

Calcium Induced Volume Transition in Polyelectrolyte Gels

Ferenc Horkay,^{1*} Peter J. Basser,¹ Anne-Marie Hecht,² Erik Geissler²

¹Section on Tissue Biophysics and Biomimetics, Laboratory of Integrative and Medical Biophysics, National Institutes of Health, Bethesda, MD 20892, USA

²Laboratoire de Spectrométrie Physique CNRS UMR 5588, Université J. Fourier de Grenoble, B.P.87, 38402 St Martin d'Hères, France

Summary: The osmotic properties and the small angle neutron scattering (SANS) behaviour of fully neutralized sodium polyacrylate gels are investigated in the presence of calcium ions. Analysis of the SANS response displays three characteristic length scales, two of which are of thermodynamic origin, while the third, associated with the frozen-in structural inhomogeneities, is static. The SANS results are consistent with direct osmotic observations which indicate that the thermodynamic properties cannot be adequately described by a single correlation length. The concentration dependence of the osmotic pressure displays a power law behaviour with an exponent that decreases with increasing calcium concentration.

Keywords: gels; neutron scattering; osmotic pressure; polyacrylate hydrogel; volume transition

Introduction

Phase transitions in polyelectrolyte systems often result in complex hierarchical structures. These structures are important in applications ranging from improved mechanical performance to specific optical, electrical and biological properties. Charged polymers having hierarchically ordered structures have great significance for biomedical uses, such as drug delivery systems or tissue scaffold materials. In general, different kinds of interactions (van der Waals, electrostatic, hydrogen bonding, etc.) play a role in driving the formation of these structures.

Recent observations^[1] indicate that swelling occurs in many physiological systems and plays a crucial role in physiological processes such as nerve excitation, muscle contraction, and cell locomotion. Previous studies on model polyelectrolyte gels have not addressed explicitly the thermodynamic conditions (ionic strength, ionic composition, etc.) that occur in biological systems. Only a few investigations have been performed on neutralized polyelectrolyte gels in solutions containing multivalent cations.^[1–3] We found that the addition of multivalent cations

to sodium polyacrylate gels is accompanied by a discrete volume transition.^[4-6] This transition, which occurs when the majority of the Na^+ counterions is replaced by Ca^{2+} ions, is reversible. Such reversibility implies that the Ca^{2+} ions are not strongly bound by the polyanion, but rather form weak interchain associations.

The aim of the present study is to identify the characteristic length scales of the different structural elements that define the sodium polyacrylate gel system in the course of the volume transition induced by the $\text{Ca}^{2+}/\text{Na}^+$ ion exchange process. We report SANS measurements over a wide range of wave vector q on these hydrogels containing different amounts of calcium. The SANS measurements are complemented by osmotic swelling pressure measurements on identical gel samples. Our intention is to distinguish those features that affect the osmotic pressure from the larger scale structures that are thermodynamically inactive.

Theory

In the case of neutral polymer gels the SANS intensity can be described by an equation containing osmotic and static terms,^[7]

$$I(q) = I_{osm}(q) + I_{stat}(q) \quad (1)$$

where

$$I_{osm}(q) = \Delta\rho^2 \frac{kT\phi^2}{M_{os}} \frac{1}{(1 + q^2\xi^2)} \quad (2)$$

Here q is the transfer wave vector, $\Delta\rho^2$ ($= 1.7 \times 10^{21} \text{ cm}^{-4}$) is the contrast factor^[8] between polymer and solvent, k is the Boltzmann constant, and ξ is the correlation length defining the thermal concentration fluctuations.^[9] M_{os} is the longitudinal osmotic modulus of the gel,^[10] while ϕ is the polymer volume fraction. The second term in Eq. 1 arises from concentration fluctuations frozen-in by the cross-links, which, owing to their static nature, contribute negligibly to the thermodynamics. Its functional form depends upon the particular system investigated.

Experimental

Sodium polyacrylate gels were synthesized by free-radical copolymerization from their respective monomers and the cross-linker *N,N'*-methylenebis(acrylamide) in aqueous solution as described previously.^[4] The concentration of the cross-linker was 0.3%. The acrylic acid units were first neutralized in NaOH and equilibrated with aqueous solutions of 40 mM NaCl. The concentration of CaCl₂ in the surrounding solution was then increased gradually up to 2.0 mM CaCl₂. At CaCl₂ concentrations higher than 1 mM a reversible volume transition occurs in this system.

Osmotic swelling pressure measurements were made by enclosing the gel sample in a dialysis membrane and allowing swelling equilibrium to be established in a polymer solution (polyvinyl pyrrolidone, $M_w=29,000$) of known osmotic pressure.^[11,12] A semi-permeable membrane was used to prevent penetration of the polymer into the network. When equilibrium was reached, the concentration of both phases was measured. This procedure gives for each gel the dependence of the swelling pressure upon the polymer volume fraction, ϕ .

The shear modulus of the gels was determined using a TA.XT2I HR Texture Analyser (Stable Micro Systems, UK). The measurements were performed under uniaxial compression on cylindrical specimens in equilibrium with salt solutions at deformation ratios $0.7 < \lambda < 1$.

The SANS measurements were made on the D22 instrument at the Institut Laue Langevin, Grenoble, France, and on the NG3 instrument at the National Institute of Standards and Technology, Gaithersburg, MD. The incident wavelength was 8 Å and the sample to detector distances were 17m, 6m and 3m (D22) and 13.1 m and 2.5 m (NG3). The ambient temperature during the experiments was 25 ± 0.1 °C. The gel samples were swollen in solutions of heavy water. After radial averaging, corrections for incoherent background, detector response and cell window scattering were applied.

Results and Discussion

Figure 1 shows the variation of the gel swelling degree ($1/\phi$) of a polyacrylate hydrogel as a function of the CaCl₂ concentration in the external liquid. CaCl₂ was added to the diluent (40 mM NaCl solution) surrounding each gel specimen.

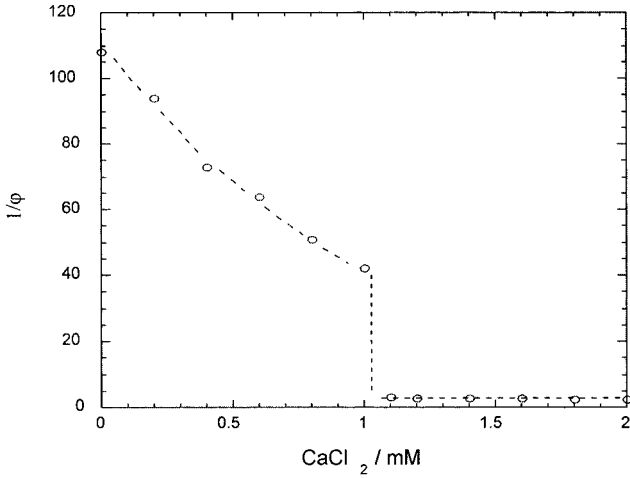


Fig. 1. Dependence of the equilibrium swelling degree of a sodium polyacrylate hydrogel on the CaCl₂ concentration in 40 mM NaCl solution.

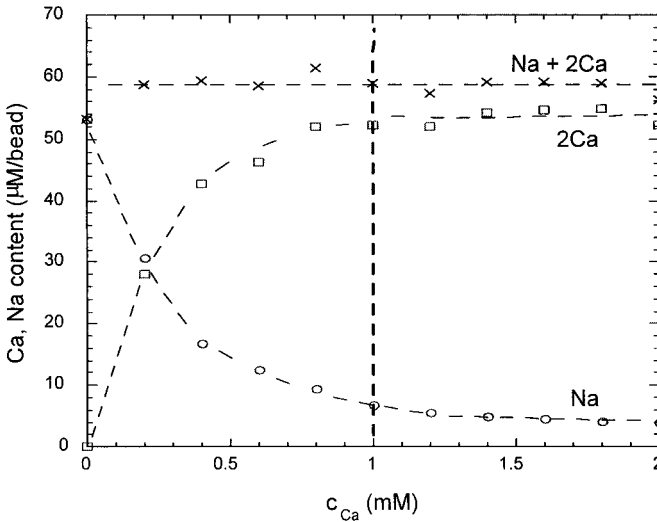


Fig. 2. Dependence of the amount of Ca²⁺ (squares), Na⁺ (circles) and the sum of these two ions (crosses) in a polyacrylate gel as a function of the CaCl₂ concentration in 40 mM NaCl solution. The vertical straight line indicates the CaCl₂ concentration at which the volume transition occurs.

It is seen that at low CaCl_2 concentrations (< 1 mM) the gel volume gradually decreases, while at approximately 1 mM a sudden contraction of the specimen occurs. This volume transition is reversible.

In Figure 2 are plotted the Ca^{2+} and Na^+ contents of a polyacrylate hydrogel as a function of the CaCl_2 concentration in the equilibrium bath. The amount of both ions varies smoothly and continuously in the gel: the Ca^{2+} concentration increases and the Na^+ concentration decreases. The total amount of these two cations, however, remains constant as required by the condition of electroneutrality.^[4] The results suggest that main effect of the calcium below the volume transition is to make the polymer uncharged and thus hydrophobic. When the concentration of the calcium ions further increases the repulsive interactions decrease and the polymer is collapsed at large length scales, as indicated by the swelling measurements.

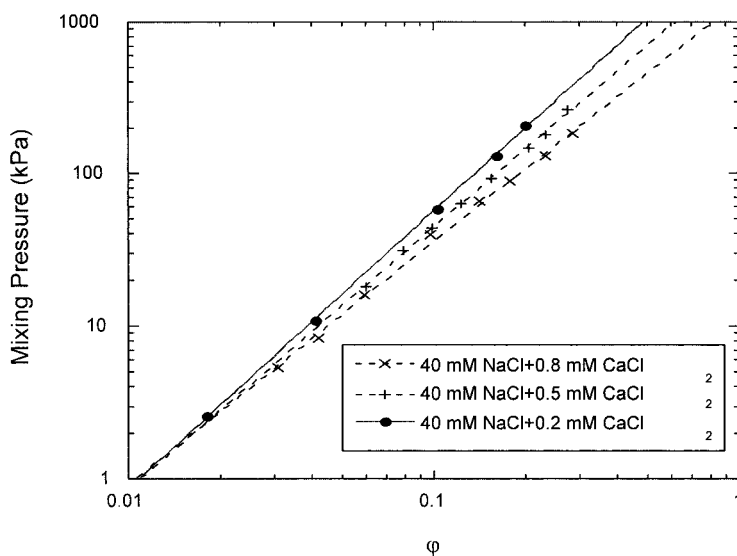


Fig. 3. Osmotic mixing pressure of polyacrylate hydrogels as a function of polymer volume fraction ϕ , in solutions containing 40 mM NaCl and different amounts of CaCl_2 . The slopes of the straight lines through the experimental data points are 1.81 (0.2 mM Ca:●), 1.71 (0.5 mM Ca: +) and 1.59 (0.8 mM Ca: ×).

In a homogeneous polyelectrolyte solution,^[13] the osmotic pressure Π is usually taken to consist of two terms. The contribution of the counterions, Π_c , is proportional to the charge density φ/A (where A is the number of monomers between effective charges on the polymer and φ is the polymer concentration) and the polymer contribution Π_p , which scales like a neutral polymer solution. Thus,

$$\Pi/kT = \varphi/A + 1/\xi^3 \quad (3)$$

where ξ is the correlation length between charged polymer subunits. The long range interactions may be expected to lead to a different concentration dependence of ξ from that in neutral polymer solutions.^[13]

In order to determine the relative importance of the two terms in Eq. (3), the osmotic pressure of the sodium polyacrylate gels was determined as a function of polymer concentration, at three different calcium concentrations (0.2 mM, 0.5 mM and 0.8 mM) below the volume transition. In Figure 3 each of these curves is linear in the double logarithmic representation with slopes ranging from 1.59 to 1.81, indicating that the first term in Eq. (3) is negligible. The decrease in the power law exponent on approaching the volume transition is contrary to what is expected for a neutral gel when a phase separation is induced by decreasing the solvent quality. In the latter case, the value of the exponent increases from 2.25 (strong excluded volume condition) to 3 (theta condition).^[9] The present results thus imply that the thermodynamic properties involve another length scale in addition to that governed by van der Waals interactions and hence eq 3 is not an adequate representation for this system.

Figure 4 shows the scattering response for a polyacrylate gel close to the volume transition. In this figure, for small values of q ($<8 \times 10^{-3} \text{ \AA}^{-1}$) power law behaviour can be seen with a slope $n = -3.6$, followed by a quasi linear region ($0.02 < q < 0.08 \text{ \AA}^{-1}$) and finally a shoulder at about 0.1 \AA^{-1} . The slope of the intensity increase at low q is characteristic of scattering from surfaces.^[14] The size of these objects exceeds 1000 \AA , but in the absence of any low- q plateau no value can be attributed to this quantity. The dotted line in Figure 4 is the osmotic term obtained from a

least squares fit to the data assuming a neutral gel system. In this fit, $I_{\text{osm}}(q)$ is given by Eq. (1) where the amplitude is left as a free parameter, while $I_{\text{stat}}(q)$ is approximated by

$$I_{\text{stat}}(q) = B q^{-3.6} \quad (4)$$

where B is a constant. In Figure 4 the value of the scattering intensity at $q = 0$, calculated from the measured osmotic swelling pressure, is indicated by an arrow. It can be seen that the intensity of the osmotic term obtained from the SANS fit to the neutral gel expression underestimates this value by a factor of approximately 2.

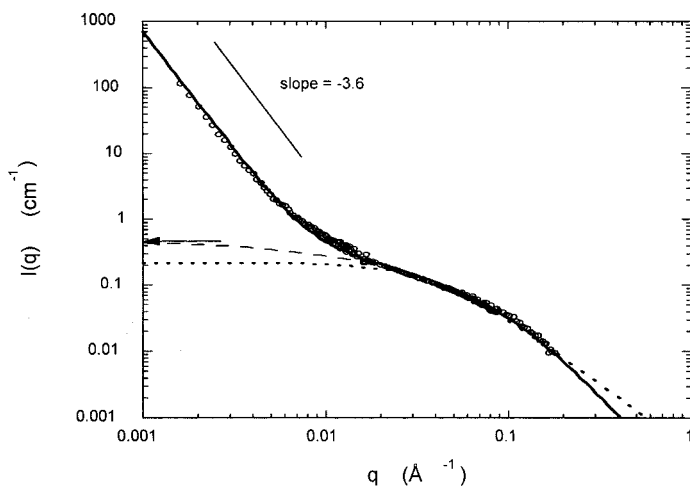


Fig. 4. SANS spectrum of a sodium polyacrylate hydrogel close to the volume transition at 0.85 mM CaCl_2 . Dotted line is the osmotic component (Eq. (2)) of the least squares fit of the data to Eq. (1). Continuous line is the least squares fit of Eq. (1) to the data, in which the osmotic component is replaced by Eq. (5), and M_{os} is calculated from the macroscopic swelling pressure and shear modulus measurements. Dashed line is the osmotic component (Eq. (5)) of this fit. The horizontal arrow indicates the numerical value of the intensity deduced from the macroscopic observations, using the neutron scattering contrast factor.

This discrepancy corroborates that the thermodynamic contribution of the gel is not completely described by Eq. (2), i.e., the structure factor of this neutralized polyelectrolyte hydrogel is different from that of a neutral polymer gel. In this fit, the value of the correlation length ξ is found to be 26 Å.

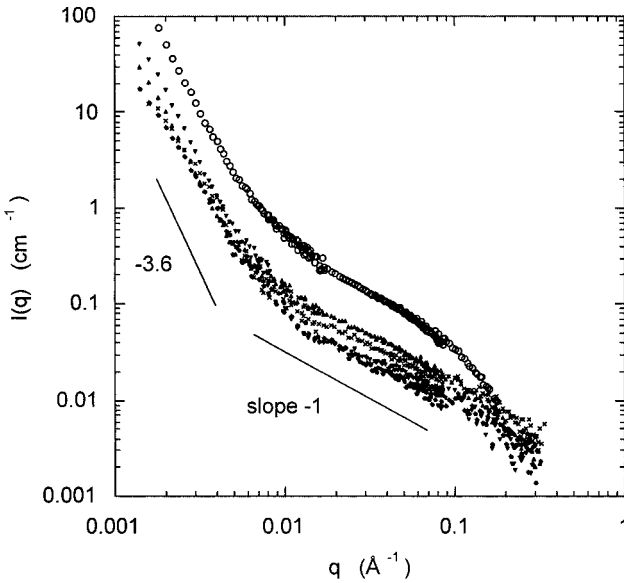


Fig. 5. Plot of SANS spectra for sodium polyacrylate gels swollen in 40 mM NaCl solution with various calcium contents indicated in box. The straight lines indicate slopes of -3.6 and -1 , respectively. CaCl_2 concentration in equilibrium bath: \bullet : 0.75 mM, \circ : 0.85 mM; \times : 1.0 mM; $+$: 1.2 mM; Δ : 1.7 mM; ∇ : 2.0 mM.

Figure 5 shows the SANS spectra for a set of polyacrylate hydrogels containing different amounts of calcium. It is clear from this double logarithmic representation, in the intermediate q -range relevant to the osmotic response, that all the curves display an intensity that varies approximately as q^{-1} . This behaviour is characteristic of linear scattering arrays, as, for instance, may be expected from polymers that are locally stretched.^[15] In this sample the transition occurs at $c_{\text{CaCl}_2} = 0.85$ mM. Close to the transition, the scattering intensity is considerably greater than below and above it.

The simplest expression that maintains the observed features of the thermal correlation length as well as reproduces the q^{-1} dependence of the scattering intensity is that of a system described by a persistence length L . In this phenomenological approach, the osmotic scattering term becomes^[16]

$$I_{\text{osm}}(q) = \Delta\rho^2 (kT\phi^2/M_{\text{os}}) (1+qL)^{-1}(1+q^2\xi^2)^{-1} \quad (5)$$

The fit of Eqs. (1), (4) and (5), in which φ^2/M_{os} is defined from the osmotic swelling measurements of Fig. 3, is shown as a heavy continuous line in Fig. 4. This fit yields $\xi \cong 9\text{\AA}$ and $L = 70\text{\AA}$. The corresponding osmotic component in this fit, i.e., Eq. (5) is shown as a dashed line in Fig. 4.

Conclusions

The present SANS results indicate that the description of neutralized polyelectrolyte hydrogels in the presence of added salt requires at least three length scales, two of thermodynamic origin and one frozen-in. The latter term is the result of scattering from the surfaces of large ($>1000\text{\AA}$) structures (e.g., cross-link zones). The thermodynamic properties are defined by two characteristic length scales, a persistence length L of locally stretched chains and the blob size ξ .

Polyacrylate chains in the presence of calcium ions form associations.^[2] It is likely that divalent calcium ions make the monomers uncharged and thus hydrophobic. But this hydrophobicity is not sufficient to induce a collapse of the chain at small length scale. When the concentration of added calcium ions increases further the repulsive interactions decrease and the polymer collapses at large length scale, as indicated by the swelling measurements (see Figure 1).

Acknowledgements

The authors acknowledge the support of the Institut Laue Langevin, Grenoble, France, and the National Institute of Standards and Technology, Gaithersburg, MD, for providing access to their neutron research facilities. We are grateful both to Drs. I. Grillo and B. Hammouda for their invaluable help in these measurements. This work is partially based upon activities supported by the National Science Foundation under Agreement No. DMR-9423101.

- [1] I. Tasaki, P.M. Byrne, *Biopolymers* **1992**, *32*, 1019; *Biopolymers* **1994**, *34*, 209.
- [2] A. Katchalsky, S. Lifson, H. Eisenberg, *J. Polym. Sci.* **1951**, *7*, 571.
- [3] J. Ricka, T. Tanaka, *Macromolecules* **1984**, *17*, 2916; *Macromolecules* **1985**, *18*, 83.
- [4] F. Horkay, I. Tasaki, P.J. Bassler, *Biomacromolecules* **2000**, *1*, 84; *Biomacromolecules* **2001**, *2*, 195.
- [5] F. Horkay, P.J. Bassler, A.-M. Hecht, E. Geissler, *Macromolecules* **2000**, *33*, 8329.
- [6] F. Horkay, A.-M. Hecht, P.J. Bassler, E. Geissler, *Macromolecules* **2001**, *34*, 4285.
- [7] F. Horkay, A.-M. Hecht, S. Mallam, E. Geissler, A.R. Rennie, *Macromolecules* **1991**, *24*, 2896.
- [8] V.F. Sears, *Neutron News* **1992**, *3*, 26.
- [9] P.G. de Gennes, "*Scaling Concepts in Polymer Physics*", Cornell University Press, Ithaca, NY, 1979.
- [10] T. Tanaka; L.O. Hocker; G.B. Benedek, *J. Chem. Phys.* **1973**, *59*, 5151.
- [11] H. Vink, *Europ. Polym. J.* **1974**, *10*, 149.
- [12] F. Horkay, M. Zrinyi, *Macromolecules* **1982**, *15*, 815.
- [13] A.V. Dobrynin; R.H. Colby; M. Rubinstein, *Macromolecules* **1995**, *28*, 1859.
- [14] O. Glatter; O. Kratky, "*Small Angle X-Ray Scattering*"; Academic Press: London, 1982.
- [15] M.N. Spiteri, F. Boué, A. Lapp, J.P. Cotton, *Phys. Rev. Lett.* **1996**, *77*, 5218.
- [16] F. Horkay, A.M. Hecht, I. Grillo, P.J. Bassler, E. Geissler, *J. Chem Phys.* **2002**, *117*, 9103.