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Fluctuation theory of hydration forces: The dramatic effects of inhomogeneous boundary conditions

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An expression for the indirect interaction of surfaces through a liquid is derived that accounts for inhomogeneity of the boundary conditions, which mimics the regular, irregular, or stochastic nature of liquid structure perturbation along the surfaces. This leads to a new picture of hydration forces, which gives an explanation of their main observable features: the dependence of the decay length on the nature of the surfaces and its variation range, and the effect of surface ordering on the magnitude of the force.

I. INTRODUCTION

The interaction between two hydrophilic surfaces in water and some other polar solvents at distances ≤ 3 nm is dominated by the so-called "hydration" (or "structural") forces.[1,2] These forces are of crucial importance in the stability of colloids,[3] for properties of wetting films,[4] and in the interaction and fusion[5] of biological membranes and macromolecules.[6,7] They result, seemingly, from an indirect interaction of the surfaces through the solvent via the spatially correlated fluctuations of some order parameter (polarization, density, etc.) perturbed at the surfaces. These forces usually decay exponentially with the distance, the characteristic length varying between 0.1 and 1 nm depending on the nature of the surfaces for a given solvent.[1,8]

The first attempt to describe this phenomenon was made by Marčelja and Radić.[9] They used a Landau free-energy gradient expansion, quadratic in the fluctuations of the order parameter, which was later interpreted as the local water polarization.[5] The interaction of the oppositely polarized water layers, adjacent to the surfaces, thus led to a repulsion force. The nonlocal electrostatic theory,[10] which fit naturally in this context, was later applied in a series of works.[11-14] All these works used homogeneous boundary conditions for the order parameter or polarization at[9,11] or near[12-14] the surfaces. The mode of the force decay so far was independent of the type of the surface, being determined only by the correlation function of the bulk water polarization fluctuations. (The difference of the nonlocal water polarizability near the interface from that of the bulk water was taken into account in a more general formalism of Ref. 13; however, its consequences were demonstrated by means of the same "bulk-like" model example.) These theories gave insight into the nonlocal nature of hydration forces. However, they did not explain many of the observable features, in particular, the dependence of the decay length on the nature of the surfaces.

These theories did not take into account the variation of water orientation along the boundaries induced by the alternation of positively and negatively charged surface groups. This variation, which is typical for the systems under study, especially for lipid membranes, would lead to an interplay between attractive and repulsive contributions and may strongly change the picture of the interaction.[15,16] This idea was emphasized in Ref. 16 where qualitative estimates were based on a superposition of attractive and repulsive contributions with phenomenological weight factors. However, no derivation of these terms was proposed and no expressions for the preexponential factors and decay lengths through the system parameters were established.

Inhomogeneous surface charge distribution was considered within the classical electrostatic approach to the interaction between surfaces due to dipole-dipole and image-charge forces.[17-20] However, it soon became clear that this approach failed to explain both the order of magnitude and the main features of hydration forces.[18] Within the nonlocal electrostatic approach, the interaction of lattices of collinear dipoles of a fixed orientation was studied in Ref. 21. This theory revealed some interesting features of the lattice discreteness effects (including, e.g., the conditions of the appearance of an attractive branch), but it did not manage to explain the variation of the repulsive force decay length with the changes in the structure of the boundary and some other important properties.

In the present work, we study the role of the ordered and stochastic (fixed or fluctuating) *inhomogeneous boundary conditions* in the self-consistent field theory of the hydration force acting between two planar surfaces. It will be shown, in particular, that the preexponential factor and the decay length in the repulsive mode of the force are determined by the lateral correlations in the values of the order parameter at the boundaries. Semimicroscopic interpretation of the boundary conditions will explain, for the first time, the main observable features of the hydration forces for lipid membranes and colloids.

II. FREE ENERGY AND DISJOINING PRESSURE

In the same way as Marčelja did,[9] we describe the water film by the Landau free-energy functional

$$F=F_0+\int\{a\varphi^2(\mathbf{r})+c[\nabla\varphi(\mathbf{r})]^2\}d^3r\ , \tag{1}$$

where φ is a scalar fluctuation field of the order parameter. Its physical meaning may be concerned with, e.g., the polarization of water, $\nabla\varphi$. The equilibrium value of φ is found from the minimum of the functional for which the Euler equation gives

$$\Delta\varphi=\kappa^2\varphi\ , \tag{2}$$

where $\kappa^{-1}=\sqrt{c/a}$ is the characteristic length of decay of the correlation function $\langle\varphi(0)\varphi(\mathbf{r})\rangle$. The value of the free energy is then given by

$$F=F_0+c\int d\mathbf{s}(\varphi\nabla\varphi)\ , \tag{3}$$

where the integration is performed over the surface, bounding water. Considering the interaction of two plane surfaces separated by the water layer, it is convenient to make the Fourier transform in the lateral plane

$$\varphi(z,\mathbf{R})=\frac{1}{\sqrt{A}}\sum_{\mathbf{Q}}\varphi(z,\mathbf{Q})e^{i\mathbf{Q}\cdot\mathbf{R}}\ , \tag{4}$$

where $(z,\mathbf{R})$ are the cylindrical coordinates with the z axis normal to the surfaces and A is the surface area. Then

$$\frac{d^2}{dz^2}\varphi(z,\mathbf{Q})=(\kappa^2+Q^2)\varphi(z,\mathbf{Q})\ . \tag{5}$$

The boundary conditions for polarization $(\nabla\varphi)$ at the surfaces (at $z=0$ and $z=L$, where L is the thickness of the water layer) are

$$\left.\frac{d\varphi(z,\mathbf{R})}{dz}\right|_{z=0}=p_1+\delta p_1(\mathbf{R})\ ,\qquad \left.\frac{d\varphi(z,\mathbf{R})}{dz}\right|_{z=L}=p_2+\delta p_2(\mathbf{R})\ . \tag{6}$$

We separated here the homogeneous and inhomogeneous parts of the polarization at the boundaries;

$$\langle\delta p_1(\mathbf{R})\rangle=\langle\delta p_2(\mathbf{R})\rangle=0\ ,$$

$\langle\ \rangle$ denotes the statistical averaging. $\delta p(\mathbf{R})$ is either a given fixed inhomogeneous field or a dynamic or random static fluctuation field. For homogeneous boundary conditions the solution is determined by the $Q=0$ eigenfunctions of Eq. (5), while this will not generally be the case for the lack of continuum translational invariance along the surfaces. Characteristic lengths other than κ^{-1} may then effectively appear in the problem.

Let us define the correlation functions

$$\tilde{S}_{ij}(\mathbf{R})=\tfrac{1}{2}\langle\delta p_i(\mathbf{r}+\mathbf{R})\delta p_j(\mathbf{r})+\delta p_j(\mathbf{r}+\mathbf{R})\delta p_i(\mathbf{r})\rangle\ , \tag{7}$$

where i $(=1,2)$ labels the surfaces. Then the solution of Eq. (5), subject to the boundary conditions (6) as substituted into Eq. (3), gives the expression for the free energy of the water film F averaged over realizations of the boundary conditions

$$\langle F\rangle=F_0+F_{\text{hom}}+\langle F_{\text{inh}}\rangle\ , \tag{8}$$

where the homogeneous and inhomogeneous terms are

$$F_{\text{hom}}=\frac{Ac}{2\kappa}[(p_1+p_2)^2\tanh(L\kappa/2)+(p_1-p_2)^2\coth(L\kappa/2)]\ , \tag{9}$$

$$\langle F_{\text{inh}}\rangle=c\sum_{\mathbf{Q}}(\kappa^2+Q^2)^{-1/2}\times\left\{\frac{S_{11}(\mathbf{Q})+S_{22}(\mathbf{Q})}{\tanh[L(\kappa^2+Q^2)^{1/2}]}-\frac{2S_{12}(\mathbf{Q})}{\sinh[L(\kappa^2+Q^2)^{1/2}]}\right\}\ . \tag{10}$$

Here,

$$S_{ij}(\mathbf{Q})=\int d\mathbf{R}\tilde{S}_{ij}(\mathbf{R})e^{-i\mathbf{Q}\cdot\mathbf{R}}\ . \tag{11}$$

In the case of dynamic fluctuations, Eq. (10) is valid under an assumption that the modes which contribute to δp are much slower than the fluctuations of water polarization.

The disjoining pressure (here the hydration force) is then given by

$$P=-\frac{1}{A}\left\langle\frac{dF}{dL}\right\rangle=-\frac{1}{A}\left[\frac{\partial\langle F\rangle}{\partial L}\right]_{S_{ij}}=P_{\text{hom}}+P_{\text{inh}}\ . \tag{12}$$

For two identical homogeneous surfaces with

$$p_1(\mathbf{R})=-p_2(\mathbf{R})=\text{const}\equiv p\ ,$$

Eqs. (9) and (12) lead to the famous Marčelja result[9]

$$P_{\text{hom}}=\frac{cp^2}{\sinh^2(\kappa L/2)}\ , \tag{13}$$

the repulsion exponentially decaying at large L with characteristic length κ^{-1}.

The contribution due to F_{inh} is much different. We shall see that for many systems the hydration force is determined just by the inhomogeneous term. For some systems the Marčelja term may give a comparable contribution and one should take into account both terms together. Below we analyze the properties of P_{inh}.

III. THE PROPERTIES OF THE "INHOMOGENEOUS" CONTRIBUTION TO HYDRATION FORCE

A. Fixed boundary conditions

For this case no averaging along the surfaces is needed:

$$S_{ij}(\mathbf{Q})=\tfrac{1}{2}[p_i(\mathbf{Q})p_j(-\mathbf{Q})+p_j(\mathbf{Q})p_i(-\mathbf{Q})] \ .$$

Let us consider, for example, the two identical periodic surface perturbations:

$$\delta p_1(\mathbf{R})=\delta p \cos(\mathbf{q}\cdot\mathbf{R})$$

and

$$\delta p_2(\mathbf{R})=-\delta p \cos[\mathbf{q}\cdot(\mathbf{R}-\Delta\mathbf{R})] \ ,$$

shifted in the lateral plane by a vector, $\Delta\mathbf{R}$; $q \neq 0$. Then

$$\begin{aligned}\delta p_1(\mathbf{Q})&=\frac{\sqrt{A}\,\delta p}{2}(\delta_{\mathbf{Q},\mathbf{q}}+\delta_{\mathbf{Q},-\mathbf{q}}) \ ,\\ \delta p_2(\mathbf{Q})&=-\delta p_1(\mathbf{Q})e^{i\mathbf{Q}\cdot\Delta\mathbf{R}} \ ,\end{aligned} \tag{14}$$

and, according to Eqs. (10) and (12),

$$P_{\text{inh}}=c(\delta p)^2\left[\frac{1+\cos(\mathbf{q}\cdot\Delta\mathbf{R})\cosh[L(\kappa^2+q^2)^{1/2}]}{\sinh^2[L(\kappa^2+q^2)^{1/2}]}\right] \ . \tag{15}$$

The surfaces which are free to adjust their mutual positions in the lateral plane will choose the energy minimum corresponding to $\mathbf{q}\cdot\Delta\mathbf{R}=(2n+1)\pi$, i.e., the dips in the $\delta p_1(R)$ profile would look at the maxima of the $\delta p_2(\mathbf{R})$. That results in a

$$P_{\text{inh}}=-\frac{c(\delta p)^2}{2\cosh^2[L(\kappa^2+q^2)^{1/2}/2]} \ , \tag{16}$$

a pure attraction exponentially decaying at large L with a *new characteristic length* $(\kappa^2+q^2)^{-1/2}$. A similar result was first obtained for the interaction of dipolar lattices in Ref. 21.

It is rather obvious that with the violations of the periodicity in $\delta p_1(\mathbf{R})$ or $\delta p_2(\mathbf{R})$ on the scales larger than L, but smaller than $\sqrt{A}$, the oscillating term in Eq. (15) vanishes or, at least, is smaller, the stronger these violations are (for two regular, but incommensurate lattices such a conclusion has been rigorously proved). The result will then be determined by the first term in the denominator of Eq. (15) which is purely *repulsive* with the decay length $[2(\kappa^2+q^2)^{1/2}]^{-1}$.

B. Fluctuation boundary conditions

The free energy described by Eq. (10) contains two contributions of different origin. The one containing $S_{11}(\mathbf{Q})$ and $S_{22}(\mathbf{Q})$ is the self-energy term. It describes the interaction of each surface with a water layer of thickness L ("surface solvation energy"). With the decrease of the thickness of the polar layer L, system energy increases, which gives rise to effective repulsion. The cross term containing $S_{12}(\mathbf{Q})$ is due to the interaction between perturbations of the order parameter at different surfaces. This contribution is always attractive because this kind of interaction will tend to reduce the system energy.[22]

Hereafter we consider systems for which we know from the experiment that the repulsion is dominating. In this case, the term determined by intersurface correlations can be neglected. The force is then given by an expression, which in the limit of $A \to \infty$, looks as

$$P_{\text{inh}}(L)=P_1(L)+P_2(L) \ , \tag{17}$$

$$P_i(L)=\frac{c}{2\pi}\int_0^\infty dQ\frac{QS_{ii}(\mathbf{Q})}{\sinh^2[L(\kappa^2+Q^2)^{1/2}]} \quad (i=1,2) \ . \tag{18}$$

[For simplicity, we consider isotropic surfaces for which $S_{ii}(\mathbf{Q})$ are the functions of $|\mathbf{Q}|$.]

As we see from Eq. (18), the mode of the hydration force decay is determined by both the water correlation length κ^{-1} and the surface structure factors $S_{11}(\mathbf{Q})$ and $S_{22}(\mathbf{Q})$. Equation (18) allows us to understand the qualitative behavior of $P_{\text{inh}}(L)$ even without particular approximations for structure factors.

Usually there are periodical oscillations in $\tilde{S}_{11}(\mathbf{R})$ with some wave number, q_*, modulated by a decaying envelope of characteristic width ξ.[23] Then $S_{ii}(\mathbf{Q})$ has a maximum centered at $Q=q_*$ with a width ξ^{-1}. In such a situation we can easily predict the results in two limiting cases.

When $\xi^2 \gg L(\kappa^2+q_*^2)^{-1/2}$, the main contribution to the integral is given by $Q=q_*$, so that

$$P_i(L)=\frac{c\langle[\delta p_i(\mathbf{R})]^2\rangle}{\sinh^2[L(\kappa^2+q_*^2)^{1/2}]} \ . \tag{19}$$

The decay length of the force is thus equal to $[2(\kappa^2+q_*^2)^{1/2}]^{-1}$. This case is equivalent to the case of a fixed periodic boundary condition with periodicity violations on large scales.

In the opposite limit, when $\xi^2 \ll L(\kappa^2+q_*^2)^{-1/2}$, the main contribution to the integral is due to the region near of $Q \sim \kappa$. The decay length then coincides with $(2\kappa)^{-1}$, the preexponential factor depending on the particular behavior of $S_{ii}(Q)$ at $Q \to 0$.

In the intermediate case there will be no single decay length but a superposition of exponentials. Since the diapason of the variation of L in the experiment is rather narrow ($1\ \text{nm} \lesssim L \lesssim 3\ \text{m}$), this might be considered as an apparent exponential with an effective decay length λ_{eff} which lies between the two limits

$$\frac{1}{2(\kappa^2+q_*^2)^{1/2}}<\lambda_{\text{eff}}<\frac{1}{2\kappa} \ . \tag{20}$$

At large L ($\gg \kappa/q_*^2$) the integrand in Eq. (18) is a product of a function which goes down exponentially with Q and of a "peak" function $QS_{ii}(Q)$ centered at a value of Q which is larger than the decay length of the first function. Therefore, the larger the width of the peak ξ^{-1} is, the larger the integral is and the stronger the force is.

There is also a peculiar consequence of the inequality (20). In the "strongly structured limit" $\xi \to \infty$, the effective decay length would no longer depend on the water correlation length κ^{-1} if q_* ($\sim 2\pi/a_0$, a_0 is the lattice constant) is considerably larger than κ^{-1}.

Thus, we may suggest three actual rules for the fluctuation mechanism of hydration forces (i.e., when the homogeneous contribution is negligible).

Rule 1. With the increase of the correlation range of the surface structure factor, the effective decay range of the hydration repulsion decreases.

Rule 2. At a large fixed distance between the surfaces, the increase of the correlation range of the surface structure factor leads to the decrease in the absolute value of the force.

Rule 3. The variation of the observable effective decay lengths is limited from below and above. The lower limit is the "period" of surface perturbation distribution ("lattice constant") divided by 4π. The upper limit is one-half of the water correlation range.

The shortest values of the lattice constant are limited to the close packing distances so that the lower limit of λ_{eff} is $\simeq 0.05$ nm. The correlation length in water, as estimated by various authors,[10,8,24,25] lies between 0.4 and 1 nm. So, the upper limit of λ_{eff} is $\simeq 0.2-0.5$ nm.

A part of rule 3 may not be approved by a more general theory which would go beyond the quadratic free-energy functional of the present "linear response theory." This concerns an evaluation of the upper limit. Indeed, the account for the φ^4 term ("the nonlinear response") might give rise to an increase of λ_{eff} with respect to the value of native water correlation length (which is likely to be seen in colloid systems). Such a study is in progress now. Within the quadratic (φ^2) approximation, we do manage to explain the variation of λ_{eff} but only down from $(2\kappa)^{-1}$. However, this just seems to be the case of lipid membrane interaction.

IV. INTERACTION OF PHOSPHOLIPID MEMBRANES

A. The nature of perturbation

To illustrate the results of the above given phenomenological analysis we consider the hydration interaction in the best studied system of smectic mesophases formed by neutral phospholipid bilayers[5,16,26] the bimolecular films composed by amphiphilic lipid molecules. The molecule has a polar head and two hydrophobic hydrocarbon tails. The tails are packed inside the film, while polar heads contact water. The bilayer has the properties of a two-dimensional (2D) liquid; the molecules in it rotate around their axes.

The water structure perturbation at the membrane surface is induced mainly by the positive and negative charged groups of the polar heads. The distance between the positive and negative charges in one dipolar head is fixed and equal to $l \simeq 0.4$ nm.[27] This dipole lies almost parallel to the surface of bilayer so that the positive and negative groups can be considered as lying in the same plane.[27,28] Then the surface perturbation can be written in the form

$$p_i(\mathbf{R})=\int d\mathbf{R}'[n_i^+(\mathbf{R}')-n_i^-(\mathbf{R}')]\Psi(\mathbf{R}-\mathbf{R}') , \tag{21}$$

where

$$n^{\pm}(\mathbf{r})=\sum_k \delta(\mathbf{R}-\mathbf{R}_k^{\pm})$$

is the surface charge density of positive and negative groups and Ψ is the form factor of the perturbation. For simplicity we assumed that + and − groups induce the similar perturbations but with opposite signs. In this case $\langle p(\mathbf{R})\rangle \equiv 0$, so that we deal with a purely inhomogeneous, fluctuating boundary condition.[29]

B. Surface structure factors

From Eqs. (7), (11), and (21) we find

$$S_{ii}(\mathbf{Q})=A|\Psi(\mathbf{Q})|^2 N_i(\mathbf{Q}) , \tag{22}$$

where we introduced the charge-density correlation function

$$\tilde{N}(\mathbf{R})=\langle [n^+(\mathbf{r}+\mathbf{R})-n^-(\mathbf{r}+\mathbf{R})][n^+(\mathbf{r})-n^-(\mathbf{r})]\rangle , \tag{23}$$

$$N(\mathbf{Q})=\int d\mathbf{R}\tilde{N}(\mathbf{R})e^{-i\mathbf{Q}\cdot\mathbf{R}} . \tag{24}$$

$N(\mathbf{Q})$ can be, in principle, extracted from the partial structure factors measured by neutron scattering.

We now consider a 2D model of a bilayer which allows us to get an analytical expression for $N(\mathbf{Q})$. Let us assume that a lipid molecule projection on a "bilayer plane" has a center of rotation, relative to which the orientation of the molecular dipole and the density of molecules are statistically independent. We furthermore assume that this center of rotation lies exactly in the middle between the positive and negative group. When the orientations of different molecules are completely *uncorrelated* we get (see the Appendix)

$$S_{ii}(\mathbf{Q})=2An_i|\Psi(\mathbf{Q})|^2[1-J_0(Ql)] , \tag{25}$$

where n_i is the mean surface density of the polar heads and J_0 is the Bessel function. In the opposite, "*strongly structured limit*" we assume that positive and negative charges form a regular square lattice with a lattice constant $2l$. Then (see the Appendix)

$$S_{ii}(\mathbf{Q})\simeq 16An_i^2|\Psi(\mathbf{Q})|^2 l\delta(Q-\pi/l) . \tag{26}$$

The intermediate case may be described by the interpolation

$$S_{ii}(\mathbf{Q})=A\frac{8n_i^2}{\pi^{5/2}}|\Psi(\mathbf{Q})|^2\left[\frac{\pi^{5/2}}{4n_i}[1-J_0(Ql)]+2\xi Q^2 l^3\right]e^{-\xi^2(Q-\pi/l)^2} . \tag{27}$$

Here ξ stands for a decay length of spatial correlation of orientational and density fluctuations. The limits described above are reproduced by, respectively, $\xi \rightarrow 0$ and $\xi \rightarrow \infty$. Plots of $P_{\text{inh}}(L)$, calculated via Eq. (27) for the case of identical bilayers ($S_{11} = S_{22}$) under the assumption $|\Psi_i(\mathbf{Q})|^2 = \Psi^2/A$ [$\Psi_i(\mathbf{R}) = \Psi\delta(\mathbf{R})$], are displayed in Fig. 1. They show the main tendencies prescribed by the phenomenological analysis.

V. COMPARISON WITH EXPERIMENTS

Let us now look how the conclusions of the theory match with the experimental facts.

A. The range of variation of the decay length

According to the present theory, three cases are possible.

(i) *Purely inhomogeneous case.* The effective decay length λ_{eff} should vary between 0.05 and 0.5 nm depending on the nature of the surfaces. For lipid membrane systems the range of observed λ_{eff} is $0.08 < \lambda_{\text{eff}} < 0.3$ nm.[5,16,26]

(ii) *Mixed case.* When both the inhomogeneous and homogeneous contributions are nonzero, at least two decay lengths should be seen. The first one is the native water correlation length κ^{-1}. The second one is determined by the nature of the surfaces and is at least two times smaller. A sum of two exponentials with $\lambda_{\text{eff}_1} \simeq 0.3$ nm and $\lambda_{\text{eff}_2} \simeq 1$ nm was observed in the interaction of mica surfaces.[3,5,8]

(iii) *Purely homogeneous case.* One exponential decay takes place here with water correlation length standing for λ_{eff}. This mode of decay is seen in the repulsion between silica surfaces with $\lambda_{\text{eff}} \simeq 0.7-1$ nm.[30]

So, data for solid surfaces can be rationalized under an assumption of nonzero mean values of polarization at each of the surfaces. Somewhat large values of λ_{eff} or λ_{eff_2} with respect to the native water correlation length suggest that the nonlinear response of water to surface perturbation might be important here. A small decay length in the interaction of lipid membranes indicates at the inhomogeneous mechanism which is in a complete agreement with the microscopic picture of surface perturbation.

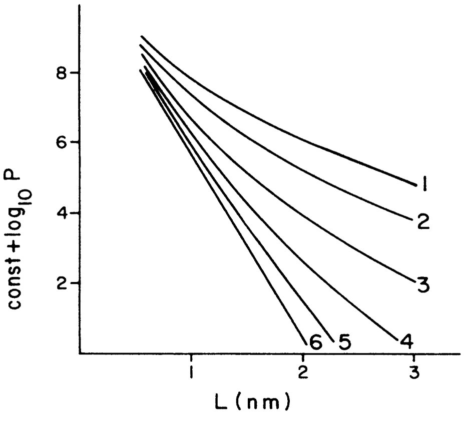

FIG. 1. Inhomogeneous contribution to the hydration force [Eqs. (17) and (18)] between two identical surfaces as calculated with the help of an interpolation formula for the surface structure factor [Eq. (27)] given in the logarithmic coordinates to the accuracy of a constant. $\kappa^{-1} = 1$ nm, $l = 0.5$ nm; surface area per unit bilayer molecule, $n_i^{-1} = 0.6$ nm^2. ξ (nm): curve 1, 0; curve 2, 0.3; curve 3, 0.5; curve 4, 0.7; curve 5, 1; curve 6, 2.

B. Peculiarities of hydration forces in lipid membrane systems

Rigorous comparison with experiments requires the knowledge of $S_{ii}(Q)$ [Eq. (22)] or, at least, of $N(Q)$ [Eq. (23)], i.e., of the partial structure factors of positively and negatively charged groups. Attempts to get such data by means of the low-angle neutron scattering experiments are in progress. However, at the moment, we may try to explain a number of qualitative effects having based our speculations on qualitative conclusions (sometimes not exactly defined, or preliminary) about the "degree of order" in the lateral arrangement of polar heads.

(i) *The dependence on the nature of the polar head.* Let us compare phosphatidylethanolamine (PE) bilayers, where lateral interaction of polar heads is supposed to be very strong,[27,15] with phospatidylcholine (PC) bilayers where the interaction is likely to be weaker. If the ordering of polar heads in PE is indeed longer than for PC, then according to rule 1, for PE the decay length λ_{eff} should be smaller due to the corresponding longer lateral correlations in the surface water perturbation. Within the framework of this picture, according rule 2, at large distances the hydration force between PE bilayers should be much smaller. Just this behavior is experimentally observed.[16,26]

(ii) *The effect of the nature or phase state of hydrocarbon tails.* The following tendency has been experimentally established. The more saturated and, consequently, more rigid the tails are, the more dense the packing of the lipids is, and the weaker the hydration force is.[5,16,26] The same tendency is observed for the liquid-gel phase transition.[5,16,26] The nontrivial explanation of this is again the strengthening of the lateral interactions among lipid molecules with the saturation of hydrocarbon chains or a liquid$\rightarrow$gel transition. A simple increase of the density of the polar heads packing (which may reach 40% here as a maximum) cannot beat the tremendous effect due to the growth of the lateral structure correlation range: the latter diminishes the hydration force by orders of magnitude (rule 2). The tendency of the decrease of λ_{eff}, prescribed in this situation by rule 1, is also in a very good agreement with the experiments.[5,16,26]

(iii) *The action of phospholipases.* These species tend to cutoff polar heads from the bilayer, leaving behind, in the lipid matrix, the hydrophobic diacylglycerol molecules (DAG). At first glance, the hydration repulsion should be diminished since the surfaces become, as a result, more hydrophobic, but this is not the case. This process increases the force at large distances.[31] Is this result, the manifestation of rule 2, due to a disordering action of DAG? The increase in λ_{eff} predicted in this case by rule 1, is also observed.[31]

(iv) *The action of cholesterol (CH).* The effect is opposite in the gel phase, where CH increases the hydration force, and in the liquid phase where the force is diminished.[16] The explanation may be concerned in a way with the well-known opposite ordering effect of CH in these phases: CH leads to a stronger ordering of the liquid and disordering of the gel.[16] The application of rule 2 then reaches the goal.

This example, however, may be not the "best" one since the discussed ordering of lipid tails might not necessarily mean the increase in ordering of the polar heads. The influence of cholesterol might be quite opposite here, which requires, in fact, a more thorough analysis.

VI. CONCLUSION

An account for spatial dispersion of the boundary conditions has led us to an entirely new picture of the hydration force. It gives a consistent physical explanation of its main features, particularly interesting for lipid membrane systems. We saw that the specific arrangement of water molecules at the interacting surfaces is not crucial for understanding the qualitative properties of hydration interaction, but the nature of perturbation and the general character of its distribution along the surfaces is crucial.

In order to verify the predictions of the theory one should either measure hydration forces in correlation to the lateral surface structure factors of polar head groups, or, at least follow the qualitative trends in hydration forces with the definite strengthening of the lateral order in the polar head distribution. We believe that the considered examples are encouraging for further applications of the theory, though one must be careful with the facts about the structure of lipid matrix and presumptions about the order in the polar head region.

Thinking of lipid bilayers as a body of biological membranes, we may now keep in mind that the strengthening of bilayer ordering may be an efficient way to reduce the hydration barriers controlling the membrane fusion. The relaxation of the surface short-range order will lead to an opposite effect making the membranes more resistive to fusion. Collective reconstructions affecting the order, manifested here via the analytical properties of the surface structure factors, may be less costly for the nature to facilitate or resist cell fusion or recognition than a realization of special chemical arrangements. We thus arrive at a possible remarkable relation between the "*function*" and statistical aspects of the *structure* of lipid membranes.

If the formation of the boundary conditions is due to hydration of negatively and positively charged groups, one should also consider the direct electrostatic contribution to the hydration force. A nonlocal electrostatic treatment of this contribution will be given in a subsequent publication.

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APPENDIX: CHARGE-DENSITY CORRELATION FUNCTIONS FOR LIPID MEMBRANES

1. Completely uncorrelated orientations of polar heads

The Fourier transform of the charge-density correlation function $N(\mathbf{Q})$ determined by Eqs. (23) and (24) may be written in the form

$$N(\mathbf{Q})=\langle |n^{+}(\mathbf{Q})-n^{-}(\mathbf{Q})|^2\rangle \ , \tag{A1}$$

where

$$n^{\pm}(\mathbf{Q})=\frac{1}{\sqrt{A}}\sum_k e^{-i\mathbf{Q}\cdot\mathbf{R}_k^{\pm}} \tag{A2}$$

are the Fourier transforms of densities of the positive and negative groups $n^{\pm}(\mathbf{R})=\sum\delta(\mathbf{R}-\mathbf{R}_k^{\pm})$. For the molecules having the center of rotation $\mathbf{R}_k$ lying in the middle between the positive and negative groups

$$\mathbf{R}_k^{+}=\mathbf{R}_k+\mathbf{l}_k/2, \quad \mathbf{R}_k^{-}=\mathbf{R}_k-\mathbf{l}_k/2 \tag{A3}$$

($l=|\mathbf{l}_k|$ is the separation between the + and − groups in a molecule). After the substitution of Eq. (A3) into Eqs. (A1) and (A2) we find

$$\begin{aligned}N(\mathbf{Q})=&\langle 2n[1-\cos(\mathbf{Q}\cdot\mathbf{l})]\rangle\\&+\frac{1}{A}\Big\langle \sum_{\substack{j,k\\ j\neq k}}[e^{-i\mathbf{Q}\cdot(\mathbf{R}_j-\mathbf{R}_k)}(e^{-i\mathbf{Q}\cdot\mathbf{l}_j/2}e^{i\mathbf{Q}\cdot\mathbf{l}_k/2}+e^{i\mathbf{Q}\cdot\mathbf{l}_j/2}e^{-i\mathbf{Q}\cdot\mathbf{l}_k/2}-e^{-i\mathbf{Q}\cdot\mathbf{l}_j/2}e^{-i\mathbf{Q}\cdot\mathbf{l}_k/2}-e^{i\mathbf{Q}\cdot\mathbf{l}_j/2}e^{i\mathbf{Q}\cdot\mathbf{l}_k/2})]\Big\rangle \ .\end{aligned} \tag{A4}$$

Here the first term reflects the rigid struture within one molecule (n is the mean density of polar heads), while the second term is responsible for intermolecular correlation functions ($j\neq k$). Since the orientations of the molecules are independent, we have

$$\langle e^{i\mathbf{Q}\cdot\mathbf{l}_j/2}e^{i\mathbf{Q}\cdot\mathbf{l}_k/2}\rangle=\langle e^{i\mathbf{Q}\cdot\mathbf{l}_j/2}\rangle\langle e^{i\mathbf{Q}\cdot\mathbf{l}_k/2}\rangle \tag{A5}$$

and

$$\begin{aligned}\langle e^{i\mathbf{Q}\cdot\mathbf{l}_j/2}\rangle&=\langle e^{i\mathbf{Q}\cdot\mathbf{l}_k/2}\rangle\\&=\langle e^{-i\mathbf{Q}\cdot\mathbf{l}_j/2}\rangle=\langle e^{-i\mathbf{Q}\cdot\mathbf{l}_k/2}\rangle \ .\end{aligned} \tag{A6}$$

After the averaging over the orientations of $\mathbf{l}$ we find

$$N(\mathbf{Q})=2n[1-J_0(Ql)] \ , \tag{A7}$$

where J_0 is the Bessel function.

2. Regular lattice of polar heads

For the sake of simplicity we consider the simpliest square lattice (with a lattice constant a) and parallel ordering of the polar heads along one of principal axes. Then from Eqs. (A1) and (A2) we find

$$N(\mathbf{Q})=2An^2\left\langle \sum_{\mathbf{q}_n} \delta_{\mathbf{Q},\mathbf{q}_n}[1-\cosh(\mathbf{q}_n\cdot\mathbf{l})]\right\rangle , \qquad \text{(A8)}$$

where $\mathbf{l}$ ($|\mathbf{l}|=l$) is the shift between positive and negative sublattices. $\mathbf{q}_n$ are the vectors of the reciprocal lattice. Since the relevant values of L are much greater than $q_1^{-1}=l/\pi$, it is possible for the calculation of $P(L)$ to keep in the sum (A8) only the first nonzero terms with the smallest vector of the reciprocal lattice, $\mathbf{q}_1$. Then, in the limit of $A\rightarrow\infty$, after averaging over the lattice orientations, we find

$$N(\mathbf{Q})=4n^2a\delta(Q-2\pi/a)[1-\cosh(2\pi l/a)] \; . \qquad \text{(A9)}$$

Usually for lipid membranes $l\simeq0.4$ nm and $a\simeq0.7-1$ nm, so we assume for simplicity that $a=2l$. Then

$$N(\mathbf{Q})=16n^2l\delta(Q-\pi/l) \; . \qquad \text{(A10)}$$

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