concentrations inside and outside is diminished. Consequently, the driving force of swelling decreases with increasing concentration of the added salt. In **Figure 1** it can also be seen that the effect of the five different salts on the swelling equilibrium concentration of the gel only slightly depends on the chemical nature of the cation. The observed deswelling increases with decreasing hydrated ionic radius of the alkaline cation and follows the Hoffmeister series (lyotropic series), i.e., Cs⁺ > Rb⁺ > K⁺ > Na⁺ > Li⁺.

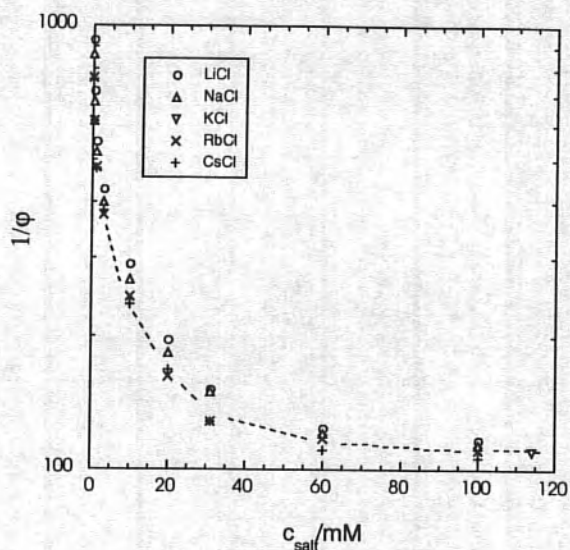


Figure 1. Effect of monovalent salts on the equilibrium swelling degree ($1/\phi$) of sodium polyacrylate gels. Dashed curve is guide for the eye.

In **Figure 2** the pressure contribution, Π_{ion} , due to the concentration difference of salt ions between the gel and the external solution calculated by eqs. 5 and 8 is plotted against Π_{tot} obtained from direct osmotic deswelling measurements performed on

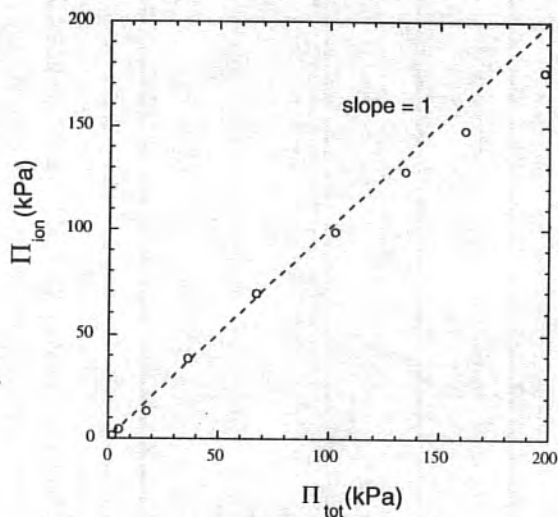


Figure 2. Swelling pressure Π_{ion} obtained from the concentration of ions in the gel plotted against swelling pressure Π_{tot} determined from direct osmotic deswelling experiments performed on salt-free gels.

salt-free gels. The values at low swelling pressures ($\Pi < 100$ kPa) are scattered around a theoretical straight line of slope unity indicating the equivalence of the response of the network in the two experiments. At higher values of Π_{ion} (i.e. at lower swelling ratios), however, the measured swelling pressure exceeds that calculated on the basis of the Donnan theory. This is expected since the Donnan model fails to account for factors, such as electrostatic interaction between the charged groups on the chains, and ion-ion interaction between the salt and the charged network.

Figure 3 shows the swelling pressure Π_{tot} and its elastic Π_{el} and mixing Π_{mix} components for a sodium polyacrylate gel measured at constant ionic concentration (c_{salt} : 40 mM NaCl solution). Π_{tot} was obtained from osmotic deswelling measurements, Π_{el} was estimated from the shear modulus ($\Pi_{\text{el}} = -G$) and Π_{mix} was calculated using the relationship $\Pi_{\text{mix}} = \Pi_{\text{tot}} + G$. Π_{tot} and Π_{mix} increases while Π_{el} decreases with increasing polymer volume fraction. The continuous curve is the least squares fit of eq. 15 to the Π_{mix} data

$$\Pi_{\text{mix}} = -RT[\ln(1-\phi) + \phi + \chi_0\phi^2 + \chi_1\phi^3] \quad (15)$$

where χ_0 and χ_1 are allowed to vary. The fit yields for the interaction parameters $\chi_0 = 0.448 \pm 0.001$ and $\chi_1 = 0.21 \pm 0.01$.

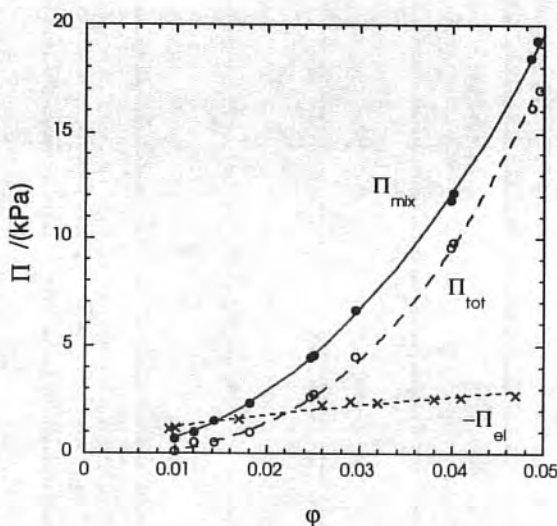


Figure 3. Variation of the swelling pressure Π_{tot} and its elastic Π_{el} and mixing Π_{mix} components with the volume fraction of the polymer in a sodium polyacrylate hydrogel swollen in 40 mM NaCl solution.

Kinetics of gel swelling in NaCl solution

In **Figure 4** are presented swelling kinetics data measured in 40 mM NaCl solution for spherical gel samples of different diameters. These samples exhibit qualitatively similar behavior: the swelling degree monotonically increases with time

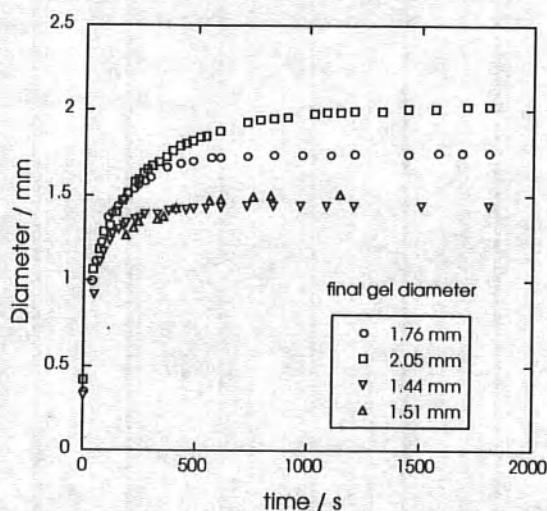


Figure 4. Swelling kinetics data for polyacrylate gels in 40 mM NaCl solution.

and asymptotically approaches a plateau. It can also be seen that the time needed to reach equilibrium strongly depends upon the size of the gel bead. Smaller gels swell faster.

In Figure 5 is shown the variation of the reduced gel diameter d/d_0 as a function of the reduced time t/τ_1 for the same gels as in Figure 4 (upper curves) and for gels swollen in 100 mM NaCl solutions (lower curves). At each salt concentration the data points lie

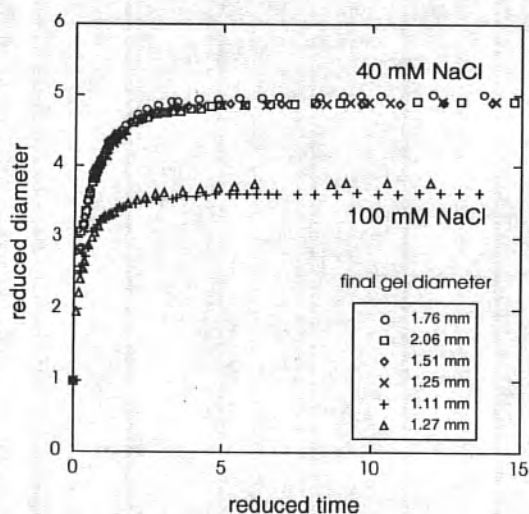


Figure 5. Reduced gel diameter d/d_0 vs reduced time t/τ_1 for polyacrylate gels swollen in 40 mM NaCl and 100 mM NaCl solutions.

on the same curve. The height of the plateau region, corresponding to the equilibrium swelling degree of the fully swollen gels, decreases with increasing salt concentration.

The analysis of the swelling kinetics data was performed using the linearized form of eq. 12

$$y = \ln [(d_{\infty} - d_t)/(d_{\infty} - d_0)] = \ln B_1 - t/\tau_1 \quad (16)$$

From the intercept of the long-time linear extrapolation of the logarithmic plot B_1 can be determined and from the slope of the straight line τ_1 . Once B_1 is known β_1 can be found since both B_1 and β_1 depend on G/M_{os} , and the dependence established numerically for spheres is available in the literature [26].

In **Figure 6** the quantity y is plotted as a function of the time for gels with different initial diameters. At higher values of t all gels exhibit a linear behavior as predicted by eq. 16. In agreement with the expectation the relaxation time decreases with decreasing gel size. B_1 is, however, the same for the four gel samples shown in **Figure 6**, indicating that the ratio of the moduli G/M_{os} is independent of the gel size. The values of τ_1 and B_1 obtained from the fits can be used to calculate D_c .

The collective diffusion coefficient D_c is presented in **Figure 7** for gels of different sizes. In the figure are also displayed the values of D_c reported for weakly charged polyacrylate gels [4] and uncharged poly(acrylamide) hydrogels [25] swollen in (salt free) water. It appears that D_c is larger for charged gels than for their neutral counterpart.

It is important to note that the ratio of the shear modulus to the longitudinal osmotic modulus can also be obtained from equilibrium swelling pressure and shear modulus measurements. The longitudinal osmotic modulus of the gel is given by [30]

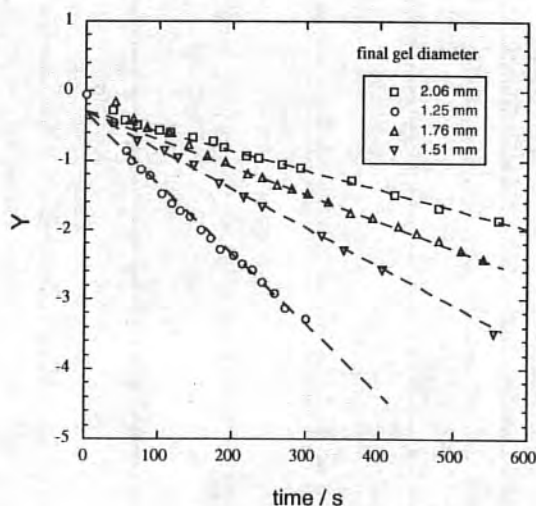


Figure 6. Variation of y in eq. 16 as a function of the swelling time for sodium polyacrylate gels swollen in 40 mM NaCl solution. Dashed curves are least squares fits to eq. 16.

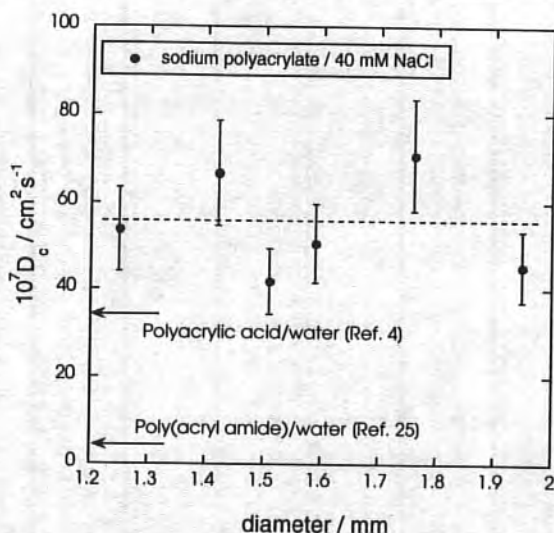


Figure 7. Collective diffusion coefficient D_c of different hydrogels.

$$M_{os} = \varphi(\partial\Pi_{tot}/\partial\varphi) + (4/3)G \quad (17)$$

For the particular gel sample investigated here $G/M_{os}(\text{swelling pressure}) = 0.34$ was found which is in reasonable agreement with the value $G/M_{os}(\text{kinetics}) = 0.32$ determined from swelling kinetics measurements.

Swelling equilibrium in salt solutions containing both monovalent and multivalent cations

Figure 8 shows the variation of the swelling degree ($1/\varphi$) of sodium polyacrylate hydrogels as a function of the salt concentration, c_{salt} in different salt solutions. The first data point on the y-axis corresponds to the degree of swelling in 40 mM NaCl solution. In general, salt addition leads to gel contraction because ions screen repulsive interactions between charged monomer units. These gels exhibit substantially different behavior in solutions containing monovalent (NaCl), divalent (CaCl_2 , SrCl_2 , NiCl_2 , CoCl_2), and trivalent cations (CeCl_3 , LaCl_3). In NaCl solution the variation of the swelling degree is relatively weak. In the presence of divalent cations at a 'critical concentration' (or critical ratio of divalent to monovalent cations) a reversible volume transition occurs. The sharp volume change indicates that the transition is a highly cooperative process. Trivalent cations shift the transition concentration toward lower salt concentrations and bind practically irreversibly to the polyanion.

Volume change results from the interplay of two main effects: attractive interactions between polymer segments that tend to shrink the gel, and repulsion between similarly charged groups (either charged units of the polymer network or mobile ions). Therefore, any change in the mixing and elastic interactions, and in the degree of ionization of the network chains should be reflected by a change in the corresponding free energy. There

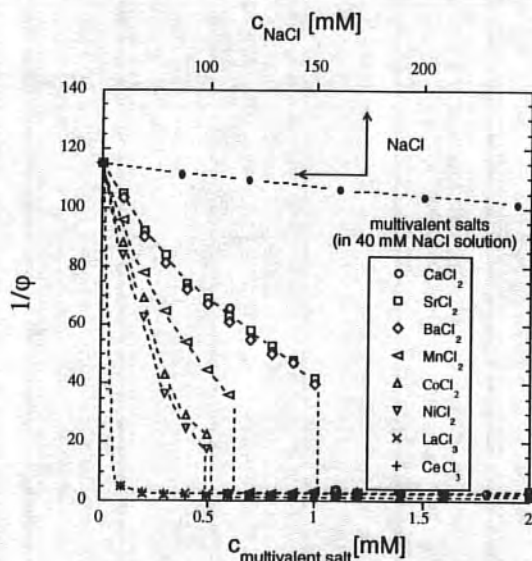


Figure 8. Volume changes of polyacrylate hydrogels induced by addition of different salts. Dashed curves are guide for the eye.

is, however, no well-established relationship between the network free energy and the ionic composition of the surrounding solution.

To reveal the effect of added salts we made an attempt to separate the elastic and mixing contributions of the free energy. It is reasonable to assume that addition of multivalent cations form bridges between the charged groups of the polyacrylate chains. In **Figure 9** is shown the dependence of the shear modulus on the equilibrium swelling degree measured in different salt solutions.

At moderate and low swelling degrees G varies according to the prediction of the theory of rubber elasticity, i.e.,

$$G = G_0 \phi^{1/3} \quad (18)$$

where G_0 is a constant ($G_0 = ARTv$). Deviation from the theoretical dependence can be observed only at the largest swelling ratios, where finite extensibility of the network chains becomes dominant, and network elasticity can no longer be described by the Gaussian elasticity theory. In these systems the elastic pressure term can be given by theories based on non-Gaussian chain statistics [17,18]. A similar upturn in the elastic modulus at high swelling degrees was observed in ionized polyacrylamide and acrylamide-sodium acrylate copolymer gels by others [4,31].

If the multivalent cation acts as a cross-linker it should affect the shear modulus of the gel. In the presence of Ca^{2+} ions all data points fall on a single curve, indicating that the elastic modulus is a function of the polymer concentration only, i.e., Ca^{2+} does not modify the effective cross-link density of the gel. Alkaline earth metal ions cause gel contraction but they do not form additional cross-links. When CaCl_2 is replaced by

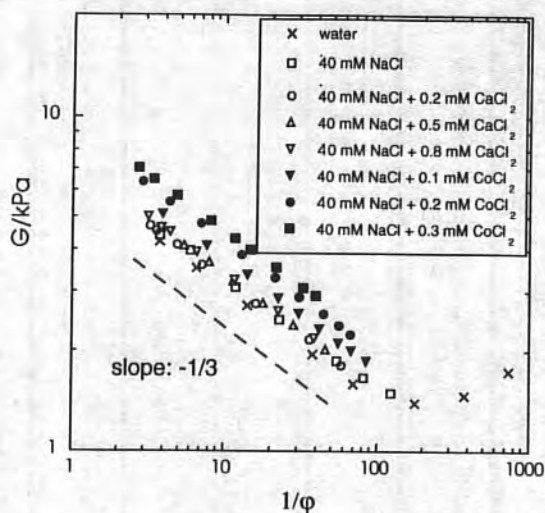


Figure 9. Dependence of the shear modulus on the swelling degree ($1/\phi$) of sodium polyacrylate gel in equilibrium with various salt solutions, and water.

CoCl_2 (or NiCl_2) the value of G increases with increasing salt concentration. A probable explanation of the increase of the elastic modulus is complex formation between the transition metal ions (Co^{2+} , Ni^{2+}) and the polyacrylate anion. Complex formation is, however, reversible, i.e., by decreasing cation concentration G decreases.

In order to gain insight into the nature of the interaction between Ca^{2+} ions and the polyanion the extent of the $\text{Ca}^{2+}/\text{Na}^+$ exchange was measured in a gel as a function of the CaCl_2 concentration of the surrounding solution using plasma optical emission and flame atomic absorption techniques (**Figure 10**) [32].

It is apparent that the amount of both ions varies smoothly and continuously within the gel despite the discontinuous change in the gel volume: the Ca^{2+} concentration increases and the Na^+ concentration decreases. The total amount of charges, however, remains constant as required by the condition of electroneutrality. It can be seen that more than 80% of the Na^+ ions is replaced by Ca^{2+} ions at a CaCl_2 concentration of 0.4 mM, while the volume transition occurs at 1 mM CaCl_2 concentration (vertical dashed line). This result indicates strong interactions between the Ca^{2+} ions and the polyacrylate anion. The fact that the Ca content and the effective cross-link density (see **Figure 9**) remains practically unchanged during the transition suggests that Ca^{2+} ions primarily affect Π_{mix} .

It is reasonable to expect that specific interactions between cations and the carboxylate groups modify the mixing contribution of the network free energy. Π_{mix} as a function of ϕ is shown in **Figure 11** for polyacrylate gels swollen in NaCl solutions containing different amounts of CaCl_2 or CoCl_2 .

It can be seen that both quality and concentration of the cations affect the mixing pressure. Π_{mix} decreases with increasing concentration of divalent cations and depends on the chemical type of the cation. At identical salt concentrations the effect of Co^{2+} significantly exceeds that of Ca^{2+} . The lines through the experimental points are the

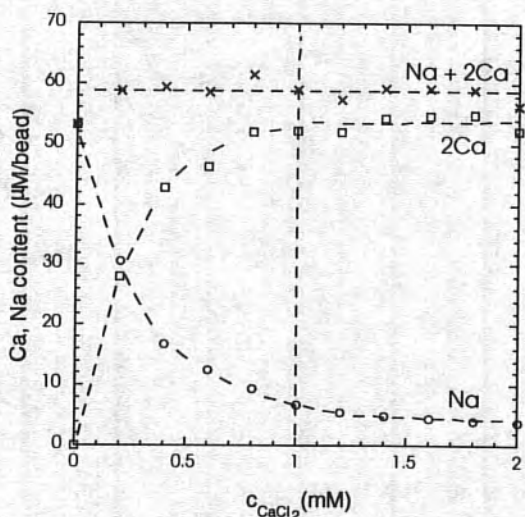


Figure 10. Variation of the amount of Ca^{2+} (squares), Na^+ (circles) and the sum of these two cations (crosses) in a polyacrylate gel as a function of the CaCl_2 concentration in the equilibrium solution. (The NaCl concentration in the solution was 40 mM.)

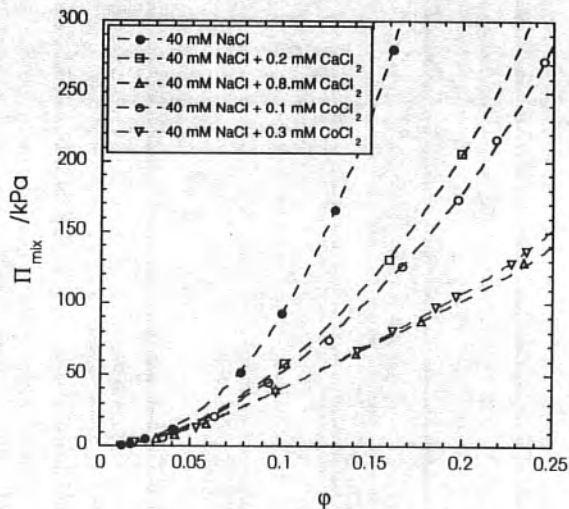


Figure 11. Mixing pressure, Π_{mix} , versus polymer volume fraction, ϕ , plots for polyacrylate hydrogels in different salt solutions. The dashed lines show the fits of eq 15 to the experimental data.

least squares fits to equation 15. As shown in **Figure 12**, the addition of calcium causes an initial jump in the value of χ_1 and thereafter a very slow increase, while χ_0 displays a weak increase over the entire concentration range explored [33].

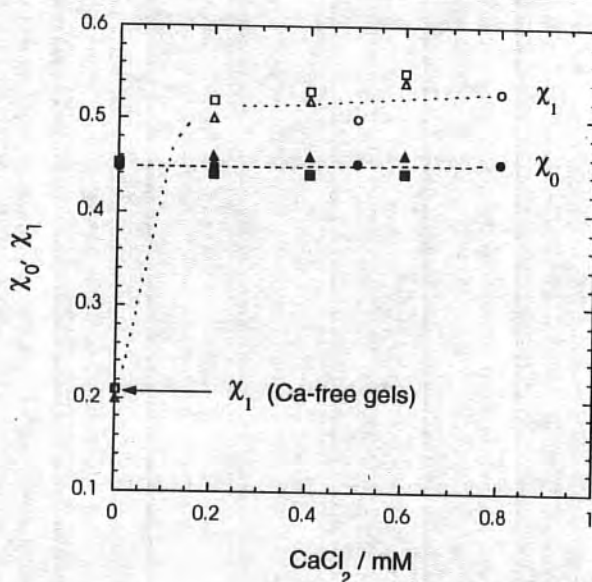


Figure 12. Variation of χ_0 (filled symbols) and χ_1 (open symbols) as a function of the CaCl_2 concentration for polyacrylate hydrogels swollen in sodium chloride solutions (squares: 10 mM NaCl, circles: 40 mM NaCl, triangles: 100 mM NaCl).

The experimentally determined concentration dependence of χ_0 and χ_1 allows us to evaluate the variation of the longitudinal osmotic modulus M_{os} as a function of the calcium concentration [34]. This quantity is important to understand the thermodynamics of volume transition induced by multivalent cations. The data shown in **Figure 13** indicate an abrupt change close to the calcium concentration at which the volume transition occurs (vertical dashed line in the figure). At the critical point of the volume transition a divergence of the osmotic compressibility is expected. This corresponds to a softening of the gel, because the osmotic compression modulus $K_{os}(= \phi \partial \Pi / \partial \phi)$ vanishes. In the figure is also shown the variation of the shear modulus G as a function of the CaCl_2 concentration. This quantity varies smoothly at the transition.

Based on the effect of ions on the apparent cross-link density and the interaction parameter a hierarchy can be established in the interaction strength according to the chemical group to which the ions belong. Alkali metal ions and alkaline earth metal ions do not affect considerably the static elastic properties of polyacrylate hydrogels. The reduction of the swelling degree with increasing concentration of alkaline earth metal salts is primarily due to modification of the mixing free energy. Experimental data indicate that addition of CaCl_2 has little effect on χ_0 , but changes χ_1 . Transition metal cations (Co^{2+} , Ni^{2+}) form stronger complexes with the polyanion, which act as additional cross-links as verified by elastic modulus measurements. In these gels cations affect both elastic and mixing free energy terms. Trivalent cations (La^{3+} and Ce^{3+}) bind practically irreversibly to the polyanion.

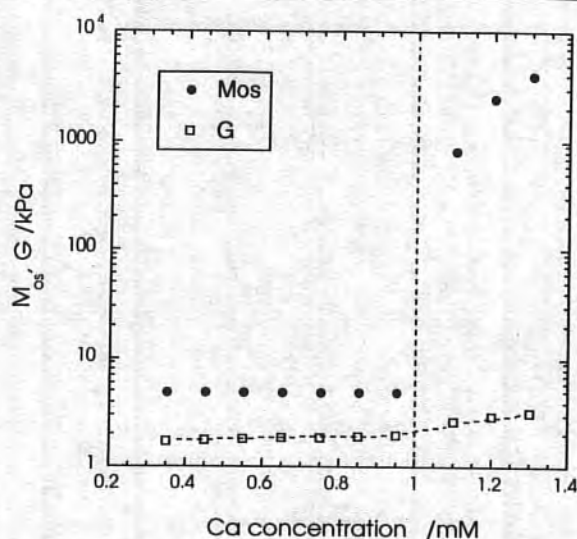


Figure 13. Dependence of the longitudinal osmotic modulus M_{0s} on the CaCl_2 concentration for a polyacrylate hydrogel. The vertical dashed line indicates the CaCl_2 concentration at which volume transition occurs.

Kinetics of gel swelling/shrinking in salt solutions containing divalent cations

The presence of divalent cations in the solution changes the swelling/shrinking kinetics of polyacrylate hydrogels. **Figure 14** shows the variation of the swelling degree after addition of CaCl_2 to the surrounding 40 mM NaCl solution. In the shrinking process three different stages can be clearly distinguished. In the first stage the swelling degree decreases slowly, practically linearly with time. During this process the Ca concentration progressively increases from the surface of the gel to the center. At a certain Ca concentration a volume transition occurs causing further shrinking. First a collapsed layer is formed on the surface. Then this layer expands as the ion exchange front moves towards the center. In this stage the collapsed network coexists with the swollen gel.

Figure 15 shows the reswelling of the same (collapsed) polyacrylate gel in 40 mM NaCl solution. First the Ca^{2+} ions diffuse from the gel into the surrounding NaCl solution, which produces a slight continuous increase in the swelling degree of the gel. When the Ca concentration in the gel falls below the transition concentration, a rapid increase in the swelling degree occurs. This is followed by a plateau stage where the network swells further while the remaining Ca^{2+} leaves the gel.

Measurement of the swelling rate provides a simple way to estimate the relative 'stability' of the collapsed state of the gel [35]. **Figure 16** compares the rate of water uptake of polyacrylate gel beads containing various multivalent cations. (To ensure a fair comparison between the swelling rates prior to the swelling experiment identical gel beads were equilibrated with salt solutions of concentration 40 mM NaCl and 2 mM of the corresponding multivalent salt. Then the collapsed gel beads were transferred into

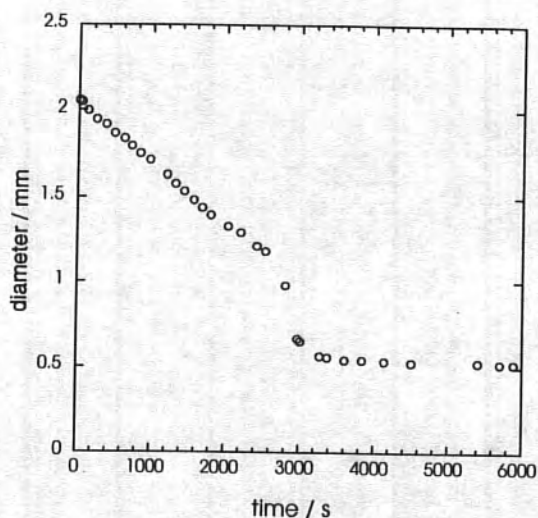


Figure 14. Kinetics of shrinking of a polyacrylate hydrogel (swollen in 40 mM NaCl solution) in 10 mM CaCl_2 solution. (The CaCl_2 was dissolved in 40 mM NaCl).

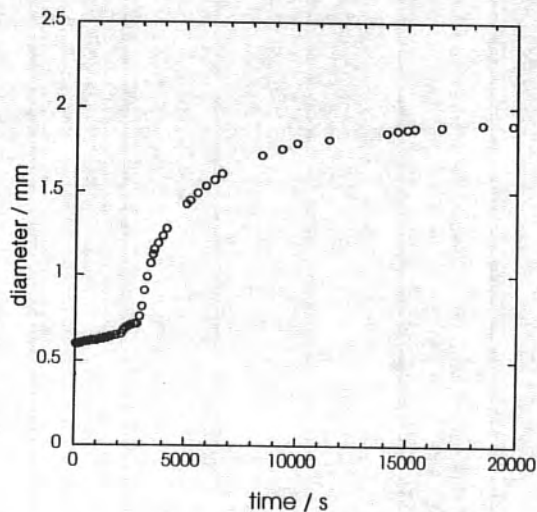


Figure 15. Kinetics of swelling of a polyacrylate gel deswollen in 10 mM CaCl_2 solution. The gel was reswollen in 40 mM NaCl solution.

40 mM NaCl solution.) There are notable differences among the swelling rates: the water uptake of gels deswollen in solutions of alkaline earth metal salts (CaCl_2 , SrCl_2) is the fastest, followed by gels containing transition metal cations (Co^{2+} , Ni^{2+}). In the case of trivalent cations no appreciable increase in the swelling degree was observed even after 3-4 weeks. On the basis of the swelling curves shown in Figure 16 the stability of

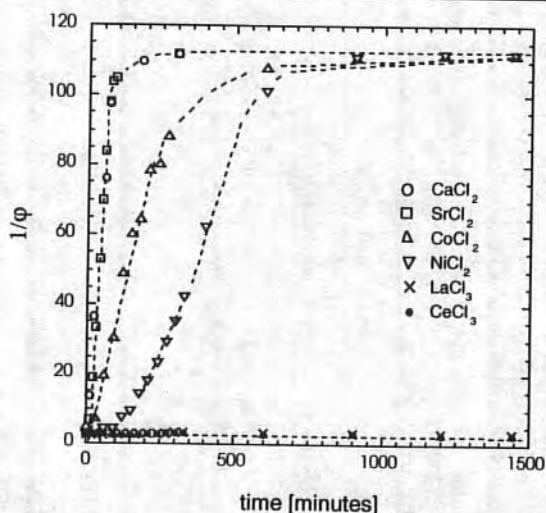


Figure 16. Kinetics of swelling of polyacrylate gels deswollen in different multivalent salt solutions. The gels were reswollen in 40 mM NaCl solution.

the collapsed state varies in the order $\text{La}^{3+} \approx \text{Ce}^{3+} > \text{Ni}^{2+} > \text{Co}^{2+} > \text{Ca}^{2+} \approx \text{Sr}^{2+}$. These results are in qualitative agreement with the osmotic and mechanical observations discussed in the previous section.

Conclusions

The effect of different cations on the osmotic properties and the swelling kinetics of fully neutralized polyacrylate hydrogels was investigated. These gels exhibit reversible volume changes in solutions containing both monovalent and divalent cations in the biologically relevant concentration range.

A hierarchy was established in the interaction strength according to the chemical group to which the ions belong. Alkali metal ions (Li^+ , Na^+ , K^+ , Rb , Cs^+) move freely all over the entire network, alkaline earth metal ions (Ca^{2+} , Sr^{2+} , Ba^{2+}) promote association of the polymer chains, but these associations are relatively weak. Transition metal ions (Co^{2+} , Ni^{2+}) form stronger (but not irreversible) bridges between the network chains. Trivalent cations (La^{3+} and Ce^{3+}) bind practically irreversibly to the polyanion.

Addition of multivalent cations to polyacrylate gels swollen in NaCl solution leads to a volume transition. The repulsion between the network chains is decreased because multivalent ions more efficiently compensate the charge of the polyanion. Due to the presence of charged groups these ions are localized near the polymer chains. Large number of such condensed counterions could bring chains together, since neighboring chains might share multivalent ions.

In the volume transition induced by $\text{Ca}^{2+}/\text{Na}^+$ exchange Ca^{2+} ions preferentially replace condensed Na^+ ions and modify the effective thermodynamic interaction between the polymer and the solvent. The reversible nature of the volume transition and the absence of measurable effect of calcium on the elastic modulus indicate that calcium

binding is not permanent. More likely Ca^{2+} ions promote weak association of the network chains.

The Flory-Huggins formalism provides a satisfactory empirical description of the effect of Ca^{2+} ions on the osmotic properties both below and in the vicinity of the volume transition region. Ca^{2+} ions primarily affect χ_1 that increases suddenly when Ca^{2+} is introduced. The subsequent gradual increase of this parameter with increasing CaCl_2 concentration of the surrounding solution is sufficient to create the conditions for volume transition.

The swelling kinetics of sodium polyacrylate gels in NaCl solution is characterized by a collective diffusion coefficient, which is independent of the initial size of the gel beads. In NaCl solutions containing Ca^{2+} ions the swelling/shrinking behavior is more complex and depends on the initial state of the gel. When a gel initially swollen in NaCl solution is immersed in a salt solution that contains CaCl_2 three different stages can be distinguished in the shrinking process. In the first stage the swelling degree decreases slowly with time. This is followed by a sudden shrinking due to the volume transition. Then gel contraction continues until the fully collapsed state is reached. When the gel is swelling from the collapsed state in NaCl solution a weak initial increase in the swelling degree precedes the steep increase accompanied by the volume transition. The last stage of the swelling process is the slow absorption of liquid as the Ca^{2+} concentration gradually decreases in the gel. Since a certain combination of monovalent and divalent ions should be present to induce volume transition it is necessary to take into account the coexistence of swollen and collapsed states in the description of the swelling and contraction of these gels.

Although the present work is confined to polyacrylate hydrogels it is likely that the behavior described in this paper is common in many other polyelectrolyte gels. Although the molecular mechanism responsible for the volume transition is not fully understood yet, the present results clearly indicate the important role of ion exchange and ion diffusion in the development of complex structures consisting of coexisting shrunken and swollen regions. Understanding the organization of charged macromolecules in nearly physiological salt solutions may also shed light on the mechanism of structure formation in biological systems, e.g., organization of nucleic acids or other structural elements of the cell or the extracellular matrix.

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