The pH Inside a pH-Sensitive Gel Swollen in Aqueous Salt Solutions: Poly(*N*-vinylimidazole)

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ABSTRACT: The pH inside a swollen polyelectrolyte network is calculated through a simple model, based on Donnan equilibrium and balance of mobile ions, extended to include the presence of a supporting electrolyte (salt) in the solution that swells the particle. This pH inside the gel, although needed to characterize the ionization properties of the polyelectrolyte, is generally not accessible to direct measurement. The main advantage of our model is that it is free from any simplification concerning the pK_a of the ionizable groups. A common univalent anion is assumed for the acid and salt. The model was applied to chemically cross-linked poly(*N*-vinylimidazole) (PVI) immersed in acidic aqueous baths containing variable concentrations of HCl and NaCl as supporting electrolyte. The imidazole units are basic and become protonated by the acid, thus changing the pH of the initial bath. The data needed for the calculation of the proton concentration inside the gel, the degree of ionization, and the pK_a of the polyelectrolyte are: polymer concentration, pH and salt concentration in the initial solution, and pH in the bath at equilibrium. All of them can be determined experimentally by a batch method, where the polymer is immersed in a different pot for each starting pH and salt concentration. It was thus found that in salt free solutions the pH inside the gel is several units higher than the pH in the external bath at equilibrium, but this difference between internal and external pH faints with added salt. The intrinsic pK_a of PVI, determined from the pH in the gel, is slightly higher than the pK_a of the model molecule, for salt free solutions, but it is lower with added salt (possibly due to the formation of a hydrogen bond between two imidazole units and its disruption by chloride). It was concluded that the pH inside the polymer must be employed instead of the pH outside, in order to calculate pK_a, not only for a swollen polymer network, but also for a dissolved coil.

Introduction

Hydrogels sensitive to pH are a class of macromolecular materials of great practical interest as drug delivery systems, reversible pH-triggered nano and microporous materials, ion exchangers, or metal ion removal devices.[1−4] The polymeric chains in these hydrogels are composed of monomer units having acid or basic groups that ionize by dissociating (acids) or accepting (basic) protons in the solution. The groups are weak acids or weak bases whose equilibrium of ionization is displaced depending on the activity of the protons (pH) in the medium. The polymers carrying charges in their chain are capable of much larger swelling than neutral polymers, and, in the case of weak polyacids or weak polybases, their degree of swelling changes with the pH of the medium, because pH modifies their degree of ionization. The medium is external to the gel, so a given pH in the solution surrounding the gel determines the swelling (and other properties) inside the gel. But the gel also influences the properties of the external solution, because it is a proton supplier (polyacid) or a proton absorber (polybase). It is a two-phase system where the properties of interest of the gel are governed by the pH of the external solution and, in turn, the pH of the solution is altered by contact with the gel. When looked from the gel side, we say that it is a pH sensitive gel; when looked from the solution side, we say that the solution is buffered by the presence of the gel.[5−7] Not only from a practical point of view but also from a fundamental interest in basic polyelectrolytic behavior, it is of utmost importance to characterize the capacity for ionization of these pH-sensitive polymers.

For a given pH of the solution, the degree of ionization of a polyelectrolyte is higher or lower depending on the acidity or basicity of the proton sensitive groups in the polymer chains. Such acidity or basicity is usually expressed through the equilibrium constant, K_a, for the reaction of dissociation of the group as an acid (in the case of bases, the dissociation of the acid conjugate to the base). The traditional way of measuring K_a for polyacids or polybases is by titration: the pH in a solution of the polyacid or the polybase is measured sequentially after additions of a strong base or a strong acid, respectively. In the case of insoluble gels, the titration is followed by measuring the pH in the solution external to the gel. The equilibrium of ionization of the acid or basic groups is established in the phase where these groups reside: the gel, but the proton activity is measured in the other phase: the solution, because the pH inside the gel is not accessible to direct measurement. In this way, the constant being determined is not the proper constant for the ionization of the polyelectrolyte in equilibrium with the protons in its same phase. The error thus committed is about equal to the difference between the proton activities in the gel phase and in the surrounding solution.

When the two phases are in equilibrium, the activities of all components are equal in both phases, but equal activity for components does not imply equal activity for the individual ions. In fact, the activity of protons has to be different inside and outside the gel because of the restraint imposed by Donnan equilibrium. Ionization of the polyelectrolyte creates fixed charges on the chains that stay within the gel and are neutralized by mobile counterions that diffuse from the solution. The activity of mobile protons cannot be the same inside and outside the gel because of the existence of these fixed charges in only one of the two phases. If the difference in proton activity between the solution inside the swollen gel and the bath solution surrounding the gel is significant, then the traditional method

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of titration cannot give a reliable characterization of the acidity or basicity of the polyelectrolyte. The difference between these two proton activities should be function of several factors. One such factor is the pH itself, because the degree of ionization or concentration of fixed charges in the gel phase changes with pH. So, the difference between internal and external pH changes along the titration curve as more acid or base is added to the solution. Another factor is the presence of a supporting electrolyte in the solution, because with increased ionic strength the charges are screened. Also an important factor is the concentration of ionizable groups inside the polyelectrolyte, because it determines the activity of the fixed charges in the gel, for a given degree of ionization. Regarding these two factors, the difference in ionic activity between the inside and the outside of the polyelectrolyte is expected to be more important with higher polymer concentrations, while such difference is expected to be attenuated with increasing ionic strength from a supporting electrolyte (that affords extra ions for diffusion into the gel).

With linear polymers, it is custom to use dilute solutions in order to avoid complications from interactions between charges of different molecules. In cross-linked gels, the concentration of polymer inside the gel is determined by the structure of the network, which is fixed at the time of the cross-linking reaction. Predominantly, it is determined by the density of cross-links in the network and, if it is a copolymer, also by the comonomer composition. With cross-linked systems, the polymer concentration in the gel is usually high enough to produce large differences in the individual ion concentrations, as found with a gel in water without electrolyte.[8]

The pH inside a gel is not amenable to direct determination through potentiometric titrations. Alternative methods, such as the use of pH sensitive dyes or fluorophores, pose problems because they cover only a narrow pH range ($pK_a \pm 1$) and their calibration depends on the ionic strength,[9] which, *a priori*, is unknown inside the gel. To develop methods for obtaining the pH inside the gel is of great importance, since such internal pH is the quantity needed to characterize the acid−base properties of the polyelectrolyte. Here, we develop a theoretical method to calculate such nonmeasurable pH inside the gel starting from the pH measured in the surrounding bath. The method is rigorous, since it uses only thermodynamics. The experimental data needed for the calculation include, obviously, the pH measured in the surrounding bath, but this is not plugged directly as substitute for the inaccessible pH inside the gel. Instead, the pH inside the gel is calculated (with no approximation) using the balance of counterions that diffuse into the gel from the solution, the corresponding equality of chemical potentials across the boundary solution/hydrogel, and the electroneutrality of both phases. No assumption about the acidity or basicity of the ionizable groups is included.

Previous attempts to obtain the pH in the gel[10−19] have usually included (never explicitly, but as a tool in other calculations) some assumption regarding the magnitude of K_a,[10−12] but this is kind of a closed loop, since one of the interests in knowing the pH inside the gel is precisely to obtain the value of K_a. Several proposed models[12,13] derive from the treatment of the Donnan equilibrium together with the condition of electroneutrality inside the gel, as reported by Rička and Tanaka.[14] Such models require to know the concentration of each ion present in the outer solution at equilibrium (which uses to be more difficult to determine than the initial concentrations) and do not allow calculation of the degree of ionization, which must be experimentally determined, e.g., by spectroscopic methods.[13] The molecular model by Dušek et al. uses equations originally derived for a particular model of polyelectrolyte solution and implicitly assumes that the polymer network is ideal, without defects.[17] It leads to quantitative agreement with experimental values only if the effective degree of ionization (which is lower than the stoichiometric degree of ionization because of the limited mobility of some counterions) is considered, and such values, as well as other parameters also needed, are hardly accessible for most systems.[18] However, it provides a very useful frame to understand the acid−base properties of polyelectrolyte gels. The method here presented serves to calculate the pH inside the gel, as well as the degree of ionization, through experimental magnitudes easily available and using simple expressions. It was previously reported[8] for salt free systems and here it is extended to salt solutions as swelling media. In our previous report it was found that the counterion condensation, while having an important incidence in the dependence of swelling on the degree of ionization,[20,21] does not involve a significant change of pK_a and here it will not be considered.

We apply here the method to study the polymer poly(*N*-vinylimidazole). Since this is a polybase, the theoretical method is developed for a polybase being titrated with an acid, but an entirely parallel treatment can be developed for a polyacid titrated with a base. The interest of the theoretical method goes well beyond its application to obtaining the acid/base characterization of a polyelectrolyte. In its more general scope, the method allows the determination of the pH inside a given inaccessible phase from measurements of the pH in a contiguous easily accessible phase. This can have implications for the study of reactions in confined media, vesicles, cellular systems, etc. The same separation in two hypothetical phases can be considered in homogeneous solutions of soluble linear polymers at concentrations and degrees of ionization where the macromolecules stay as nonoverlapping coils. Such polyelectrolyte solutions are nonuniform (in contrast to solutions of simple electrolytes), with high concentration of ionizable groups inside the volume pervaded by the coils and zero concentration in-between the coils.

Besides describing the general formalism, we apply it here to determine the K_a of cross-linked poly(*N*-vinylimidazole). Chemically cross-linked poly(*N*-vinylimidazole) is a pH-sensitive hydrogel.[1,2] As such, it is neutral, but the imidazole rings are proton accepting (basic) groups that ionize by the following protonation:[8,20−22]

$$P + H^+ = PH^+ \quad (1)$$

Each monomer in the polymer gel carries a ring that can be protonated. The imidazole molecule anchored to small size compounds has an equilibrium constant sensitive to the microenvironment with pK_a close to 7 (7.3 for *N*-ethylimidazole at 25 °C in salt free aqueous solution,[23] 6.08 for free histidine or 6.56 for histidine residues inside transferrin[24]). This means that an acid medium is needed to substantially ionize the imidazole ring. When the ring is part of the monomer unit in a macromolecule, its basicity may be modified with respect to that of the free molecule. There are many examples in the literature reporting that the acidity (or basicity) of a group in the monomer unit of a polymer chain is diminished with respect to that of the same group in a free molecule.[2] Besides, it depends on the degree of ionization and therefore, the acid dissociation constant of a polymer is in fact an apparent equilibrium constant, not a true thermodynamic one.[2] The reasons for these ambiguities in the value of pK_a for a given polyelectrolyte are several[17] and will be discussed below. Hence, there is interest in having a reliable method to determine K_a. The method here developed is applied to determine pK_a in the presence of variable concentrations of a supporting electrolyte, thus extending a preliminary report for salt-free solutions.[8]

The plan is as follows: first the experimental results of pH measured at equilibrium for different initial concentrations of

acid and salt; then, the theoretical model to calculate pH inside the gel; finally, the application of this method to the experimental results in order to obtain pK_a.

Experimental Results

The specimens of the polyvinylimidazole hydrogel (PVI) here employed were synthesized by radical cross-linking copolymerization of *N*-vinylimidazole (VI) and *N,N′*-methylenebis(acrylamide) (BA) in aqueous solution, with 2,2′-azobis(isobutyronitrile) (AIBN) (6×10^{-3} M) as initiator, with total comonomer concentrations, $C_T = 4.2$ M, and BA concentration [BA] = 0.054 M, following the protocol described.[21,25] The polymerization proceeded at 90 °C throughout 2 h and the conversion of the several specimens here employed ranged from 85 to 90%, which is an important datum regarding the cross-linking density and derived properties.[26] This particular sample composition will be denoted, as in previous reports,[20−22] by PVI40(2). The cross-linking density of this sample obtained at total conversion is 0.07 mol/L and the corresponding average molecular weight of elastic chains between adjacent knots is 17500 g/mol.[21]

Xerogels of well-known mass (m), were immersed in a much larger volume (V_T) of an aqueous solution of known pH (pH_i), containing HCl as acid and the salt NaCl, at concentration $[NaCl]_i$. The number of proton accepting units (or monomers) in the gel is as follows: m/M_0 (M_0 being the molecular weight of a monomer unit bearing imidazole). Then, we define the effective molar concentration of proton accepting units in the system as:

$$C = \frac{m}{M_0 V_T} \tag{2}$$

The masses of the xerogel specimens were chosen to yield a fixed value, $C = 0.01$ M, for the effective concentration of monomer units. This C is a formal concentration, not a real one. A given xerogel could have different values of the effective concentration, C, simply by putting different masses (m) in the same volume V_T. If only some of the monomeric units would bear the proton accepting unit, eq 2 should be corrected with the copolymer composition. Formally, the cross-linker contribution to m should be discounted, since it is not bearing imidazole groups, but the cross-linker ratio of this particular sample is very low and its contribution can be neglected.

The xerogel specimens used here for pH measurements were handled as unshaped pellets about 1 mm thick, in order to minimize the time required to reach equilibrium, i.e., constant pH.[22] Upon swelling of the xerogel, the initial aqueous solution is divided into the swollen gel phase and the remaining bath solution surrounding the gel. The equilibrium pH in the surrounding bath solution (pH_S) was measured, at room temperature, two days after preparation. It should be remarked that measurements were not made as in a continuous titration; a different pot with a different PVI specimen was employed for each starting value of pH_i and of $[NaCl]_i$. So, in each pot, we have a trio of experimental values: the equilibrium pH_S, and the initial pH_i and $[NaCl]_i$. Forward and backward continuous titrations of cross-linked polymers give, very often, hysteresis[27] due to incomplete diffusion of the titrant into the gel between two successive additions. Such problem is avoided by using the above method.

The pH reached at equilibrium by immersion of PVI40(2) in HCl aqueous solution with different salt concentrations, are shown in Figure 1. Several features are to be noted in these results. The pH that remains in the bath at equilibrium is higher than the pH of the initial solution ($pH_S > pH_i$), and a plateau (almost constant pH_S) is observed with initial solutions of low acidity (pH_i above 4.5), this plateau extending to more acid solutions as $[NaCl]_i$ increases (Figure 1). The same trend was found for other polybases, such as uncross-linked poly(2-vinylpyridine)[28] and poly(2-vinylquinoline),[29] as well as for gels,[8] microgels, and nanogels containing imidazole swollen in salt free aqueous solutions,[30] and even for spores able to act as proton reservoirs.[31]

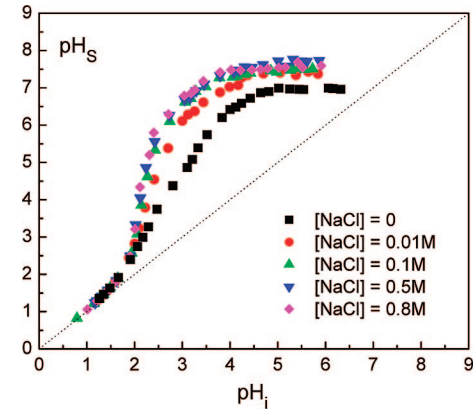

Figure 1. Equilibrium pH in the solution surrounding the gel (pH_S), reached after PVI40(2) is immersed in HCl aqueous solutions with different initial pH (pH_i) and different NaCl concentrations, $[NaCl]_i$, at an effective polymer concentration $C = 0.01$ M.

That $pH_S > pH_i$ is understandable, because the protonation of PVI (eq 1) drains free protons from the solution. The trend is that this effect is larger in the presence of salt than in the salt-free case. As we can see, the curves for the salt solutions are shifted up and left with respect to the curve for the salt-free solutions. In other words: with salt, the equilibrium pH is more basic, and is reached from more acid initial solutions. In the case of the plateau, the almost constant pH_S is practically 7 for the salt free solutions, and shifts to 7.4−7.7 for salt containing solutions. The mechanism behind this neutralization of the initially acid solutions has been described elsewhere as a buffering effect working in two phase systems.[6,7]

Theory

We proceed to calculate the pH inside the swollen gel, in order to determine the ionization constant of the polyelectrolyte hydrogel. The initial solution is water to which a strong acid, H^+A^-, and an inert salt, M^+A^-, with a common anion, have been added, up to concentrations $[A^-]_i - [M^+]_i$, and $[M^+]_i$, respectively. The proton concentration in this same initial solution is $[H^+]_i$. In the surrounding bath, after reaching equilibrium, there are these same species, at concentrations $[A^-]_S$, $[M^+]_S$, and $[H^+]_S$, respectively. In the swollen hydrogel at equilibrium the concentrations of these same species are, respectively: $[A^-]_G$, $[M^+]_G$, $[H^+]_G$, and in the gel there are additionally the concentrations of protonated and unprotonated base groups, $[PH^+]$, [P], respectively ([P] and $[PH^+]$ do not need a subindex to specify in which phase they are).

In order to calculate the pH inside the gel, the protonation degree, and the ionization constant, we have seven variables that correspond to the concentrations of ionic species inside the hydrogel and in the external bath, namely: $[PH^+]$, $[H^+]_G$, $[A^-]_G$, $[M^+]_G$ (inside the gel), and $[H^+]_S$, $[A^-]_S$, $[M^+]_S$ (in the external bath). Several conditions must be met by these variables: Donnan equilibrium, mass balance, and electro-neutrality, which together allow for a solution of the problem. Before showing the details of these conditions, let us explain first the relationships between the volumes of the phases.

We call V_G the volume of the swollen hydrogel, and V_S the volume of the surrounding bath (remember V_T is the volume of the initial solution to which the xerogel is added). Inside the hydrogel phase, the volume of liquid is $(1 - v_2)V_G$, and the

volume of polymer network is v_2V_G, where v_2 represents the polymer volume fraction in the swollen gel. At equilibrium, the molar concentration of proton accepting units in the gel phase is as follows:

$$C_G = \frac{m}{M_0 V_G} = \frac{v_2 \rho_2}{M_0} \tag{3}$$

Here ρ_2 (in g/L) is the xerogel density. (C_G in a coil can be calculated with the intrinsic viscosity, $[\eta]$ in dL/g, as $10/M_0[\eta]$). Obviously the eighth variable is $[P] = C_G - [PH^+]$.

The volume ratio of the initial solution to the swollen gel is as follows:

$$\frac{V_T}{V_G} = \frac{C_G}{C} \tag{4}$$

The volume ratio of the surrounding bath to the swollen gel is as follows:

$$\frac{V_S}{V_G} = \frac{C_G}{C}\sigma \tag{5}$$

where σ (the fraction of initial solution that remains as bath surrounding the gel after swelling equilibrium) is as follows:

$$\sigma = 1 - \frac{(1 - v_2)C}{C_G} \tag{6}$$

Now we proceed with the conditions of equilibrium in the two phases, swollen hydrogel and surrounding bath.

Equality of Activities. Since in the initial solution two electrolytes have been added independently (the acid, AH, and the salt, MA), there are two equalities of electrolyte activities:

$$[H^+]_G[A^-]_G = [H^+]_S[A^-]_S \tag{7}$$

$$[M^+]_G[A^-]_G = [M^+]_S[A^-]_S \tag{8}$$

Electroneutrality. The initial solution is electroneutral, and the same are each one of the two phases at equilibrium. The contribution from the charge of water hydroxyl ions has to be taken into account when the pH approaches 7 or is above 7. Therefore

$$[A^-]_i = [H^+]_i + [M^+]_i - K_w/[H^+]_i \tag{9}$$

$$[A^-]_S = [H^+]_S + [M^+]_S - K_w/[H^+]_S \tag{10}$$

$$[A^-]_G = [H^+]_G + [PH^+] + [M^+]_G - K_w/[H^+]_G \tag{11}$$

where K_w has its usual meaning of constant for water dissociation, and molar concentrations are not distinguished from activities of individual ions, as is repeatedly the use.

Mass Balance. The two ionic species A^- and M^+ are neither involved directly in the protonation equilibrium (eq 1), nor in the autodissociation of water. Their partition between the two phases at equilibrium obeys solely to their diffusion from the initial solution to the gel phase. So, we can apply the mass balances:

$$[A^-]_G = ([A^-]_i - [A^-]_S\sigma)\frac{C_G}{C} \tag{12}$$

$$[M^+]_G = ([M^+]_i - [M^+]_S\sigma)\frac{C_G}{C} \tag{13}$$

Substituting in eq 12the electroneutrality conditions, for the initial solution (eq 9), and for the surrounding bath (eq 10), we get

$$[A^-]_G = [[\tilde{H}^+]_i + [M^+]_i - ([\tilde{H}^+]_S + [M^+]_S)\sigma]\frac{C_G}{C} \tag{14}$$

where we have abbreviated the notation by defining the differences of proton minus hydroxyl concentrations in each solution as

$$[\tilde{H}^+]_x = [H^+]_x - K_w/[H^+]_x \tag{15}$$

x being i, S, or G.

Proton Concentration Inside the Gel. In the thermodynamic equilibrium for electrolyte HA (eq 7), we substitute the condition of electroneutrality (eq 10) and the mass balance (eq 14), obtaining:

$$[H^+]_G = \frac{[H^+]_S([\tilde{H}^+]_S + [M^+]_S)}{[[\tilde{H}^+]_i + [M^+]_i - ([\tilde{H}^+]_S + [M^+]_S)\sigma]\frac{C_G}{C}} \tag{16}$$

In this expression, all quantities are amenable to experimental determination without approximations: the proton and salt concentrations in the initial solution ($[H^+]_i$ and $[M^+]_i$), as well as the effective gel concentration (C), are determined when preparing the system; the proton and salt concentrations in the surrounding bath at equilibrium ($[H^+]_S$ and $[M^+]_S$) can be measured experimentally in the external solution ($[M^+]_S$ can also be calculated as explained below); and the polymer volume fraction in the swollen gel, v_2 (needed for σ and C_G) can be determined from measurements of degree of swelling of the gel. So, the proton concentration inside the gel can be calculated entirely from experimental data.

Ionization Degree. The degree of protonation, α, is:

$$\alpha = \frac{[PH^+]}{[P] + [PH^+]} = \frac{[PH^+]}{C_G} \tag{17}$$

Therefore, the concentration of fixed protons, or charges on the polymer network, referred to the volume of the gel phase, is: $[PH^+] = \alpha C_G$. This concentration of fixed protons is related to the other concentrations in the gel as (eq 11):

$$[PH^+] = [A^-]_G - [M^+]_G - [\tilde{H}^+]_G \tag{18}$$

Substituting with eqs 13 and 14, we get

$$\alpha = \frac{1}{C}([\tilde{H}^+]_i - [\tilde{H}^+]_S\sigma) - \frac{[\tilde{H}^+]_G}{C_G} \tag{19}$$

This expression does not contain the concentration of salt, it is therefore the same as for salt-free solutions.[8] However, α values for a given pH_i are obviously different with and without salt because of changes in $[H^+]_S$ and $[H^+]_G$.

Dissociation Constant. The protonation of the imidazole rings in the monomer units of the gel follows eq 1. The equilibrium constant for this protonation is the reciprocal of K_a, the equilibrium constant for the dissociation of the acid PH^+:

$$K_a = \frac{[P][H^+]_G}{[PH^+]} \tag{20}$$

All three concentrations: [P], $[PH^+]$, and $[H^+]_G$, refer to the gel phase, as argued before. Also as before, we neglect here the difference between molar concentrations and activities, with the knowledge that refinement of the results will require contributions from activity coefficients.

The pK_a of the polyelectrolyte is obtained from the pH inside the gel (pH_G) and the ionization degree, α, by rewriting eq 20 in log−log form (the so-called Henderson−Hasselbalch equation):

$$pK_a = pH_G - \log\frac{1-\alpha}{\alpha} \quad (21)$$

We have already the theoretical expressions to obtain the concentration of protons in the gel (eq 16) and the degree of ionization (eq 19), both in terms of experimentally accessible quantities. So, we can calculate pK_a directly from experiment (next section).

Calculations and Discussion

We now proceed to calculate the proton concentration inside the gel, $[H^+]_G$, and the degree of ionization, α, as functions of the initial acid and salt concentrations, $[H^+]_i$, $[M^+]_i$, using the experimental $[H^+]_S$ from the pH results measured in the surrounding bath, which are shown in Figure 1. The additional data needed to apply eqs 16 and 19 are the salt concentration in the surrounding bath, $[M^+]_S$, and the concentration of proton accepting units in the gel, C_G.

This C_G is obtained from υ_2 values calculated with experimental measurements of swelling degree previously reported.[21] The degree of swelling (expressed as mass of solvent absorbed per unit mass of xerogel) shows a maximum (minimum υ_2) for acid solutions in the pH_i range 0−3 and levels off for larger pH's.[21,22] Since the swelling degree values available were taken at intervals of pH_i not so fine as those used here for the measurement of pH_S, a smoothing of υ_2 was performed to interpolate the values that correspond to the present intermediate pH_i's. The results are shown in Figure 2. The fitting appears as rather crude, but it is valid here, because the uncertainty in the interpolated values of υ_2 has a much lesser effect on the final results than the accuracy of the pH values measured in the bath and in the initial solution.

The other unknown, $[M^+]_S$, can be obtained from the same set of experimental measurements, namely: from the pH measured in the external bath at equilibrium, the pH and salt concentration of the initial solution, plus the degree of gel swelling. This is possible thanks to the condition of thermodynamic equilibrium for electrolyte MA (eq 8) and the mass balance of ions M^+ (eq 13). By combining eqs 7 − 10, and 12, 13, we get an equation of second degree in $[M^+]_S$ as the only unknown, with solution

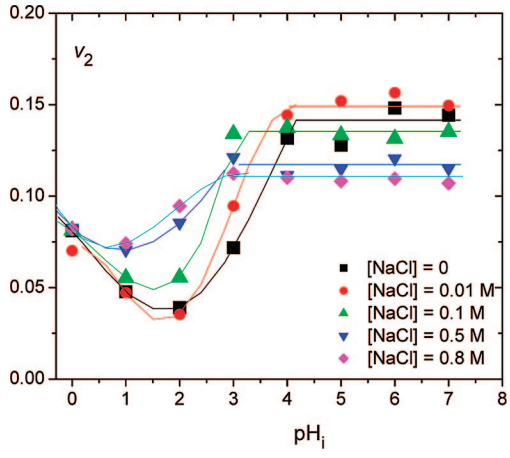

Figure 2. Polymer volume fraction in the swollen gel, υ_2, reached at equilibrium when PVI40(2) is immersed in HCl aqueous solutions with different initial pH (pH_i) and different NaCl concentrations, $[NaCl]_i$, at an effective polymer concentration $C = 0.01$ M. The points are values calculated from experimental swelling degree,[21] and the lines are their smoothing for interpolation, using a polynomial fit for low pH, and an average value for high pH, where the swelling degree is practically constant.

$$[M^+]_S = \frac{2[M^+]_i + [\tilde{H}^+]_i - \sigma\mu[\tilde{H}^+]_S - \Delta^{1/2}}{2\sigma\mu} \quad (22)$$

where

$$\Delta = 4(1-\mu)[M^+]_i([M^+]_i + [\tilde{H}^+]_i) + ([\tilde{H}^+]_i - \sigma\mu[\tilde{H}^+]_S)^2 \quad (23)$$

and

$$\mu = 1 - \left(\frac{C}{\sigma C_G}\right)^2 \quad (24)$$

Ionization Degree. The degree of protonation, α, calculated with eq 19, is shown in Figure 3, as function of pH_S. The same results (within 2% deviation), for α in the range 0.002−0.5, are obtained when α is calculated with the simplified expression[20−22]

$$\alpha \cong \frac{[H^+]_i - [H^+]_S}{C} \quad (25)$$

The difference becomes 10% for α close to 1 and low salt concentrations.

Figure 3 shows that salt concentration modifies α significantly, when plotted versus pH_S. However, α does not depend appreciably on salt concentration when plotted versus pH_i (because $[H^+]_i$ is the dominant term in eqs 19 and 25). In other words, for a given initial pH, the salt has practically no influence on the degree of protonation, but modifies strongly the final equilibrium pH.

pH Inside the Gel. The pH inside the gel (pH_G), corresponding to the proton concentration calculated with eq 16, is shown in Figure 4A, as function of the pH in the initial solution (pH_i).

The pH inside the gel at equilibrium is much higher than in the initial solution, which means that the protons diffusing into the gel are mainly used in the protonation of imidazole, and very few remain as mobile ions. The trend of pH_G versus pH_i has two significant characteristics: a level off in the region of high pH_i, and an inflection around pH_i 2. This inflection corresponds to the equivalence point for this polybase that is at effective concentration $C = 0.01$ M. It is about the same regardless of the salt concentration, but it gets steeper with increasing salt concentration. The plateau is the behavior expected for a weak base that acts as buffering agent both inside the swollen gel (pH_G constant)[6] and in the outside solution (pH_S constant).[6,7]

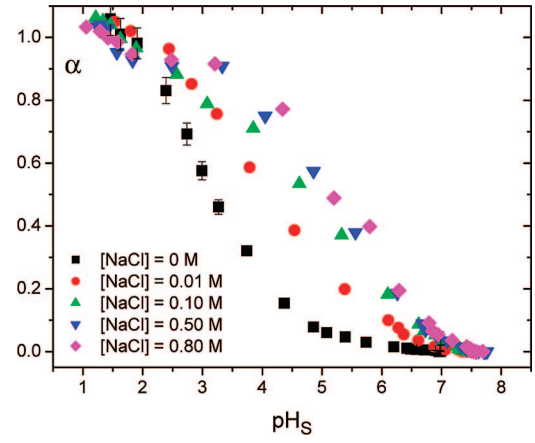

Figure 3. Degree of protonation of the PVI40(2) gel, α, calculated through eq 19 with the results of Figures 1 and 2, as function of the equilibrium pH in the surrounding solution, pH_S, (for different NaCl concentrations, $[NaCl]_i$). Error bars (5%) are plotted only for salt free systems.

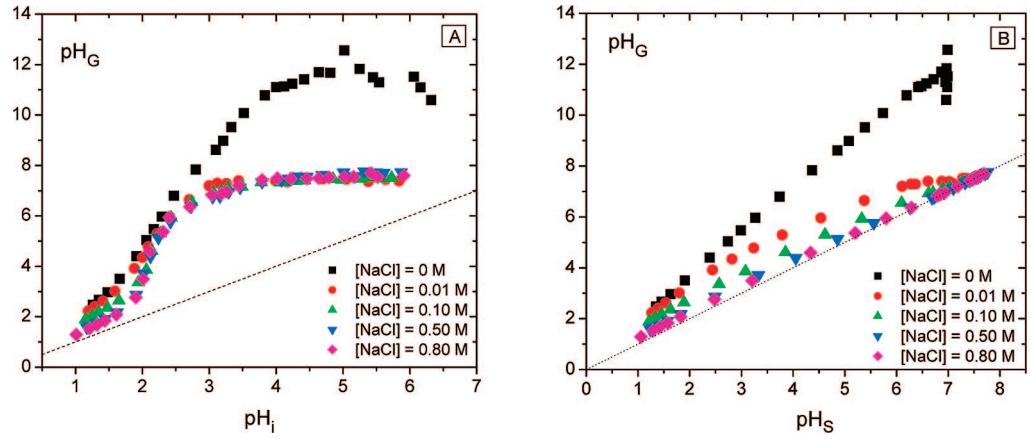

Figure 4. pH inside (pH_G) the PVI40(2) gel, swollen in HCl aqueous solutions with different initial pH (pH_i) and different NaCl concentration, $[NaCl]_i$. It is compared with the pH outside (pH_S) the gel: (A) pH_G plotted versus pH_i; (B) pH_G plotted versus pH_S.

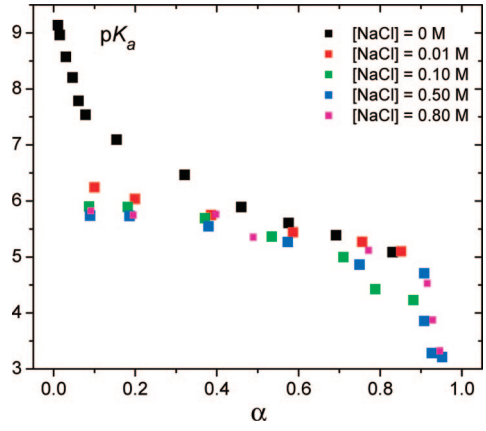

Figure 5. Basicity of the PVI40(2) gel (pK_a for its acid dissociation), as function of the degree of protonation, α, attained with HCl in solutions containing different NaCl concentrations, $[NaCl]_i$. Points are pK_a values calculated with pH_G (eq 21).

Let us compare now the pH inside the gel (pH_G) with the pH outside the gel (pH_S), as shown in Figure 4B. The pH inside the gel is always higher than the pH outside the gel, which seems reasonable since the polybase is a sink of free protons. The difference between pH_G and pH_S is very sensitive to the presence of salt: it is largest in salt-free solutions and decreases abruptly as the concentration of salt increases. $pH_G - pH_S$ reaches up to 5 pH units in salt-free solutions, it drops to a maximum of 2 pH units with the smallest concentration of salt (0.01 M), and it reduces still further with higher salt concentrations. This is due to the anions contributed by the salt. Just 0.01 M of NaCl provides a concentration of anions equal to that provided by the acid in a solution of pH = 2. The total amount of anions available is so large with salt added, that the equilibrium is no longer linked exclusively to the diffusion of acid into the gel. Formally, we can trace it to the mass balance of anions in eq 14, where the concentrations of acid and salt appear combined, but the concentration of salt dominates. This effect of the supporting electrolyte is typical of membrane equilibria, where the concentrations of the individual ions in both sides of the membrane approach each other, as the concentration of the supporting electrolyte exceeds that of the fixed charges present in only one side of the membrane.

Dissociation Constant. For the calculation of pK_a according to eq 21, we use the pH inside the gel (pH_G) and the ionization degree (α), both already obtained. Figure 5 shows the values of pK_a thus calculated, as a function of α. As we can see, the calculated pK_a is not constant, which means that it is not a true equilibrium constant intrinsic to the imidazole group (pK_a^o), but an apparent one. From now on, it will be called pK_a^{app}.

For $0.1 < \alpha < 0.8$, PVI40(2) swollen in any of the NaCl solutions shows a uniform weak decrease of pK_a with increasing α, the slope of this decrease being notably steeper in the absence of salt. The decrease of pK_a^{app} as the degree of ionization increases is a behavior commonly observed for polybases, while for polyacids pK_a^{app} increases with increasing degree of dissociation.[2,33−36] In the case of polybases (such as PVI), it was interpreted as due to repulsive interactions of (positive) fixed charges and protons approaching the polymer, which makes more difficult the protonation as α increases. In the presence of salt, such repulsive interactions are shielded[2,32] and pK_a changes less with α, except for conformational transitions.[32,33] In fact, around $\alpha = 0.8-0.9$ there is a sudden decrease of pK_a^{app} (Figure 5), that can be ascribed to a conformational transition.[32] In this case, a conformational transition that makes more difficult the protonation, since pK_a decreases.

Intrinsic and apparent values of pK_a for the equilibrium of protonation (eq 1) are related in the model developed by Katchalsky[37] by the expression

$$pK_a^{app} = pK_a^{o} + \frac{0.434}{kTn_p}\left(\frac{\partial G_{el}}{\partial \alpha}\right)_{nH,h} \qquad (26)$$

where pK_a^{app} is obtained with eq 21, G_{el} is the electrostatic free energy due to repulsive interactions of neighbor fixed charges and to the polymer configurational energy, nH and n_p are the mole number of protons and of ionizable groups fixed to the gel and h is the distance between two adjacent knots of the polymer network.

Analogously, the model[17] by Dušek et al. expresses the difference between intrinsic and apparent pK_a values as the sum of three contributions: (i) the Donnan effect, which includes the activity coefficients of counter-ions and coions inside the gel; (ii) conformational aspects as changes in the number of monomer units in the statistical segment with the degree of neutralization; (iii) repulsive interactions of fixed charges, which justify changes of pK_a^{app} with α. Within this framework, the ionic strength influences pK_a through the activity coefficients of the Donnan term and through the electrostatic free energy of repulsive interactions responsible of changes of pK_a^{app} with α.

In practice, pK_a^o is obtained free of the influence of repulsive interactions by extrapolation of pK_a^{app} to zero degree of ionization. In this extrapolation, the term log α of the Henderson−Hasselbalch equation (eq 21) poses some problems because it strongly deviates from linearity when α approaches 0, giving place to a pronounced downward curvature in plots such as that in Figure 5. Good linearity holds in the range 0.1

Table 1. Intrinsic Acid Dissociation Constant of Cross-Linked PVI, pK_a^o, determined for Acid Solutions Containing Different NaCl Concentrations[a]

[NaCl] (M)	pK_a^o
0	7.5; 9.3
0.01	6.35
0.10	6.1
0.50	6.0
0.80	6.0

[a] Two pK_a^o values are obtained without salt, by extrapolating: in the range $0.1 \leq \alpha \leq 0.8$ or in the range $0.01 < \alpha < 0.1$.

$\leq \alpha \leq 0.8$, so this range is adequate in order to avoid artifacts (Figure 5). pK_a^o values obtained from this extrapolation are shown in Table 1, for the different salt concentrations. It is seen that pK_a^o decreases somewhat when salt is present. The influence of salt on pK_a has been interpreted, as due to the dependence of the activity coefficient of polyelectrolyte units on ionic strength through the Debye−Hückel law.[38] Here, it is not evident what is the influence of the activity coefficients, because of the mixed use of activities and concentrations. Activities enter through the measured initial and equilibrium pH (the raw data in our calculation of pK_a), and concentrations enter through the electroneutrality and mass balances.

Without salt, a different extrapolation is obtained if the range is extended down to $0.01 < \alpha$. The meaning of the pK_a^{app} trend in this region of very low α is not clear at present. Whether the range is $0.1 \leq \alpha$ or it is $0.01 < \alpha$, pK_a^{app} extrapolates to values (7.5 or 9.3, respectively) larger than pK_a of the monomeric analog ($pK_a = 7.3$ for *N*-ethylimidazole at 25 °C in salt free aqueous solution[23]). Possibly, there is a cooperative effect[39] in the limit of zero degree of protonation without salt, which can be related with the formation of hydrogen bonds between protonated and neutral imidazole groups, as previously observed for related systems.[40,41] Sharing a proton by two imidazole groups makes easier protonation (and larger pK_a^o) in conditions of very low degree of protonation ($\alpha < 0.1$) without salt, i.e., with counterions which are, in part, hydroxyl groups, since pH_G is larger than 7. On increasing α, the repulsive interactions between neighboring fixed charges (an anticooperative effect[35]) prevail and pK_a^{app} decreases.

When the salt is present, it provides chloride counteranions in concentration sufficient to make negligible the contribution of hydroxyls (pH_G about 7 or lower) and the cooperative effect at $\alpha \rightarrow 0$, is no longer observed. In coherence with this observation, it was reported for similar systems that $NH^+\cdots N$ bonds are ruptured when each imidazolium ring has a chloride counterion.[41]

Let us compare now the results for cross-linked PVI, summarized in Table 1, with results reported for linear PVI. The pK_a^{app} of linear PVI depends on chain molecular weight, ranging from 4.9, in salt free aqueous solution, to 5.45, in 2 M NaCl, for a sample[42] with molecular weight 7.6×10^4, while $pK_a^{app} = 2.6$ for another sample,[43] with 3.0×10^5 molecular weight, in water, all of them determined at 50% degree of ionization.[37] It was also reported,[44] that the pK_a^{app} versus α curves of linear PVI (9.4×10^4 molecular weight), determined under various NaCl concentrations, converge to a single pK_a^o value (7.0) at the complete neutral condition. Values of pK_a^o for linear PVI (7.0×10^4 molecular weight) going from 5.6 without salt to 6.5 with 1.0 M NaCl, were also reported.[45] All these values are smaller than pK_a of the monomeric analog, the same as pK_a^o of cross-linked PVI with salt (Table 1), but the ionic strength dependence is opposite: while pK_a^o values of linear PVI are larger with salt,[46] the corresponding values of cross-linked PVI are lower.

It must be emphasized that pK_a^o of linear and cross-linked polymer are obtained from different pH data. The values shown in Table 1 come from extrapolation of pK_a^{app} calculated with the pH inside the gel (pH_G in eq 21), while those for the linear polymers come from the pH in a homogeneous solution. With the cross-linked polymer we could use the pH in the external solution, (pH_S) instead of pH_G, in order to obtain the so-called pK_a^S, equivalent to those shown in ref.[22] Then, pK_a^o obtained by extrapolation of such pK_a^S would be larger with salt than without salt, the same that happens with the linear polymer. One is tempted to think that the solution external to the gel in cross-linked polymer plays a role similar to the homogeneous solution of the dissolved linear polymer. There is reason for this, because the solutions of linear polymers at concentrations below the overlapping of coils are spatially nonuniform (albeit macroscopically homogeneous) with separate swollen coils that swim in a sea of solvent. It is inside the coil volume that the protonation equilibrium takes place, but the pH measured may be that of solvent spaces empty of polymer.

As a corollary, one can ask whether the pH to be used in conjunction with α, when applying eq 21, can be the pH measured in the surrounding bath, pH_S (as is the usual practice), or it has to be necessarily the pH inside the gel, pH_G. Rigorously, it has to be pH_G. The difference between pK_a and pK_a^S can be very large (up to 3−5 units), but it diminishes drastically as ionic strength increases.

Concluding Remarks

The model here proposed is a reliable method for determining the inner pH (pH_G), the degree of ionization (α), and the ionization equilibrium constant (pK_a), suitable, not only for chemically cross-linked polymer networks, but also for an ample set of systems: soluble polyelectrolytes, biopolymers, physically cross-linked gels, particles (soluble or insoluble) acting as proton reservoirs, homopolymers or copolymers as well. The main advantage of our model, with regard to others based on the titration of polyelectrolytes, is that here we measure both the initial pH and the final pH of each solution, thus being able to calculate the balance of mobile ions going from one phase to the other as equilibrium is being established. Another advantage over usual titrations is that our model is free from any assumption concerning the pK_a of the ionizable groups in the polyelectrolyte.

When the model is applied to the hydrogel of chemically cross-linked poly(*N*-vinylimidazole) (PVI) immersed in acidic baths containing variable concentrations of the supporting electrolyte NaCl, the following features appear. The solution inside the hydrogel reaches basic pH much higher than the pH of the external bath, when no salt is present, but with added salt both pH are similar, because of the extra ions afforded by the salt. For a given initial pH, the ions of the salt scarcely disturb the degree of ionization of the imidazole units up to $\alpha = 0.4$, and above that value, α increases with salt concentration. But the basicity of the imidazole groups in the polyelectrolyte is significantly larger (pK_a higher) and more dependent on the degree of ionization if no salt is present. The opposite effect of salt is obtained with pK_a^S calculated using the pH in the external solution (pH_S). This increase of pK_a^S with ionic strength is similar to that observed in the titration of homogeneous solutions of linear PVI, which casts doubts on the adequacy of the pH measured in such solutions, because the protonation equilibrium takes place only inside the volume pervaded by the coils.

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