

Charge fluctuations on membrane surfaces in water

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We generalize the predictions for attractions between overall neutral surfaces induced by charge fluctuations or correlations to nonuniform systems that include *dielectric discontinuities*, as is the case for mixed charged lipid membranes in an aqueous solution. We show that the induced interactions depend in a nontrivial way on the dielectric constants of membrane and water and show different scaling with distance depending on these properties. The generality of the calculations also allows us to predict under which dielectric conditions the interaction will change sign and become repulsive.

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I. INTRODUCTION

In recent years there has been a growing interest in electrostatic systems that are dominated by ion fluctuations and ion distributions around larger charged objects. In some of these systems one finds attraction between like charged objects [1] and direct *electrostatic* contributions in systems that are overall *neutral* [2,3].

In this paper we will generalize some theoretical results for systems of neutral surfaces (membranes) that nonetheless interact electrostatically via ion fluctuations and correlations. These predictions are relevant to the experimental work done both on biological systems and on artificial systems where charges are introduced in order to improve membrane characteristics. Examples are the charged membranes in membrane-DNA complexes [4] used for gene transvection and the formation of equilibrium bilayer vesicles from mixed charged lipids [5].

Recently it has been shown [2] that charge fluctuations can lead to attractions between overall neutral surfaces. However, the system treated was the somewhat artificial case of uniform layers where the interacting surfaces separate regions of the *same* dielectric. In this paper we specifically focus on the role of the dielectric discontinuities in systems of lipid membranes in an aqueous solution and how they affect these interactions. In Sec. II we introduce a model system for the membrane which includes two surfaces charged with both positive and negative mobile ions (charged lipid heads at the bilayer surface) that are overall neutral. The system is treated within the Debye-Hückel model [6,7] for a two-dimensional salt solution [2,8]. We calculate the interaction between these two surfaces resulting from the fluctuations and correlations of the mobile charges, and find that the resulting attraction depends in a nontrivial way on the *dielectric discontinuity* between lipid and water.

II. INTERACTION BETWEEN TWO SALTY SURFACES

In this section we calculate the effective interaction between two surfaces that contain mobile charges but are overall neutral. This is a model system for mixed charged lipid

membranes [5] or for membranes that are very highly charged to the extent that their counterions are restricted to a nearby layer that is thin enough to be considered as a two-dimensional surface. Pincus and Safran [2] have calculated this interaction within the Debye-Hückel approximation for a uniform system, i.e., a system with no dielectric discontinuities. We will follow their method, while introducing the dielectric contributions to this model.

A. Model

The Debye-Hückel model is an expansion of the energy to second order in the charge density fluctuations [10] and includes both the electrostatic and entropic contributions due to these fluctuations:

$$\delta H = \int d\rho d\rho' \left[\frac{1}{2} \sum_{i=1,2} \left(\frac{\delta(\vec{\rho} - \vec{\rho}')}{\sigma_0} + \phi(\vec{\rho} - \vec{\rho}', z=0) \right) \times \delta\sigma_i(\vec{\rho}) \delta\sigma_i(\vec{\rho}') + \phi(\vec{\rho} - \vec{\rho}', z=d) \delta\sigma_1(\vec{\rho}) \delta\sigma_2(\vec{\rho}') \right]. \quad (2.1)$$

The self-energy of each of the surfaces separately is given by the first two terms while the third term is the interaction term between charges on the different surfaces. $\sigma_{1,2}$ are the charge densities on the surfaces (the index $i=1,2$ denotes the surface number) while ρ is the in-plane coordinate and z is the coordinate perpendicular to the surface. The first term (δ function) is the entropic contribution from the charge density fluctuations in both surfaces. In this expression we have assumed, for the sake of simplicity and without taking away from the generality of the treatment, that the charge fluctuations are due only to density fluctuations of *one* type of charge while the other sign does not fluctuate and therefore does not contribute to the free energy to this order. Thus the entropic contribution can be written in terms of the total charge density fluctuations on each surface, where σ_0 is the average charge density of each species (separately). The electrostatic contributions ϕ both between charges in the same surface ($z=0$) and between charges on the opposite surfaces ($z=d$) are not trivial because of the dielectric discontinuities that are formed by these surfaces (Fig. 1). The

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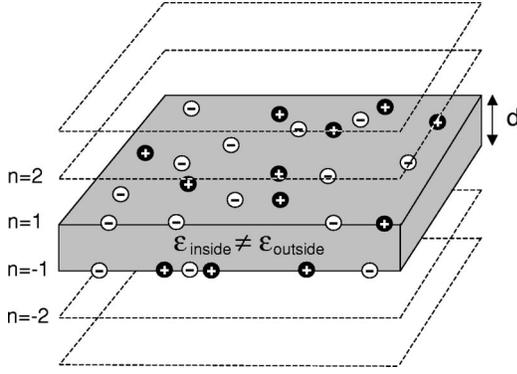


FIG. 1. Schematic of model system. [For example, membrane ($\epsilon=2$) in water ($\epsilon=80$). The lipid heads are charged with both positive and negative charges but the membrane is overall neutral.] The dashed lines indicate the virtual surfaces where the image charges show up. Because there are two dielectric discontinuities, there are infinitely many such surfaces at equal distances d apart.

discontinuities reflect the fields, thus creating image charges in the region outside the membrane [9]. Because this system has two such discontinuities on either side of the membrane, each image charge is reflected over and over again so that we have an infinite number of charges over which to sum when calculating the potential. We require expressions for the interactions between charge fluctuations in the same surface (they will also contribute to the intersurface interaction via the reflections) and fluctuations on opposite surfaces. The interaction potential of two charges that are in the same surface is

$$\phi(\vec{\rho}-\vec{\rho}', z=0) = \frac{e^2}{\bar{\epsilon}} \left(\frac{1}{|\vec{\rho}-\vec{\rho}'|} + \frac{\epsilon_{in}}{\bar{\epsilon}} \sum_{n=1}^{\infty} u^{2n-1} \times \frac{1}{\sqrt{|\vec{\rho}-\vec{\rho}'|^2 + (2nd)^2}} \right), \quad (2.2)$$

while the interaction energy for two charges on the two different sides of the membrane is given by

$$\phi(\vec{\rho}-\vec{\rho}', z=d) = \frac{e^2 \epsilon_{in}}{\bar{\epsilon}^2} \sum_{n=1}^{\infty} u^{2n-2} \times \frac{1}{\sqrt{|\vec{\rho}-\vec{\rho}'|^2 + [(2n-1)d]^2}}. \quad (2.3)$$

Here $\epsilon_{out, in}$ are the dielectric constants of the outer and inner layers respectively, $\bar{\epsilon} = (\epsilon_{out} + \epsilon_{in})/2$, $u = (\epsilon_{in} - \epsilon_{out})/(\epsilon_{in} + \epsilon_{out})$, and d is the membrane thickness.

The sums in Eqs. (2.2) and (2.3) are easily performed if we use the identity $\int e^{-qz} J_0(qr) dq = 1/\sqrt{r^2 + z^2}$ to transform them into simple geometric series. The resulting energy in momentum space has the form

$$\delta H = \sum_q \left(\frac{1}{2} [|\delta\sigma_1(q)|^2 + |\delta\sigma_2(q)|^2] A(q) + \delta\sigma_1(q) \delta\sigma_2(q) B(q) \right). \quad (2.4)$$

The coefficients are given by

$$A(q) = \frac{1}{\sigma_0} + \frac{2\pi\langle l \rangle}{q} + \frac{2\pi\delta l}{q} \frac{\exp(-2qd)}{1 - u^2 \exp(-2qd)},$$

$$B(q) = (2\pi l_{in}/q) \exp(-qd) / [1 - u^2 \exp(-2qd)].$$

Here we have defined three different ‘‘Bjerrum lengths:’’ $\langle l \rangle = e^2/\bar{\epsilon} k_B T$, $\delta l = \langle l \rangle 2(\epsilon_{in} - \epsilon_{out})\epsilon_{in}/\bar{\epsilon}^2$, and $l_{in} = \langle l \rangle \epsilon_{in}/\bar{\epsilon}$.

At this point it is worth noting the differences between this expression and that which is found for the uniform case [2] of no dielectric variations: The differences are expressed through the various effective Bjerrum lengths. In the uniform case there is only one such length scale, which would be equal to $\langle l \rangle$ where $\bar{\epsilon} = \epsilon$. In that case $l_{in} = \langle l \rangle = l_B$ and $\delta l = 0$. Hence the differences enter not only in the way they change the interaction amplitude through l_{in} and $\langle l \rangle$, but also by adding an additional interaction term that is d dependent, but that is also proportional to the dielectric difference $\epsilon_{in} - \epsilon_{out}$, through δl , and affects the resulting interaction in a nontrivial way, as will be seen below [11].

The Gibbs free energy for these fluctuations is now given by the logarithm of the partition function:

$$\frac{G}{k_B T} = -\ln \left(\int \Pi_q d\sigma_q \exp(-\Delta H/k_B T) \right) = \ln[A(q)^2 - B(q)^2]. \quad (2.5)$$

The pressure between the two surfaces due to charge fluctuations as a function of membrane thickness is given by the negative derivative of the Gibbs free energy with respect to the thickness:

$$\Pi(d) = \frac{k_B T}{A} \sum_q q e^{-2qd} \times \frac{(\delta l/\langle l \rangle)[\lambda q + 1 + (\delta l/\langle l \rangle)e^{-2qd}] - (l_{in}/\langle l \rangle)^2}{[\lambda q + 1 + (\delta l/\langle l \rangle)e^{-2qd}]^2 - (l_{in}/\langle l \rangle)^2 e^{-2qd}}, \quad (2.6)$$

where we have introduced a Gouy-Chapman length scale $\lambda = 1/2\pi\langle l \rangle\sigma$. In integral form we find the expression

$$\Pi(d) = k_B T \frac{1}{2\pi d^3} \int dx x^2 e^{-2x} \times \frac{(\delta l/\langle l \rangle)[(\lambda x/d) + 1 + (\delta l/\langle l \rangle)e^{-2x}] - (l_{in}/\langle l \rangle)^2}{[(\lambda x/d) + 1 + (\delta l/\langle l \rangle)e^{-2x}]^2 - (l_{in}/\langle l \rangle)^2 e^{-2x}}. \quad (2.7)$$

B. Results and discussion

The most convenient way to analyze the results of the previous section is by looking at the various limits of the

integral Eq. (2.7). We have three dimensionless parameters that determine the behavior of this integral and thus the d and $\epsilon_{out}, \epsilon_{in}$ dependence of the pressure. The first is the ratio between the two length scales in the problem,

$$\frac{\lambda}{d} = \frac{1}{2\pi\langle l \rangle \sigma d},$$

which parametrizes the strength of the charging in the membrane relative to the distance between the surfaces. The other two parameters are the ratio of the dielectric constants and also their relative difference:

$$\frac{\delta l}{\langle l \rangle} = \frac{2(\epsilon_{in} - \epsilon_{out})\epsilon_{in}}{\bar{\epsilon}^2} \quad \text{and} \quad \frac{l_{in}}{\langle l \rangle} = \frac{\epsilon_{in}}{\bar{\epsilon}}.$$

The first of these two ratios reflects the effect of image charges on the fluctuation induced interactions, while the second measures the relative weakening or strengthening of the primary interactions between fluctuations on the two sides due to the difference in dielectric response of the material between them.

We have three different parameters with which we find three different limiting regimes. The first regime is reached when we take the limit $\lambda/d \ll 1$ (high ion density: the average distance between ions $\ll \sqrt{d\langle l \rangle}$):

$$\Pi(d) \propto \frac{k_B T}{\pi d^3} \left[\frac{\delta l}{\langle l \rangle} - \left(\frac{l_{in}}{\langle l \rangle} \right)^2 \right] \propto - \frac{k_B T}{d^3} \frac{\epsilon_{in}(2\epsilon_{out} - \epsilon_{in})}{\bar{\epsilon}^2}. \quad (2.8)$$

The $1/d^3$ behavior remains the same throughout this regime, although the sign of the pressure changes from being attractive for $\epsilon_{out} > \epsilon_{in}$ (as is expected for a lower dielectric between the surfaces and is the case for a biomembrane) and even ϵ_{in} slightly bigger than ϵ_{out} , becoming repulsive only when the internal dielectric ϵ_{in} is at least twice as big as the external one ϵ_{out} . In this limit the effect of the variation in the dielectric between the surfaces is just on the size (and eventually the sign) of the pressure, but the dependence on distance is unaltered from the uniform case, which was described in [2] as a fluctuation effect and compared with the van der Waals attraction also because of its linear dependence on temperature [12].

The next main regime is the opposite one when $\lambda/d \gg 1$. Here we distinguish between two regimes. The first is that when the dielectric contrast is not very big [compared with $(l_{in}/\langle l \rangle)^2 d/\lambda$] and in this case the behavior is, as expected, similar to that found for the uniform case in this limit [2]:

$$\Pi(d) \propto - \left(\frac{l_{in}}{\langle l \rangle} \right)^2 \frac{k_B T}{d \lambda^2} \propto - \left(\frac{\epsilon_{in}}{\bar{\epsilon}^2} \right)^2 \frac{\sigma^2}{d} \frac{e^4}{k_B T}. \quad (2.9)$$

In this case the pressure is inversely proportional to the temperature (through the λ dependence) and is argued to be a correlation, rather than a fluctuation, effect [2]. The dielectric effects enter in the coefficient $(l_{in}/\langle l \rangle)^2$ and reduce the interaction as the internal dielectric (lipid) becomes smaller than the external one (water) and the dielectric contrast increases. However, as this contrast increases another effect

becomes important—the effect of the image charges, which dominate when $|\delta l/\langle l \rangle|$ is not small compared with $(l_{in}/\langle l \rangle)^2 d/\lambda$ —and we find

$$\Pi(d) \propto \frac{\delta l}{\langle l \rangle} \frac{k_B T}{d^2 \lambda} \propto - \frac{(\epsilon_{out} - \epsilon_{in})\epsilon_{in}}{\bar{\epsilon}^3} \frac{\sigma e^2}{d^2}. \quad (2.10)$$

Here once again we find that the interaction will change sign when the internal and external dielectrics reverse roles. However, the dominant effect is that the power law changes from d^{-1} to d^{-2} , and therefore for smaller d this effect becomes more important than the previous result, Eq. (2.9). Note that in this regime the pressure is independent of T and is therefore neither pure fluctuation nor correlation effect. Moreover, it is linearly dependent on the surface charge density σ (and not quadratically), indicating that the correlations lead to an average charge distribution that is temperature independent and the result is an interaction between each charge and its effective image charge which does not include, to first order, the rest of the mobile charges.

Although one can find systems composed of charged layers of relatively similar dielectric content, most charged layered structures are included within the first ($\lambda \ll d$) and last ($d \ll \lambda$ and large dielectric contrast) regimes. The case of membranes in water clearly belongs to these two limits. Moreover, such a structure can exhibit both regimes simultaneously since in a stacked arrangement one can consider both the membrane and the water as being the internal layer. Although membrane thickness is predominantly determined by forces resulting from the hydrophobicity and length of the carbon chains, it is still interesting to compare this charge fluctuation induced pressure with the van der Waals forces [13] in the system. Taking the membrane Hamaker constant to be of the order of $2 \times 10^{(-21)}$ J [13], the ratio between the pressures for highly charged membranes ($\lambda \ll d$) turns out to be $\Pi_{charge}/\Pi_{vdW} \sim 8$ (independent of d). In this limit the charge fluctuation pressure is stronger than van der Waals forces. Since they both have the same sign and order of magnitude (both tend to squeeze the membrane), and both show the same dependence on thickness, the two interactions plainly add up to an enhanced dispersion force. What happens in the opposite limit, when the charging is weak so that $\lambda > d = 40$ Å (typical membrane thickness)? It turns out that at this limit the charging is too weak and van der Waals pressure always dominates strongly.

On the other hand, when the water layer is not constrained by a fixed layer thickness we can expect to see both regimes expressed. Moreover, because the internal and external phases are reversed the size of the interactions is $\epsilon_{water}/\epsilon_{oil} \approx 40$ times larger than in the previous case. Hence for thick water layers ($\lambda \ll d$) the enhanced fluctuation pressure, which now tends to swell the water layer, clearly dominates over the attractive van der Waals pressure that tends to thin it. In the low charging limit ($d \ll \lambda$) we now find that $\Pi_{charge}/\Pi_{vdW} \approx 25d/\lambda$. This means that even at the low charging limit there is a regime where the fluctuation pressure dominates over the van der Waals forces. These two have opposite signs and also different functional dependences on the thickness of the layer, d . This means that for moderately charged layers ($\sigma = 10^{(-3)} \text{ Å}^2$), for spacings

larger than 1 \AA but smaller than $\lambda \approx 10 \text{ \AA}$, we can expect a $1/d^2$ power law for swelling that will cross over into a $1/d^3$ behavior for larger distances.

In summary, we have shown that fluctuation induced interactions are strongly dependent on the dielectric properties of the system not only quantitatively but also qualitatively. The lower dielectric constant of the lipid will reduce the strength of the interaction between the two surfaces of the membrane but will also change the scaling with the membrane thickness. When looking at interactions in a stack the reverse happens: the interaction is enhanced by a factor of $\epsilon_{out}/\bar{\epsilon} \approx 2$ with respect to the uniform case, and we might

also be able to see the effects of dielectric reflections when looking at the intermembrane interactions.

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