Effects of pH on ion transport in weak amphoteric membranes

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Abstract

We have studied theoretically the effects of pH on the ion transport through amphoteric polymer membranes composed of weak polyelectrolytes where the charged groups are randomly distributed along the axial direction of the membrane. This system serves as a simplified model for the pH controlled ion transport and drug delivery through membranes of biological interest. The theoretical approach employed is based on the Nernst-Planck equations. The complete system of electrical charges formed by: (i) the pH dependent, amphoteric membrane fixed charge, and (ii) the four mobile charges (the two salt ions and the hydrogen and hydroxide ions) have been taken into account without any additional assumption. The model predictions show that the ionic fluxes and the membrane potential are very sensitive to the external pH, and the potential utility of these predictions for the analysis of experiments involving pH dependent passive transport through membranes is emphasized. © 1997 Elsevier Science S.A.

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1. Introduction

Amphoteric membranes contain both positively and negatively fixed charge groups chemically bound to the membrane constituents. Early studies on amphoteric membranes were carried out by Sollner [1], Neihof and Sollner [2], Sollner [3], Weinstein and Caplan [4], and Weinstein et al. [5,6], who considered the case of the charge-mosaic membranes on the basis of the Non-Equilibrium Thermodynamics formalism developed by Kedem and Katchalsky [7]. It is also possible to prepare amphoteric polymer membranes composed of weak polyelectrolytes where the charged groups are randomly distributed along the axial direction of the membrane, as has been done by Yamauchi et al. [8], Hirata et al. [9], Saito and Tanioka [10], and Saito et al. [11]. In the latter studies, it was shown that the membrane properties were very sensitive to the external pH, and then amphoteric membranes could be of potential utility for biochemical sensors and pH-controlled drug delivery systems.

Polymer membranes composed of silk fibroin have also been reported to have amphoteric properties [12,13] due to the existence of weakly acidic carboxyl groups and weakly basic amino groups. Since ionizable protein amino acid residues (i.e. carboxylic acid groups) and protonated amine groups are very common in biological systems, the study of ion transport in weak amphoteric membranes can be of relevance also for the biophysical chemistry of biological membranes. This is the case of the cornea, for instance, where the ion permselectivity appears to be controlled by the degree of protonation of ionizable sites within the tissue [14]. In the above study, the permselectivity was analyzed in terms of diffusion and streaming potential measurements, and the effect of the external pH on these potentials suggested that the cornea contains acidic and basic charge groups that could be responsible for the observed differences in the permeabilities between cationic and anionic species [14].

Although the permselectivity of biological membranes is certainly a complicated phenomenon that involves not only passive electrostatic barriers (due probably to membrane fixed charges) but also active elements like carriers and pumps [15,16], we propose here to study theoretically an ideal case which considers only one major effect: the pH dependence of passive transport through a weak amphoteric membrane carrying both positive and negative fixed charge groups. This case serves as a simplified physical model for many real systems, and can thus be of relevance for the biophysical chemistry of pH controlled
ion transport and drug delivery through thick membranes (membrane thickness of the order of or higher than 10^{-5} cm) of biological interest. For these membranes, bulk rather than surface effects are rate limiting for ion transport.

The theoretical model employed for studying the pH dependence of ion transport in weak amphoteric membranes is based on the Nernst–Planck equations. The physical basis and limitations of these equations as applied to membrane systems can be found elsewhere [17,18]. Several useful theoretical models based on a number of assumptions are already available [1–13]. The present modelling differs from most of these models in that we consider the four nonlinear (diffusion + migration) Nernst–Planck equations which are strongly coupled by the three local chemical reactions occurring in the membrane (the two membrane fixed charge dissociation equations and the water dissociation equation). The full system of nonlinear differential equations is solved numerically without any additional simplifying approximation (such as the Goldman constant field assumption [15,16]) in order to obtain the local profiles across the membrane of all the physical variables (the four ion concentrations and the electric potential) involved. The membrane characteristics studied are the ionic fluxes and the membrane potential.

We believe that the model predictions can be useful for the analysis of future experiments because of the following reasons: (i) experiments involving electrolyte transport through biomembranes, biochemical sensors and pH-controlled drug delivery systems are often conducted using buffer solutions and the measured ternary ion system properties are analyzed in many cases in terms of binary system equations [14,19]; (ii) simplifying assumptions such as equal pH values inside and outside the membrane and a constant electrical field within the membrane [15,16] are sometimes used without a clear verification of the validity of these assumptions; and (iii) most of the experiments are conducted with the same pH value in the two external solutions bathing the membrane [10,11,14,19–21], and thus the effects of imposing a pH gradient through the membrane are not well known.

2. Theoretical model

The system considered is shown schematically in Fig. 1. The amphoteric membrane extends from $x = 0$ to $x = d$, and separates two solutions of the same uni-univalent electrolyte. The solutions are assumed to be perfectly stirred. $c_i(x)$ stands for the concentration of the $i$th-species at a point of coordinate $x$ within the membrane ($i = 1$ for salt cations, $i = 2$ for salt anions, $i = 3$ for hydrogen ions, and $i = 4$ for hydroxide ions). $c_i$ denotes the concentration of the $i$th-species in the bulk of the $j$th-solution ($j = L$ for the left hand solution and $j = R$ for the right hand solution). $\text{pH}_j$, ($j = L, R$) refers to the pH value of solution $j$. The whole system is assumed to be isothermal and free from convective movements.

The amphoteric membrane contains acidic (N) and basic (P) groups homogeneously distributed throughout its volume. These groups are assumed to be monovalent, and can be charged or not depending on the local value of the pH within the membrane. We denote by $N_c$ and $N_N$ the concentrations of the charged (N*) and neutral (N°) acidic groups, and by $P_c$ and $P_P$ the concentrations of the charged (P*) and neutral (P°) basic groups, respectively. The equations describing the local equilibria between neutral and charged groups are:

\begin{align}
N^0 & \Leftrightarrow N + \text{H}^+ , \quad (1a) \\
P^* & \Leftrightarrow P^0 + \text{H}^+ , \quad (1b)
\end{align}

where $K_N$ and $K_P$ are the equilibrium constants. From Eqs. (1a) and (1b), the local concentrations of charged groups within the membrane are:

\begin{align}
N_c &= \frac{1}{1 + c_i/K_N} N_T , \quad (2a) \\
P_c &= \frac{c_i/K_P}{1 + c_i/K_P} P_T , \quad (2b)
\end{align}

and the local concentration $X$ of the net fixed charge in the membrane is defined as:

\begin{equation}
X = P_c - N_c , \quad (3)
\end{equation}

where we have included the sign (positive or negative) of this charge in the value of $X$, and $N_T = N_N + N_c$ and $P_T = P_P + P_c$ are the total concentrations of acidic and basic groups. The concentrations of $\text{H}^+$ and $\text{OH}^-$ ions verify the equilibrium condition:

\begin{equation}
c_1 + c_2 = K_w , \quad (4)
\end{equation}

with $K_w = 10^{-14} \text{ mol}^2 \text{ L}^{-2}$ through the whole system. The ion concentrations obey the electroneutrality conditions:

\begin{align}
c_{1j} + c_{3j} = c_{2j} + c_{4j}, \quad j = L, R, \\
c_1 + c_3 + X = c_2 + c_4 . \quad (5a) \\
(5b)
\end{align}
in the bulk of the two bathing solutions and in the membrane phase, respectively.

Bulk solution and inner (membrane phase) concentrations are connected through the following Donnan equilibrium conditions \([15,16]\) at the interfaces \(x = 0\) and \(x = d\):

\[
\frac{c_i(0)}{c_{IL}} = \frac{c_i(d)}{c_{IR}} = \frac{c_{IL}}{c_{IR}}, \quad (6a)
\]

\[
\frac{c_i(d)}{c_{IR}} = \frac{c_i'(d)}{c_{IR}} = \frac{c_{IR}}{c_{IL}}. \quad (6b)
\]

From Eqs. (2a), (2b), (3), (4), (5a), (5b), (6a) and (6b), it follows that:

\[
\frac{c_i}{K_i} \frac{c_i(-)}{K_i} = \left[ \frac{c_i}{K_i} + \frac{c_i}{K_i} + \frac{c_i}{K_i} \frac{P}{1 + c_i/c_i} \right] u_i + \left[ 1 - \frac{c_i}{K_i} \frac{c_i}{K_i} \frac{P}{1 + c_i/c_i} \right] u_i - 1 = 0, \quad j = 1, L, R. \quad (7)
\]

where \(u_i = c_i(0)/c_{IL}\) and \(u_i = c_i(d)/c_{IR}\). Eq. (7) can be solved numerically for \(u_{1L}\) and \(u_{1R}\) using a standard procedure. Then, the inner membrane phase concentrations \(c_i(0)\) and \(c_i(d)\), \(i = 2, 3, 4\), can be obtained from Eqs. (6a) and (6b) in terms of the electrolyte concentrations and the pH values in the external bathing solutions. Once all the concentrations \(c_i(0)\) and \(c_i(d)\) have been determined, the Donnan potential differences at the left (\(x = 0\)) and right (\(x = d\)) interfaces, \(\Delta \phi_L\) and \(\Delta \phi_R\), can be computed as:

\[
\Delta \phi_L = \frac{RT}{F} \log \frac{c_{IL}}{c_i(0)}, \quad (8a)
\]

\[
\Delta \phi_R = \frac{RT}{F} \log \frac{c_i(d)}{c_{IR}}. \quad (8b)
\]

The electric potential and the ion fluxes in the bulk of the amphoteric membrane can be calculated solving the Nernst–Planck equations \([17,18]\):

\[
J_i = -D_i \left[ \frac{d c_i}{d x} + (-1)^{i+1} \frac{F}{RT} \frac{d \phi}{d x} \right]
\]

\[i = 1, 2, \ldots, 4, \quad (9)\]

with the condition of zero total current:

\[
J_1 - J_2 + J_3 - J_4 = 0. \quad (10)
\]

In Eq. (9), \(D_i\) and \(J_i\) stand for the diffusion coefficient in the membrane and the flux of the \(i\)th-species, respectively, \(\phi\) is the local electric potential, and the constants \(F, R\) and \(T\) have their usual meaning.

Fluxes \(J_1\) and \(J_2\) correspond to the salt ions (the sodium and chloride ions coming from the NaCl dissociation in water, for instance) and are constant through the membrane under steady state conditions because of the continuity (mass conservation) equations: there are neither local sources nor local sinks for these ions due to the complete dissociation of the strong electrolyte in pure water. Fluxes \(J_3\) and \(J_4\) correspond to the water (hydrogen and hydroxide) ions and are not constant through the membrane because these ions participate in the local dissociation reactions at the membrane fixed charge groups. The dissociation reactions constitute local sources and sinks for these ions (see Eqs. (1a) and (1b)).

Substituting Eq. (4) into Eq. (9) for \(i = 3\) and \(4\), and taking into account Eq. (10), we obtain:

\[
J_3 = \frac{J_2 - J_1}{1 + K_{C, D, C, C}^2}, \quad (11a)
\]

\[
J_4 = -\frac{D_i K_i}{D_{IR} c_i^2} J_4. \quad (11b)
\]

Eqs. (11a) and (11b) show that the fluxes of H\(^+\) and OH\(^-\) ions are not constant through the membrane in the general case where \(c_i\) changes with \(x\).

We have used the following iterative procedure to integrate the system of differential equations given by Eq. (9). First, we assume some initial values for the ion fluxes and integrate Eq. (9) using a fourth-order Runge–Kutta method with the boundary conditions at the interface \(x = 0\). Then, we check whether the solutions satisfy the boundary conditions at \(x = d\) or not. If not, the initial estimation is changed until the boundary conditions at \(x = d\) are satisfied. This allows us to obtain the ion concentration and electric potential profiles, \(c_i(x)\) and \(\phi(x)\), and the ion fluxes \(J_i\). Then, the profile of the fixed charge concentration \(X(x)\) through the membrane can be determined from Eqs. (2a), (2b) and (3). Finally, the membrane potential is computed as:

\[
\Delta \phi_M = \Delta \phi_L + \Delta \phi_R, \quad (12)
\]

where \(\Delta \phi_M = \phi(d) - \phi(0)\) is the diffusion potential in the membrane.

3. Results and discussion

In this section, we present a set of model calculations concerning the fixed charge concentration profiles, the membrane potential and the ionic fluxes in the amphoteric membrane. In all the calculations, we have considered the symmetrical case \(N_T = P_T = 5 \times 10^{-2}\) mol l\(^{-1}\), and assumed the values \(d = 10^{-5}\) cm for the membrane thickness and \(pK_N = 4\) for the \(pK\) value of the acidic groups. The particular concentration and pH values employed here are those typical of the cornea ion transport and pH-controlled drug delivery experiments \([14,19,21]\). The \(pK\) values used (see Fig. 2) are characteristic of ionizable protein amino acid residues (i.e., carboxylic acid groups) and protonated amine groups \([10,11,14,19,21]\). We have also used the following values for the diffusion coefficients of the ionic species within the membrane: \(D_1 = 10^{-7}\).
cm$^2$ s$^{-1}$, $D_L = 2D_I$, $D_A = 9D_I$ and $D_T = 5D_I$. These ion diffusion coefficients are one/two orders of magnitude lower than those corresponding to a free aqueous solution, according to the typical experimental results obtained for charged membranes [15,16].

The steady state values for the membrane potential and the ion fluxes are zero when the pH values and the electrolyte concentrations in the left and right hand bathing solutions are equal ($pH_L = pH_R$ and $c_L = c_R$). In this case, the concentrations of charged acidic and basic groups are constant through the membrane, and the net fixed charge

$$X$$

concentration $X$ within the membrane is homogeneous. Fig. 2 shows this fixed charge concentration vs. $pH_L = pH_R = pH$ in the case $c_L = c_R = 5 	imes 10^{-2}$ mol $1^{-1}$. The numbers in the curves correspond to the $pK_p$ values considered. The concentrations $P_L$ and $N_L$ have been calculated solving Eq. (7) for $u = u_R$ and substituting the result in Eqs. (6a), (6b), (2a) and (2b). As expected, $X = P_T$ ($X = -N_T$) for $pH < pK_N$ ($pH > pK_p$) and $X = P_T/2$ ($X = -N_T/2$) for $pH = pK_N$ ($pH = pK_p$). It is also observed that the membrane becomes uncharged in the vicinity of the isoelectric point, $pI = (pK_N + pK_p)/2$, and that the pH value region where the net fixed charge concentration is practically zero becomes enlarged as the difference between $pK_p$ and $pK_N$ is increased.

Figs. 3–5 illustrate the case $pH_L = pH_R = pH$ and $c_L = 5c_R$. The model calculations have been performed using $c_L = 5 	imes 10^{-2}$ mol $1^{-1}$ and $pK_p = 6$. Fig. 3 shows the net fixed charge concentration profiles within the membrane. The curves are parametric in the pH value, which is indicated in each curve. Again, we see that $X = P_T$ ($X = -N_T$) for $pH < pK_N$ ($pH > pK_p$) and that $X = 0$ near the isoelectric point $pI = (pK_N + pK_p)/2$. However, in the regions $pH < pK_N$ and $pH > pK_p$, the net fixed charge concentration profiles become inhomogeneous due to local variations in the pH values within the membrane.

Fig. 4 shows the calculated membrane potential vs. pH for the same conditions as in Fig. 3. The continuous line corresponds to the results obtained using the numerical procedure described in the previous section. The dashed line has been calculated assuming that the pH value within the membrane is equal to that of the bathing solutions and that the fluxes of the $H^+$ and $OH^-$ ions can be neglected. Under these assumptions, the net fixed charge concentration $X$ within the membrane is homogeneous and can be

$$X$$

Fig. 4. Calculated membrane potential of the amphoteric membrane vs. pH for the same conditions as given in Fig. 3. The continuous line corresponds to the exact numerical results. The dashed and dotted–dashed lines correspond to the approximations given by Eq. (13a) and Eqs. (12) and (14a), respectively.

Fig. 5. Ion fluxes (exact numerical values) vs. pH for the same conditions as given in Fig. 3 and Fig. 4.
calculated from Eqs. (2a), (2b) and (3) for each pH value. The membrane potential and the fluxes of salt ions can be obtained using the equations [15]:

\[
\Delta \phi_M = \frac{RT}{F} \left\{ \log \frac{c_L}{c_R} \frac{X^2 + 4c_L^2}{X^2 + 4c_R^2} - X \right\} + U \log \frac{X^2 + 4c_L^2 + UX}{X^2 + 4c_R^2 + UX},
\]

\[J_i \approx J_2 = \frac{D_3D_1}{D_2 + D_1} \frac{1}{d} \left( \sqrt{X^2 + 4c_L^2} - \sqrt{X^2 + 4c_R^2} \right) + UX \log \frac{X^2 + 4c_L^2 + UX}{X^2 + 4c_R^2 + UX},
\]

where \( U = (D_1 - D_3)/(D_2 + D_1) \). This approximation gives very good results in the range \( 8 < \text{pH} < 10 \), where the membrane has a negative value of \( X \) (\( X = -N_t \), see Fig. 3) and the membrane potential is nearly constant \( (\Delta \phi_M \approx -14 \text{ mV}) \) obtained with the numerical procedure near the isoelectric point. However, the results given by this approximation deviate from the exact numerical ones in the low pH region because in this region the flux of the \( \text{H}^+ \) ions is no longer negligible. The deviations in the pH range \( 4 < \text{pH} < 8 \) must be ascribed to the fact that the net fixed charge concentration within the membrane is not homogeneous.

A more accurate analytical approximation for the calculation of the membrane potential can be achieved using the so called constant field approximation [15,16] which assumes that \( d\Phi/dx = \Delta \phi_D/d = \text{constant} \). In this case, Eq. (9) can be readily integrated for \( i = 1, 2 \) and 3 in the low pH region (note that in this limit \( J_2 \approx 0 \) and \( J_3 \approx J_1 \approx \text{constant} \), see Eqs. (10), (11a) and (11b)). Under these assumptions, we obtain [15,16]:

\[
\Delta \phi_D \approx \frac{RT}{F} \log \frac{D_1c_L(0) + D_2c_L(d) + D_1c_1(0)}{D_1c_L(d) + D_2c_L(0) + D_1c_1(d)},
\]

\[
J_1 \approx \frac{F}{RT} \frac{D_3\Delta \phi_D}{d} \frac{c_1(0)}{1 - \exp\left[ -F\Delta \phi_D/RT \right]} - c_1(0),
\]

\[
J_2 \approx -\frac{F}{RT} \frac{D_2\Delta \phi_D}{d} \frac{c_L(d) \exp\left[ -F\Delta \phi_D/RT \right] - c_L(0)}{1 - \exp\left[ -F\Delta \phi_D/RT \right]},
\]

\[
J_3 \approx \frac{F}{RT} \frac{D_3\Delta \phi_D}{d} \frac{c_3(0) \exp\left[ -F\Delta \phi_D/RT \right] - c_3(d)}{1 - \exp\left[ -F\Delta \phi_D/RT \right]}.
\]

Substituting Eq. (14a) in Eq. (12), the membrane potential can be calculated. A similar procedure can be followed to obtain the constant field approximation for the membrane potential in the limit \( \text{pH} \gg 7 \). The dotted--dashed line in Fig. 4 corresponds to the results given by this approximation.

Fig. 5 shows the dependence of the ion fluxes on the pH for the same conditions as in Fig. 4. The results have been obtained using the numerical procedure described in the previous section. As expected, we see that \( J_1 = J_2 \) and \( J_3 = J_4 = 0 \) in the intermediate range \( 4 < \text{pH} < 10 \). It can also be observed that the ion fluxes \( J_1 \) and \( J_2 \) attain a local maximum at the pH value where \( \Delta \phi_M = 0 \) in Fig. 4 (this pH value does not coincide exactly with \( \text{pH} = 5 \) because the pH within the membrane is not equal to the external pH). Again, the constant value \( J_1 = J_2 \approx 4.9 \times 10^{-7} \text{ mol cm}^{-2} \text{ s}^{-1} \) in the region \( 8 < \text{pH} < 10 \) and the value \( J_1 = J_2 \approx 5.3 \times 10^{-7} \text{ mol cm}^{-2} \text{ s}^{-1} \) for \( \text{pH} = \text{pI} = 5 \) can be anticipated from Eq. (13b) taking \( X = N_t \) and \( X = 0 \), respectively. As discussed above, we see that the fluxes \( J_3 \) and \( J_4 \) can not be neglected for the low and high pH values (compare Figs. 4 and 5). In these limits, the constant field approximation given by Eqs. (14a), (14b), (14c) and (14d) can provide good analytical approximations for the ion fluxes.

The case \( c_L = 5c_R \) and \( \text{pH}_L = \text{pH}_R \) is considered in Figs. 6–8. We have fixed \( c_L = 5 \times 10^{-2} \text{ mol}^{-1} \), \( \text{pH}_L = 6 \) and \( \text{pK}_a = 9 \) in the calculations. Fig. 6 shows the profiles of the net fixed charge concentration within the membrane. The numbers close to each curve correspond to the pH value considered. We see that the profiles are highly inhomogeneous except for the case \( \text{pH}_L = \text{pH}_R = 6 \), where the membrane is practically uncharged (\( X \approx 0 \)). As could be anticipated, the inhomogeneity of the membrane increases as \( \text{pH}_L \) decreases with respect to the value in the right hand solution, \( \text{pH}_R = 6 \).

Fig. 7 shows the membrane potential of the amphoteric membrane for the same case as in Fig. 6. The exact

![Fig. 6. Net fixed charge concentration profiles within the amphoteric membrane in the case \( \text{pH}_L = \text{pH}_R \). We have used \( N_t = P_t = 5 \times 10^{-2} \text{ mol}^{-1} \), \( c_L = 5 \times 10^{-2} \text{ mol}^{-1} = 5c_R \), \( \text{pK}_a = 4 \) and \( \text{pK}_b = 9 \) in the model calculations. The curves are parametric in \( \text{pH}_L \), with \( \text{pH}_R = 6 \). The case \( \text{pH}_L = \text{pH}_R = 6 \) gives \( X = 0 \).](image)
We have carried out also other calculations for different values of the parameters involved, but we obtained qualitatively similar results for reasonable choices of these parameters (for instance, an increase in the membrane thickness $d$ does not change the membrane potential values but decreases the ion fluxes as $1/d$, as could be anticipated for relatively thick membranes).

Two additional effects that could be present in weak amphoteric membranes have not been taken into account in our study. One of these is the variation of the water content of the membrane associated with the change of the ionization degree of the fixed charge groups. The other is the possibility of having cross electrical neutralization between ionized fixed groups of opposite charge. Let us discuss these questions qualitatively now. The ionization of the membrane fixed charge groups produces an uptake of additional water from the solution [22]. Since the membrane swells, the effective fixed charge volume concentration $X$ decreases. The decrease in the effective value of $X$ with the degree of hydration of charged membranes is well documented [23] and would make less dramatic some of the pH effects discussed in our study. We must recognize that the omission of the swelling effect is a major limitation of our results, though this effect should not be so important here as it is in the case of ampholytic hydrogels of low crosslinker content [24]. Note that there is a limit in the charged membrane swelling because of the restoring elastic forces exerted by the crosslinker chains inserted between the fixed charge chains [22]. The second effect mentioned above, the cross electrical neutralization between ionized membrane groups of different charge, can probably be discarded on the basis of the following reasoning [25,26]. Since the fixed charge groups are randomly distributed in the membrane, an average distance between groups is 

$$r = \left(1/N_m\right)^{1/3}$$

where $N_m$ is Avogadro's constant. If $X = 10^{-2}$ mol l$^{-1}$, then $r = 50 \text{ Å}$. Now, a typical Debye length for electrical screening within the membrane is $\Lambda_0 = (eRT/2F^2c_m)^{1/2} = 20 \text{ Å}$ for $c = 40$ $e_0$ [27] and $c_m = 10^{-2}$ mol l$^{-1}$ where $e_0$ is the vacuum electrical permittivity and $c_m$ is a typical mobile ion concentration within the membrane. The electrical screening factor [25,26] is then $\exp(-r/\Lambda_0) = 0.08$. This factor is small enough to neglect the electrostatic attraction between nearest neighbor membrane fixed groups of opposite charge [25,26]. Therefore, the condition of local electroneutrality in the membrane must be assured by the mobile electrolyte ions taken from the solution (see Eq. (5b)) and the electrical state of the fixed charge groups must be dictated by the local concentrations of the mobile ions in the vicinity of the fixed charge groups (see Eqs. (1a) and (1b)).

In summary, we have presented a set of model calculations concerning the membrane potential and the ionic fluxes in weak amphoteric membranes. The whole system of equations including the four Nernst–Planck equations and the equations for the local dissociation equilibria within the membrane have been solved numerically without any additional simplifying assumption. The comparison of the exact results with those obtained by using numerical results have been plotted in a continuous line. The dashed and the dotted–dashed lines correspond to the approximations given by Eq. (13a) and Eqs. (12) and (14a), respectively. The exact numerical results for the ion fluxes vs. pH are shown in Fig. 8. As in the previous case (see Figs. 4 and 5), the behavior of the membrane potential is closely related to the behavior of the ionic fluxes through the membrane. We can distinguish three different regions in Fig. 7: first, the membrane potential decreases with $\text{pH}_L$, then attains a plateau region characterized by a constant value $\Delta \phi_M = -30 \text{ mV}$, and, finally, decreases again with $\text{pH}_L$. These regions correspond to $J_2 > J_1$, $J_1 = J_2$ and $J_1 < J_2$ in Fig. 8, respectively.

The approximate solution for $\Delta \phi_M$ given by Eq. (13a) deviates significantly from the exact solution except for the pH region $5 < \text{pH}_L < 7$, where $X = 0$, $J_1 = J_2 = 5.3 \times 10^{-2} \text{ mol cm}^{-2} \text{s}^{-1}$ and $J_3 = 0$ (see Figs. 6–8). The results for $\Delta \phi_M$ obtained using Eqs. (12) and (14a) do not agree with the exact numerical results over the entire range of $\text{pH}_L$ values considered, and thus the constant field assumption constitutes a poor approximation when a pH gradient exists through the membrane.

![Fig. 7. Calculated membrane potential of the amphoteric membrane vs. pH for the same conditions as given in Fig. 6. The curves correspond to numerical calculations (continuous line), results of Eq. (13a) (dashed line), and results of Eqs. (12) and (14a) (dotted–dashed line).](image)

![Fig. 8. Ion fluxes (exact numerical values) vs. pH for the same conditions as given in Fig. 6 and Fig. 7.](image)
several approximations has shown the potential utility of the numerical solution, especially when a pH gradient is imposed through the membrane. Since the pH dependence of passive transport in weak amphoteric membranes is a subject of great importance in thick biological membranes [14,15] and pH-controlled drug delivery systems [19–21], the model calculations presented here could be of interest for the analysis of future experiments.

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