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pH dependence of electrostatic interaction between ion-penetrable membranes

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A theory on the electrostatic repulsion between ion-penetrable membranes proposed previously by us is extended by taking into account the degree of dissociation of the membrane-fixed ionizable groups. A system of equations which determines the pH dependence of the membrane interaction is presented. The density of membrane-fixed charges is consistently determined as a function of the electric potential so that both the membrane-fixed charge density and the potential are not constant but functions of the membrane separation. The pH at the surface of interacting membranes is also calculated as a function of the membrane separation.

1. Introduction

Electrostatic interaction between biocolloids such as cells or their membranes plays an important role in various interfacial electric phenomena in biological systems. A number of studies [1–3] have been carried out on the membrane interaction on the basis of the DLVO theory of colloid stability [4,5]. These studies, however, employ the assumption that the membrane surface is ion-impenetrable and that the membrane-fixed charges are located only at the membrane surface (of zero thickness). This assumption is by no means a close approximation to real biological membranes, since their fixed charges are considered to be distributed through an ion-penetrable surface layer of nonzero thickness. Recently, we have proposed a novel model for the electrostatic interaction between ion-penetrable membranes, by taking into account the above-mentioned membrane surface structure [6–10]. In refs. 7 and 8, in particular, it is assumed that the electric potential far inside the membrane remains constant at the Donnan potential during interaction. We refer to this type of interaction as the double-layer interaction regulated by the Donnan potential. This model, therefore, is completely different from the conventional interaction models for ion-impenetrable solid surfaces, which assume that the surface potential [4,5] or surface charge density [1,3,11–13] remains constant during interaction.

Our previous theory [6–10], however, assumes that the density of the membrane-fixed charges, which arise mostly from dissociation of ionizable groups distributed within the membrane, is constant and is independent of membrane separation. This theory can therefore be applied only to the pH region where the membrane ionizable groups can be considered to be completely dissociated, since the degree of dissociation of the membrane-

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fixed groups at a given point should generally depend on the electric potential at the same point, as has previously been shown for a noninteracting single membrane [14]. Although Ninham and Parsegian [2] take into account the degree of dissociation of the membrane-ionizable groups in their theory of membrane interaction, they treat ion-impenetrable membranes. In the present paper, we consider these effects in the case of ion-penetrable membranes and treat both the density of the membrane-fixed charges and the potential consistently as functions of membrane separation. This approach therefore makes it possible for us to discuss the pH dependence of the electrostatic interaction between ion-penetrable membranes.

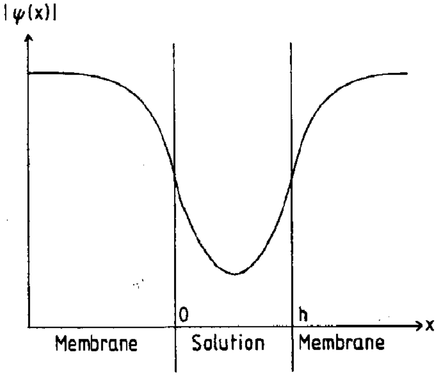

Fig. 1. Schematic representation of potential distribution ($\psi(x)$) between and within two interacting ion-penetrable membranes at separation h.

2. Theory

Consider two parallel planar ion-penetrable membranes at separation h immersed in a monovalent electrolyte solution. Let n be the total concentration of free mobile ions, i.e., electrolyte ions, H^+ and OH^- in the bulk solution, with n_H being the bulk concentration of H^+ only. Inside the membrane, monovalent acidic ionizable groups AH are distributed according to a uniform density N. Dissociation of these groups, i.e., $AH = A^- + H^+$, renders the membranes negatively charged. We assume that the electric potential far inside the membrane remains constant at the Donnan potential (which will be given later by eq. 23) during interaction. We take an x-axis perpendicular to the membrane with its origin at the boundary between the membrane on the left and the solution, as shown in fig. 1. From the symmetry of the system, only the region $x \leqq h/2$ need be considered.

We regard the two membranes as an open system in a large reservoir of small mobile ions. In order to calculate the free energy of the system, we shall employ a procedure used for calculation of the free energy increase of membranes due to the adsorption of cations [15,16]. We regard the dissociation reaction $AH = A^- + H^+$ as being desorption of H^+ from AH and adsorption of H^+ onto A^-. In accordance, we consider the electrochemical potential μ_H of adsorbed H^+, which, at equilibrium, is equal to the chemical potential of AH (μ_{AH}) minus the electrochemical potential of A^- (μ_{A^-}). The increase in the Helmholtz free energy of the membranes due to ionization of membrane groups, $F(h)$, can be expressed as

$$F(h) = 2\int_{-\infty}^{0} f(x)\,\mathrm{d}x, \qquad (1)$$

where $f(x)$ is the corresponding free energy density at position x within the left membrane and the factor 2 arises from the same contribution from the membrane on the right-hand side. We introduce the electric potential $\psi(x)$ at position x relative to the bulk solution phase. Then, $f(x)$ can be given by

$$f(x) = \int_0^{\sigma(x)} \psi(x)\,\mathrm{d}\sigma - \mu_0^m N_H(x) - TS(x),$$

$$x \leqq 0 \qquad (2)$$

with

$$\sigma(x) = -\,eN_H(x), \qquad (3)$$

$$S(x) = k\,\ln\left\{\frac{N!}{N_H!(N-N_H)!}\right\}$$

$$\approx k\{N\ln N - N_H \ln N_H - (N-N_H)\ln(N-N_H)\}, \qquad (4)$$

where $N_H(x)$ denotes the number density of ionized groups A^- at position x (in other words, the number density of H^+ desorbed from AH at position x is $N_H(x)$), $\sigma(x)$ the charge density at position x, e the elementary electric charge, μ_0^m a constant, T the absolute temperature, k Boltzmann's constant and $S(x)$ the configurational entropy at position x. In deriving the second relation of eq. 4, the Stirling formula has been used. The electrochemical potential $\mu_H(x)$ of adsorbed H^+ at position x within the membrane (whose number density equals that of undissociated groups AH, $N - N_H(x)$) is given by

$$\mu_H(x) = \frac{\partial f}{\partial(N - N_H)} = \mu_0^m + e\psi(x) - kT \ln\left(\frac{N_H(x)}{N - N_H(x)}\right), \quad (5)$$

(which is equal to $\mu_{AH} - \mu_{A^-}$).

At thermodynamic equilibrium, $\mu_H(x)$ must be equal to the chemical potential of H^+ in the bulk solution phase, μ_H^w, viz.,

$$\mu_H(x) = \mu_H^w, \quad (6)$$

with

$$\mu_H^w = \mu_0^w + kT \ln(n_H/n_0), \quad (7)$$

where μ_0^w is a constant and n_0 the number of water molecules per unit volume of the bulk solution. Substituting eqs. 5 and 7 into eq. 6 yields

$$N_H(x) = \frac{N}{1 + \frac{n_H}{K} \exp(-e\psi(x)/kT)}, \quad (8)$$

where

$$K = n_0 \exp[(\mu_0^m - \mu_0^w)/kT] \quad (9)$$

is the dissociation constant of the membrane ionizable groups. Eq. 8 represents the mass action law for the reaction $AH = A^- + H^+$.

Now we define a thermodynamic potential, $\tilde{F}(h)$, by

$$\tilde{F}(h) = 2\int_{-\infty}^{0} \tilde{f}(x)\, dx, \quad (10)$$

with

$$\tilde{f}(x) = f(x) + \mu_H(x) N_H(x). \quad (11)$$

Note that $\tilde{F}(h)$ corresponds to the Helmholtz free energy of the total system, i.e., the membranes plus the reservoir (the surrounding solution). Substituting eqs. 2–5 and 8 into eq. 11, we obtain

$$\tilde{f}(x) = \int_0^{\sigma(x)} \psi\, d\sigma - \sigma(x)\psi(x) - NkT \ln\left[1 + \frac{K}{n_H} \exp(e\psi(x)/kT)\right]. \quad (12)$$

The derivative of $\tilde{F}(h)$ with respect to h gives the electrostatic repulsion $P(h)$ between the membranes per unit area, viz.,

$$P(h) = -\frac{\partial \tilde{F}}{\partial h}, \quad (13)$$

and the difference $\tilde{F}(h) - \tilde{F}(\infty)$ equals the potential energy of interaction per unit area, $V(h)$, viz.,

$$V(h) = \tilde{F}(h) - \tilde{F}(\infty). \quad (14)$$

By using eq. 12, we obtain the following expression for the repulsion $P(h)$ via eq. 13 after lengthy algebraic treatment:

$$P(h) = 4nkT \sinh^2[e\psi(h/2)/2kT], \quad (15)$$

which can also be derived from direct consideration of Maxwell's stress and the osmotic pressure acting on the membranes.

In order to calculate $P(h)$ and $V(h)$, one must obtain the electric potential $\psi(x)$, which satisfies the Poisson-Boltzmann equations, viz.,

$$\frac{d^2\psi}{dx^2} = \frac{2en}{\varepsilon_r\varepsilon_0}[\sinh(e\psi/kT) - \sigma(x)/2en], \quad x < 0, \quad (16)$$

$$\frac{d^2\psi}{dx^2} = \frac{2en}{\varepsilon_r\varepsilon_0}[\sinh(e\psi/kT)], \quad 0 < x \leq h/2, \quad (17)$$

where ε_r and ε_0 denote the relative permittivity of the solution and permittivity of a vacuum, respectively. The second term in brackets on the right-hand side of eq. 16 corresponds to the contribution from the membrane-fixed charges.

The boundary conditions are

$$\psi(-0)=\psi(+0), \tag{18}$$

$$\left.\frac{\mathrm{d}\psi}{\mathrm{d}x}\right|_{x=-0}=\left.\frac{\mathrm{d}\psi}{\mathrm{d}x}\right|_{x=+0}, \tag{19}$$

$$\psi(x)\xrightarrow[\substack{|x|\gg 1/\kappa\\ x<0}]{}\psi_{\mathrm{DON}}, \tag{20}$$

$$\left.\frac{\mathrm{d}\psi}{\mathrm{d}x}\right|_{x=h/2}=0, \tag{21}$$

where

$$\kappa=\left(2ne^2/\varepsilon_r\varepsilon_0 kT\right)^{1/2} \tag{22}$$

is the Debye-Hückel parameter and ψ_{DON} the Donnan potential, given by the solution of the following transcendental equation

$$\sinh\left(\frac{e\psi_{\mathrm{DON}}}{kT}\right)+\frac{N}{2n}\frac{1}{1+(N_{\mathrm{H}}/K)\exp(-e\psi_{\mathrm{DON}}/kT)}=0, \tag{23}$$

Eq. 23 can be obtained by putting the right-hand side of eq. 16 equal to zero (and using eqs. 3 and 8), since at points far inside the membrane, where the potential equals the Donnan potential ψ_{DON}, the condition of electroneutrality holds, i.e., $\mathrm{d}^2\psi/\mathrm{d}x^2=0$. Eq. 18 and 19 express the conditions of continuity of the electric potential and of the electric displacement at $x=0$. Eq. 20 corresponds to the assumption that the potential far inside the membrane remains constant at the Donnan potential during interaction. Eq. 21 derives from the symmetry of the system.

The solution to the coupled eqs. 16 and 17 subject to the boundary conditions, eqs. 18–21, completely determines the potential distribution between and inside the two interacting membranes.

3. Results and discussion

The aim of this paper has been to derive equations describing the pH dependence of the electrostatic interaction between ion-penetrable membranes. We have assumed that the electric potential far inside the interacting membranes is always equal to the Donnan potential. We have taken into account the degree of dissociation of the membrane-fixed ionizable groups so that the density of the membrane-fixed charges $\sigma(x)$ at position x within the membrane is a function of the electric potential $\psi(x)$ at the same point. We have obtained expressions for the free energy (eq. 10 with eq. 12) and force (eq. 15) of the electrostatic interaction between two parallel planar ion-penetrable membranes. These expressions involve the potential distribution $\psi(x)$, which is the solution of the Poisson-Boltzmann equations (eqs. 16 and 17) subject to the boundary conditions (eqs. 18–22). Note that $\tilde{F}(h)$ includes terms that become infinity, which can be interpreted as the inherent free energy of the membrane itself, but these terms are independent of membrane separation and therefore make no contribution to the membrane interaction.

Eq. 12 for the free energy density $\tilde{f}(x)$ consists of three terms: the first one expresses the electric work needed to charge the membrane and the second and third terms represent the chemical contribution, the third term arising from the configurational entropy of adsorbed H^+.

Figs. 2–5 show examples of the numerical calculation. We have used numerical values $N=0.69$ M, $K=10^{-4}$ M (an appropriate value for carboxylic acid groups), $n=0.1$ M, $\varepsilon_r=78.54$ and $T=298$ K. Fig. 2 depicts the repulsion P as a function of h for various values of pH in the bulk solution phase. For bulk pH values above 7, $P(h)$ shows only a slight dependence on the bulk pH, since in this pH region the membrane ionizable groups in the present system are almost completely dissociated. The repulsion P reaches its maximum at $h=0$. The maximum is given by

$$P_{\max}=4nkT\sinh^2(e\psi_{\mathrm{DON}}/2kT), \tag{24}$$

since $\psi(h/2)$ becomes equal to ψ_{DON} at $h=0$. Fig. 2 shows that $P(h)$ is almost directly proportional to $\exp(-\kappa h)$, which implies that the linear superposition with respect to the potential $\psi(h/2)$ holds well, i.e., the potential $\psi(h/2)$ can be closely approximated by the sum of the potentials which

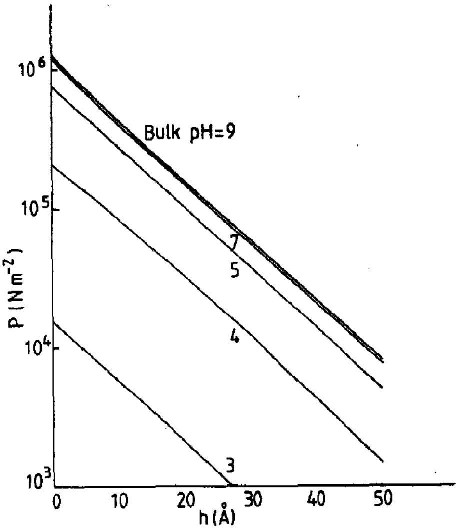

Fig. 2. Electrostatic repulsion (P) between two ion-penetrable membranes as a function of membrane separation (h) for several values of bulk pH. Calculated using $N = 0.69$ M, $K = 10^{-4}$ M, $n = 0.1$ M, $\varepsilon_r = 78.5$ and $T = 298$ K.

would be produced at a distance $h/2$ from the surface of the respective membranes in the absence of interaction.

In fig. 3, $P_{\max}$, ψ_{DON} and the membrane surface potential $\psi(0)$ at $h = \infty$, which we denote by ψ_s^{∞}, are plotted as functions of bulk pH. As h decreases from infinity to 0, the membrane surface potential ψ_s ($= \psi(0)$) increases from ψ_s^{∞} to ψ_{DON}, namely, the value of ψ_s at arbitrary h lies between ψ_s^{∞} and ψ_{DON}. In order to see this more clearly, in fig. 4, we display ψ_s as a function of h for various values of the bulk pH. The value of ψ_s at $h = 0$ equals the Donnan potential ψ_{DON}. For bulk pH values above 7, the dependence of ψ_s on bulk pH is very small due to nearly complete dissociation of the membrane ionizable groups.

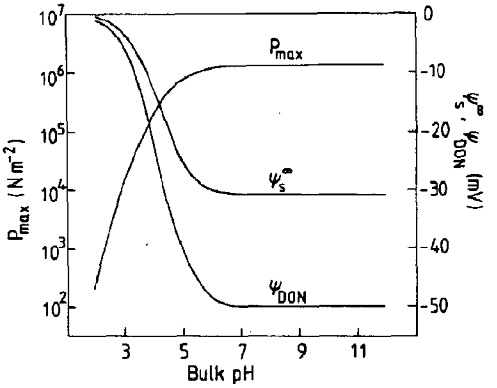

Fig. 3. Maximum repulsion ($P_{\max}$; $= P(0)$), and Donnan potential (ψ_{DON}) and surface potential at infinite separation (ψ_s^{∞}) as functions of bulk pH. Calculated using $N = 0.69$ M, $K = 10^{-4}$ M, $n = 0.1$ M, $\varepsilon_r = 78.5$ and $T = 298$ K.

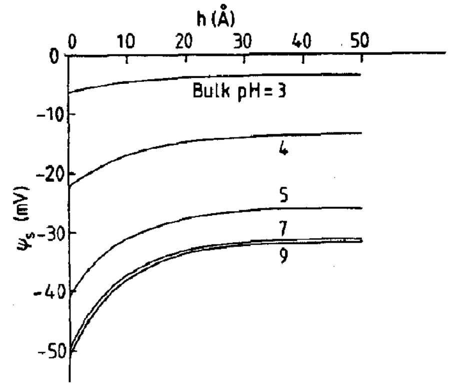

Fig. 4. Surface potential (ψ_s; $= \psi(0)$) as a function of membrane separation (h) for several values of bulk pH. Calculated using $N = 0.69$ M, $K = 10^{-4}$ M, $n = 0.1$ M, $\varepsilon_r = 78.5$ and $T = 298$ K. The value of ψ_s at $h = 0$ coincides with the Donnan potential (ψ_{DON}).

The theory presented here also predicts how the surface pH, i.e., the value of pH at $x = 0$, changes with membrane separation h. It should be stressed

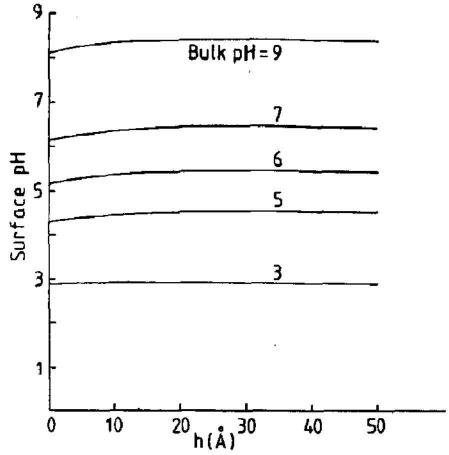

Fig. 5. Surface pH as a function of membrane separation (h) for several values of bulk pH. Calculated using $N = 0.69$ M, $K = 10^{-4}$ M, $n = 0.1$ M, $\varepsilon_r = 78.5$ and $T = 298$ K.

that even at infinite h, the surface pH differs from the corresponding bulk pH [14]. In the present case, in which the membranes are negatively charged, the H^+ concentration is higher at the membrane surface than in the bulk solution phase, so that the surface pH is lower than the bulk pH. With decreasing h, the membrane surface potential ψ_s becomes more negative (as shown in fig. 4) and the surface H^+ concentration becomes higher, resulting in a further decrease in surface pH. An example of the calculation is given in fig. 5, which shows that for pH > 7, for example, the surface pH at $h = 0$ is lower than the bulk pH by about 0.8 pH units.

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