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Control of Gel Swelling and Phase Separation of Weakly Charged Thermoreversible Gels by Salt Addition

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ABSTRACT: Doping of thermoreversible polymer gels with charged monomers provides a way to control phase separation and gelation conditions by coupling the properties of the gel with a tunable ionic environment. We analyze the dependence of the gelation and phase separation conditions on the amount of salt present using a mean field model of weakly charged associative polymers. The ions and co-ions present are explicitly considered at the mean field level, and we determine their concentrations in the different equilibrium phases when the system undergoes phase separation. For weak polymer charge, the entropic contributions of the ions to the free energy of the system play a central role in the determination of the location of phase equilibrium. In the simplest case, when the associative interaction responsible for gel formation is independent of the electrostatic interaction, the addition of salt changes the polymer equilibrium concentrations and indirectly changes the measurable swelling of the gel. We construct phase diagrams of these systems that exhibit the location of the coexistence region, the gel−sol boundary, and the location of the tie lines. We determine the swelling of the gel within the coexistence region. Our main result is that the effect of the salt on the properties of the weakly charged gel can be described through an extra contribution to the effective immiscibility parameter χ proportional to the square of the doping degree f^2 and to the inverse square of the added salt concentration s^{-2}.

I. Introduction

Thermoreversible gels are important materials with a large number of potential applications as drug delivery systems[1−5] and as injectable, in-vivo-forming biomaterials.[6−9] These materials have not been investigated as extensively as chemically cross-linked charged gels. Important lessons from the study of chemical gels, however, can be applied to the tailoring of properties of thermoreversible gels. A key method for controlling the degree of swelling of chemical gels, from small changes to full phase separation, is the incorporation of charged monomers into the polymer chains.[4,5,10] The counterions to the polymer charges provide large entropic barriers to phase separation, but their effects are also highly tunable as their concentration can easily be changed. Further, the degree of ionization of the gel can be controlled by the pH of the environment. Recently, this idea has been shown useful in the context of thermoreversible gels as well. For example, we have shown that the transition temperature for fixed concentration of poly(*N*-isopropylacrylamide) (NIP) can be modified by copolymerization with acrylic acid (AAc) and maleic acid (MAc) and that the change is directly related to the charges carried by the comonomers.[11]

In this article we present a model that provides simple relations between the properties of the gelling polymer and the salt of the environment. We obtain the approximate location of the phase coexistence region in the phase diagram by determining the spinodal curves of the model. Our central result is that the spinodal condition can be written as a single variable equation, similar to the classical Flory−Huggins spinodal for a polymer−solvent system, with extra terms that account for the excess pressure due to the different salt concentrations in the separated phases. The gelation of the system is treated using the incorporation of the classical Flory−Stockmayer theory[12] into solution thermodynamics following the work of Semenov and Rubinstein and others.[13−17] The charged nature of the polymers used is treated through a simple mean field theory as developed by Warren,[18] some of whose results we rederive. This approach leads to simple rules for the partition of the salt into the coexisting phases and for the construction of tie lines. In the approximation employed, the gel transition does not in fact change location within homogeneous states, but the conditions for its observation are modified by changes in phase boundaries induced by changes in salt concentration. We present phase diagrams derived from the model and derive simple rules for the effect of salt addition in the swelling of phase-separated gels.

Recent theoretical research has addressed several aspects of the phase diagrams of gel polyelectrolytes. These works have considered the possibility of association by electrostatic interactions and the determination of the contribution of charge fluctuations to the net free energy of these system.[19,20] These issues are not as directly relevant to the case of weakly charged polymers. Closer to the case dealt with in this article is the examination of microphase separation and gelation of charged polymers by Kudlay et al.[15] Our article presents a simpler approach to the problem as we determine the location of the spinodals against macroscopic, instead of microscopic, phase segregation. Also, our main interest lies in the effect of added salt concentration, not discussed in that work. Macroscopic segregation is a more likely phenomenon in the presence of substantial amounts of salt as the formation of macroscopic phases of high polymer density are not obstructed by the large entropic penalties of the salt-free case. The entropic barrier to phase separation has been previously explored in the context of physical gel formation by Potemkin et al.;[21,22] our work addresses the structure of a full phase diagram.

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II. Model and Phase Equilibrium Conditions

We set our model in a lattice with site size a and write a model free energy F per lattice size, in energy units of kT, with T the temperature and k the Boltzmann constant. The polymer occupies a volume fraction ϕ, and we assume a monodisperse system with polymers chains of size N (in lattice size units). The average charge per monomer of the polymer is f, so that each chain has charge fN. The density of associative units, gel-forming contacts, of the polymer is h, so that the total number of possible associations of a chain is hN. The salt ions concentrations are s_A for co-ions and s_B for counterions. The magnitude of the charge of the ions (in proton charges) is z_A and z_B, respectively. We write the free energy as a sum of three different contributions: the standard Flory−Huggins polymer solution model F_s, the contribution of the gel-forming interactions F_g, and the contribution of the charged monomers and salt F_c.

$$F = F_s + F_g + F_c \tag{1}$$

The first term is the Flory−Huggins contribution

$$F_s = \frac{\phi}{N}\ln\phi + s_A \ln s_A + s_B \ln s_B + (1-\phi-s_A-s_B)\ln(1-\phi-s_A-s_B) - \chi_0\phi^2 \tag{2}$$

In this expression, we use a "bare" χ parameter χ_0 that includes interactions other than those responsible for associative behavior and electrostatic interactions. Terms proportional to the volume fraction of the polymer have been omitted. The volume fraction available to the solvent is obtained from subtraction of the monomers and salt ions volume fractions.

Our second term is the contribution of gel-forming associations. We assume that each polymer can form at most a fixed number of pairwise associations, sN, where s can be considered the density of associating segments of the chain. Each association produces a contribution to the free energy of gkT per each of the chain segments involved. The mean field estimate of the free energy of configurations with a fraction Γ of actually associated elements gives the contribution to the free energy as

$$F_g = -\phi h\frac{\Gamma}{2}(\ln[\phi h] - 1) + g\phi h\Gamma + \phi h\left[\frac{\Gamma}{2}\ln\Gamma + (1-\Gamma)\ln(1-\Gamma)\right] \tag{3}$$

For each given temperature and concentration, the actual association rate Γ is determined from minimization of the free energy with respect to that variable.

Finally, the salt ions contribute to the solution entropy in a standard way. Each phase of the system is macroscopically electroneutral. However, fluctuations of the local density of salt and polymer ions do contribute to the free energy. This contribution can be taken to be a Debye−Huckel term, which can be derived from the random phase approximation to the fluctuations contribution. The electroneutrality condition, $f\phi - z_A s_A - z_B s_B = 0$, can be enforced at the free energy level by a Lagrange multiplier ψ. Thus, we have

$$F_c = -\frac{1}{12\pi}\kappa^3 - \psi(f\phi - z_A s_A - z_B s_B) \tag{4}$$

with an inverse screening length κ dominated by the "light" charges, the co-ions and counterions:

$$\kappa^2 = 4\pi l_B({z_A}^2 s_A + {z_B}^2 s_B) \tag{5}$$

where $l_B = e^2/\epsilon kT$ is the Bjerrum length (in lattice units), with e the charge of the proton and ϵ the permittivity of the medium. More precise determinations of this contribution can be found in the literature where the proper weight of the fluctuations of the polymer bound ions is taken into account. For weakly charged polyelectrolytes, and moderate salt concentrations, the contribution of the fluctuations, the Debye−Huckel term, is smaller than the entropic contribution of the ions and can be neglected. We will do so in deriving the approximate rules for salt partition in the phase diagram. This term can be reinstated in more precise calculations as needed.

Determination of the phase diagram may proceed as follows. The values of the fraction of associated monomers are obtained by minimization of the free energy with respect to the associated fraction Γ. This determination has been presented in the literature many times, and we simple show the main results below, in section III. Upon evaluation of the free energy at this value of the association fraction, the free energy can be presented as a function of the polymer volume fraction, the salt concentrations, and a set of parameters. We can now determine the equilibrium conditions for the multicomponent system.

The equilibrium conditions between two states labeled 1 and 2 require (1) equality of the chemical potential of each species and (2) equality of the total pressure of the nonsolvent particles, namely

$$\mu_{\phi 1} = \mu_{\phi 2} \tag{6}$$

$$\mu_{A1} = \mu_{A2} \tag{7}$$

$$\mu_{B1} = \mu_{B2} \tag{8}$$

and

$$p_1 = p_2 \tag{9}$$

In these expressions, the subindices 1 and 2 indicate the phase, and subindices ϕ, A, and B refer to the polymer, the co-ions, and counterions. The chemical potentials, also in units of kT, per lattice site volume, are

$$\mu_\phi = \frac{\partial F}{\partial \phi} \tag{10}$$

$$\mu_A = \frac{\partial F}{\partial s_A} \tag{11}$$

$$\mu_B = \frac{\partial F}{\partial s_B} \tag{12}$$

while the pressure is obtained as

$$p = -F + s_A\mu_A + s_B\mu_B + \phi\mu_\phi \tag{13}$$

The set of four equations (6−9) determines the coexistence points. The equations can be further reduced using the electroneutrality condition. This condition defines a two-dimensional subspace in the ions−polymer concentration space. The equilibrium of salt ions between coexisting phases defines a subset of points within this subspace. The solution to the equilibrium of the salt ions gives a slope for the tie lines: a construction shown before by Warren[18] and implicit in many previous treatments. Application of this result leaves us with just two equations for the chemical potential of the polymer and the pressure. These last two equations can be replaced by a single spinodal condition which in the coexistence region has two solutions that approximate the positions of the two points of coexistence along the tie line. We carry out this procedure in the next sections and discuss the results later on.

III. Gelation Conditions and Gel Formation Energies

In the classical theory of gelation of Flory,[12] the onset of the gel conditions corresponds to the requirement that all polymer chains be connected. Ignoring self-associations, this requirement is that the fraction of associated segments be larger than the critical value Γ_g given by

$$\Gamma_g = \frac{1}{hN - 1} \qquad (14)$$

The actual degree of association is determined from minimization with respect to the variable Γ. The basic result for the association extent, as a function of the concentration, is the mass action law

$$\frac{\Gamma}{(1-\Gamma)^2} = e^{-2g} h\phi \qquad (15)$$

In this approximation, the location of the sol−gel boundary is simply given by the solution of the previous equation for the concentration ϕ_g, for which the association fraction takes the gel value Γ_g.

We assume that the mass action law above leads to values of the association rate that are not close to full saturation $\Gamma \ll 1$. This condition still allows the formation of gels under a large variety of conditions as the critical value Γ_G can also be very small. Evaluation of the free energy contribution of the gel-forming associations gives approximately

$$F_g = -\frac{1}{2} e^{-2g}(h\phi)^2 \qquad (16)$$

That is, the gelation acts as a simple two-body term in effective free energy. We can define an effective contribution of gelation to the net χ parameter of the system as

$$\chi_g = h^2 e^{-2g} \qquad (17)$$

This result is useful in the construction of phase diagrams presented in terms of an effective χ parameter. In particular, we note that we can express the critical association value in terms of this parameter only. The critical concentration required for gelation is given by

$$\phi_g = \frac{h}{2\chi_g} \frac{hN - 1}{(hN - 2)^2} \qquad (18)$$

In the case of a relatively large number of associating units hN, the result reduces to the even simpler condition $\phi_g = 1/(2\chi_g N)$.

The previous expressions and, in particular, the evaluation of the effective χ parameter are valid in a regime where the density of the polymer is low. Expansions in powers of the volume fractions are well justified. Far away from the critical temperature, the coexisting phase with larger monomer volume fraction might not satisfy the low concentration approximation. The theoretical description of dense polymer phase is complicated by the multibody interactions of the polymers, and some of the approximations used above might break down. To complement the previous collapse of the description of the gel by a single two-body term, we consider two complementary expressions of the free energy. First we point out that in the strongly associative regime, where $\Gamma \approx 1$, the evaluation of the free energy gives the approximate result

$$F_g = -h\phi \ln(h\phi) + gh\phi \qquad (19)$$

This expression can be interpreted as the reduction in entropy freedom of all the associative segments and the gain in energy gkT for near all associative segments. Note that the last term of this expression cannot be eliminated from the free energy in spite of being just linear in the concentration as this expression for the free energy does not apply uniformly to all concentration regimes. A second direction to improve the description of the dense phase is the use of virial coefficients. We assume that, as with the χ parameter, we may separate contributions of these virial coefficients into gel association dependent and independent parts. The expansion of the free energy in powers of the polymer concentration can be written as

$$F = -\chi\phi^2 + \frac{B}{6}\phi^3 \qquad (20)$$

Taking the third virial coefficient B as a function of salt concentration and other parameters, this expression can replace the gel association contributions and the excluded-volume effects.

IV. Electroneutrality and Salt Partition

Upon phase separation of the polymer into a dense (gel) and dilute phase, the concentration of the salt ions in both phases is not equal. The electroneutrality condition is

$$f\phi - z_A s_A - z_B s_B = 0 \qquad (21)$$

so that a change in the concentration of polymer is always accompanied by a change in the concentrations of ions. When the activity of the salts, as quantified by the Debye−Huckel contribution to the energy, is small, the equilibrium conditions that arise from the equality of chemical potentials for these species can be solved in a simple way.

The chemical potential for the ions derived from our free energy contains a term proportional to the Lagrange multiplier enforcing charge neutrality that can be identified with the Donnan potential[23] and the regular contribution μ^o. Explicitly

$$\mu_A = \mu_A{}^\circ - z_A\psi \qquad (22)$$

$$\mu_B = \mu_B{}^\circ + z_B\psi \qquad (23)$$

The multiplier creates an apparently nontrivial contribution that disappears when electroneutrality is preserved. The equilibrium equations for the ions, eqs 7 and 8, become

$$\Delta\mu_A{}^\circ = z_A \Delta\psi \qquad (24)$$

$$\Delta\mu_B{}^\circ = -z_B \Delta\psi \qquad (25)$$

where the delta symbol indicates the difference between the two phases in equilibrium, for example $\Delta\psi = \psi_2 - \psi_1$. Eliminating the multiplier, we obtain

$$z_A \Delta\mu_B{}^\circ + z_B \Delta\mu_A{}^\circ = 0 \qquad (26)$$

When the Debye−Huckel contributions to the activity of the salt are small, the chemical potentials are dominated by the logarithm of the concentrations of the species, $\mu^\circ \approx \ln(s)$. Replacing this approximation into our equilibrium relation and exponentiating, we recover the Donnan condition:

$$s_{A1}^{z_B} s_{B1}^{z_A} = s_{A2}^{z_B} s_{B2}^{z_A} \tag{27}$$

The polymer concentrations in a pair of equilibrium phases can be written as ϕ_1, and $\phi_2 = \phi_1 + \Delta\phi$. Using the electroneutrality condition, we can now write the equilibrium equation as

$$s_{A1}^{z_B}\left(\frac{z_A s_{A1} + f\phi_1}{z_B}\right)^{z_A} = (s_{A1} + \Delta s_A)^{z_B} \left(\frac{z_A(s_{A1} + \Delta s_A) + (f\phi_1 + f\Delta\phi)}{z_B}\right)^{z_A} \tag{28}$$

The amount of charge from the polymer can be assumed to be always small compared to the concentration of co-ions, i.e., the concentration of added salt. Expanding this equation with respect to the change in polymer charge, we obtain the approximate result for the difference in co-ion concentration:

$$\Delta s_A = -\frac{z_A}{z_B^{\,2} + z_A^{\,2}} f\Delta\phi = -xf\Delta\phi \tag{29}$$

where we have introduced and defined the factor x to simplify our later formulas.

Using again electroneutrality, we obtain the condition for the counterions:

$$\Delta s_B = \frac{z_B}{z_B^{\,2} + z_A^{\,2}} f\Delta\phi = yf\Delta\phi \tag{30}$$

where the factor y is defined by the second equality. Note that in the case of monovalent ions we have the following simple result: the excess charge due to the polymer $f\Delta\phi$ is compensated by an increase of $f\Delta\phi/2$ in the counterion concentration and a decrease of $f\Delta\phi/2$ in the co-ion concentration.

To use these results in the determination of the phase diagram, we first point out their geometrical meaning. The three-dimensional space specified by the variables ϕ, s_A, and s_B is reduced to a two-dimensional surface due to the electroneutrality condition. The tie lines of the coexistence region join pairs of points of the form (ϕ, s_{A1}, s_{B1}) and (ϕ_2, s_{A2},s_{B2}). The tie line has then a tangent vector proportional to (1, $-fx$, fy). By looking at sets of points along such lines only, the spinodal condition becomes a single equation in one variable. That is, we will look for unstable points with negative second derivative along those lines. The location of the tie lines is sketched in the three-dimensional space and its projections into two-dimensional planes in Figure 2. The approach presented above is very similar to the use of Warren's full spinodal condition. The main difference is our use of a reduction of variables by first determining the slope of the tie lines. Our approach leads more directly to the determination of the equilibrium rules of eqs 26 and 27.

V. Phase Diagrams

We have already determined the location of the gelation curves. We can now, using the results of the previous section, determine the location of the coexistence region. We have already used the equation of electroneutrality and the conditions of equality of the chemical potentials of the salt. We are left with the equation of pressure and chemical potential for the monomer. The dimensional reduction obtained from using our previous result has led to a problem on a single variable, the location along the tie line. The line can be parametrized by the value of the polymer concentration there ϕ. Instead of solving the pressure and chemical equilibrium conditions on this single species, we obtain the conditions of stability and reproduce the phase diagram on the basis of the location of the spinodal lines.

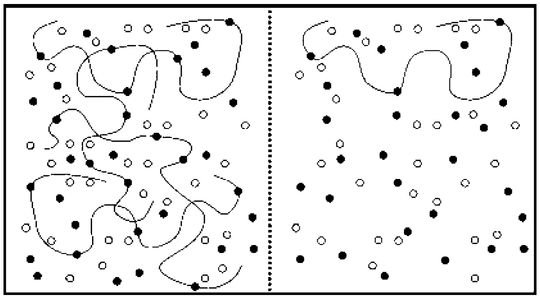

Figure 1. Scheme of two phases of a weak polyelectrolyte in coexistence. The weakly charged polymers, represented by thin continuous lines, are charged, and their ions are represented by black dots. In the presence of salt, further charges of the same sign, co-ions, are also present. For electroneutrality, the same number of counterions (for 1:1 valencies) are present in each phase. Polymers and ions can transverse the boundary between phases here indicated by a dashed line. The excess charge associated with the polymers in the dense phase (left), compared to that of the dilute phase (on the right), is compensated by changes in the co-ion and counterion densities in each phase. The simplified equilibrium rules presented in the text require that the excess charge due to polymers in the dense phase, compared to the dilute phase, $f\Delta\phi$, be compensated by a reduction in the number of co-ions in that phase of $\Delta s_a = -{}^1/_2 f\Delta\phi$ and an increase in counterions of the same magnitude $\Delta s_b = {}^1/_2 f\Delta\phi$.

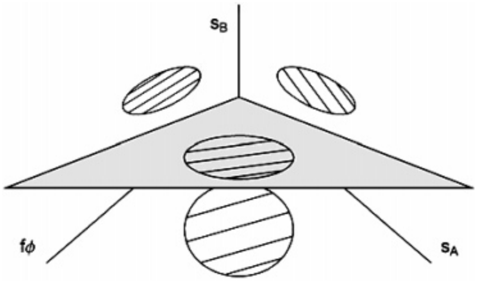

Figure 2. The scheme shows the electroneutral subspace, as a shaded plane, within the larger space defined by concentrations of charged monomers $f\phi$, co-ions s_A, and counterions s_B. States within this plane are the only physically realizable macroscopic states. The electroneutral plane crosses the origin of the three-dimensional space. At the center of the plane we sketch a region of phase coexistence and show the projections of this area into the three bounding planes. The tie lines are obtained according to the approximation discussed in the text.

The spinodal condition locates the boundaries of stability along the tie lines. Stability requires that the second derivative of the energy be positive. The boundary satisfies

$$\left.\frac{d^2F}{d\phi^2}\right|_{\text{tie}} = 0 \tag{31}$$

The derivative along the tie line is calculated as

$$\left.\frac{d}{d\phi}\right|_{\text{tie}} = \frac{\partial}{\partial\phi} - xf\frac{\partial}{\partial s_A} + yf\frac{\partial}{\partial s_B} \tag{32}$$

Applying the derivative twice on our model energy, with the approximate evaluation of the gelation contribution discussed in section III, we obtain the spinodal condition:

$$\frac{f^2x^2}{s_A^{\,2}} + \frac{f^2y^2}{s_B^{\,2}} + \frac{1}{N\phi} + \frac{(1 + fx - fy)^2}{1 - s_A - s_B - \phi} - 2(\chi_0 + \chi_g) = 0 \tag{33}$$

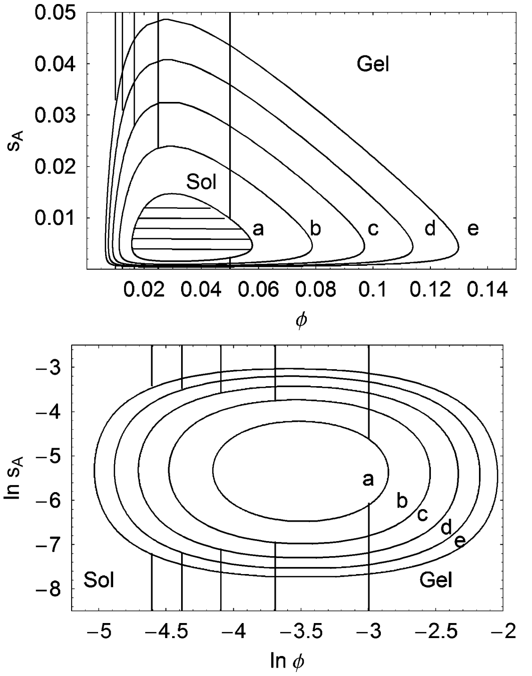

Figure 3. Example of a projection of the phase diagram into the polymer−co-ion plane. The closed loops bound the coexistence regions and correspond to fixed values of the composite parameter $\chi_0 + \chi_g$. Maintaining the bare parameter χ_0 constant, the change in the gel contribution χ_g (associated with changes in temperature) leads to changes in the boundary between gel−sol states. The gel−sol boundaries, within our model, are independent of the co-ion concentration. Tie lines for the coexistence region are shown for the innermost loop. These lines have slight negative slope, $-f/2 = -0.005$ in this case. At bottom, the same curves, except for the tie lines, are shown on a logarithmic scale. The system shown has monovalent ions, and $N = 1000$, $f = 0.01$, $\chi_0 = 0.53$, and $\chi_g = 0.01$, 0.02, 0.03, 0.04, and 0.05 for curves a−e, respectively.

To further simplify this equation, we use electroneutrality and the condition that the amount of ions from the polymer is much smaller than the salt ion concentrations. We can present the final result in terms of two variables; we choose the concentrations of monomers and co-ions:

$$\frac{f^2(x^2+(z_By/z_A)^2)}{{s_A}^2}+\frac{1}{N\phi}+\frac{(1+fx-fy)^2}{1-(1+z_B/z_A)s_A-\phi}-2(\chi_0+\chi_g)=0 \quad (34)$$

This equation implicitly defines the boundary of the unstable region in the co-ions−polymer diagram. Similar equations, without the salt terms, appear in the theory of phase separation of homogeneous polymer solutions. In contrast to that case, however, we note that the equation above defines a curve on the ϕ−s plane, instead of simply determining a pair of volume fraction values for every temperature. Further, for a given salt concentration value, the two solutions for the volume fraction, if they exist, do not lie at the end points of the same tie line; the tie lines connect points with different salt concentrations.

Using the spinodal condition determined above, we construct the phase diagram and can present its projection onto the ϕ−s plane. Plots of the unstable region, in these coordinates, appear in Figure 3. The figure shows results for fixed values of the χ parameter combination χ_0+ χ_g. When the contribution of the gel-forming contacts vary, the location of the gel−sol transition changes. In the figure, this effect is shown by maintaining a constant value of the bare parameter χ_0, while changing the χ_g contribution. Note that the gel−sol boundaries are straight lines as we have assumed that the interaction between polymers is not affected by the amount of salt present.

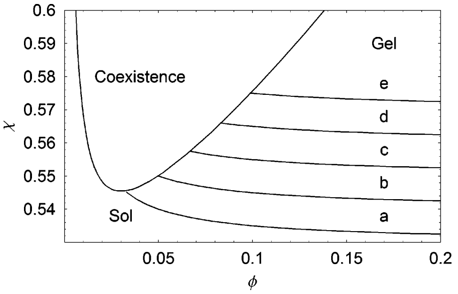

Figure 4. A slice of the phase diagram for a constant value of co-ion concentration. The vertical axis is the value of the combined parameter $\chi_0 + \chi_g$. Changes in the ratio between the contributions to the net parameter by the bare interaction and the gel-forming contacts do not change the coexistence region but change the location of the gel−sol boundary. The cases shown correspond to different fixed values of the bare parameter. The system shown has monovalent ions, and $s_A = 0.01$, $N = 1000$, $\phi = 0.01$, and $\chi_0 = 0.53$, 0.54, 0.55, 0.56, and 0.57 for curves a−e, respectively.

In Figure 4, we show a slice of the phase diagram obtained by taking a constant value of the co-ion concentration. As discussed above, this is similar to imposing a value of added slat concentration. The coexistence region depends again only on the $\chi_0 + \chi_g$ parameter combination. The gel−sol line depends only on the value of the χ_g parameter. The figure shows the gel−sol boundaries for different values of the bare parameter when the gel parameter changes. The values used for Figures 3 and 4 are chosen to show the gel and coexistence boundaries in the same region of the phase diagram. In practice, most systems will not show this convergence of effects, and gel−sol boundaries might appear at concentrations much lower than those near the critical point of the coexistence region. Phase diagrams presented with temperature as an independent variable can be recovered from our results through suitable assumptions of the behavior of the different χ parameters with respect to temperature. The phase diagrams shown can be read as temperature diagrams by simply exchanging the χ parameter axis by a temperature one and assuming a linear relation between them. Applying such a procedure to the case shown in Figures 3 and 4 leads to a case with a temperature-independent bare parameter χ_0 and a fast changing gel contribution χ_g. Many other combinations are possible, with both parameters increasing or decreasing simultaneously or even showing opposite behaviors. The complex phase diagrams that can be obtained when the two parameters change have been examined, in the absence of modifying charges, by Erukhimovich et al.[16,17] In that work, furthermore, the properties of the postgel region are considered in more detail including, for example, the effects of the presence of cycles in the gel network. These corrections lead to the broadening of the gel−sol line into a finite but narrow two-phase coexistence region. Quantitatively, for a large variety of conditions, these corrections are small and do not disturb the general shape of the coexistence region of the phase diagram; the reader may observe these effects by comparing Figure 7b,c of ref 16 with the phase diagram in Figure 3.

Back to our basic result, eq 34, we note that it is reminiscent of the standard result for phase separation of polymer solutions. We can further enhance this similarity by noting that the first term is independent of concentration and therefore can also be absorbed into a total χ parameter:

$$\chi = \chi_0 + \chi_g + \chi_c = \chi_0 - h^2 e^{-2g} - \frac{f^2(x^2 + (z_B y/z_A)^2)}{s_A^{\ 2}} \tag{35}$$

Note that the changes in salt concentration along a given tie line are always assumed smaller than the magnitude of the initially added salt, so that the denominator of the last term is approximately constant. The main conclusion of this analysis is that the control exerted by the salt on the shape of the phase diagram is equivalent to a simple change in the interaction parameters of the polymer backbones. Upon addition of salt, the phase diagram retains its shape, but it is shifted in the temperature axis (through its dependence on the χ parameter). Some of the limitations of this approach are discussed in the final section.

For completeness, we record another approximate version of the spinodal equation. When the contribution of the gel formation term in the free energy is large, this term dominates the concentration-dependent terms relevant at large concentrations. We can then replace the excluded volume term for a term including the third virial coefficient contribution:

$$\frac{f^2(x^2 + (z_B y/z_A)^2)}{s_A^{\ 2}} + \frac{1}{N\phi} - 2(\chi_0 + \chi_g) - \frac{B\phi}{2} = 0 \tag{36}$$

The virial coefficient B is only weakly sensitive to the density concentration.

We close this section stating a simplified version of the critical point position for fixed amount of added salt (i.e., co-ions). This point is determined by setting to zero both the second and third derivatives of the free energy with respect to the volume fraction along the tie line. Combining these equations results in a single condition that implicitly determines the critical temperature as a function of the parameters χ and B. The relation is

$$\frac{f^2(x^2 + (z_B y/z_A)^2)}{s_A} - \frac{1}{2N} - 2(\chi_0 + \chi_g) - 2B = 0 \tag{37}$$

To obtain this expression, we have neglected terms that appear in the partial derivatives that are of higher order with respect to the ionized fraction f. This final result is of course expected from analogies to noncharged polymer systems.

VI. Swelling Control

The basic application of the previous analysis lies in the prediction of swelling upon addition of salt. In biomedical applications, delivery of a prepared solution into an environment with physiological salt and pH conditions will drive the degree of swelling of the gel away from the preparation conditions. Often, the prepared gel sate will lie near the high-density coexistence region or will be in a mixed state with the components lying at coexisting states that we label I and II, with concentrations (ϕ_I, s_{AI}, s_{BI}) and (ϕ_{II}, s_{AII}, s_{BII}). We are mostly interested in the fate of the gel-rich state, phase II. We can define the degree of swelling w of a gel by comparing the total volume occupied by the gel phase with the volume occupied by the polymer.[10] That is, swelling is simply the inverse of the volume fraction.

$$w = \frac{1}{\phi} \tag{38}$$

In situations of coexistence, we define the swelling as that of the dense gel phase only.

$$w_{co} = \frac{1}{\phi_{II}} \tag{39}$$

This is the most useful definition, as the actual ratio of polymer to solvent can be modified by simply adding solvent and increasing the fraction of the system volume in phase I. The concentration ϕ_{II} remains constant and thus the swelling ratio.

The relation between swelling and added salt ions is obtained by analyzing the change in the boundary concentration ϕ_{II} as the ions concentrations change. Away from the critical points, we expect the change to be linear in the salt change:

$$\Delta w_{co} = \frac{\partial w}{\partial s_A}\Delta s_A = -\frac{1}{\phi_{II}^{\ 2}}\frac{\partial \phi_{II}}{\partial s_A}\Delta s_A \tag{40}$$

The derivative in this expression can be evaluated from the implicit relation given by the spinodal condition given above. To obtain a more practical simplified result, we consider the following set of approximations. First, we assume that the point in the phase diagram under consideration is in an intermediate concentration region, concentrations greater than the critical point, so that the changes in swelling are well described by the linear approximation, $\phi > \phi_c$, but less than concentrations where the monomers constitute the majority component in the system, $\phi < 0.5$. In that case, the polymer-rich region branch of the spinodal is approximately determined by the equilibrium between the polymer–polymer interaction and the solvent entropy, namely

$$\frac{(1 + fx - fy)^2}{1 - (1 + z_B/z_A)s_A - \phi} \approx 2\chi \tag{41}$$

where χ includes the gel and salt generated terms. Solving this expression for ϕ leads to a simple linear dependence on s_A. This region can be easily identified in the phase diagram of Figure 3 where the upper right boundary of the phase coexistence region approaches a straight line. In this region we have then

$$w = \left[1 - (1 + z_B/z_A)s_A - \frac{(1 + fx - fy)^2}{2\chi}\right]^{-1} \tag{42}$$

In this region, the local rate of change of swelling approximately obeys the relation

$$\frac{\partial w}{\partial s} = -w^2(1 + z_B/z_A) \tag{43}$$

The previous analysis is useful in the near-linear region of the phase coexistence boundary of the phase diagram. These results are modified according to the details of the model since, for example, when higher order correction in the virial coefficients are required, the boundary is no longer linear. In the general case, when a suitable model can be constructed, it is possible to simply determine the value of the equilibrium concentration in the gel-rich phase. In Figure 5 we present examples of the phase coexistence value and the swelling ratio for different values of the gelation parameter χ_g for fixed initial polymer concentration. The relations obtained in the previous paragraph operate in the region of decreasing swelling of the gel.

We have assumed that the gel formation, as quantified by the association fraction Γ, is not strongly affected by the presence of the salt. As was the case of the swelling ratio, however, the fact that in conditions of coexistence the volume fraction takes different values at different salt concentrations induces a salt dependence in the gel fraction in the coexisting

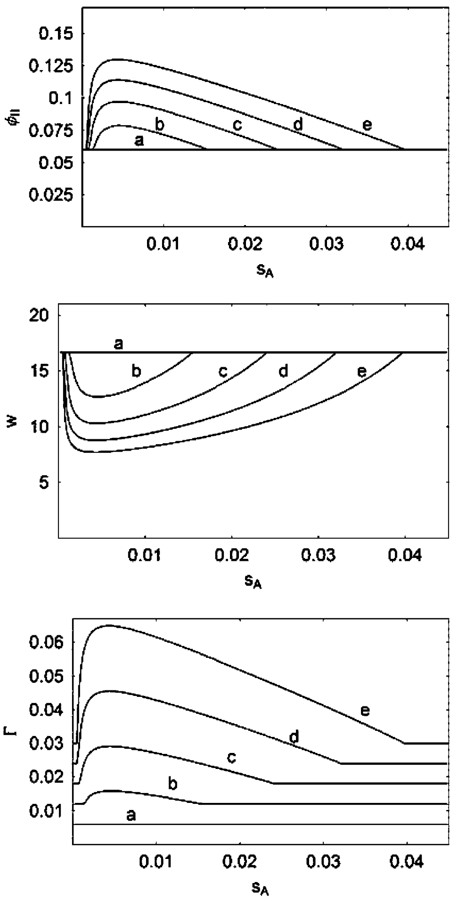

Figure 5. Equilibrium monomer concentration (top), swelling (middle), and gel fraction (bottom) as a function of salt concentration for a system with $N = 1000$, $f = 0.01$, $h = 0.1$, $\chi_0 = 0.53$, and $\chi_g = 0.01$, 0.02, 0.03, 0.04, and 0.05 for curves a−e, respectively. The concentration of monomers in the system is $\phi = 0.6$. Line a corresponds to a case where there is no phase separation. For all other cases, the system shrinks and expands before becoming a homogeneous state again. Note that after quick shrinking the dependence of the volume fraction decreases linearly with the salt concentration.

phases. Evaluation of the gel fraction at these locations is obtained by substitution into eq 15 of the values obtained above for the equilibrium volume fractions. In the dense gel phase we obtain the defining relation

$$\frac{\Gamma_{\mathrm{II}}}{(1-\Gamma_{\mathrm{II}})^2} = \phi_{\mathrm{II}} h \mathrm{e}^{-2g} \tag{44}$$

We use the subindex II to indicate the evaluation of the association fraction at the dense phase. In cases where the coexistence regions is small, the association fraction is, to first approximation, linear in the volume fraction $\Gamma_{\mathrm{II}} \sim \chi_g \phi_{\mathrm{II}}$. In the third panel of Figure 5, we plot the induced dependence of the gel fraction on the salt concentration, for the values of the parameter listed. In this case, the change in the assumed value of the parameter χ_g also changes the base value of the graph. For a fixed value of this parameter, the association fraction follows the behavior of the equilibrium volume fraction in its dependence on the salt concentration.

VII. Conclusions

The swelling of charged thermoreversible gels upon salt addition is, of course, an expected result. Our calculation shows, in more detail, the specific dependence of these changes on the salt concentration. The overall behavior of the swelling, as determined here, reveals great sensitivity on the salt presence and is clearly a useful way to control the properties of the gel. Our central result, eq 34, shows that most of the effects of the presence of salt can be summarized by stating that the change in the concentration of environmental salt can be thought of as a modification of the properties of the polymer backbone. The net contribution to the effective χ parameter is proportional to the square of the doping fraction f^2 and inversely proportional to the s^2 salt concentration.

In our presentation we have chosen to work with an effective χ parameter χ_g that incorporates the basic information regarding the gel properties of the polymer. This approach is valid for not highly connected gels ($\Gamma \ll 1$), and it simplifies the resulting expression used to calculate the phase diagram and discuss the response to salt changes. The fact that a gel, or an associative polymer in the pregel state, is present is somewhat obscured in our formulation, but information about the state of the gel (the degree of association) is easily retrieved from eqs 15 and 17. As we have also assumed independence between associative strength and salt concentration, it is easy to read the gel presence in the phase diagrams that use salt and monomer concentration variables as in Figure 3. In those diagrams, the gel fraction is simply proportional to the monomer concentration, and the gel−sol boundary is a vertical line.

There are several limits to the applicability of the theoretical approach presented. We have treated the electrostatic interactions in the system in the limit of low salt concentrations. Contributions to the free energy arising form electrostatic interactions become important when the inverse screening length of the ions κ is large. Further, when the distance κ^{-1} approaches values comparable with the monomer size a, not only corrections to the free energy are important but also a strong renormalization of the charge appears as ion pairing begins. The polymeric nature of the system imposes further limits. Semenov and Rubinstein[13] have described the conditions in which the Flory approach is valid. They discuss in detail the effects of a good solvent and the changes induced in the sol−gel transition. These effects appear, for the most part, on regions above the phase coexistence region and do not have a major impact in the coexistence regime of the phase diagram, the main concern of this article. A second important result is the fact that self-interactions renormalize the number of effective bonds hN that a chain may form. These renormalization effects appear at low concentrations, below the overlap concentration, and do modify our results. While the shape of the phase diagram remains similar, the precise values of the location of the phase boundaries are modified. We have omitted the discussion of these effects, as further assumptions on the nature of the gel-forming contacts are required.

There are several directions in which the current work must be extended for more specific applications. In particular, it is important to consider the possibility of doping the polymer chains with monomers capable of different states of ionization. It will also be of interest to consider the case of polymer backbones that lead to lower critical solution temperatures (LCST-type materials). The effects of ionization, i.e., nonfixed backbone charge, have been considered in the context of non-gelling, weakly charged polymers[18] as well as for charged chemical gels. Many of the properties described in those works are likely to carry over to the case of weakly charged thermoreversible gels.[24] We have also previously reported that addition of doubly ionizing monomers to the polymer backbone (of LCST type) induces features in the swelling and phase separation behavior that might quantitatively different from those of equivalent systems with double amount of singly ionizable monomers.[11] Another previous work by our group has also considered a model for the generation of concurrent gelation and LCST-type behavior in polymers.[25] It seems also possible to directly introduce the present treatment of charges into that framework. Finally, we point out that salt concentration is capable to induce important changes in the behavior of gelling polymers even when they are not explicitly charged.[26,27] These effects require a different theoretical treatment and unfortunately complicate the modeling of those materials.

We can contrast our results with those derived for chemical gels. Models that predict the phase transitions in charged chemical gels, such as the original work of Flory[12] and later refinements,[28] must account for the elastic behavior of the gel. Often, it is the competition between elastic stretching and the osmotic pressure of the gel that leads to volume transitions. In the model we have considered the equilibrium is established between the ion pressure and the associative contacts. We have neglected the elastic contribution of the system. This seems an adequate approximation for thermodynamic properties, but elasticity is likely to be relevant in the case of dynamical processes and in particular to the rheological properties of these systems. We expect, however, that many of these properties will be independent of salt presence. That is, once the static properties of the gel are established with the help of salt control, the dynamic properties will follow the same pattern as unsalted gels.

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