

The influence of ion binding and ion specific potentials on the double layer pressure between charged bilayers at low salt concentrations

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Measurements of surface forces between double-chained cationic bilayers adsorbed onto molecularly smooth mica surfaces across different millimolar salt solutions have revealed a large degree of ion specificity [Pashley *et al.*, *J. Phys. Chem.* **90**, 1637 (1986)]. This has been interpreted in terms of highly specific anion binding to the adsorbed bilayers. We show here that inclusion in the double layer theory of nonspecific ion binding and ion specific nonelectrostatic potentials acting between ions and the two surfaces can account for the phenomenon. It also gives the right Hofmeister series for the double layer pressure. © 2008 American Institute of Physics.
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I. INTRODUCTION

Specific ion effects in colloid science and membrane biology change the apparent surface charge properties of membranes and their electrostatic double layer interactions. For example, Pashley *et al.*¹ demonstrated that surface forces between double-chained cationic bilayers adsorbed onto molecularly smooth mica surfaces across different millimolar salt solutions have a large degree of ion specificity. The origin of such Hofmeister phenomena has been unexplained for a very long time. They have been observed in a wide variety of systems. A few typical examples include growth rates of *Staphylococcus Aureus*,² the ion specific swelling of neutral lipid bilayers,^{3(a),3(b)} of charged bilayers, and surface tension of salt solutions.⁴

Recently there has been some hints and progress in pinning down the source of such effects.^{5–7} In a series of papers we have demonstrated that some of the specific ion effects fall into place if quantum mechanical nonelectrostatic (NES) forces acting between each ion and a macromolecule (e.g., a protein) are included consistently.^{5,6} These many body potentials due to the totality of electrodynamic many body fluctuation forces are accessible in principle via Lifshitz theory.^{7(a)} They are not included in standard theories which, by and large, focus on electrostatic and hydration effects alone. At and above biological concentrations ($\sim 0.15M$) electrostatic effects are strongly screened, and the ionic dispersion potentials become important. In this regime usually neglected highly ion specific forces^{7(a)} and ion binding^{7(b)} emerge as dominant. The generic “Hofmeister series” phenomenon is captured in part and related to the ideas devel-

oped by Collins^{7(d)} on how ions destroy the natural hydrogen bonded network of water.^{7(d)} This and the different short range forces due to the overlap of hydration shells (Gurney potentials) are built into and implicit in the cosmotropic, chaotopic classification of ions. The forces between surfaces will also be influenced by image charges^{7(c)} and “ion size effects.”^{7(e)} We focus here on a related but different effect which emerges from inclusion of NES forces and how they affect ion binding. Rydall and Macdonald, e.g., used NMR to demonstrate that anions “bind” to lipid membranes following a so-called Hofmeister series. The ²H NMR quadrupole splitting near a charge neutral phosphatidylcholine membrane increased in the order $NO_3^- \ll I^- < SCN^- < ClO_4^-$.⁸ More recently Petrasche *et al.* demonstrated that specific ion adsorption can explain the ion specific swelling of neutral lipid membranes.^{3(a)} Dubois *et al.* have in a series of careful experiments shown that both the osmotic pressure versus membrane separation and the head group area depend on counterion.^{3(b)} Both effects are related to ion specific NES forces acting between ions and the surface head groups. However, ion specific changes in area per head group appear to be insufficient to explain the ion specific double layer pressure between charged membranes. Here we will neglect changes in head group area that reflect short range interactions between ions and surface head groups. Instead we focus on and show that there is an equally important direct role for NES forces on the double layer pressure between two charged bilayers.

McLaughlin *et al.*⁹ showed that the surface potentials of bilayer membranes follow the standard Hofmeister sequence. The inference from his work is that large polarizable ions such as perchlorate and thiocyanate “adsorb” to phospholipid bilayers to a much larger degree than chloride and even more

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so than acetate. We have shown elsewhere that this circumstance can be traced to and is largely due to these NES or ionic dispersion potentials.^{5,6}

There has up to now been no understanding of how, at low salt concentrations below 0.1M, ions can influence the forces between bilayers and ion binding, with high specificity. It is to be expected that ionic dispersion potentials could account for large Hofmeister effects (ion specificity) at and above biological (>0.15M) salt concentrations. In that regime electrostatic effects are screened, with a Debye length less than 0.8 nm, a distance of just a few water molecules. So the dominating short range interactions between anions and cations, and between ions and interfacial headgroup moieties ought to be specific. What is surprising are the specific counterion effects that occur at much lower salt concentrations. This effect is here traced to adsorption of polarizable counterions. The specific adsorption is linked to the magnitude of NES potentials acting between ions and the surface, and so affects the effective double layer forces.

We first recapitulate the modified ion specific double layer theory required in Sec. II, then present numerical results for forces between model charged bilayers in Sec. III, and finally, summarize what can be concluded.

II. THEORY

In the standard DLVO theory of particle interactions in colloid science, the forces operating are considered to be repulsive electrostatic double layer, and attractive quantum mechanical, van der Waals–Lifshitz forces. These contributions are treated separately. This ansatz is too drastic an approximation. A consequence is that ion specific forces are ignored. They are included in principle but contribute insignificantly because the Lifshitz or Hamaker theory of forces is linear, whereas the double layer forces are treated in a non-linear theory. In a correct theory they must be treated at the same level as the electrostatic forces acting on ions.⁷ This has been demonstrated in a number of previous papers.^{5–7} One overview of the present state of the understanding of the Hofmeister effect is given by Kunz *et al.*¹⁰ Following earlier work, we use an ion specific Poisson–Boltzmann equation with charge regulated boundary condition.^{3,11,12} This allows the determination of the ion distributions between two charged membrane surfaces a distance L apart. The appropriate equations for monovalent ions are⁶

$$\frac{d^2\phi}{dx^2} = -\frac{ec_0}{\epsilon_w\epsilon_0}(\exp[-(e\phi + U_+(x))/kT] - \exp[(e\phi - U_-(x))/kT]), \quad (1)$$

$$\left. \frac{d\phi}{dx} \right|_{x=L/2} = 0, \quad \left. \frac{d\phi}{dx} \right|_{\text{surface}} = \frac{\sigma}{\epsilon_w\epsilon_0} \quad (2)$$

$$\sigma = eN_s \frac{10^{-pK}}{10^{-pK} + [\text{anion}^-]_s}. \quad (3)$$

Here ϵ_w is the dielectric constant of water, N_s is maximum number of charges per unit area, ϕ is the self-consistent electric potential, σ is the (positive) surface charge, and $[\text{anion}^-]_s$

is the anion surface concentration. We consider a system where the anions adsorb so we can use a site-binding model to calculate a dissociation constant.^{1,3,11,12} We then assume as a realistic model example that $pK=1.09$. The exact value is not so important since we are here focusing on the general principle that ion specific NES forces influence surface ion concentrations and ion binding. U_{\pm} is the ionic dispersion potential acting between each ion and the two surfaces,⁶

$$U_{\pm} = B_{\pm} \left(\frac{1}{x^3} + \frac{1}{(L-x)^3} \right). \quad (4)$$

Here the dispersion coefficient (B_{\pm}) for different combinations of ion and membrane can be calculated from the frequency dependent ionic excess polarizability (this is the difference in polarizability compared to the surrounding water), and the dielectric functions of water and of the surface. In a complete theory the B coefficients will include contributions from not just the visible to UV frequency region van der Waals dispersion forces. They also include (many body) dipole-induced dipole and permanent dipole-dipole forces.

We choose the maximum number of charges per unit area of a positively charged model surface to be $1.7 \times 10^{18} \text{ m}^{-2}$ as for the double-chained cationic surfactant adsorbed on mica. This corresponds to the experimental system considered by Pashley *et al.*¹ For sodium, chloride, bromide, and iodide the following estimates for the ionic dispersion coefficient have been used: $-0.5 \times 10^{-50} \text{ J m}^3$, $-3 \times 10^{-50} \text{ J m}^3$, $-6 \times 10^{-50} \text{ J m}^3$, and $-9 \times 10^{-50} \text{ J m}^3$, respectively. The magnitudes of these values are consistent with refractive index data and with other ion specific experiments, such as surface tension of electrolytes⁵ and surface potentials of membranes in salt solutions.⁷ (Recent unpublished *ab initio* calculations by Parsons and Ninham will allow these values to be much more precisely quantified.)

The ion distributions obtained are used to calculate the pressure between two parallel charged membranes. The double layer pressure between two planar plates a distance L apart can then be written as¹³

$$P = kT \sum_i [c_i(L/2) - c_{0,i}] - 2 \sum_i \int_{x_0}^{L/2} c_i \frac{dU_i}{dL} dx - \frac{H}{6\pi L^3}, \quad (5)$$

where k , T , $c_{0,i}$, $c_i(L/2)$, $x_0=2 \text{ \AA}$, and U_i are Boltzmann's constant, temperature, ion concentration in bulk solution, ion concentration at the midplane between the two surfaces, ion size (which is the closest distance the ions can come to the interface), and the ionic dispersion potential acting between each ion and the two interacting surfaces. The last term is the direct van der Waals interaction between the two planar surfaces across water. H is the Hamaker constant which is estimated to be 10^{-20} J .

III. NUMERICAL RESULTS

Pashley *et al.*¹ demonstrated that there can be large ion specificity for the pressure between mica surfaces coated with bilayers of double-chained quaternary ammonium acetate and bromide surfactants. The force could be up to ten

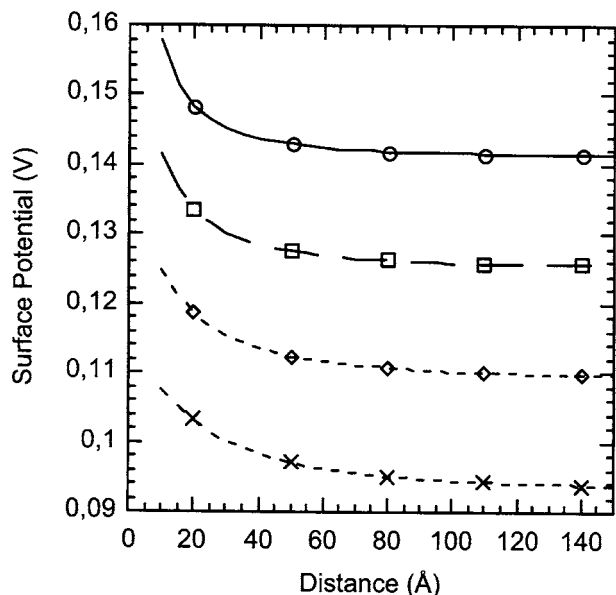


FIG. 1. The calculated surface potential as a function of distance between a pair of bilayers as described in the text across a 2 mM salt solution of nonpolarizable salt (circles), NaCl (squares), NaBr (diamonds), or NaI (crosses).

times smaller with more polarizable bromide ions than in a solution with, say, acetate or chloride. We stress again that the same Hofmeister phenomena occur with “ion binding” to micelles, cationic or anionic, for microemulsions and for polyelectrolytes.^{7(a)} For such systems the phenomenological ion binding model, used, e.g., for interpretation of NMR measurements of binding, is exactly equivalent to an electrostatics-only model. It “works” loosely only in the limit of strong counterion “binding” due to electrostatics. For other counterions and coions, e.g., Ac versus Cl, the “binding” makes no sense. For such systems one needs to include ionic dispersion and other NES forces in the ion binding theory to effect a reconciliation between ion binding required to explain force measurements and that for single interfaces such as lipids or micelles.^{7(a)} The ion and distance specific surface potential and surface charge density shown in Figs. 1 and 2 are for two model surfaces. These correspond to insoluble double-chained cationic surfactants adsorbed on mica interacting across different 2 mM salt solutions. We note that the effective surface charge density depends on the choice of background salt solution and on the distance between the two bilayers. It is 0.04 C m^{-2} for the system with 2 mM nonpolarizable salt when the two bilayers are far apart. The nonpolarizable salt roughly corresponds to sodium acetate. The surface charge density calculated decreases when the bilayer separation decreases or when the ionic excess polarizability (or strength of the ionic dispersion potential) increases. Part of the ion specific surface charge density is here due to the ionic dispersion potentials. If these forces are ignored, as in the usual Poisson–Boltzmann treatment of the double layer interactions, this surface charge would be interpreted incorrectly by assigning an ion specific pK value. An apparent ion specific pKa value can then come about because of the effects of NES potentials are missing from the classical double layer theory. There is a coupling of direct

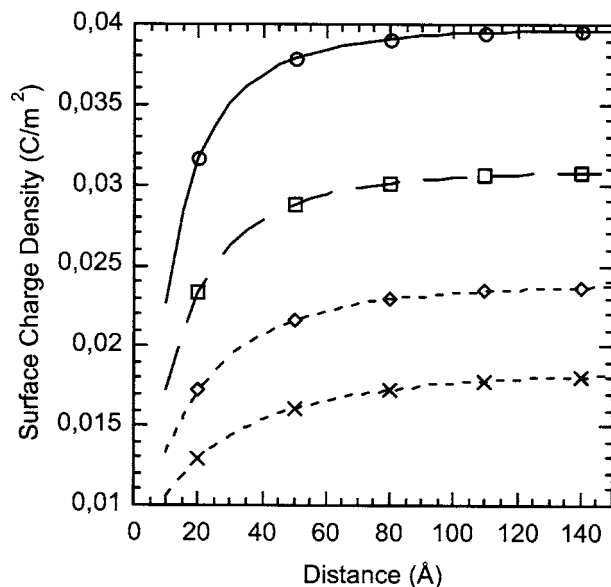


FIG. 2. The calculated surface charge density as a function of distance between a pair of bilayers across a 2 mM salt solution of nonpolarizable salt (circles), NaCl (squares), NaBr (diamonds), or NaI (crosses).

ion binding and physisorption which is due to the electrostatic and electrodynamic ionic forces. Such apparent binding is more likely to happen when there is an enhanced surface concentration.

The corresponding double layer pressure is shown in Fig. 3. It includes the total DLVO pressure (that is, Eq. (5) using a Hamaker constant of 10^{-20} J^1). Notice that the standard DLVO theory would give results that not only miss specific ion effects but are also much different in magnitude. We remark that linearization of the dispersion part of the ionic distribution in the nonlinear double layer potential we have used gives back the ordinary result from Lifshitz theory. However, to pin down the sources of ion specificity one

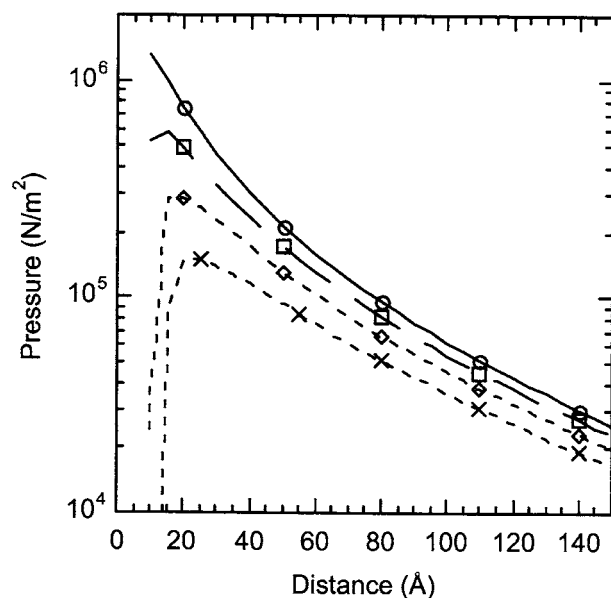


FIG. 3. The calculated double layer pressure as a function of distance between a pair of bilayers across a 2 mM salt solution of nonpolarizable salt (circles), NaCl (squares), NaBr (diamonds), or NaI (crosses).

needs the full nonlinear distribution, for both electrostatic and dispersion forces acting on ions. As can be seen in Fig. 3 the pressure between two closely spaced charged bilayers in the presence of salt can be up to ten times smaller in an electrolyte with highly polarizable anions than in one with low polarizability anions. There are clear Hofmeister effects observed at short separation distances. Even more noticeable is the fact that there is a noticeable shift downward in the long range asymptotic pressure for the 2 mM salt system with increasing ionic dispersion potentials.

IV. CONCLUSIONS

It is well known that there are ion specific effects at biological salt concentrations. However, there are ion specific effects also in the 1–10 mM range which have so far remained unaccounted for. At these low concentrations the effects cannot be due to the bulk effects such as possible water structure in, e.g., activity coefficients. The low salt Hofmeister phenomena are not restricted to bilayers of membrane mimetic surfactants or of lipids. They occur par excellence, e.g., in the pioneering force measurements of Pashley and Israelachvili with mica surfaces.¹⁴ It is known that electrostatic double layer theory applied to ionic micellization gives the phenomenological theory of ion binding as a special case and is inconsistent with the specific binding required to account for double layer force measurements.^{7(a)} The pressure is reduced more in a salt solution with the more polarizable anions than it is in a solution with less polarizable anions. The trend at least is in qualitative agreement with the results obtained by Pashley *et al.*¹ There is a correlation between the resulting pressure and the ionic dispersion potentials, and hence with the excess polarizabilities. Pashley *et al.* suggested ion binding of Br⁻ ions to explain the large deviations between forces measured in bromide compared to in acetate. This ion binding explanation has also been given to explain ion specific swelling of charge neutral lipid membranes.³ For charge neutral lipid zwitterionic bilayers, this ion binding gives rise to a repulsive double layer force. In that case the binding probably does involve real compatibility of hydration and association of ions and surface zwitterions. So our inference is not that specific ion binding in the chemical sense does not exist. It is rather that before considering chemical binding, one must first do the zeroth order theory of interactions correctly, with nonelectrostatic and electrostatic forces treated together in a proper nonlinear theory.^{7(a)} Chemical binding is more likely to occur when there is an enhanced surface concentration due to the ion specific physisorption. Ion binding occurs not just through the influence of electrostatic potentials but also from nonelectrostatic potentials that enhance adsorption. These potentials include ionic dispersion potentials. However, they also include of course solvation energy changes in regions with a varying water density or with changes in hydrated ion size. The essential point is that in order to understand ion specificity in the millimolar, as well as in the biological, regime one has to include NES potentials.

Summarizing, we would like to attract the simulation community to complement this work. In the future there

would be a great value provided by novel atomistic simulations in elucidating the specificity of ions on the electrostatics of lipid bilayers and the resulting changes in membrane behavior. There is a lack of previous simulation studies where the nature and especially the specific effects of ions on membrane systems would have been accounted for. However, the development of force fields relevant for the experimental membrane system considered by Pashley *et al.*¹ could be carried out in a similar way to previous simulations that neglected specific ion effects.^{15–18} These related papers highlight the fact that current resources and force fields are good enough for dealing with these interesting phenomena related to specific ion induced effects, and we would like to encourage the simulation community to initiate simulation studies to support our theoretical work. By appropriate combination of models for cationic membranes and various ion types, studies of the specificity of related effects are feasible and would benefit both theory and experiments.

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