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Molecular Theory of Weak Polyelectrolyte Gels: The Role of pH and Salt Concentration

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ABSTRACT: We develop a detailed molecular theory that describes the response of weak polyelectrolyte gels to changes in both the pH and salt concentration, c , of the solution. This approach includes specific molecular details and conformational degrees of freedom of the polymeric gel, acid–base equilibrium, and solution entropy as well as electrostatic, van der Waals, and excluded-volume interactions. Here, we study polyacid gels in good solvent. The physical properties of the gel are found to depend on the coupling between charge regulation and the molecular interactions. In particular, the gel's degree of dissociation is not only determined by the bath pH and ionic strength but also by the polymer's ability in regulating charge to modify the local environment and in swelling or shrinking that depends on the externally controlled variables. The gel pH can be several units smaller than the bath pH depending on the salt ion concentration. The gel pH does not respond linearly to changes in neither bath pH nor c , and its behavior results from the complex interplay between the conformational degrees of freedom and all of the interactions mentioned above. The gel system swells if $\text{pH} > \text{pK}_a$ and collapses if $\text{pH} < \text{pK}_a$. The continuous transition between collapsed and swollen regimes occurs in a very narrow range of bath pH around pK_a whose width depends on the salt concentration. In this intermediate region the volume fraction of the polyacid can be controlled by both c and pH.

1. Introduction

Charged gels undergo large volume changes induced by external stimuli that include changes of temperature and/or osmotic pressure variations^{1–3} and electric field.⁴ Because of their large deformations and fast responses to external stimuli, hydrogels of charged chains have generated great interest for potential applications such as microactuators,⁵ muscle-like actuators,^{6–8} and filtration/separation⁹ and microfluidic¹⁰ devices. Moreover, it has been argued that hydrogels have structures and properties that resemble biological tissues^{11,12} and biological networks.^{13,14} Indeed, nucleoids of bacteria such as *E. coli*¹⁵ and mitotic chromosomes have been described to show many of the physical¹⁶ and mechanical¹⁷ properties of hydrogels: these biological networks undergo large salt-induced volume changes.¹⁸ In addition, mammalian cytoplasm responds to extracellular pH resembling the physical behavior of hydrogels, having the ability to absorb large quantities of water and modify its volume manifold.¹⁹

There are two types of polyelectrolytes: strong and weak polyelectrolytes. The acid (basic) groups of strong polyelectrolytes are deprotonated (protonated) in the typical range of pH values. Therefore, they have charge densities that are nearly insensitive to pH changes; their volume and thermodynamics are controlled by the salt concentration and the valency of the salt in a rather universal way.^{20–23} This group includes nucleic acids and polystyrenesulfonate. In the presence of gelling molecules, such as proteins capable of hydrogen bonding to their backbone, they can also form gels.^{24–27} The physical properties of strong polyelectrolyte gels, including swelling, have been previously analyzed mainly using linear-response theory.^{28–30} In addition, simulations have been used to analyze gels of charged chains in

different solvent conditions^{31,32} that includes the case of multivalent ions presence.³³

On the other hand, the state of charge of polyacids or polybases depends more strongly on the acid–base equilibrium. These polymers are often referred to as weak polyelectrolytes. In weak polyelectrolyte chains, not only the salt concentration but also the pH controls the effective charge of the chains,³⁴ i.e., the fraction of chain monomers whose acid (basic) groups are dissociated or degree of dissociation, f_d . Salt-free solutions of weak polyelectrolytes³⁵ and grafted layers of polyacids^{36–38} have been theoretically studied before. In many applications, gels of weak polyelectrolyte chains are preferred. These gels are ubiquitous in nature and can be formed, for example, using triblock copolymers with associating end groups.¹ If the chain ends undergo thermoreversible reactions with the ends of other chains, charged gels that are highly regular are formed.³⁹ In this work, we analyze permanently cross-linked chains that form regular gels as a function of their degree of ionization; we assume the backbone is in good-solvent conditions.

There are various competing physicochemical interactions that determine the size of weak polyelectrolyte gels. The acid–base equilibrium must be established inside the gel under the constraint of fixed chemical potential of the protons given by the bath solution in contact with the gel. Charge dissociation is favored by an entropy increase in production of charged groups. However, the charge present on the chain backbone swells the gel and consequently decreases the entropy of the chains. Moreover, ions are required to cancel the charge of the chains, which generate a strong penalty to charge dissociation. These competitions determine the charge and size of the swollen gel: charge dissociation of the chains favors homogeneous mixing of hydrated counterions and of swollen charged chains. The macroscopic shrinking of the gel occurs when the charge of the chains is screened by salt and/or

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pH changes, such that the degree of dissociation is negligible. In present paper, we develop a theory to determine how the equilibrium conformation of weak polyelectrolyte hydrogels changes in response to external stimuli. The contributions to the free energy of the acid–base equilibrium, the solution mixing entropy, the steric repulsions, the van der Waals attractions, and the conformational degrees of freedom of the gel molecule are all explicitly included. In addition, starting from the electrostatic energy, we derive a generalized nonlinear Poisson–Boltzmann equation whose solution provides the electrostatic potential. In this theoretical approach, the thermodynamic equilibrium is determined by the coupling between all of these contributions. We ask the question of how the thermodynamic equilibrium of the hydrogel changes as a consequence of externally fixing the pH and ionic salt concentration of the outer bath solution in equilibrium with the gel.

This work is organized as follows: In section 2, the general molecular-level theory is introduced, while the molecular model used to evaluate the approach is presented in section 3. Then, in section 4, the behavior of the polyacid gel, whose total number of cross-links is independent of its density, in good solvent is described using results obtained with our general theoretical method. Finally, concluding remarks and directions for future work are presented in the last section.

2. Theoretical Approach

Consider a weak polyelectrolyte gel (G) with n_G monomer units in a solution containing water (w), protons (H^+), hydroxyl ions (OH^-), and completely dissociated salt, resulting in the presence of anions ($-$) and cations ($+$). Each monomer has one acid group that can be either protonated (AH) or deprotonated (A^-). Namely, we are considering a polyacid such as poly(acrylic acid). This system is in equilibrium with a homogeneous solution that provides a bath for all of the free species whose chemical potentials are determined by the bath pH and salt concentration, c . Our approach to this problem consists of defining a detailed molecular-level theory,^{37,38} which is described in the following.

First, we write the free energy of the system, which explicitly includes the conformational entropy of the flexible gel molecule, the mixing entropy of the different free species in the solution, the repulsive excluded volume interactions as well as the attractive van der Waals interactions, the chemical equilibrium resulting from the acid–base reaction, and the electrostatic interactions due to both charged free species and dissociated acid groups in the gel monomers. This free energy is expressed as a functional of the probability of the different molecular conformations of the gel, the local density distribution of the mobile species in the solution, the gel degree of dissociation, and the electrostatic field. Then, this free energy is optimized with respect to those functions subject to two constraints: the incompressibility constraint, which accounts for the intermolecular repulsions, and the global electroneutrality constraint, which requires the total charge of the system be zero. Finally, any thermodynamic quantity of interest can be computed after all these functions are determined by taking the proper derivative of the minimized thermodynamic potential.

In this framework, the total Helmholtz free energy of the system can be expressed as

$$F = -TS_{\text{conf}} - TS_{\text{mix}} + U_{\text{vdw}} + F_{\text{chm}} + U_{\text{elec}} \quad (1)$$

where T is the temperature and S_{conf} , S_{mix} , U_{vdw} , F_{chm} , and U_{elec} denote the configurational entropy of the gel, mixing entropy of the free species, van der Waals interaction energy, chemical free energy associated with the acid–base equilibrium, and

electrostatic interaction energy arising from charged species, respectively. The conformational entropy of the gel is given by

$$-\frac{S_{\text{conf}}}{k_B} = \sum_{\alpha} P(\alpha) \ln(P(\alpha))$$

where $P(\alpha)$ is the probability of finding the gel in conformation α . A conformation denotes a given spatial distribution of all the monomers of the gel.

The mixing (translational) entropy of the free species within the hydrogel is

$$-\frac{S_{\text{mix}}}{k_B} = \sum_{\gamma} \int d^3r \rho_{\gamma}(\mathbf{r}) [\ln(\rho_{\gamma}(\mathbf{r})v_w) - 1]$$

$$(\gamma = w, +, -, H^+, OH^-)$$

where v_w is the volume of a solvent molecule and $\rho_w(\mathbf{r})$, $\rho_+(\mathbf{r})$, $\rho_-(\mathbf{r})$, $\rho_{H^+}(\mathbf{r})$, and $\rho_{OH^-}(\mathbf{r})$ are the local number density of the different mobile species in the solution.

The total van der Waals attractive energy between gel monomers can be written as

$$\beta U_{\text{vdw}} = \sum_{\alpha} P(\alpha) \beta U_{\text{vdw}}(\alpha) = \frac{1}{2} \sum_{\alpha} P(\alpha) \sum_{i,j} \beta u_{\text{mm}}(r_{ij}^{\alpha})$$

where $\beta = 1/k_B T$ and $u_{\text{mm}}(r_{ij}^{\alpha})$ is the pairwise attractive interaction between monomers i and j : in configuration α , these two monomers are a distance r_{ij}^{α} apart, and $U_{\text{vdw}}(\alpha) = \frac{1}{2} \sum_{i,j} u_{\text{mm}}(r_{ij}^{\alpha})$ is the total van der Waals energy of the gel in that conformation. Note that this expression considers the exact van der Waals attractive energy of the gel.

On the other hand, the repulsive interactions are separated into intramolecular and intermolecular. The intramolecular repulsions are exactly taken into account through the gel conformations which are self-avoiding while the intermolecular ones are included in an approximate fashion through the use of local packing (incompressibility) constraints.

The free energy term describing the chemical reactions takes into account the acid–base equilibrium ($AH \rightleftharpoons A^- + H^+$) as follows:

$$\begin{aligned} \beta F_{\text{chm}} = & \int d^3r \frac{\langle \phi_G(\mathbf{r}) \rangle}{v_G} f_d(\mathbf{r}) (\ln f_d(\mathbf{r}) + \beta \mu_{A^-}^0) \\ & + \int d^3r \frac{\langle \phi_G(\mathbf{r}) \rangle}{v_G} (1 - f_d(\mathbf{r})) [\ln(1 - f_d(\mathbf{r})) + \beta \mu_{AH}^0] \\ & + \int d^3r (\rho_{OH^-}(\mathbf{r}) \beta \mu_{OH^-}^0 + \rho_{H^+}(\mathbf{r}) \beta \mu_{H^+}^0) \end{aligned}$$

where $\phi_G(\alpha, \mathbf{r})$ is the local volume fraction of gel in conformation α at \mathbf{r} , and $\langle \phi_G(\mathbf{r}) \rangle = \sum_{\alpha} P(\alpha) \phi_G(\alpha, \mathbf{r})$. The quantity $\langle \rangle$ represents the ensemble average over the set of configurations $\{\alpha\}$. The volume of a gel segment is v_G , and $\langle \phi_G(\mathbf{r}) \rangle / v_G$ is the average local polymer number density. The quantity $f_d(\mathbf{r})$ is the local degree of dissociation, which gives the fraction of monomers that are charged in the element of volume between \mathbf{r} and $\mathbf{r} + d\mathbf{r}$. The quantities $\mu_{A^-}^0$ and μ_{AH}^0 are the standard chemical potentials of charged and uncharged monomers, respectively. In addition, $\mu_{H^+}^0$ and $\mu_{OH^-}^0$ are respectively the standard chemical potentials of protons and hydroxyl ions which are needed since we explicitly consider the self-ionization of water ($H_2O \rightleftharpoons OH^- + H^+$).

The electrostatic energy term in eq 1 is given by

$$\beta U_{\text{elec}} = \int d^3r \left[\langle \rho_q(\mathbf{r}) \rangle \beta \Psi(\mathbf{r}) - \frac{1}{2} \beta \epsilon(\mathbf{r}) (\nabla \Psi(\mathbf{r}))^2 \right]$$

where $\Psi(\mathbf{r})$ is the electrostatic potential, $\varepsilon(\mathbf{r})$ denotes the dielectric permittivity of the medium at \mathbf{r} , and $\langle \rho_q(\mathbf{r}) \rangle$ is the ensemble average total charge at \mathbf{r} which is given by

$$\langle \rho_q(\mathbf{r}) \rangle = f_d(\mathbf{r}) \frac{\langle \phi_G(\mathbf{r}) \rangle}{v_G} q_G + \sum_{\gamma} \rho_{\gamma}(\mathbf{r}) q_{\gamma} \quad (\gamma = +, -, \text{H}^+, \text{OH}^-)$$

The quantity q_G in the total charge density represents the electric charge of the deprotonated gel monomer, while q_+ , q_- , q_{H^+} , and q_{OH^-} denote the electric charge of the various charged free species.

To the above total free energy of the gel system, we now impose two physical constraints: the incompressibility constraint that accounts for the intermolecular repulsions (excluded volume) in the system. Namely, at each position \mathbf{r} the total volume must be completely filled by some of the molecular species, i.e.

$$1 = \langle \phi_G(\mathbf{r}) \rangle + \sum_{\gamma} \rho_{\gamma}(\mathbf{r}) v_{\gamma} \quad (\gamma = \text{w}, +, -, \text{H}^+, \text{OH}^-) \quad (2)$$

where v_+ , v_- , v_{H^+} , and v_{OH^-} are the volume of the corresponding molecules. In addition, we require the system to be globally electroneutral, i.e.

$$\int d^3r \langle \rho_q(\mathbf{r}) \rangle = 0 \quad (3)$$

In total, the unknowns in eq 1 consist of the probability density function, $P(\alpha)$, the free species local densities, $\rho_{\gamma}(\mathbf{r})$ ($\gamma = \text{w}, +, -, \text{H}^+, \text{OH}^-$), the local degree of dissociation, $f_d(\mathbf{r})$, and the electrostatic potential, $\Psi(\mathbf{r})$. To obtain these quantities, a functional minimization of the free energy with respect to each of these variables is performed, subject to the two aforementioned constraints. Once these functions are obtained, any thermodynamic quantity can be derived in a straightforward manner.

The explicit function to minimize is

$$\begin{aligned} \beta F = & \sum_{\alpha} P(\alpha) [\ln(P(\alpha)) + \beta U_{\text{vdw}}(\alpha)] \\ & + \sum_{\gamma = \text{w}, +, -, \text{H}^+, \text{OH}^-} \int d^3r \rho_{\gamma}(\mathbf{r}) [\ln(\rho_{\gamma}(\mathbf{r}) v_{\gamma}) - 1] \\ & + \int d^3r \frac{\langle \phi_G(\mathbf{r}) \rangle}{v_G} f_d(\mathbf{r}) (\ln f_d(\mathbf{r}) + \beta \mu_{\text{A}^-}^0) \\ & + \int d^3r \frac{\langle \phi_G(\mathbf{r}) \rangle}{v_G} (1 - f_d(\mathbf{r})) [\ln(1 - f_d(\mathbf{r})) + \beta \mu_{\text{AH}}^0] \\ & + \int d^3r (\rho_{\text{OH}^-}(\mathbf{r}) \beta \mu_{\text{OH}^-}^0 + \rho_{\text{H}^+}(\mathbf{r}) \beta \mu_{\text{H}^+}^0) \\ & + \int d^3r \left[\langle \rho_q(\mathbf{r}) \rangle \beta \Psi(\mathbf{r}) - \frac{1}{2} \beta \varepsilon(\mathbf{r}) (\nabla \Psi(\mathbf{r}))^2 \right] \quad (4) \end{aligned}$$

Minimization subject to the constraints leads to

$$\begin{aligned} \rho_{\text{w}}(\mathbf{r}) &= \frac{1}{v_{\text{w}}} \exp(-\beta \pi(\mathbf{r}) v_{\text{w}}) \\ \rho_{\gamma}(\mathbf{r}) &= \frac{\rho_{\gamma}^{\text{hm}}}{(v_{\text{w}} \rho_{\text{w}}^{\text{hm}})^{v_{\gamma}/v_{\text{w}}}} \exp(-\beta \pi(\mathbf{r}) v_{\gamma} - \beta \Psi(\mathbf{r}) q_{\gamma}) \\ (\gamma &= \text{H}^+, \text{OH}^-, +, -) \quad (5) \end{aligned}$$

for the mobile species where $\pi(\mathbf{r})$ are the local Lagrange multipliers conjugated with the packing constraint, eq 2, at each point in space. $\rho_{\gamma}^{\text{hm}}$ ($\gamma = \text{w}, +, -, \text{H}^+, \text{OH}^-$) is the density of free species

γ in the homogeneous bath solution. These quantities are input constants that depend only on bath pH and c and appear since we require the free species to have a constant chemical potential which must be that of the bath solution. Moreover, the probability of a gel conformation α is given by

$$P(\alpha) = \frac{1}{Q} \exp(-\beta U_{\text{vdw}}(\alpha) - \int d^3r \phi_G(\mathbf{r}, \alpha) \beta \pi(\mathbf{r})) \exp \left[- \int d^3r \frac{\phi_G(\mathbf{r}, \alpha)}{v_G} (\beta \Psi(\mathbf{r}) q_G + \ln f_d(\mathbf{r})) \right] \quad (6)$$

where the factor Q imposes $\sum_{\alpha} P(\alpha) = 1$. The functional form of the probability density function shows the very strong coupling expected between the physical interactions in the system, the gel conformation, and the local degree of dissociation. The manifestation of this coupling will be discussed in the next section together with the presentation of the results. The local degree of dissociation, $f_d(\mathbf{r})$, that minimizes the free energy functional, after algebraic manipulation, is given by

$$\frac{f_d(\mathbf{r})}{1 - f_d(\mathbf{r})} = \frac{K_{\text{a}}^0}{v_{\text{w}} \rho_{\text{H}^+}^{\text{hm}}} (v_{\text{w}} \rho_{\text{w}}^{\text{hm}})^{v_{\text{H}^+}/v_{\text{w}}} \exp(-\beta \Psi(\mathbf{r}) q_G) \quad (7)$$

where K_{a}^0 is the dimensionless standard equilibrium constant, which is proportional to the standard equilibrium constant of the acid–base reaction, K_{a} , expressed in molar units, and defined by

$$K_{\text{a}} = \frac{[\text{A}^-][\text{H}^+]}{[\text{AH}]} \quad (8)$$

The standard chemical potentials of the protons and the hydroxyl ions can be expressed in terms of the densities of the free species in the homogeneous bath (see section A of the Appendix), and the standard chemical potential of the ionized acid groups is obtained using $K_{\text{a}}^0 = \exp(\beta \mu_{\text{AH}}^0 - \beta \mu_{\text{H}^+}^0 - \beta \mu_{\text{A}^-}^0)$.

Furthermore, the variation of the free energy with respect to the electrostatic potential results in the Poisson equation:

$$\varepsilon \nabla^2 \Psi(\mathbf{r}) = -\langle \rho_q(\mathbf{r}) \rangle \quad (9)$$

where it is clear the strong coupling that exists between the electrostatic potential and all the other degrees of freedom and the chemical equilibrium through the average of the local charge density.

The unknowns left after minimization of the free energy are the Lagrange multipliers, $\pi(\mathbf{r})$, and the electrostatic potential, $\Psi(\mathbf{r})$, which are obtained by solving, at each position, the packing constraint, eq 2, and the Poisson equation, eq 9, respectively. The pH and salt concentration are input variables of the molecular theory and determine bath densities of the free species. Moreover, a molecular model of the polyelectrolyte gel must be defined to obtain the set of gel conformations needed to calculate results using this theory. We introduce the molecular model used in this work in the next section. Further details on the molecular theory of the polyelectrolyte gel are presented in section A of the Appendix.

3. Molecular Model

As an initial approach to the problem, a simple model of polyelectrolyte (PE) gel molecule is considered (see Figure 1). The gel is modeled as monodisperse chains connected at nodal monomers. Each chain has 25 segments excluding the nodes. In the calculations, a cubic box of volume V is considered, and periodic boundary conditions are imposed. There are 64 nodes in

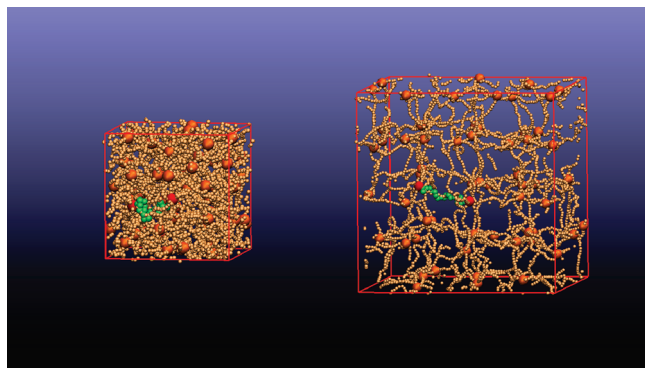


Figure 1. Molecular model of the polyelectrolyte gel at two different volume fractions, $\phi_G = 0.095$ (left) and $\phi_G = 0.013$ (right). Nodes are represented by larger spheres, and one chain is shown in a different color (for illustration purposes only).

the calculation box, each connected to six chains. Thus, the total number of monomers in the box is $n = 64 + 64 \times 6/2 \times 25 = 4864$. All monomers, including the nodes, are set to have the same volume, v_G . As such, the global gel volume fraction is given by $\phi_G = (1/V) \int d^3r \langle \phi_G(\mathbf{r}) \rangle = n(v_G/V)$. Different box sizes with box length between 9.84 and 25.87 nm (ϕ_G between 0.334 and 0.0184) were considered. The system size is chosen as large as possible to reduce box size effects but still allow the computation of our results. For each volume fraction, a large set ($\sim 10^4$) conformations are generated using molecular dynamics simulations whose technical details are presented in section C of the Appendix.

The PE gel is taken under good solvent conditions, which is modeled by selecting $u_{mm} \equiv 0$. The monomer segment length is taken as $l_G = 0.5$ nm, its volume $v_G = (\pi/6)l_G^3 = 0.0655$ nm³, and its charge either zero or $q_G = -e$, with e being the absolute value of the electron charge. The acid–base equilibrium constant is taken $pK_a = 5$.

The water dissociation equilibrium constant is $pK_w = 14$. The aqueous medium is assumed to have a homogeneous dielectric constant, $\epsilon(\mathbf{r}) \equiv \epsilon_w \epsilon_0$, with $\epsilon_w = 80$ and ϵ_0 denoting the vacuum permittivity.

The monovalent salt is taken as sodium chloride, which is assumed to be completely dissociated in solution. Salt ions are described by $v_+ = v_- = 0.0335$ nm³ and $q_+ = -q_- = e$. For the rest of the mobile species in the solution, the values used are $v_{H^+} = v_{OH^-} = v_w = 0.03$ nm³ and $q_{H^+} = -q_{OH^-} = e$.

4. Results

Consider the acid–base reaction, described by eq 8, taking place in a bulk system, where all of the reacting species are mobile in the solution. Under the assumption of ideal solution, the degree of dissociation, which is the fraction of unprotonated acid groups, is given by

$$f_{\text{bulk}} = \frac{[A^-]}{[AH] + [A^-]} = \frac{1}{1 + \frac{[H^+]}{K_a}} \quad (10)$$

where $[H^+]$ is the bulk concentration of protons. Then, given the pK_a of the acid, f_{bulk} depends only on the pH of the solution.

In the gel, the acid groups are part of the interconnected polyelectrolyte chains, which imposes a constraint that modifies the equilibrium conditions as compared to the bulk reaction. f_{bulk} is, however, often used to estimate the gel degree of dissociation. We shall show that this is a poor approximation and that the gel degree of dissociation can deviate substantially from f_{bulk} , and it does so in a nontrivial way.

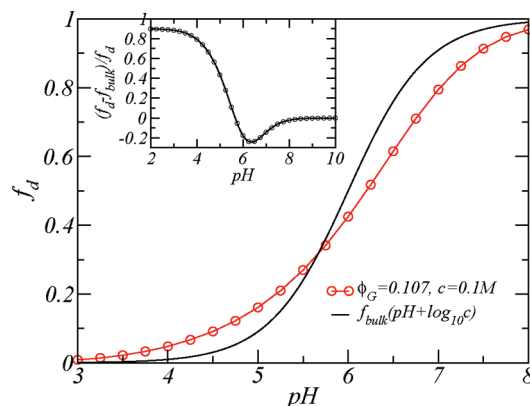


Figure 2. Our results (open red circles) are compared to the bulk degree of dissociation, f_{bulk} , including the correction for Donnan effect (black curve). The relative difference between the curves, $(f_d - f_{\text{bulk}})/f_d$, is shown in the inset as a function of pH.

Following eq 7, the local degree of dissociation, $f_d(\mathbf{r})$, can be expressed as

$$f_d(\mathbf{r}) = \frac{1}{1 + \frac{[H^+]}{K_a} C_1 \exp(\beta \Psi(\mathbf{r}) q_G)} \quad (11)$$

where C_1 is a constant close to unity, whose dependence on the salt concentration of the solution is very weak. The quantity $[H^+]$ is the concentration of protons in the bath solution. Comparison between eqs 11 and 10 seems to suggest that the only difference between the bulk and the local gel expression is given by the local electrostatic potential. However, one should recall that the electrostatic potential is the result of the interplay between the packing of the different species, gel-chain statistics, distribution of free species, and chemical equilibrium, which is clear by looking at the Poisson equation (eq 9) where this coupling enters through the total charge density. Therefore, as we will show, the acid–base equilibrium behaves in a nontrivial way as compared to the bulk solution. Furthermore, the local dissociation is only defined in the regions of space where there is polymer, something that cannot be deduced from eq 11. To quantify the comparison between the dissociation in the bulk and within the gel, we define the gel degree of dissociation, f_d , as the spatial average of the local degree of dissociation weighted by the polymer volume fraction, i.e., $f_d = (\int d^3r f_d(\mathbf{r}) \langle \phi_G(\mathbf{r}) \rangle) / (\int d^3r \langle \phi_G(\mathbf{r}) \rangle)$.

Figure 2 compares the dependence on bath pH of the gel and bulk degrees of dissociation. In the presence of salt ions, it is more natural to consider the bulk degree of dissociation as a function of $pH + \log c$ due to the Donnan effect.⁴⁰ This is, simply, a translation by $\log c$ along the abscissa of the $f_{\text{bulk}}(pH)$ curve given by eq 10. When pH is increased, the gel degree of dissociation varies with a slope that changes more smoothly as compared to the bulk situation. The bulk system goes from uncharged to completely dissociated in a narrow range of pH values. The PE gel responds less abruptly to changes in bath pH, and there is a wider range of pH values for which the protonated and unprotonated monomers are mixed. The more broad transition between charged and uncharged segments can be explained by noticing that in the gel the chemical equilibrium between protonated and unprotonated species does not only depend on the local concentration of both species but also on the local electrostatic potential, which in turn results from the solution of a Poisson equation in which all of the interactions in the system are coupled. The gel degree of charge results from the complex balance between electrostatic interactions, chemical equilibrium osmotic pressure, counterion release, and the conformational degrees of freedom of the gel. We will

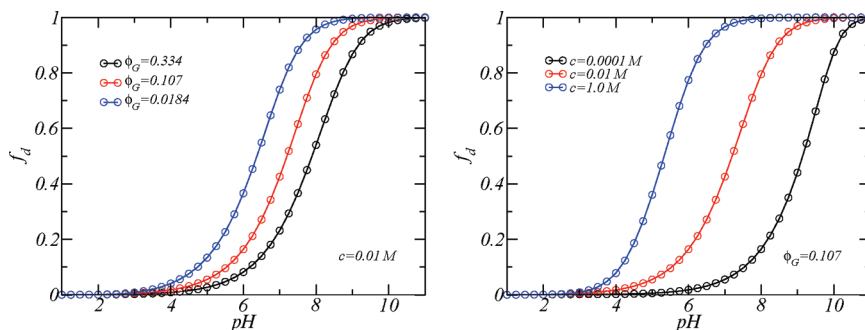


Figure 3. Degree of dissociation, f_d , as a function of pH. Left: different volume fraction curves are shown. Right: f_d vs pH at various salt concentrations.

show how this interplay works by describing a variety of conditions below.

Deviations of the gel degree of dissociation from the bulk are large in most of the pH range studied. The difference between the bulk and gel degrees of dissociation relative to the gel value, $(f_d - f_{\text{bulk}})/f_d$, is shown in the inset of Figure 2. Note that using f_{bulk} as an approximation to f_d leads to an underestimation of the gel charge of as much as 90% at low pH and close 30% near $\text{pH} = \text{pK}_a = 5$. For larger pH values, the gel degree of ionization can be overestimated by as much as 20% using such an approximation, which is only justified at very large pH. In absolute terms, the difference between bulk and gel degrees of dissociation ($|f_d - f_{\text{bulk}}|$) can be as much as 0.1 at low pH or 0.15 at high pH, in the case shown in Figure 2. We conclude that the gel degree of ionization cannot be approximated by using the bulk value because such huge deviations of f_d from f_{bulk} can have important physical consequences. For example, we will show later that the difference between the degree of ionization in the collapsed and swollen regimes of the gel is less than that observed between our results and the bulk curve.

The dependence of f_d on pH for different volume fractions and different salt conditions is shown in Figure 3. The results are presented for fixed values of the volume fraction of the gel, $\phi_G = (1/V) \int d^3r \langle \phi(\mathbf{r}) \rangle$. Compressing the gel (by increasing ϕ_G) results in a much less charged system at fixed pH, except in the regions where the system is either uncharged or minimally charged ($f_d \approx 0$, $\text{pH} \ll \text{pK}_a$) and in the region where the gel is fully charged ($f_d \approx 1$, large pH). This is expected since, for intermediate values of pH, compressing the gel implies higher electrostatic repulsions between the monomers, and the system responds by decreasing the number of charged monomers in order to mitigate the increasing repulsions. Namely, the system sacrifices chemical free energy in order to relax some of the electrostatic repulsions and gain in counterion release at the same time. The effect of salt concentration can be also interpreted in terms of the balance between electrostatic repulsions and chemical free energy. Increasing the salt concentration at fixed pH and ϕ_G results in a larger screening of the repulsions between monomers, and therefore the hydrogel increases its degree of dissociation. However, a description of the gel behavior based only on the electrostatic interaction is too simplistic and may lead to wrong conclusions: the degree of dissociation as a function of pH, c , and ϕ_G is the result of the coupling between the acid–base equilibrium, the gel conformational degrees of freedom, mobile species entropy, and excluded volume as well as electrostatic interactions.

Let us now define pK_{app} as the pH at which the degree of dissociation is one-half, i.e., $f_d(\text{pH} = \text{pK}_{\text{app}}) = 1/2$. This quantity is experimentally known as the apparent pK_a . The dependence of pK_{app} on salt concentration and polymer volume fraction is displayed in Figure 4. The apparent pK_a increases monotonically with increasing gel volume fraction or decreasing salt concentration. This quantity can be thought as an intrinsic property of the

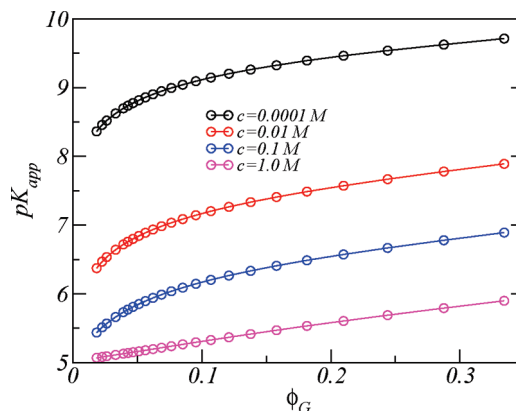


Figure 4. Apparent pK_a , pK_{app} , vs gel volume fraction at different salt concentration conditions. The apparent pK_a is defined by the equation $f_d(\text{pH} = \text{pK}_{\text{app}}) = 1/2$.

PE gel that measures when (in terms of varying pH) the gel becomes charged: if $\text{pH} > \text{pK}_{\text{app}}$, most of the acid groups in the gel will be deprotonated (charged). In the case of the bulk reaction of the isolated acid group, $\text{pK}_{\text{app}} = \text{pK}_a$. The lower the salt concentration, the largest the minimum pH needed to charge the system. In fact, for the lowest salt concentration shown in the figure the gel is uncharged in almost all the range of pH values studied. Namely, all this can be interpreted as a local Le Chatelier principle, where the equilibrium is shifted as a response to changes in the environment. The interesting and important finding is that in gels this is a local effect since the gel is locally inhomogeneous. For more compressed systems ($\phi_G > 0.15$, for example) the different c curves are roughly parallel, and the difference in pK_{app} can be mainly attributed to salt concentration differences. In the limit of infinite dilution, $\phi_G \rightarrow 0$, and high c , pK_{app} seems to converge to pK_a as expected. Note, however, that as the salt concentration decreases, the variation from pK_{app} to pK_a , at very low gel volume fractions, has a very steep gradient.

The hydrogels we consider are in equilibrium with a bath solution whose pH and c are the variables controlled experimentally; i.e., their bath values determine the constant chemical potential of charged mobile species in the gel. In other words, the chemical potentials of the charged free species are identical in the gel and the bath solution. The concentration of protons in the gel is found to be different from that of the bath solution. To quantify the difference between the proton concentration in the bath solution and inside the gel, we define the gel pH as $\overline{\text{pH}} = 1/V \int d^3r \text{pH}(\mathbf{r})$, where the local gel pH is $\text{pH}(\mathbf{r}) = -\log([H^+](\mathbf{r})) = -\log(\rho_{H^+}(\mathbf{r})/N_A)$ with N_A denoting Avogadro's number, and show in Figure 5 how this quantity varies as a function of the bath pH. The two different panels in the figure illustrate the dependence of $\overline{\text{pH}}$ on both volume fraction and salt concentration. The dashed line represents the case in which the pH inside the gel and that of the bath are identical.

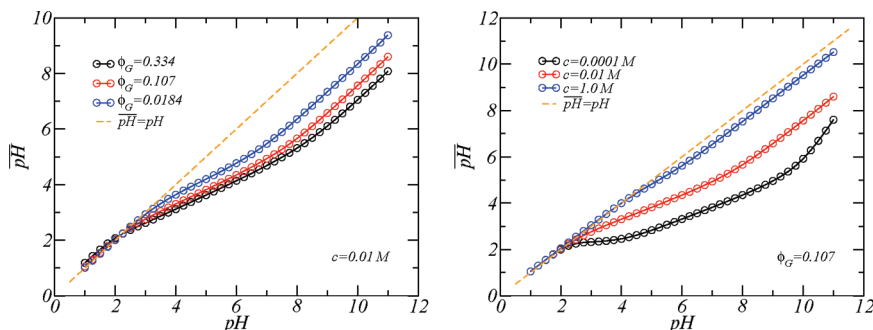


Figure 5. Gel pH, $\overline{\text{pH}}$, vs the pH of the bath solution.

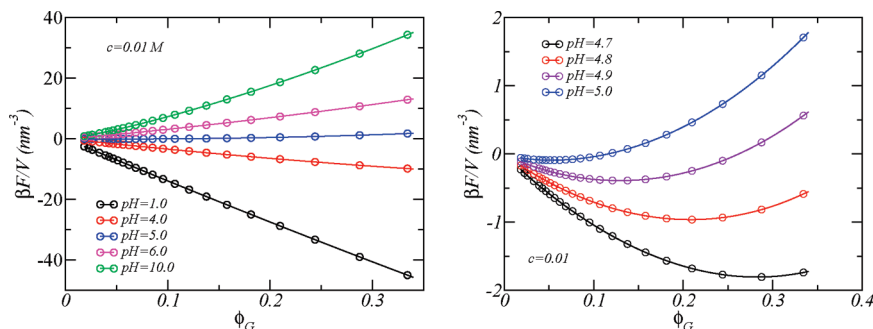


Figure 6. Free energy density vs gel volume fraction for different values of pH. Left: all pH range is represented. Right: a close-up of the cases $\text{pH} \sim \text{p}K_a = 5$.

For very low pH, the concentration of protons is roughly the same in the bath solution as in the gel, but there is a particular pH value at which $\overline{\text{pH}}(\text{pH})$ starts to deviate from the bath value ($\overline{\text{pH}}(\text{pH}) = \text{pH}$). This value depends strongly on the salt concentration and more weakly on the gel's volume fraction. In most of the range pH values, $\overline{\text{pH}}$ is lower than the bath pH, which means that the concentration of protons is higher in the hydrogel than in the bath. Moreover, depending on the ionic strength of the solution, the proton concentration can be several orders of magnitude larger in the gel. There is a contribution to this phenomenon resulting from the Donnan potential, established because the deprotonated monomers cannot cross to the bath solution. However, this contribution alone is not enough to describe the behavior of the system; otherwise, different c curves should be parallel, and there should be no dependence on ϕ_G ; see also Figure 2 which demonstrates that the Donnan potential is not enough to even quantitatively explain the predictions of the molecular theory. The gel pH is the consequence of the complex balance between acid–base equilibrium, the gel molecular organization, and the resulting electrostatic interactions. These contributions are coupled in our approach, resulting in the observed nonlinear behavior of the PE gel which means that the response of the system to external stimuli cannot be analyzed in terms of just one of such contributions, except in very limiting cases. The reason for the pH inside the gel to be higher than in the bath solution under all conditions can be explained on the basis of a local Le Chatellier principle or more formally due to the proton activity. Namely, inside the gel there is always a tendency to have a larger proton concentration in order to shift the chemical equilibrium toward the protonated (uncharged) state. This is due to the increased chemical potential that arises from the electrostatic interactions. To decrease the chemical potentials, the gel becomes uncharged. This effect is stronger when the ionic strength is lower and the gel volume fraction increases, since both effects increase the strength of the electrostatic repulsions. Therefore, we see the tendencies shown in Figure 5 where the chemical equilibrium strongly couples to the steric and electrostatic interactions by reducing the gel's pH.

In all the preceding discussion, we have assumed that the volume fraction of polyelectrolyte gel was an externally controlled variable. Let us now consider the case in which the polyacid gel can find its optimal volume fraction once the external variables, pH and c , have been set. Figure 6 shows the free energy as a function of polymer volume fraction at different bath solution pH values. Three different regimes are observed here: if $\text{pH} < \text{p}K_a = 5$, the gel shrinks to a highly dense state. The optimal volume fraction ϕ_0 , such that $(\partial(\beta F/V(\phi_G))/\partial\phi_G)_{\phi_0} = 0$, is actually larger than the volume fractions considered in this study. However, even though the exact value is not obtained, it is clear by looking at the trend of the free energy that ϕ_0 corresponds to a highly collapsed hydrogel (ϕ_0 very large). On the other side, if $\text{pH} > \text{p}K_a$, the optimal volume fraction corresponds to a swollen state ($\phi_0 \sim 0$). Interestingly, if $\text{pH} \sim \text{p}K_a$, the free energy displays a minimum that does not correspond to either a collapsed or a swollen state of the gel. It is also worth noticing that varying the pH by a small amount leads to big changes in the optimal volume fraction.

Figure 7 shows the free energy of the gel as a function of the volume fraction in the three distinctive regimes. In this case, we try to analyze the role of salt concentration in determining the gel equilibrium conformation in the different regimes. In the collapsed regime ($\text{pH} < \text{p}K_a$), the free energy as a function of the volume fraction is almost independent of c . The electrostatic interactions do not play a significant role since effectively the gel is uncharged, and the system finds equilibrium by optimizing the packing of the gel segments. On the contrary, the free energy depends strongly on the salt concentration for the swollen state ($\text{pH} > \text{p}K_a$) because in this case the degree of dissociation is significantly higher than in the collapsed regime. Near the optimal volume fraction, however, all curves seem to converge since it is expected that all of them have a very small ϕ_0 . As such, the differences between the optimal volume fraction at different c will be even smaller. Here, the deprotonated (charged) PE gel minimizes the free energy by expanding and thereby reducing electrostatic repulsions. Thus, changing the salt concentration cannot cause further structural changes in the already swollen gel, and this explains the system behavior near the optimal volume

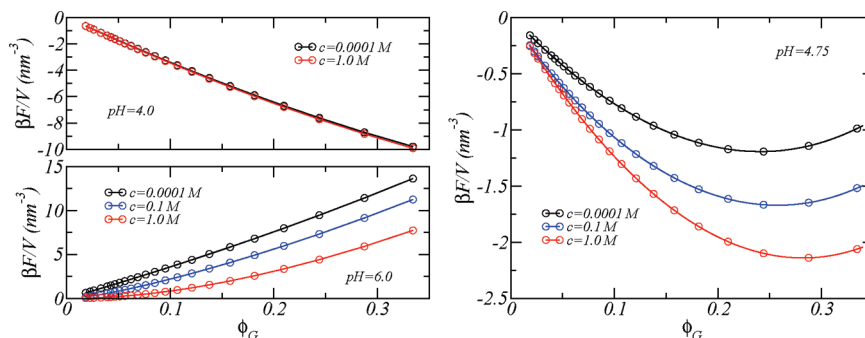


Figure 7. Dependence of the free energy density, $F(\phi_G)/V$, on the ionic strength of the solution for the collapsed (left upper panel), swollen (left lower panel), and intermediate (right panel) gel volume fraction regimes.

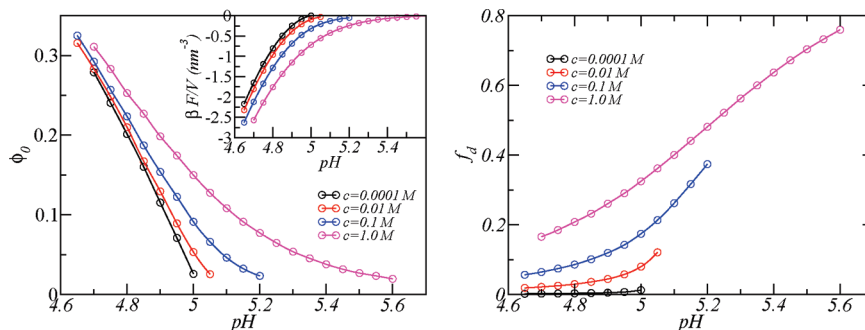


Figure 8. Left: the optimal gel volume fraction, ϕ_0 as a function of pH. The free energy density at the optimal gel volume fraction is shown in the inset. Right: the degree of dissociation at the optimal gel volume fraction. In both panels different salt conditions are included.

fraction. In the intermediate cases (right panel, $\text{pH} \sim \text{pK}_a$), both the free energy and the exact location of the minima depend on the concentration of salt ions and higher ionic salt concentrations shift the minimum to higher volume fractions: as the screening increases, the polymers are more charged and thus the volume fraction of the equilibrium state is larger. Namely, the degree of gel swelling is the optimal interplay between the dual action of adding salt to the system, which decreases the range of the interactions and at the same time increases the electric charge of the gel. This interplay is ubiquitous in the charge regulation of confined weak polyelectrolytes; similar behavior is found, for example, in grafted layers of polyacids.^{36,38}

The left panel of Figure 8 shows the dependence of the optimal volume fraction on pH at different c conditions. The $\phi_0(\text{pH})$ curves are very steep and go from high (collapsed) to low (swollen) values of ϕ_0 within a very narrow range of pH. The transition from one regime to the other, however, seems to be continuous. Decreasing c leads to a more sudden transition with respect to the pH. In transitioning from the collapsed to the swollen regime, the gel increases its charge. At low salt concentrations, increasing the degree of dissociation will lead to a sharp swelling due to the large Debye length, and therefore one expects this transition from uncharged to charged states to be sharp. Higher concentrations of salt allow the hydrogel more flexibility in terms of modifying the local environment via charge regulation with less degree of swelling. At lower salt concentrations, on the other hand, the increase in monomer ionization has to be accompanied by a higher degree of swelling. This behavior can also be observed by looking at the degree of dissociation for the unconstrained gel, which is displayed in the right panel of Figure 8. The gel is always uncharged for low salt concentrations, while for high ionic concentrations, the system transitions from a poorly charged state (at low ϕ_0) to a highly charged state (at high ϕ_0) in the intermediate range of pH. Note that in the collapsed regime a poorly charged gel is always the case independently of the salt concentration. In contrast, the gel in the swollen regime can have different degrees of charge depending on c , though a highly charged

PE gel is expected, if the pH is high enough (see for example Figure 3). These effects are also a manifestation of the dual role of the solution ionic strength to screen the electrostatic interactions while increasing the charge on the polymers.

5. Concluding Remarks

In this work, we describe a theory designed to analyze the response of weak polyelectrolyte gels to changes in pH and salt concentration. This theoretical approach incorporates specific molecular details pertaining to the gel molecule, including its conformational degrees of freedom, coupled to the acid–base equilibrium, as well as to the underlying electrostatic, attractive van der Waals, and repulsive excluded-volume interactions and solution entropy. Specifically, we have applied the theoretical approach developed here to study a polyacid gel under good solvent conditions.

The hydrogel's local degree of charge is a function of the externally imposed pH and of the local electrostatic potential. This electrostatic potential results from a generalized Poisson equation in which the contributions from the various interactions described in the previous paragraph are coupled with the acid–base chemical equilibrium. As a result, the average degree of dissociation differs from the bulk value which is normally considered for these systems. Depending on the ionic strength of the solution, these differences in polymer charge can be higher than those observed between swollen and collapsed regimes. Therefore, we conclude that the common use of the bulk formula to estimate the gel degree of dissociation is incorrect, and the interplay between acid–base equilibrium and local interactions needs to be appropriately treated.

The polyacid gel can regulate charge and modify its local environment. We found that the pH within the gel's surrounding can drop significantly when compared to that of the bath solution. This nonlinear dependence of the gel pH with respect to the bath medium's pH has an enormous importance in, for example, the design of hydrogel applications such as pH-controlled drug delivery systems.^{41,42}

In a good solvent, the weak PE gel responds to external changes of pH in a dramatic way. If pH is near pK_a , the volume fraction of gel can be controlled, depending on the exact value of pH and on the ionic strength of the solution. However, slightly increasing the pH rapidly leads to a swollen state, while a small reduction of pH results in a collapsed gel. Therefore, fluctuations in bath pH could potentially lead to large fluctuations in the gel volume fraction. The collapsed state corresponds always to a poorly charged system, where excluded-volume interactions are dominant. In the swollen state, on the other hand, electrostatic forces are dominant, and therefore the degree of charge depends more critically on the salt concentration. These interactions, however, are coupled in our approach and their net contribution to determining the gel's thermodynamic equilibrium cannot be clearly separated. The transition between those two regimes is continuous and drastic, occurring within a very narrow range of pH whose width depends upon the bath salt concentration.

The presence of salt ions in the system has two opposing roles. On the one hand, increasing salt concentration decreases the range and strength of the electrostatic interactions. On the other hand, an increase in salt concentration results in a more charged system which augments the importance of the electrostatic interactions in determining the behavior of the system, particularly its swelling. This coupling between charge regulation, electrostatic interactions, and gel swelling shows the importance of optimizing all the degrees of freedom together within a single theoretical framework, and it explains why considering the charge state of weak polyelectrolytes to be homogeneous and given by the bath value provides with the incorrect qualitative behavior.

The theoretical approach presented here can be applied using any molecular model of the weak polyelectrolyte gel. As our initial approach to the problem, we have chosen a relatively simple and regular model in which the connectivity of all monomer nodes is the same and in which all the chains are monodisperse. However, the degree of cross-linking and the molecular weight of gel chains modify the quantitative swelling behavior in response to external stimuli.⁴³ Therefore, this molecular model will need to be refined in future applications of such molecular theory. In addition, further research using this approach should include the study of weak PE gels under bad solvent conditions, which requires a non-negligible definition of monomer–monomer van der Waals attractive interactions as opposed to the case studied here.

In poor solvent conditions charged gels undergo large volume changes induced by external changes.² These changes have been associated with the formation of nanophase or microphase segregation transitions.⁴⁴ Polyelectrolyte gels with attractive interactions, such as those induced by hydrophobic backbones, can form locally segregated patterns in aqueous solutions¹⁴ that consist of regions where the gel is locally collapsed, interdispersed in regions where the gel is expanded. In the case of gels with acid groups and poor solvent backbones, one expects self-regulated local composition, charge, and pH heterogeneities, which can be controlled by temperature, ionic concentrations, pH values, and electric fields as it has been found to be the case in grafted hydrophobic weak polyelectrolyte layers.³⁸

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Appendix

A. Molecular Theory. In this work, the theoretical approach developed previously in refs 37 and 38 is now extended to investigate the behavior of a weak PE gel under different pH and salt concentration conditions. The previous studies described extensively the application of the theory in examining weak polyacid-grafted layers. In this section, we

only describe the most important aspects of the theoretical framework as well as introduce the necessary modifications.

The hydrogel system is in equilibrium with a homogeneous solution that provides a bath for all of the mobile species. In this context, homogeneity means that the densities of the different species in this bath solution are independent of position. Namely, in this region of the solution, the quantity $\rho_\gamma(\mathbf{r}) \equiv \rho_\gamma^{\text{hm}}$ ($\gamma = w, +, -, H^+, OH^-$) is a constant that depends only on pH and c .

The thermodynamic equilibrium is, therefore, given by the Lagrange transform of the free energy that is a function of the chemical potentials for the mobile species, which consist of the water molecules, the protons, the hydroxyl ions, and the salt anions and cations. The existence of two constraints reduces the total number of independent thermodynamic variables by two.³⁷ Thus, we can introduce exchange chemical in such a way that those of water, protons, and hydroxyl ions do not represent relevant thermodynamic variables. Then, the semi-grand canonical potential, $W = F - \mu_+ N_+ - \mu_- N_-$, with μ_+ and μ_- being the exchange chemical potentials conjugated to the number of salt cations (N_+) and anions (N_-), respectively, is indeed the thermodynamic potential whose minimum yields the equilibrium state. In our formalism, W is expressed as

$$W = F - \mu_+ \int d^3r \rho_+(\mathbf{r}) - \mu_- \int d^3r \rho_-(\mathbf{r})$$

Furthermore, the solution to our problem must satisfy both incompressibility and electroneutrality constraints (eqs 2 and 3). To impose each of these constraints, the Lagrange multipliers $\pi(\mathbf{r})$ and λ need to be introduced, respectively. In its complete form, the functional that we need to extremize becomes

$$\Phi = \beta W + \int d^3r \beta \pi(\mathbf{r}) [\langle \phi_G(\mathbf{r}) \rangle + \sum_\gamma \rho_\gamma(\mathbf{r}) v_\gamma - 1] + \lambda \int d^3r [\rho_q(\mathbf{r})]$$

Minimization of Φ yields the following results for the densities of the free species:

$$\rho_w(\mathbf{r}) = \frac{1}{v_w} \exp(-\beta \pi(\mathbf{r}) v_w)$$

$$\rho_\gamma(\mathbf{r}) = \frac{\rho_\gamma^{\text{hm}}}{(v_w \rho_w^{\text{hm}})^{v_\gamma/v_w}} \exp(-\beta \pi(\mathbf{r}) v_\gamma - \beta \Psi(\mathbf{r}) q_\gamma) \\ (\gamma = H^+, OH^-, +, -)$$

Moreover, assuming that the dielectric constant of the medium is homogeneous ($\epsilon(\mathbf{r}) \equiv \epsilon$), the probability density function of gel conformations is given by

$$P(\alpha) = \frac{1}{Q} \exp(-\beta U_{\text{vdw}}(\alpha)) \\ - \int d^3r \phi_G(\mathbf{r}, \alpha) \beta \pi(\mathbf{r}) \exp \left[- \int d^3r \frac{\phi_G(\mathbf{r}, \alpha)}{v_G} (\beta \Psi(\mathbf{r}) q_G + \ln f_d(\mathbf{r})) \right]$$

where the factor Q ensures the satisfaction of $\sum_\alpha P(\alpha) = 1$.

For the local degree of dissociation, we obtain

$$\frac{f_d(\mathbf{r})}{1 - f_d(\mathbf{r})} = \frac{K_a^0}{v_w \rho_{H^+}^{\text{hm}}} (v_w \rho_w^{\text{hm}})^{v_{H^+}/v_w} \exp(-\beta \Psi(\mathbf{r}) q_G)$$

where K_a^0 is the dimensionless thermodynamic equilibrium constant for the acid–base reaction, related to the standard

chemical potentials of the protons, the unprotonated and protonated species via $K_a^0 = \exp(\beta\mu_{\text{AH}}^0 - \beta\mu_{\text{H}^+}^0 - \beta\mu_{\text{A}^-}^0)$. Note that the more commonly mentioned experimental equilibrium constant K_a , given in molar units, is defined by

$$K_a = \frac{[\text{A}^-][\text{H}^+]}{[\text{AH}]}$$

so that K_a and K_a^0 are proportional. The standard chemical potentials of the protons and the hydroxyl ions are respectively given by

$$\exp(-\beta\mu_\gamma^0) = \frac{v_w \rho_\gamma^{\text{hm}}}{(v_w \rho_w^{\text{hm}})^{v_\gamma/v_w}} \quad (\gamma = \text{H}^+, \text{OH}^-)$$

while the chemical potential of the salt ions are expressed as

$$\exp(\beta\mu_\gamma) = \frac{v_w \rho_\gamma^{\text{hm}}}{(v_w \rho_w^{\text{hm}})^{v_\gamma/v_w}} \quad (\gamma = +, -)$$

In addition, the variation of Φ with respect to the electrostatic potential readily yields the Poisson equation

$$\varepsilon \nabla^2 \Psi(\mathbf{r}) = -\langle \rho_q(\mathbf{r}) \rangle$$

Because we are modeling a volumetric hydrogel, periodic boundary conditions are imposed to the electrostatic potential; this periodicity of $\Psi(\mathbf{r})$ guarantees electroneutrality.

At this point, the free energy have been expressed in terms of the position-dependent osmotic pressure, $\pi(\mathbf{r})$, the electrostatic potential, $\Psi(\mathbf{r})$, the densities of the different mobile species in the bath homogeneous solution, ρ_γ^{hm} ($\gamma = \text{w}, \text{H}^+, \text{OH}^-, +, -$) as well as inputs provided by the molecular model that include the polymer pK_a ($pK_a = -\log K_a$), the gel volume fraction distribution, $\phi_G(\mathbf{r}, \alpha)$, etc. Once the independent variables of a calculation, pH, c , and ϕ_G are set, all of the homogeneous bath densities ρ_w^{hm} , $\rho_{\text{H}^+}^{\text{hm}}$, $\rho_{\text{OH}^-}^{\text{hm}}$, ρ_+^{hm} , and ρ_-^{hm} can be obtained via imposing the incompressibility and electroneutrality constraints in the bath solution. Another relationship to be used at this point is the self-ionization of water described by $K_w = [\text{OH}^-][\text{H}^+] \propto \exp(-\beta\mu_{\text{OH}^-}^0 - \beta\mu_{\text{H}^+}^0)$. Lastly, the quantities $\pi(\mathbf{r})$ and $\Psi(\mathbf{r})$ are determined by substituting the expressions for the local densities of free species and ensemble average local gel volume fraction into the incompressibility constraint (eq 2) and the Poisson equation (eq 9). The solution can then be obtained numerically (see section A.1 of the Appendix).

Finally, it is important to mention that the theory requires the input of the complete set of gel conformations for each volume fraction. The free energy term, $-k_B \sum_\alpha P(\alpha) \ln P(\alpha)$, represents the exact conformational entropy of the gel if all possible molecular configurations are included in the sum. It is, however, only possible to include a finite number of conformations in practice. To calculate the conformational entropy, we define $-k_B \sum_\alpha P(\alpha) \ln P(\alpha) = -k_B \sum_{\tilde{\alpha}} P(\tilde{\alpha}) \ln P(\tilde{\alpha}) + \Delta_\alpha F$, where $\{\tilde{\alpha}\}$ is a finite set of conformations, large enough to describe the gel's conformational degree of freedom properly, and $\Delta_\alpha F$ is the correction needed as a result of this truncation of the gel's conformational space. It is important to mention that the main contribution to the conformational entropy comes from the term $-k_B \sum_{\tilde{\alpha}} P(\tilde{\alpha}) \ln P(\tilde{\alpha})$ and not from the correction (see Figure 11 in Appendix B). The gel conformations included in $\{\tilde{\alpha}\}$ are generated using molecular dynamics simulations as described in section 3 and Appendix C. At fixed volume fraction, $\Delta_\alpha F$ represents only an additive constant to the free energy in which case it can be ignored. However, this

correction needs to be considered when comparing thermodynamic states having different volume fractions because of the different dimensions of the conformational space. In section B of the Appendix, we derive an exact expression for $\Delta_\alpha F$ and then use an approximation to estimate its value.

A.1. Numerical Solution. To obtain results from the microscopic-level theory that incorporates molecular details as presented here, we must numerically solve the nonlinear integro-differential equations described in the previous section. To this end, the volume of the system is discretized in cubic cells of length $\delta = 0.5$ nm. The number of equations to be solved after discretization ranges from 2×10^4 for the largest gel volume fraction to 2.5×10^5 for the smallest gel volume fraction, with each equation containing roughly 10^4 terms (the number of gel conformations included). Note that because the volume fraction is inversely proportional to the system volume (the total number of gel segments is constant), the number of equations increases with decreasing gel volume fraction. These equations are solved using Jacobian-free Newton method. Figure 9, for example, shows the free energy as a function of the pH of the bath solution, at different gel volume fractions and salt conditions. Each point in these curves represent a single calculation.

B. Free Energy Correction. For each volume fraction, the complete set of gel conformations should be included when calculating the free energy of the system using the approach presented in this work. Unfortunately, this is impossible from a practical standpoint, and we consequently include a large but finite set of gel conformations that is adequate enough to describe the behavior of the system.

At fixed volume fraction, if the set of configurations included is large enough, this truncation of the conformational space results merely in a translation of the free energy, which is of no importance. The problem arises, however, from comparing calculations at different volume fractions, since the relative dimension of the conformational space contributes to the entropy difference between the states under consideration.

In this section, we estimate the corrections to the system entropy that must be included due to the truncation of the gel conformational space.

B.1. Conformational Entropy of a Finite Set. Let $\{\alpha\}$ be the complete set of gel configurations. The conformational entropy is given by

$$S = \sum_{\alpha \in \{\alpha\}} P(\alpha) \ln(P(\alpha))$$

Suppose that $\{\alpha\}$ contains many configurations that are equivalent (in a sense that will be clear later). Let now $\{\alpha'\}$ be the minimal (degenerate) set of independent configurations. A conformation α' in $\{\alpha'\}$ is an arbitrary choice within the many configurations α_k in $\{\alpha\}$, for $k = 1, \dots, n(\alpha')$ that satisfies $P(\alpha') = P(\alpha_k)$. The quantity $n(\alpha')$ is the degeneracy of α' , and the system entropy can then be written as

$$S = \sum_{\alpha' \in \{\alpha'\}} n(\alpha') P(\alpha') \ln(P(\alpha'))$$

In general, the average value of a quantity O is defined as

$$\langle O \rangle_\alpha = \sum_\alpha P(\alpha) O(\alpha) = \sum_{\alpha'} n(\alpha') P(\alpha') O(\alpha')$$

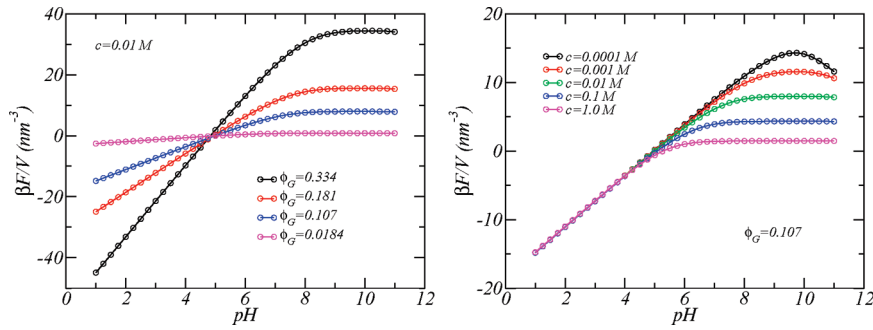


Figure 9. Free energy density $\beta(F/V)$ vs pH for different volume fractions, ϕ_G , and salt concentrations, c .

with $\sum_{\alpha} P(\alpha) = \sum_{\alpha'} n(\alpha') P(\alpha') = 1$. Now, we generate a set of configurations $\{\tilde{\alpha}\}$ that is a subset of $\{\alpha\}$. The subset $\{\tilde{\alpha}\}$ is such that the ensemble average value of a quantity O over the subset, $\langle O \rangle_{\tilde{\alpha}}$, is equal to that over the complete set, i.e., $\langle O \rangle_{\tilde{\alpha}} = \sum_{\tilde{\alpha} \in \{\alpha\}} R(\tilde{\alpha}) O(\tilde{\alpha}) = \sum_{\alpha} P(\alpha) O(\alpha) = \langle O \rangle_{\alpha}$. Here, the quantity $R(\tilde{\alpha})$ is the probability of a configuration $\tilde{\alpha}$.

Configurations in $\{\tilde{\alpha}\}$ are randomly generated from $\{\alpha\}$. Therefore, the probability of generating a configuration α' of $\{\alpha'\}$ within the subset $\{\tilde{\alpha}\}$ is $n(\alpha')/(\Omega)$, where $\Omega = \dim\{\alpha\}$ is the total number of configurations in $\{\alpha\}$. If the $\tilde{\Omega}$ configurations are generated in $\{\tilde{\alpha}\}$, the degeneracy of a configuration α' is given by $\tilde{\Omega}[n(\alpha')/\Omega]$, where $\tilde{\Omega}$ is large enough so that $\langle O \rangle_{\alpha} = \langle O \rangle_{\tilde{\alpha}}$. Therefore, we must have the following relation

$$\langle O \rangle_{\tilde{\alpha}} = \sum_{\tilde{\alpha}} R(\tilde{\alpha}) O(\tilde{\alpha}) = \sum_{\alpha'} \tilde{\Omega} \frac{n(\alpha')}{\Omega} O(\alpha') R(\alpha')$$

However, since by definition

$$\langle O \rangle_{\tilde{\alpha}} = \langle O \rangle_{\alpha'} = \sum_{\alpha'} P(\alpha') n(\alpha') O(\alpha')$$

which implies that we must have the following relation:

$$R(\alpha') \frac{\tilde{\Omega}}{\Omega} = P(\alpha')$$

Substituting this last expression into S , we then obtain the following:

$$\begin{aligned} S &= \sum_{\alpha} P(\alpha) \ln(P(\alpha)) = \sum_{\alpha'} P(\alpha') n(\alpha') \ln(P(\alpha')) \\ &= \sum_{\alpha'} n(\alpha') P(\alpha') \ln\left(R(\alpha') \frac{\tilde{\Omega}}{\Omega}\right) \\ &= \sum_{\alpha'} n(\alpha') P(\alpha') \ln(R(\alpha')) + \sum_{\alpha'} n(\alpha') P(\alpha') \ln\left(\frac{\tilde{\Omega}}{\Omega}\right) \\ &= \langle \ln(R) \rangle_{\alpha} + \ln\left(\frac{\tilde{\Omega}}{\Omega}\right) \sum_{\alpha'} n(\alpha') P(\alpha') = \langle \ln(R) \rangle_{\alpha} + \ln\left(\frac{\tilde{\Omega}}{\Omega}\right) \end{aligned}$$

Since $\langle \ln(R) \rangle_{\alpha} = \langle \ln(R) \rangle_{\tilde{\alpha}} = \sum_{\tilde{\alpha}} R(\tilde{\alpha}) \ln(R(\tilde{\alpha}))$, the conformational entropy can be now expressed in terms of $\{\tilde{\alpha}\}$ in the following form:

$$S = \sum_{\tilde{\alpha}} R(\tilde{\alpha}) \ln(R(\tilde{\alpha})) + \ln\left(\frac{\tilde{\Omega}}{\Omega}\right) \quad (12)$$

B.2. Volume-Fraction Dependence of the Correction. From eq 12, we see that the correction to the entropy at constant

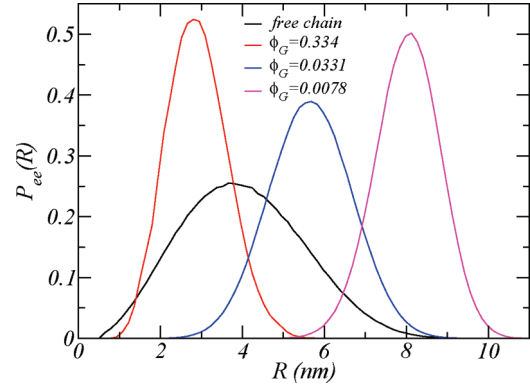


Figure 10. End-to-end distance distribution for different gel volume fractions.

volume (fraction) is given by

$$\Delta_{\alpha} S = \ln\left(\frac{\Omega(\phi_G)}{\Omega_1(\phi_G)}\right)$$

where $\Omega(\phi_G)$ is the number of gel configurations included [$\Omega(\phi_G) = \dim\{\alpha(\phi_G)\}$] and $\Omega_1(\phi_G)$ denotes the total number of configurations [$\Omega_1(\phi_G) = \dim\{\alpha(\phi_G)\} + \dim\{\alpha(\phi_G)^c\}$].

Consider a reference state ϕ_G^0 . At volume fraction ϕ_G , the free energy needs to be corrected by a factor of

$$\begin{aligned} \Delta_{\alpha} F(\phi_G) &= \ln\left(\frac{\Omega(\phi_G)}{\Omega_1(\phi_G)}\right) - \ln\left(\frac{\Omega(\phi_G^0)}{\Omega_1(\phi_G^0)}\right) \\ &= \ln\left(\frac{\Omega(\phi_G)}{\Omega(\phi_G^0)} \frac{\Omega_1(\phi_G^0)}{\Omega_1(\phi_G)}\right) \end{aligned}$$

Note that up to this point, we have not made any approximation, and the previous expression is general. In our calculations, we include the same number of gel configurations for all volume fractions, which means that $\Omega(\phi_G)/\Omega(\phi_G^0) = 1$ and that

$$\Delta_{\alpha} F(\phi_G) = \ln\left(\frac{\Omega_1(\phi_G^0)}{\Omega_1(\phi_G)}\right) \quad (13)$$

B.3. Estimation of the Correction. Let us first assume that the chains connecting the nodes are independent. Then, it follows that

$$\Omega_1(\phi_G) = \Omega_1(\phi_G) n_{\text{chains}}$$

where $\Omega_1(\phi_G)$ denotes the number of configurations of a chain in the gel and n_{chains} represents the total number of chains.

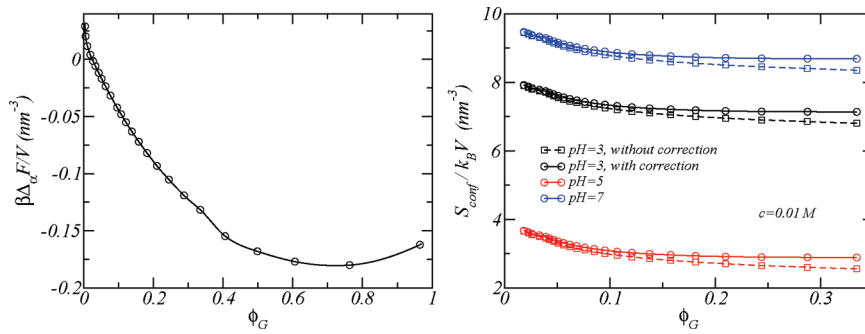


Figure 11. Left: free energy correction $\Delta_\alpha F$ vs gel volume fraction. Right: configurational entropy density vs volume fraction, for three typical cases, with (open circles-solid lines) and without (open squares-dashed lines) including the correction.

If the chain is free and not connected to the network, we must have

$$\Omega_{1,\text{free}}(\phi_G) \equiv \Omega_{1,\text{free}} = \int \omega_{1,\text{free}}(R) d^3R$$

where $\omega_{1,\text{free}}(R)$ is the number of configurations of the free chain with end-to-end distance between R and $R + dR$.

In the gel, however, end-to-end distances are constrained by the network:

$$\Omega_1(\phi_G) = \int \omega_{1,\text{free}}(R) P_{\text{node}}(R, \phi_G) d^3R$$

where $P_{\text{node}}(R, \phi_G)$ denotes the probability that the nodes connecting the chain are separated by a distance R given that the volume fraction of the gel is ϕ_G . Let us now define the quantity $P_{1,\text{free}}(R) = (\omega_{1,\text{free}}(R))/\Omega_{1,\text{free}}$, which represents the probability that the free chain has end-to-end distance R . We thus have

$$\Omega_1(\phi_G) = \Omega_{1,\text{free}} \int P_{1,\text{free}}(R) P_{\text{node}}(R, \phi_G) d^3R$$

and

$$\Omega_t(\phi_G) = (\Omega_{1,\text{free}} \int P_{1,\text{free}}(R) P_{\text{node}}(R, \phi_G) d^3R)^{n_{\text{chains}}}$$

Using eq 13, the correction to the free energy is therefore given by

$$\Delta_\alpha F(\phi_G) = n_{\text{chains}} \ln \left(\frac{\int P_{1,\text{free}}(R) P_{\text{node}}(R, \phi_G^0) d^3R}{\int P_{1,\text{free}}(R) P_{\text{node}}(R, \phi_G) d^3R} \right) \quad (14)$$

Figure 10 shows the end-to-end distance probability distribution, $P_{\text{cc}}(R)$, for the different gel volume fractions ($P_{\text{node}}(R, \phi_G)$) and for the free chain ($P_{1,\text{free}}(R)$). In the case of the gel, the distributions correspond to the set of conformations used in this work and averaged over the different chains. The quantity R is the distance between two nodes that are connected by a chain. The free-chain distribution is obtained by performing a MD simulation under the same conditions as described for each volume fraction of gel (see section C). Each chain includes two additional segments representing the nodes, which allows for the proper comparison with gel chains. In both cases, once a large number of configurations have been generated, the criterion to stop

further generation of gel configurations hinges on the condition that adding more conformations would not modify the quantity $P_{\text{cc}}(R)$ any further.

Finally, Figure 11 shows the magnitude of the free energy correction as a function of the gel volume fraction. Note that only changes in $\Delta_\alpha F$ are important, since the free energy itself can be defined with respect to an arbitrary constant. The right panel also shows that the main contribution to configurational entropy comes from the Gibbs entropy, $-k_B \sum_{\tilde{\alpha}} P(\tilde{\alpha}) \ln(P(\tilde{\alpha}))$, over the truncated set of gel configurations, $\{\tilde{\alpha}\}$, generated as described in section 3.

C. Molecular Dynamics. The specification of conformations of the gel molecule, which is needed for the evaluation of our theory, is obtained by molecular dynamics simulations using GROMACS 3.3.2.^{45,46} For each volume fraction, the system is equilibrated for 500 ps, and then the simulation is continued for another 10 ns. During the production time, one configuration is recorded during every 1 ps, which results in a total of 10^4 configurations.

The force field used in the MD simulations has been described previously.⁴⁷ All monomers interact via a repulsive (shifted) Lennard-Jones potential of the following form:

$$U^{\text{LJ}}(r_{ij}) = \begin{cases} 4\epsilon \left[\left(\frac{\sigma}{r_{ij}} \right)^{12} - \left(\frac{\sigma}{r_{ij}} \right)^6 + \frac{1}{4} \right] & \text{if } r_{ij} \leq 2^{1/6}\sigma \\ 0 & \text{if } r_{ij} > 2^{1/6}\sigma \end{cases}$$

where r_{ij} is the distance between monomers i and j . Neighboring monomers along the chain interact additionally via a FENE potential:

$$U^{\text{FENE}}(r_{ij}) = \begin{cases} -\frac{kR_0^2}{2} \ln \left[1 - \left(\frac{r_{ij}}{R_0} \right)^2 \right] & \text{if } r_{ij} \leq R_0 \\ \infty & \text{if } r_{ij} > R_0 \end{cases}$$

Here we set $\sigma = 1$ and $\epsilon = 1$, since all energetic and spatial dimensions can be rescaled later by the values assigned to these parameters. We set $R_0 = 1.5\sigma$ and $k = 30(\epsilon/\sigma^2)$ in order to avoid any bond crossing.⁴⁷ The distance between bonded monomers was found to be larger than 0.87σ for all simulations across different volume-fraction values. As such, we set this value as the segment length l_G .

References and Notes

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