

Nonlocal polarizability of water and hydration interaction between lipid membranes

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A theory of hydration interaction of lipid membranes in an aqueous solution is proposed and is based on the premise that water is a medium with large spatial dispersion of the static dielectric constant $\epsilon(q)$. It is shown that the parameters of the function $\epsilon(q)$ can be determined by a detailed measurement of the interaction between closely spaced membranes.

1. INTRODUCTION

The structure and properties of water have been attracting considerable interest recently. There are grounds for assuming that water has a definite local structure whose characteristic dimension exceeds substantially the distance between the molecules (see the review by Stillinger¹). This raises the question of the dielectric response of water to static electric fields having short spatial periods. Many data favor the assumption that the static response of water has an appreciable spatial dispersion if the characteristic lengths over which the electric field varies are small enough,^{2,3} i.e., water is a nonlocally polarizable dielectric medium.

We consider in this paper the effects of nonlocal polarization in a lamellar liquid-crystal structure made up of phospholipid molecules in water. We shall show that the interactions of polar surfaces (produced on the interface of phospholipid bilayers and water) at short distances are determined by the effects of spatial dispersion of the linear response of the water. Accordingly, a detailed experimental study of interactions of this type permits an investigation of the static dielectric properties of water in very small spatial scales ($\sim 10 \text{ \AA}$) that are difficult to achieve by other methods. Individual lamellas of phospholipid lamellar structures are similar to lipid bilayers of cellular and intracellular biomembranes.⁴ A phospholipid molecule consists of a hydrophilic "head" and two hydrophobic "tails," each constituting a small hydrocarbon chain $(\text{CH}_2)_n$ ($n = 8-12$). The "head" of the molecule consists of phosphate and nitrate groups joined by a short flexible hydrocarbon $(\text{CH}_2)_2$ chain (see Fig. 1). The nitrate group is positively charged, and the phosphate negatively, i.e., the "head" of a phospholipid has an appreciable dipole moment, and it is this which makes it hydrophilic. "Heads" of certain phospholipids can dissociate into ions and acquire thereby, besides a dipole moment, also an electric charge (usually negative).

Phospholipid molecules in the lamellar phase form extended flat layers—lamellas—separated by water. Each such layer consists of molecules whose hydrophobic tails are turned to one another and hydrophilic heads are turned towards the water⁴ (see Fig. 2). A phospholipid bilayer is a splendid model object that permits investigation of important biological processes, especially the interaction and fusion of cellular membranes. Experimental investigations of multilamellar phospholipid systems have shown that the

long-range interaction of bilayers is determined by electrostatic and Van der Waals forces, and is described by the Derjagin-Landau-Verwey-Overbeek theory.⁵ Recent experiments⁶⁻⁸ have shown that at short distances (at water gap thicknesses $h \lesssim 30 \text{ \AA}$) the interaction forces between phospholipid layers are quite considerable and have the following unusual properties.

1. For h in the interval $5-25 \text{ \AA}$, the wedging action (i.e., the specific repulsion force between plane surfaces) P is quite appreciable and is approximated by the exponential relation

$$P = P_0 \exp(-h/h_0) \quad (1)$$

with $h_0 \approx 3 \text{ \AA}$ and $P_0 = 5 \cdot 10^9 - 5 \cdot 10^{10} \text{ dyn/cm}^2$ (Refs. 6-8). (This interval of P_0 is typical of various phospholipids.)

Note that the usual electrostatic repulsion between maximally charged lipid bilayers is smaller by two decades than P_0 at $h \sim h_0$.

2. The parameters h_0 and P_0 are practically independent of the surface charge of the bilayer.

3. Variation of the concentration of salts dissolved in water, in the range from distilled water to an electrolyte with a Debye screening length $\kappa^{-1} \sim 10 \text{ \AA}$, affects the values of h_0 and P_0 little.

The phenomenon considered was named hydration⁶ (or the structural component of wedging pressure).

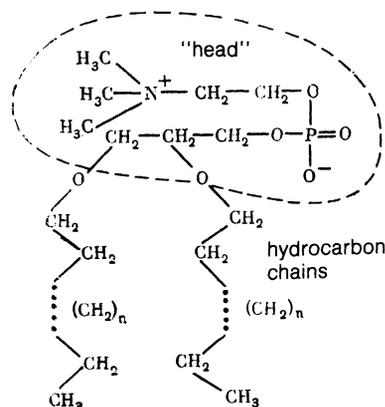


FIG. 1. Structure of phosphatidiquinoline molecule.

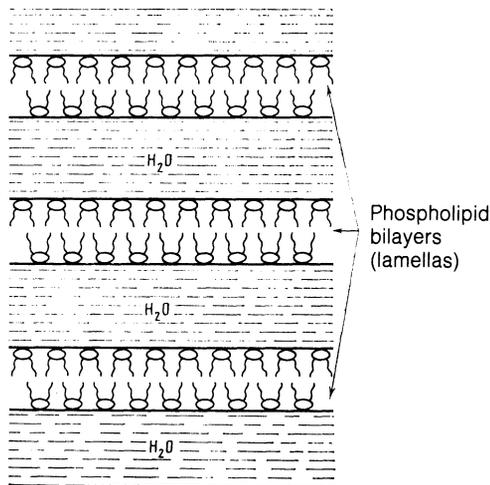


FIG. 2. Multilamellar structure of phospholipid dispersions.

The first attempt to explain the hydration forces was made by Marcelja and Radic,⁹ who proposed that the hydrophilic surface of a lipid bilayer alters the structure of adjacent water and leads to appearance of a certain local "order parameter" whose value decreases exponentially in the interior of the liquid. It was subsequently proposed to identify this order parameter with the normal component P_x of the polarization vector P (Refs. 3, 11–13). It seems to us that these theories are inadequate, since they do not explain the observed values of the parameters P_0 and h_0 , but merely express them in terms of corresponding fit parameters of the theory.

We propose here a phenomenological theory of hydration forces, based on consideration of water as a nonlocally polarizable medium. We shall show that the spatial dispersion of the static dielectric constant $\varepsilon(q)$ of water leads to a strong interaction between the surface dipoles of the surface bilayers that face one another.

Note that if effects of nonlocal polarizability of the medium are neglected, neutral surfaces do not interact at all with dipole moments. A singular property of lipid bilayers is precisely the presence of large dipole moments while the total charge is usually small (or even nonexistent). Allowance for nonlocal-polarizability effects is therefore of fundamental importance here.

Under the simplest assumptions concerning the form of $\varepsilon(q)$, the interaction of the bilayers takes the form (1). Setting the experimental value at $h_0 \approx 3 \text{ \AA}$, the factor that precedes the exponential agrees qualitatively with experiment. The proposed approach will be used also to analyze the interaction of charged membranes in an aqueous electrolyte. The obtained dependences of the interaction parameters on the electrolyte concentration can be used for a quantitative check on the theory. We show also that nonlocal-polarizability effects should increase the observable screening length in the electrolyte compared with its Debye value. This increase should be quite appreciable ($\sim 50\%$) at an electrolyte concentration corresponding to biological conditions.

2. NONLOCAL ELECTROSTATIC OF WATER

We discuss briefly the physical causes of the substantial nonlocality of the dielectric response of water in the scales of interest to us (see also Ref. 2). It is known that the high value of the static dielectric constant, $\varepsilon_0 \approx 80$, is due to the fact that water is a highly polar liquid and has therefore a soft orientational degree of freedom (rotation of the molecular dipoles), which is indeed the one that makes the main contribution to ε_0 . Measurements of the frequency dispersion $\varepsilon(\omega)$ at radio frequencies¹⁴ point to a Debye character of the relaxation:

$$\varepsilon(\omega) = \varepsilon_1 + \frac{\varepsilon_0 - \varepsilon_1}{1 + i\omega\tau} \quad (2)$$

with a characteristic time $\tau = 10^{-11}$ s. At $\omega\tau \gg 1$ we have $\varepsilon(\omega) \rightarrow \varepsilon_1 \approx 5$. It is natural to assume that the value ε_1 is due to the faster (vibrational and electronic) modes, while the orientational mode is "frozen." It is quite probable that just such a "freezing" of the orientational mode should take place also for static fields that change abruptly in space, with the corresponding length scale ξ_0 at least not smaller than the size of the water molecule ($\sim 3 \text{ \AA}$). The upper bound on ξ_0 follows (indirectly) from experiments on hypersound dispersion in water.¹⁵ The absence of such a dispersion (accurate to about 1%) for hypersound wave vectors $q \lesssim 10^6 \text{ cm}^{-1}$ shows apparently that $\xi_0 \lesssim 10 \text{ \AA}$. Note that the ratio $\varepsilon_0/\varepsilon_1 \approx 16$ is quite large, so that noticeable deviation of the static dielectric response $\varepsilon(q)$ from ε_0 should be observed over spatial scales q^{-1} substantially larger than ξ_0 . For the vibrational modes, the corresponding scale ξ_1 should be noticeably smaller, as should also be the change of the dielectric susceptibility ε when these modes are frozen: $\varepsilon_1/\varepsilon_2 \approx 2.5$ ($\varepsilon(\omega) = \varepsilon_2 = 2$ corresponds to the optical band). There exists therefore a certain wave-vector region $\xi_1^{-1} \gg q \gg \xi_0^{-1}$ in which $\varepsilon(q) \approx \varepsilon_1$. The foregoing arguments allow us to express $1/\varepsilon(q)$ in the form

$$\frac{1}{\varepsilon(q)} = \frac{1}{\varepsilon_0} + \frac{\alpha(q)(q\xi_0)^2}{1 + (q\xi_0)^2}, \quad (3)$$

where $\alpha(q) = \varepsilon_1^{-1} - \varepsilon_0^{-1}$ at $\xi_1^{-1} \gg q \gg \xi_0^{-1}$; $\alpha(q) \rightarrow \text{const}$ as $q \rightarrow 0$.

The Green's function corresponding to (3) takes at $r \gg \xi_0$ the asymptotic form

$$G(\mathbf{r}) = \int \frac{4\pi}{\varepsilon(q)q^2} e^{i\mathbf{q}\cdot\mathbf{r}} \frac{d^3q}{(2\pi)^3} = \frac{1}{\varepsilon_0 r} + \frac{\alpha(i/\xi_0)}{r} e^{-r/\xi_0}. \quad (4)$$

The second term of (4) describes nonlocal-polarizability effects. Assuming that the function $\alpha(q)$ has no scales other than ξ_0^{-1} (in the region $q \lesssim \xi_0^{-1}$), we have

$$\alpha(i/\xi_0) = c_1/\varepsilon_1 = 1/\varepsilon_1, \quad c_1 \sim 1, \quad (5)$$

i.e., the second term of (3) can be neglected only if $r \gg \xi_0 \ln \varepsilon_0/\varepsilon_1$.

Note that the electric field of a point dipole μ , determined from (4) at $r \gg \xi_0$, is

$$\mathbf{E}_\mu = \frac{1}{\varepsilon_0 r^3} [3(\boldsymbol{\mu}\mathbf{n})\mathbf{n} - \boldsymbol{\mu}] + \frac{e^{-r/\xi_0}}{\varepsilon_1 \xi_0^2 r} (\boldsymbol{\mu}\mathbf{n}), \quad (6)$$

The second term of (6), in contrast to the first, does not

vanish after averaging over the directions of the vector $\mathbf{n} = \mathbf{r}/r$, and this leads (as we shall show below) to the existence of an electric field near a homogeneous dipole layer.

The simplest interpolation of the function $\varepsilon(q)$ between ε_0 (for $q = 0$) and ε_1 (for $q \gg \xi_0^{-1}$) is similar in form to the real part of Eq. (2):

$$\varepsilon(q) = \varepsilon_0 \varepsilon_1 \frac{1 + (q\xi_0)^2}{\varepsilon_1 + \varepsilon_0 (q\xi_0)^2} \quad (7)$$

and corresponds to $\alpha(q) = \text{const} = \varepsilon_1^{-1} - \varepsilon_0^{-1}$.

The dielectric-response function (7) had previously been used in connection with electrochemistry problems.²

3. ELECTRIC FIELD OF A LIPID BILAYER MEMBRANE IN AN AQUEOUS SOLUTION

The electric-field sources of lipid membranes are the charges and dipole moments of the hydrophilic heads of the lipid molecules. The distance l_0 between the molecules in the bilayer plane is about 6–7 Å. This allows us to regard the field sources as continuously spread out in the plane, since the difference between a field obtained in this manner and a true exponential field decreases with increasing distance from the membrane, with a characteristic length $l_0/2\pi \approx 1 \text{ \AA} \ll h_0$. Thus, we must determine the one-dimensional distribution of the field $E_x(x) \equiv E(x)$ produced by a plane with a surface charge density σ and a dipole moment M ($M > 0$ and is perpendicular to the plane) near the boundary of the phospholipid membrane and the aqueous electrolyte. The water molecules adhere quite tightly to the phospholipid heads.¹⁶ We shall therefore assume that a plane with field sources is located in the water at a distance l from the interface with the membrane. The quantity l is a phenomenological parameter that describes the degree of penetration of the water into the region of the polar heads of the phospholipids. To determine this parameter consistently we must determine accurately the field distribution for the real geometry of the membrane-water interface. It appears that l can vary in the interval 0.5–3 Å, depending on the density of the bilayer (if the lateral density is increased, the water is expelled from the region of the polar heads and l decreases). In a number of cases we shall simplify the equations by writing them in the limit as $l \rightarrow +0$. (Note that the solution is not analytic in l at $l = 0$, since the membrane is approximated by a continuous medium.) The membrane can be regarded as infinitely thick, in view of its thickness $\delta \approx 50 \text{ \AA} \gg h_0$. The coordinate x will be measured from the membrane boundary, and the region occupied by the electrolyte corresponds to $x > 0$.

We begin with the case of an uncharged membrane in pure water. In multilamellar structures⁶⁻⁷ the field $E(x)$ inside each membrane is zero by virtue of symmetry (in the case of interaction of two separate bilayers this field differs from zero, but is small in terms of the parameter h_0/δ). We must thus solve the equation

$$\frac{d}{dx} \left[\int_0^\infty K(x-x') E(x') dx' \right] = 4\pi \rho_{st}(x) = -4\pi M \delta'(x-l) \quad (8)$$

with the boundary condition $E(x < 0) = 0$. In Eq. (8), the function $K(x)$ is the one-dimensional Fourier original of the

dielectric susceptibility $\varepsilon(q)$ given by (3). Generally speaking, near the membrane-water interface the properties of the dielectric response of water differ from the bulk properties, but we shall neglect this possible difference (i.e., we use the so-called dielectric approximation²⁶). Equation (8) can be integrated once with respect to x (with zero integration constant), after which this equation takes the standard Wiener-Hopf form and can be solved by known methods¹⁷ for any function $\varepsilon(q)$. It is useful to note, however, that the asymptotic form of $E(x)$ of interest to us is determined at $x \gg \xi_0$ by the position and residue of the pole of the function $1/\varepsilon(q)$ [just as the asymptotic Green's function $G(r)$ in (4)]. We can therefore use, in place of the true (and unknown) $\varepsilon(q)$, the interpolation (5), substituting $\varepsilon_1 \rightarrow \tilde{\varepsilon}_1 = \varepsilon_1/c_1$ [see (5)]. The regular part of the field $E(x)$ is then found to be a sum of terms of form $\exp(-x/\xi_0)$, with coefficients that are determined by direct substitution. As a result we get ($x > l$)

$$E(x) = \gamma \frac{4\pi M}{\tilde{\varepsilon}_1 \xi_0} \exp(-x/\xi_0), \quad (9)$$

where

$$\beta = \frac{\varepsilon_0}{\tilde{\varepsilon}_1} \approx 16, \quad \gamma = \text{ch} \frac{l}{\xi_0} - \frac{1}{\beta^{1/2}} \exp\left(-\frac{l}{\xi_0}\right) - \frac{1}{\beta} \text{sh} \frac{l}{\xi_0}.$$

The total value of the dipole moment of the phospholipid molecule is $d = 30\text{--}40 \text{ D}$, depending on the type of lipid.¹⁸ The exact value of the dipole-moment component d_1 is unknown, but the estimate $d_1 \sim 10\text{--}15 \text{ D}$, seems reasonable and leads to $M = d_1/S_0 \sim 2 \cdot 10^{-3} \text{ CGS}$ ($S_0 = 50\text{--}70 \text{ \AA}^2$ is the area per molecule in the bilayer). It is useful to compare (9) with the equation for the electric field of a charged membrane in an ordinary Debye electrolyte with a screening length κ^{-1} :

$$E_{Deb}(x) = \frac{4\pi\sigma}{\varepsilon_0} e^{-\kappa x}. \quad (10)$$

Using the value $\xi_0 = h_0 \approx 2.5\text{--}3 \text{ \AA}$ (the basis for this will be made clear presently) we obtain a ratio on the order of 10 for the factors preceding the exponentials, even for the lipids with the highest charges. The nonlocality of the polarizability of water leads thus to the presence of a very strong electric field even near a neutral phospholipid membrane.

We proceed now to investigate the general case of a charged membrane in an aqueous electrolyte, confining ourselves to not excessively high ion densities, with a Debye radius $\kappa^{-1} \gtrsim \xi_0 \beta^{1/2}$. In this case we can neglect the influence of the ions on the nonlocal-polarizability mechanisms, so that their role reduces to replacing the electric response $\varepsilon(q)$ by $\tilde{\varepsilon}(q) = \varepsilon(q) + \varepsilon_0 \kappa^2/q^2$ (see also Ref. 2). In lieu of (8) we have now an equation for the potential φ :

$$-\frac{d}{dx} \left[\int_0^\infty K(x-x') \frac{d\varphi(x')}{dx'} dx' \right] + \varepsilon_0 \kappa^2 \varphi = 4\pi\sigma \delta(x-l) - 4\pi M \delta'(x-l). \quad (11)$$

Using, as above, the approximation (7) we obtain for the electric field (in the limit as $l \rightarrow +0$)

$$E(x) = E_1 \exp(-q_1 x) + E_2 \exp(-q_2 x), \quad (12)$$

where

$$q_{1,2}^2 = \frac{q_0^2 + \beta \kappa^2}{2} \pm \left[\frac{(q_0^2 + \beta \kappa^2)^2}{4} - \kappa^2 q_0^2 \right]^{1/2} \quad (q_1 > q_2, q_0 = \xi_0^{-1}), \quad (13)$$

$$E_1 = \frac{4\pi q_1^2}{\varepsilon_1 Q} \left[M - \frac{\sigma q_2^2}{\beta \kappa^2} \frac{\beta^{1/2}}{\beta^{1/2} q_2 - q_0} \right], \quad (14)$$

$$E_2 = -\frac{4\pi q_2^2}{\varepsilon_1 Q} \left[M - \frac{\sigma q_1^2}{\beta \kappa^2} \frac{\beta^{1/2}}{\beta^{1/2} q_1 - q_0} \right], \quad (15)$$

$$Q = \frac{\beta^{1/2} q_1^2}{\beta^{1/2} q_1 - q_0} - \frac{\beta^{1/2} q_2^2}{\beta^{1/2} q_2 - q_0}. \quad (16)$$

The electric field of the membrane is thus a sum of two terms that decrease exponentially with lengths $\xi_1 = q_1^{-1} < \xi_0$ (polarization term) and $\xi_2 = q_2^{-1} > \kappa^{-1}$ (Debye term). For $\kappa \ll q_0 \beta^{-1/2}$ we have $\xi_1 \rightarrow \xi_0$ and $\xi_2 \rightarrow \kappa^{-1}$. For $\kappa \sim q_0 \beta^{-1/2}$ Eq. (13) is by way of an interpolation, since the influence of the ions can no longer be described by a simple replacement of $\varepsilon(q)$ by $\tilde{\varepsilon}(q)$. The second term in the square brackets of (14) is always small compared with the first, so that the "polarization" contribution to the electric field is determined just by the density (more accurately, by the normal component) of the dipole moment M . Both terms in (15) can be of the same order. Note that $E_1/E_2 \sim q_1^2/q_2^2 \approx \beta$, therefore the polarization contribution exceeds the Debye contribution right up to

$$x \sim x_m = \frac{2}{q_1 - q_2} \ln \frac{q_1}{q_2} \gg q_1^{-1}.$$

Great interest attaches to the case $\sigma = 0$, when the polarization and Debye contributions have opposite signs, so that $E(x)$ is zero at $x \approx x_m$. At large distances $x \gg x_m$ such a membrane appears charged with a charge density (determined by comparison with Eq. (10))

$$\sigma_{eff} = -\beta q_2^2 M / q_1. \quad (17)$$

4. INTERACTION OF MEMBRANES. HYDRATATION FORCES

The specific force of interaction between membranes separated by a distance h is $P(h) = -\partial F / \partial h$, where F is the free energy of the system with given field sources, and is equal to

$$F = \frac{1}{8\pi} \int_0^h [E(x)D(x) + \varepsilon_0 \kappa^2 \varphi^2(x)] dx, \quad (18)$$

where $D(x)$ and $\varphi(x)$ are the induction and the field potential.

Expression (18) for a system of two identical membranes can be reduced (accurate to terms independent of h) to the following simple form:

$$F = -ME(l) + \sigma\varphi(l). \quad (19)$$

To calculate $E(l)$ and $\varphi(l)$ we must solve an equation that generalizes (11) to the case of two membranes:

$$\begin{aligned} -\frac{d}{dx} \left(\int_0^h K(x-x') \frac{d\varphi(x')}{dx'} dx' \right) + \varepsilon_0 \kappa^2 \varphi \\ = 4\pi\sigma [\delta(x-l) + \delta(x-h+l)] \\ - 4\pi M [\delta(x-l) - \delta(x-h+l)]. \end{aligned} \quad (20)$$

$$\begin{aligned} E(x) = E_1(\exp[-q_1 x] - \exp[-q_1(h-x)]) \\ + E_2(\exp[-q_2 x] - \exp[-q_2(h-x)]). \end{aligned} \quad (21)$$

where $E_{1,2}$ are determined by equations similar to (14)–(16):

$$E_1 = \frac{4\pi q_1^2}{\varepsilon_1 \alpha_1 Q(h)} \left[M - \frac{\sigma q_2^2}{\beta \kappa^2} \frac{\gamma_2}{\alpha_2} \right], \quad (22)$$

$$E_2 = -\frac{4\pi q_2^2}{\varepsilon_1 \alpha_2 Q(h)} \left[M - \frac{\sigma q_1^2}{\beta \kappa^2} \frac{\gamma_1}{\alpha_1} \right], \quad (23)$$

$$Q(h) = \frac{\gamma_1}{\alpha_1} q_1^2 - \frac{\gamma_2}{\alpha_2} q_2^2. \quad (24)$$

Here

$$\alpha_i = 1 - \exp[-q_i h],$$

$$\gamma_i = (q_i - q_0 \beta^{-1/2})^{-1} + (q_i + q_0 \beta^{-1/2})^{-1} \exp[-q_i h].$$

Substituting (21)–(24) in (19) (at $l = 0$) we obtain the free energy F in the form

$$\begin{aligned} F = \frac{4\pi}{\varepsilon_1 Q(h)} \left\{ -M^2 (q_1^2 - q_2^2) + \sigma M \left[\frac{q_1^2 q_2^2}{\beta \kappa^2} \left(\frac{\gamma_2}{\alpha_2} - \frac{\gamma_1}{\alpha_1} \right) \right. \right. \\ \left. \left. + q_1 \frac{2 - \alpha_1}{\alpha_1} - q_2 \frac{2 - \alpha_2}{\alpha_2} \right] + \frac{\sigma^2 q_1 q_2}{\beta \kappa^2} \left[q_1 \frac{\gamma_1}{\alpha_1} \frac{2 - \alpha_2}{\alpha_2} - q_2 \frac{\gamma_2}{\alpha_2} \frac{2 - \alpha_1}{\alpha_1} \right] \right\}. \end{aligned} \quad (25)$$

We shall not write down for $P(h)$ the cumbersome general equation that corresponds to (25), but analyze various limiting cases.

For neutral membranes ($\sigma = 0$) in pure water:

$$P(h) = \frac{8\pi M^2 \eta \exp[-h/\xi_0]}{\varepsilon_1 \xi_0^2 (1 + \eta \exp[-h/\xi_0])^2}, \quad (26)$$

where $\eta = (\beta^{1/2} - 1) / (\beta^{1/2} + 1) \approx 0.6$. For $h \gg \xi_0$, Eq. (26) reduces to (1) with

$$h_0 = \xi_0, \quad P_0 = 8\pi M^2 \eta / \varepsilon_1 \xi_0^2.$$

We present the asymptotic expression for $P(h)$ at $h \gg \xi_0$ for neutral membranes in an electrolyte; we confine ourselves furthermore to first order in the parameter $q_2^2/q_1^2 < \kappa^2 \xi_0^2 \leq 0.1$:

$$\begin{aligned} P(h) = \frac{8\pi M^2}{\varepsilon_1} q_1^2 \left[\frac{\beta^{1/2} q_1 - q_0}{\beta^{1/2} q_1 + q_0} \exp[-q_1 h] \right. \\ \left. + \frac{q_2^4 (\beta^{1/2} q_1 - q_0)^2}{q_1^4 (q_0^2 - \beta q_2^2)} \frac{1}{4 \operatorname{sh}(q_2 h/2)} \right]. \end{aligned} \quad (27)$$

For charged membranes in a weak electrolyte ($\beta^{1/2} \kappa \ll q_0$) we get

$$P(h) = \frac{8\pi M \eta}{\varepsilon_1 \xi_0} \left(\frac{M}{\xi_0} + \frac{2\sigma}{\beta^{1/2}} \right) \exp\left(-\frac{h}{\xi_0}\right) + \frac{2\pi\sigma^2}{\varepsilon_0} \operatorname{sh}^{-2} \frac{\kappa h}{2}. \quad (28)$$

Note that the last term of (28) diverges formally as $x \rightarrow 0$. The reason for this divergence is that the membranes are assumed to be infinitely thick, an assumption valid, as follows from the results of Ref. 19, only if $\kappa \gg 2(\varepsilon_m / \varepsilon_0 h \delta)^{1/2}$ (here $\delta \approx 50 \text{ \AA}$ is the membrane thickness and $\varepsilon_m = 2$ is its dielectric constant). This condition is actually not too re-

strictive, in view of the large $\varepsilon_0\delta/\varepsilon_m \approx 2000 \text{ \AA}$. At sufficiently large h , the main contribution to (28) is made by the second term that accords with the usual double-layer theory.

Of interest, finally, is the dependence of $P(h)$ on the parameter l that determines the location of the dipole layer relative to the membrane-electrolyte interface (see the discussion at the beginning of Sec. 3). To find this dependence we must obtain a solution similar to (21) at arbitrary l . As a result we get $P(h)$ in the form (we confine ourselves here to a neutral membrane in pure water):

$$P(h) = \frac{8\pi M^2}{\varepsilon_1 \xi_0^2} \frac{\eta \exp[-h/\xi_0]}{(1 + \eta \exp[-h/\xi_0])^2} \bar{\gamma}, \quad (29)$$

$$\bar{\gamma} = (\text{ch } al + \beta^{-1/2} \text{sh } al)^2. \quad (30)$$

As l varies from 0 to ξ_0 the parameter $\bar{\gamma}$ changes from 1 to 3.6.

5. DISCUSSION OF RESULTS

We have shown that the interaction of polar planes in water is exponentially decreasing repulsion [see (26) and (29)] if account is taken of the effects of nonlocal polarizability of the water. The parameter ξ_0 that determines the dispersion of the dielectric constant $\varepsilon(q)$ is unknown at present. By comparing the derived expression (26) with the experimental relation (1), however, we obtain the estimate $\xi_0 = h_0 = 3 \text{ \AA}$.

The factor preceding the exponentials in (26)

$$P_0 = 8\pi M^2 \gamma \eta / \varepsilon_1 \xi_0^2$$

is estimated at $10^{10} - 10^{11} \text{ dyn/cm}^2$ [an estimate of M is given in the text following Eq. (9)], which exceeds on the average by half a decade the experimental range of P_0 . It is reasonable to assume that this overestimate of P_0 is due to our present use of an approximation linear in the electric field. In the immediate vicinity of the membrane there should actually exist substantial nonlinear effects that lower the electric field of the membrane and with it P_0 . Note that when these effects are taken into account $P(h)$ becomes exponential at $h \gg \xi_0$.

The theory proposed explains some unusual properties of hydration forces, particularly the decrease of these forces on transition of the bilayer from the "liquid" to the "solid" phase⁸ (the ensuing increase of the dipole surface density notwithstanding).

In the course of this transition, the water is crowded out of the region of the polar heads, meaning a decrease of the parameter l and hence of the factor $\bar{\gamma}$ that enters in P_0 [see (29)]. Effects due to fluctuation of the bilayer surface may also be important here—see Ref. 20). The lowering of the hydration forces with decrease of area per phospholipid molecule can be similarly explained.²¹

Our analysis allow us therefore to attribute the hydration forces⁶⁻⁸ to dipole-dipole interaction of polar surfaces in nonlocally polarizable water. Nonetheless, one cannot exclude as yet the possibility of another (non-electrostatic) origin of the hydration forces. For example, the order parameter of a liquid, introduced in Ref. 9, may turn out to be connected with the orientational order parameter introduced in a number of papers (see, e.g., Refs. 22 and 23) in connection with the description of the melting phase transi-

tion. Unfortunately, no estimates whatever are available for the interaction forces in the latter mechanism.

An indirect check on the hydration-forces theory proposed by us would be a correct experimental determination of the dependence of the "hydration" radius q_1^{-1} on the electrolyte density, and also measurement of the deviation, due to spatial dispersion, of the electrolyte screening length q_2^{-1} from the Debye value κ^{-1} (see (13), and also Ref. 24). This deviation should be quite noticeable ($\sim 50\%$) at an electrolyte concentration corresponding to biological conditions ($\kappa^{-1} \approx 10 \text{ \AA}$). If the mechanism proposed by us for the onset of hydration forces is confirmed, the two parameters $\bar{\varepsilon}_1$ and ξ_0 of the dielectric response of water can be determined by comparing the experimental values of P_0 and the lengths q_1^{-1} and q_2^{-1} with Eqs. (25) and (13).

Note also the unusual behavior of the field of a neutral membrane in an electrolyte [see (12), (14), and (15)], viz., $E(x)$ vanishes at

$$x = x_m = \frac{2}{q_1 - q_2} \ln \frac{q_1}{q_2};$$

whereas at $x \gg x_m$ the membrane seems to be negatively charged (see also Ref. 3).

After completing this work, we learned of a paper by Cevs,²⁵ in which nonlocal electrostatics is used to analyze hydration forces and solvation phenomena in pure water. Cevs's approach differs only in that different sources are chosen for the membrane field.

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