Poisson–Boltzmann Theory for Membranes with Mobile Charged Lipids and the pH-Dependent Interaction of a DNA Molecule with a Membrane

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ABSTRACT We consider a planar stiff model membrane consisting of mobile surface groups whose state of charge depends on the pH and the ionic composition of the adjacent electrolyte solution. To calculate the mean-field interaction potential between a charged object and such a model membrane, one needs to solve a Poisson–Boltzmann boundary value problem. We here derive and discuss the boundary condition at the membrane surface, a condition that is generally appropriate for biological membranes where two charge-regulating mechanisms are present at the same time: the pH-dependent chemical charge regulation and a regulation through the in-plane mobility of the surface groups. As an application of this general formalism, we consider the specific example of a single DNA molecule, approximated by a cylinder with smeared-out surface charges, interacting with such a model membrane. We study the effect that the two competing charge-regulating mechanisms have on the DNA/membrane interaction and the distribution of surface ions in the plane of the membrane. We find that, at short DNA/membrane distances, membrane fluidity can have a considerable impact on the DNA adsorption behavior and can lead to such counterintuitive phenomena as the adsorption of a negatively charged DNA onto a (on average) negatively charged membrane.

INTRODUCTION

Most biomembranes are charged. These charges arise from charged headgroups of phospholipids, adsorbed ions, and proteins. Phospholipids, the basic structural component of membranes, are charged due to the dissociation of protons. Depending on the charges of additional groups that may be bound to the phosphate group, phospholipids in water can have a valency between -2 and +1, and also neutral groups are possible (Cooper, 2000). The state of charge of a phospholipid is not a fixed quantity, but depends on the pH and the ionic composition of the adjacent electrolyte solution. For this reason, a specific phospholipid group is best characterized by a chemical-binding constant rather than by a fixed charge.

Biomembranes are usually in a fluid state in which individual membrane components are free to move in lateral directions, i.e., within the plane of the membrane, whereas their normal movements are highly restricted (Almeida and Vaz, 1995). Depending on their specific biological function, membranes are composed of mixtures of many different lipids and amphiphilic proteins, and it is, in particular, the proteins that are decisive for their specific function. However, if more general properties of membranes are concerned, it often makes sense to neglect this diversity (and especially the proteins), and to study a model membrane solely made of phospholipids (Sackman and Lipowsky, 1995).

In this article, we study such a model membrane. It is assumed to be a collection of surface groups, specified not other than that they can become charged and that they are mobile in the membrane plane. The membrane shape changes are neglected. Different types of groups are allowed for, each type being characterized by a chemical dissociation constant rather than a charge. With such a model, we take account of three basic properties of a lipid bilayer: that it may be composed of different types of phospholipids, that the state of charge of each surface group is controlled by a pH-dependent chemical reaction, and that the surface groups can diffuse laterally.

Specifically, this article addresses the question of how such a model membrane interacts electrostatically with other charged objects in an electrolyte solution. The interaction between charged macroscopic objects in an electrolyte solution is, in fact, an “effective” one (Löwen and Hansen, 2000), meaning that, in addition to the direct Coulomb interaction between both objects, there is a contribution to the interaction energy coming from the distance-dependent density distribution of the electrolyte ions around both objects. More precisely, the effective interaction can be viewed as the free energy of the whole system (composed of both macroions and microions) as a function of the distance between the macroions. In a mean-field approach, the essential input to calculate this free energy, and thus the effective interaction, is the electrostatic mean-field potential; it can be obtained from a Poisson–Boltzmann (PB) (Barrat and Joanny, 1996; Andelman, 1995) boundary value problem (BVP), where the boundaries are the surfaces of the two objects carrying the fixed charges. Important here is the choice of the boundary conditions, which must be made on physical grounds. Besides the constant-charge and constant-potential boundary condition, fixing either the potential or
its derivative at the boundary, a third boundary condition is well established, the charge-regulation boundary condition, where the surface charge is assumed not to be fixed, but to result from ionization of discrete surface sites (Ninham and Parsegian, 1971; Healy and White, 1978; Healy et al., 1980; Chan et al., 1976). The surface-charge density distribution is then a result, not a parameter, of the calculation; input parameters are rather the set of acid dissociation constants and the pH value.

This charge-regulation boundary condition is based on the assumption that the ionizable groups are locally fixed, and is thus not adequate for our case of a model membrane composed of mobile groups. This brings us to the major point of this paper. We derive a boundary condition for a PB BVP that goes beyond the traditional charge-regulation boundary condition by taking explicit account of surface group mobility. Once this point is clarified, the calculation of effective interactions is—though technically involved—conceptually simple. We then calculate the effective interactions between a charged rod and a charged membrane. Here we think of a DNA molecule interacting with a lipid membrane, which we see as a potential field of application of our results.

The issue of mobility of surface groups in an electrostatic context has been addressed before by Guttman and Andelman (1993) and Fogden and Ninham (1991), who investigated the interplay of a spontaneous curvature of a single membrane and the spatial modulation of the surface-charge density of mobile and immobile ions (Andelman, 1995). The effect of mobile surface charges has also been investigated treating the surface charges and counterions as strongly correlated two-dimensional (2D) liquids, which is a valid approximation at very large coupling parameters (i.e. low temperature or multivalent counterions) (Nguyen et al., 2000). Motivated by the recent interest in the DNA-cationic liposome complexes observed by Rädler et al. (1997) and Salditt et al. (1997), a sequence of theoretical papers appeared in which a periodic array of charged rods is considered that is adsorbed onto an oppositely charged surface with mobile charged groups (Menes et al., 1998; Dan, 1997; Bruinsma and Mashl, 1998; Harries et al., 2000; Wagner et al., 2000; Mashl et al., 1999; Mashl and Gronbech-Jensen, 1998). In the work of Harries et al. (2000), the appropriate boundary condition is derived by minimizing a free-energy functional. Quite recently, May et al. (2000a) considered the adsorption of charged proteins on membranes, taking explicit into account surface-group mobility. However, in all these works, the equilibrium between dissociated and associated surface groups was not considered. The case of a membrane consisting of equal amounts of negative and positive mobile lipids has been of special interest. The effective interaction between two fluid membranes is, in this case, solely due to correlation of in-plane charge fluctuations of mobile surface groups (Attard et al., 1988a; Pincus and Safran, 1998). The effect of such lateral charge fluctuations on the elastic properties of a membrane has been considered by Lau and Pincus (1998), and the effective interaction with test charges has been calculated using a generalized Green’s formalism (Netz, 1999).

The outline of this paper is as follows. In the section Formulation of the Problem, we formulate the theoretical problem and present the results to make clear the underlying physics. The Theory section contains the formal solution that is derived from the grand-canonical partition function, a somewhat technical analysis that, however, is unnecessary to an understanding of the main result. In the Discussion, various simple limiting cases are considered to make the result more transparent and intuitively understandable. The next section is devoted to a typical application of our theory; we set up a PB BVP and calculate numerically the interaction of a charged cylinder approaching an oppositely charged wall consisting of mobile surface groups.

**FORMULATION OF THE PROBLEM**

We consider a charged surface $S$ embedded in an aqueous electrolyte solution. In addition to the mobile electrolyte ions, there are ions on the surface that we assume to result from a dissociation of ionizable groups. We assume that there are $M$ different types of such groups, each denoted by the symbol $A_{i}H_{c}$ ($i = 1, \ldots, M$). In water, these groups dissociate according to the reaction formula,

$$A_{i}H_{c} + v_{i}H_{2}O \rightleftharpoons A_{i}^{+} + v_{i}H_{3}O^{+} \quad i = 1, \ldots, M,$$  

where $v_{i}$ are the stoichiometric coefficients of the reaction and $A_{i}^{+}$ denote the negatively charged ions that remain at the surface. The valency of the ion of type $i$, $q_{i}$, is therefore $-v_{i}$. Each of the $M$ different reactions in Eq. 1 is characterized by a dissociation constant $K_{i}$ given by the law of mass action. For the moment, only simple acid reactions are allowed for, but generalization to basic groups is straightforward. Neutral surface groups are also included in the scheme, and can be realized by setting the corresponding dissociation constant equal to zero. We assume each surface group to cover some small area $a_{i}^{2}$ of the surface, which we assume to be the same area for every surface group type $i$. We can then regard the surface as being entirely composed of such groups. Every point on the surface belongs to one specific surface group. This leads to the idea of a regular lattice of site area $a_{i}^{2}$ being superposed on the surface, with each lattice site being occupied by one and only one surface group.

Inside the electrolyte solution and close to the surface, there is a charged object, which, for the moment, we need not specify further. Essential is that, in a mean-field description, the reduced electrostatic mean-field potential $\phi(r)$—that is, the potential multiplied by $eB$ with $e$ being the elementary charge and $\beta = 1/kT$, the inverse temperature—is now a function of all three spatial dimensions.
Because of the presence of the charged object, there is a variation of $\phi(r)$ directly on the surface. Let us denote the position vector on the surface, $r \in S$, by $r_S$. Far away from the object, the surface potential $\phi(r_S)$ approaches the constant value $\phi^\infty$. Note that this implies that the perturbation of the system due to the presence of the charged object is local.

What we calculate here is the partial surface density $\rho_i(r_S)$ of the ion type $A_i^q$ for 1) a given surface potential $\phi(r_S)$, 2) a given pH value of the electrolyte solution, and 3) a given set of dissociation constants $K^i_j (i = 1, \ldots, M)$. This we want to do under the additional assumption that the surface groups are free to move in the surface. To set the stage, let us briefly consider the opposite case of immobile surface groups, where our task is easily solved. In case $\phi(r_S) = \phi^\infty$, $\rho_i$ is a constant, $\rho^\infty_i$, and the law of mass action reads

$$ K^i_j = \frac{\rho^\infty_i e^{-(pH \ln 10 - \phi^\infty)}}{c_i - \rho^\infty_i} , $$

with exp($-pH \ln 10 - \phi^\infty$) the concentration of $H^+$ ions at the surface, and $c_i$ the number of surface ionizable groups of type $i$ per area. Note that the concentration of water molecules is adsorbed into the definition of $K^i_j$. Hence,

$$ \frac{\rho^\infty_i}{c_i} = (e^{pK^i_j - pH} e^{\phi^\infty} + 1)^{-1} = \alpha_i , $$

where $pK^i_j = -\ln K^i_j/\ln 10$. In the following, we refer to the ratio $\rho^\infty_i/c_i$ as the degree of dissociation $\alpha_i$. For neutral surface groups ($K^i_j = 0$), the degree of dissociation becomes zero. If $\phi(r_S)$ is now a function slowly varying on a length scale that is large compared to the lattice constant $a$ of our regular lattice, then, Eqs. 2 and 3 should be valid for every single lattice cell and $\rho_i(r_S)/c_i$ results from simply replacing $e^{\phi^\infty}$ by $e^{\phi(r_S)}$ in Eq. 3. Expressing the resulting formula in terms of the degree of dissociation $\alpha_i$ defined in Eq. 3, one obtains

$$ \frac{\rho_i(r_S)}{c_i} = \frac{\alpha_i e^{-\Delta \phi(r_S)}}{(1 - \alpha_i) + \alpha_i e^{-\Delta \phi(r_S)}} , $$

with $\Delta \phi(r_S) = \phi(r_S) - \phi^\infty$. In the same way, one obtains the surface density of the associated (A) groups $A_iH_i$ of type $i$, which we denote by $\rho_i^A(r_S)$,

$$ \frac{\rho_i^A(r_S)}{c_i} = \frac{1 - \alpha_i}{(1 - \alpha_i) + \alpha_i e^{-\Delta \phi(r_S)}} . $$

Obviously,

$$ \rho_i^A(r_S) + \rho_i(r_S) = c_i $$

for all points $r_S$ on the surface. Eq. 4 then is the partial surface density $\rho_i(r_S)$ for given values of pH and $K^i_j$, and a given surface potential caused by the presence of the charged object in the vicinity of the membrane. The main message of the last three equations is that the degree to which a certain ionizable group dissociates, now depends on its position on the surface. As a result of such a spatial dependence of the degree of dissociation, a 2D surface-charge distribution forms. Eq. 6 states, in essence, that the surface groups are immobile: a group at $r_S$ can dissociate or not, but it can never leave its position, so that the surface density of the dissociated and associated species must everywhere add up to $c_i$.

Things are different if the surface groups can freely move in the interfacial plane. There are now two possibilities for the surface groups to respond to the surface potential $\phi(r_S)$. The first is the old one, the charge-regulation mechanism of adjusting the degree of dissociation to $\phi(r_S)$, which is still effective, as in the case of immobile ions. However, in addition, the free energy of the system can now be lowered further by allowing the surface charges to move to their most favorable position in the 2D surface potential $\phi(r_S)$.

The quantity that governs the movement of the surface groups is the set of chemical potentials $\mu_i$ for all types of surface groups. They regulate the exchange of surface groups with a reservoir. A change of sites between two groups of type $i$ and $j$ at lattice positions $r_i$ and $r_j$ is then to be understood as a process consisting of four steps: transferring particle at $r_i$ to the reservoir (energy change $-\mu_i$), putting ion of type $j$ from the reservoir to site $r_j$ ($+\mu_j$), removing particle at $r_j$ ($-\mu_j$) to the reservoir and inserting particle of type $i$ at $r_i$ ($\mu_i$). The net energy change for a site change of two groups is thus zero, which is why we say that the groups can move freely. If, however, there is a $r_S$ dependence of the surface potential, an exchange of sites can cause a change of energy, because it is now the $r_S$-dependent electrochemical potential $\mu_i - q_i \phi(r_S)$ rather than the chemical potential that regulates the exchange of sites.

With these few remarks, it should have become clear that the case of mobile surface groups is not simply a straightforward generalization of the results obtained for immobile ions, but that another charge-regulating mechanism is allowed for, and that more input parameters, as the chemical potentials of all groups, must now be incorporated into the theory. Starting from the grand-canonical partition function, we derive, in the next section, the following for the partial surface density of mobile ions of type $i$,

$$ \rho_i(r_S) a^2 = \frac{c_i a^2 \alpha_i e^{-q_i \phi(r_S)}}{\sum_{j=1}^M c_j a^2 (1 - \alpha_j) + \alpha_i e^{-q_i \phi(r_S)}} , $$

which is the pendant of Eq. 4, now for the case of mobile surface groups. We will also show that Eq. 5, for the case of mobile ions, becomes

$$ \rho_i^A(r_S) a^2 = \frac{c_i a^2 (1 - \alpha_i)}{\sum_{j=1}^M c_j a^2 (1 - \alpha_j) + \alpha_i e^{-q_i \phi(r_S)}} , $$

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and one can recognize already that Eq. 6 is no longer valid, a feature that best shows the basic difference between the case of mobile and immobile ions. We continue this discussion after having derived Eqs. 7 and 8.

Once we know $\rho_i(r_i)$ for all group types $i$, we can calculate the total surface charge density distribution $\rho(r_s)$,

$$\rho_i(r_s) = \sum_{i=1}^{M} q_i \rho_i(r_i), \quad (9)$$

which, via Eq. 7, still depends on the 2D surface potential $\phi(r_s)$. So far, we have assumed this surface potential to be a quantity known a priori. In practice, the spatially dependent electrostatic potential $\phi(r)$, and with it $\phi(r_s)$, must be calculated in a self-consistent way from the PB BVP in which $\rho_i(r_s)$ (and thus $\phi(r_s)$) enter as boundary condition (see section DNA Near an Oppositely Charged Planar Membrane).

**THEORY**

We start with the grand partition function for a multicomponent electrolyte consisting of $Q$ different types of ions, free to move in the three-dimensional configuration space $G \cap G^*$, where $G$ is the configuration space for the whole system and $G^* = S \cup C$. $S$ is a 2D smooth manifold embedded in $G$, and $C$ is the region occupied by an additional arbitrary distribution of fixed charges, denoted by $\sigma(r)$, located somewhere in $GS$. On $S$, we define an regular lattice, i.e., the area per site is constant. Each site is occupied by one out of $M$ different surface groups. The area per site can be understood as the size of the surface group; all surface groups are thus assumed to be of the same size. A surface group on site $i$ can be in one of two possible states (associated/dissociated), which yields in total $2M$ possible states per site. We label each site $n$ with a state variable $S_n$ similar to the spin variable in the Ising model. $S_n$ can be any integer between 1 and $2M$. We introduce the particle density for the mobile electrolyte ions of type $j$ in $G \cap G^*$,

$$\rho_j^m(r) = \sum_{k=1}^{N_j} \delta(r - r_k), \quad (10)$$

where $r_k$ denotes the position vector of particle $k$ of species $j$, and $N_j$ the total number of particles of type $j$. Similarly, we write for the density of surface groups of type $i$ in $S$,

$$\rho_i(r) = \sum_{n=1}^{P} \delta_{S_n} \delta(r - r_n). \quad (11)$$

Here, $P$ is the number of lattice sites and $r_n$ is the position vector of lattice site $n$. All together, we have three different sorts of ions, mobile electrolyte ions (density $\rho_j^m(r)$) in $G \cap G^*$, fixed ions in $G \cap S$ (density $\sigma(r)$) and charged/un-

charged surface groups (density $\rho_i(r)$) in $S$, and the total charge density reads accordingly,

$$\rho^{tot}(r) = \sum_{j=1}^{Q} q_j \rho_j^m(r) + \sum_{i=1}^{2M} q_i \rho_i(r) + \sigma(r), \quad (12)$$

with $q_j$ ($q_i$) being the valency of the surface groups (bulk ions) ($q_i = 0$ for an uncharged group). These charges interact via the Coulomb interaction, $\nu(r, r')$, so that the Hamiltonian of our system takes the simple form

$$H(\{r_i\}, \{S_n\}) = \frac{1}{2} \int dr \int dr' \rho^{tot}(r) \nu(r, r') \rho^{tot}(r'). \quad (13)$$

We introduce the fugacities $\lambda_j = e^{\beta \mu_j / \lambda^3}$ and chemical potentials $\mu_j$ for the $Q$ different types of bulk ions ($\lambda_i$ the thermal wave length), and the fugacities and chemical potentials for the $2M$ different types of surface groups, $\lambda_i = e^{\beta \mu_i / \lambda^3} (i = 1, \ldots, 2M)$. The grand partition function of this system can then be written in the form,

$$\Xi = \prod_{j=1}^{Q} \sum_{N_j=0}^{\infty} \frac{\lambda_j^{N_j}}{N_j!} \int_{G \cap G^*} \left( \prod_{k=1}^{N_j} dr_k \right) P \prod_{n=1}^{2M} \sum_{S_n=1}^{2M} \left( \prod_{i=1}^{2M} \lambda_i^{S_n} \right) \times e^{-H(\psi, \{r_i\}, \{S_n\})}. \quad (14)$$

With Eq. 14, we have brought our problem into a form well suited for applying standard field-theoretical methods. The details of what follows now are not specific to this calculation, and has been described elsewhere; we refer the reader, for example, to Netz and Orland (1999, 2000) Netz (1999, 2000), and continue with a more condensed description of the calculation. After renormalizing the fugacities to get rid of diagonal terms, a Hubbard–Stratonovich transformation leads us to

$$\Xi = \prod_{j=1}^{Q} \sum_{N_j=0}^{\infty} \frac{\lambda_j^{N_j}}{N_j!} \int_{G \cap G^*} \left( \prod_{k=1}^{N_j} dr_k \right) \times \prod_{n=1}^{2M} \sum_{S_n=1}^{2M} \left( \prod_{i=1}^{2M} \lambda_i^{S_n} \right) e^{-H(\psi, \{r_i\}, \{S_n\})}, \quad (15)$$

where

$$H(\psi, \{r_i\}, \{S_n\}) = \frac{k_B T}{8 \pi e^2} \int_G \left( \nabla \psi(r) \right)^2 e(r) \, dr + \int_G \int_G \nabla \psi(r) \, \nabla \psi(r') \, \rho^{tot}(r) \, dr \rho^{tot}(r') \, dr' - \int_{G \cap G^*} \int_{G \cap G^*} \int_{G \cap S} \sum_{j=1}^{Q} \rho_j^m(r) \, h_j(r) \, dr \, \rho_j^m(r) \, h_j(r), \quad (16)$$

with $\psi$ being a fluctuating field and $e(r)$ a dielectric field defined on $G$. To be able to calculate later the expectation
values of the charge density operators, we introduce at this point, the generating fields \( h_i(\mathbf{r}) \) and \( h_l(\mathbf{r}) \), which couple to the densities \( \rho_i(\mathbf{r}) \) and \( \rho_l(\mathbf{r}) \), respectively. Resolving our abbreviations in Eq. 16, Eqs. 10, 11, and 12, performing the sums and making use of the series expansion of the exponential function, we can bring the partition function into the form,

\[
\Xi = \int \frac{\mathcal{D}\psi}{\sqrt{\det \nu}} e^{-H_{\psi}[\psi]} \prod_{n=1}^{P} \sum_{S_n=1}^{2M} \prod_{i=1}^{2M} (\lambda_n e^{h_i(r_n)} - i\phi_n(r_n)) \delta_{\nu},
\]

with the abbreviation

\[
H_{\psi}[\psi] := \frac{k_B T}{8\pi e^2} \int_G d\mathbf{r} (\nabla \psi(\mathbf{r}))^2 e(\mathbf{r}) + \int_G d\mathbf{r} \sigma(\mathbf{r}) i\psi(\mathbf{r}) - \frac{\phi}{\lambda_1} \int_{G_1 G^*} d\mathbf{r} e^{h_i(r_i) - \phi(\mathbf{r})}. \tag{17}
\]

This can be further simplified to

\[
\Xi = \int \frac{\mathcal{D}\psi}{\sqrt{\det \nu}} e^{-H_{\psi}[\psi]} \prod_{n=1}^{P} \sum_{S_n=1}^{2M} \prod_{i=1}^{2M} (\lambda_n e^{h_i(r_n)} - i\phi_n(r_n)). \tag{18}
\]

If the physical properties of the system vary on a much larger scale than the size of a lattice site, we can avoid the sum over a discrete lattice. Introducing the functional,

\[
H_3[\psi] := -\frac{1}{a^2} \int_S d\mathbf{r} \ln \left( \sum_{i=1}^{2M} \lambda_i e^{h_i(r_i) - \phi(\mathbf{r})} \right), \tag{19}
\]

we can rewrite Eq. 18 as

\[
\Xi = \int \frac{\mathcal{D}\psi}{\sqrt{\det \nu}} e^{-H_{\psi}[\psi] - H_3[\psi]} \tag{20}
\]

We approximate the integral over all possible configurations by the configuration for which the partition function is stationary (saddle-point approximation),

\[
\Xi_{SP} = e^{-H_{\psi}[\psi_{SP}] - H_3[\psi_{SP}]}, \tag{21}
\]

where the mean-field potential \( \psi_{SP} \) results from,

\[
\frac{\delta(H_{\psi} + H_3)}{\delta\psi(\mathbf{r})} \bigg|_{\psi=\psi_{SP}}^{\mu} = 0. \tag{22}
\]

From the mean-field partition function, Eq. 21, we can now derive all quantities needed for the following. We start with the densities of the electrolyte ions; it can be obtained with the help of the functions \( h_i(\mathbf{r}) \),

\[
\rho_i(\mathbf{r}) = \frac{\delta \ln \Xi_{SP}}{\delta h_i(\mathbf{r})} \bigg|_{h_i=h_l=0} \quad \mathbf{r} \in G \cap G^*, \tag{23}
\]

which yields

\[
\rho_i(\mathbf{r}) = \lambda_i e^{-\phi(\mathbf{r})} \quad \mathbf{r} \in G \cap G^*, \tag{24}
\]

where we have introduced \( \phi := i\psi_{SP} \). The bulk ion fugacities \( \lambda_i \) may be determined from the ion densities far away from the surface \( S \) and the fixed charge distribution \( \sigma \) where one may safely assume that \( \rho_i(\mathbf{r}_m) = c_i^0 \) with \( c_i^0 \) being the concentration of electrolyte ions of type \( j \) \((\sum_{i=1}^{M} q_i \rho_i = 0) \). This leads to \( \lambda_i = c_i^0 \). The densities of the surface groups in mean-field approximation can be calculated from \( (\mathbf{r}_S = \mathbf{r} \in S) \)

\[
\rho_i(\mathbf{r}_S) = \frac{\delta \ln \Xi_{SP}}{\delta h_i(\mathbf{r}_S)} \bigg|_{h_i=h_l=0}, \tag{25}
\]

resulting in the expression

\[
\rho_i(\mathbf{r}_S) = \frac{1}{a^2} \sum_{j=1}^{M} \lambda_j e^{-\phi(\mathbf{r}_S)}. \tag{26}
\]

Again the fugacities need to be determined. Henceforth, we denote the density of the associated species by \( \rho_i^A \), the fugacity of the associated species by \( \lambda_i \), and that of the dissociated one by \( \lambda_i \lambda_i^D \) \((i \in \{1, \ldots, M\}, \lambda_i^D = e^{\mu_D}) \). Furthermore, we set the valencies of the neutral surface groups to zero. For \( \mathbf{r}_S \) far away from any fixed charge distribution \( \sigma(\mathbf{r}) \) we expect a homogeneous density,

\[
a^2 \rho_i^\infty + a^2 \rho_i^\infty \lambda^D = a^2 c_i \]

\[
= \frac{\lambda_i \lambda_i^D e^{-\phi(\mathbf{r})} + 1}{\sum_{i=1}^{M} \lambda_i \lambda_i^D e^{-\phi(\mathbf{r})} + 1}, \tag{27}
\]

and hence,

\[
\lambda_i = \frac{a^2 c_i}{1 - a^2 c_i} \sum_{j=1}^{M} \lambda_j \frac{\lambda_j^D e^{-\phi(\mathbf{r})} + 1}{\lambda_j^D e^{-\phi(\mathbf{r})} + 1}. \tag{28}
\]

This is an eigenvalue equation for the fugacities for the eigenvalue 1 with the eigenvector,

\[
\lambda_i = \frac{c_i a^2}{1 + \lambda_i^D e^{-\phi(\mathbf{r})}}. \tag{29}
\]

We determine the \( \lambda_i^D \) by means of the mass action law, Eqs. 2 and 3. At infinity, the ratio of \( \rho_i^\infty \) and \( \rho_i^\infty \lambda^D = c_i - \rho_i^\infty \) must
be equal to \( \alpha_i/(1 - \alpha_i) \) as defined in Eq. 3. In contrast, Eq. 26 yields \( \rho_i^\alpha/\rho_i^\beta = \lambda_i^D e^{-\alpha_i} \) so that
\[
\lambda_i^D = e^{\phi_r^+} \frac{\alpha_i}{1 - \alpha_i}.
\] (30)

Inserting the expression for \( \lambda_i \) and \( \lambda_i^D \) in Eq. 26 leads us directly to the main result of this paper, Eqs. 7 and 8.

The mean-field partition function provides us also with the grand potential, \( \beta \Omega = -\ln \Xi_{SP} \bigg|_{h_n = h_0} = H_G[\phi/i] + H_S[\phi/i] \bigg|_{h_n = h_0} \). (31)

It is important to realize that this equation is only valid if we use the mean-field potential defined by Eq. 22 in \( H_G \) and \( H_S \). Using Eqs. 17 and 19, we obtain for the grand potential
\[
\beta \Omega = -\frac{k_B T}{8 \pi e^2} \int_G \nabla \phi \phi(r) \psi(r) + \sum_{j=1}^M c_j \int_G e^{-\phi_j(r)}
\]
\[
- \frac{1}{\alpha^r_s} \int_S \ln \left( \sum_{i=1}^M c_i^e \left( \alpha_i e^{-\phi_i(r)} + (1 - \alpha_i) \right) \right).
\] (32)

An interesting property of the system is that the partition function factorizes due to the mean-field description,
\[
\Xi_{SP} = Z_G[\phi] Z_S[\phi],
\] (33)

with \( Z_G[\phi] := \exp\{ -H_G[\phi/i] \} \) and \( Z_S[\phi] := \exp\{ -H_S[\phi/i] \} \). Therefore, it is easy to extend our model to several independent lattice systems. Let us denote the \( k \)th of these lattices by \( S_k \). The partition function for each lattice factors itself and is just the product of the partition functions of each single lattice site as can be seen in Eq. 18. Allowing on \( S_k \), \( 2M_k \) different states on each site, we get for the partition sum of this sub-system \( Z_{S_k} \)
\[
Z_{S_k} = \prod_{n=1}^{2M_k} \lambda_i^D e^{\phi_i^+(r) - \phi_i^-(r)}
\] (34)

which, for a slowly varying field \( \phi \), can be approximated by
\[
Z_{S_k} = \exp \left( \frac{1}{\alpha^r_k} \int_{S_k} \ln \left( \sum_{i=1}^{2M_k} \lambda_i^D e^{\phi_i^+(r) - \phi_i^-(r)} \right) \right).
\] (35)

It is not needed that the lattices are spatially distinct. Due to this property, we are capable of describing a system of several interpenetrating lattices and thus modeling a surface with various immobile surface groups. The partition function for a system with \( L \) different lattices hence reads,
\[
\Xi_{SP} = Z_G[\phi] \prod_{k=1}^L Z_{S_k}[\phi].
\] (36)

If we determine the fugacities for each lattice similar to the procedure for one lattice done above, we arrive at the following expression for the grand potential:
\[
\beta \Omega = -\frac{k_B T}{8 \pi e^2} \int_G \nabla \phi \phi(r) \psi(r) + \int_G \nabla \nabla \phi \phi(r) \psi(r)
\]
\[
- \sum_{j=1}^M c_j \int_{G^*} e^{-\phi_j(r)} - \frac{1}{\alpha^r_k} \int_{S_k} \ln \left( \sum_{i=1}^{2M_k} c_i^e \left( \alpha_i e^{-\phi_i(r)} + (1 - \alpha_i) \right) \right),
\] (37)

where \( G^* \) now becomes \( \cup_k S_k \). If we specialize to one ionizable surface group on each lattice, i.e., two different states on each lattice site (\( M_k = 1 \)), we readily arrive at the densities given by Eqs. 4 and 5 above.

Note that it is an inherent assumption for our present treatment of the model, that the fixed charge distribution perturbs the surfaces \( S_k \) only locally. Only under this condition we can chose the fugacities in the way we did above. Furthermore, we can show that, in the case of local perturbation, the relative number fluctuation of the particle of type \( i \) in the surface goes like \( 1/\sqrt{N} \), where \( N \) is the total number of particle in the surface. Thus, in the case of large particle numbers, i.e. large surfaces, our description of the system is equivalent to the case where the particle numbers are fixed.

**DISCUSSION**

Having derived the two expressions, Eqs. 7 and 8, we now want to convey a more intuitive understanding of their meaning. For that purpose, we consider a few simple cases. We re-iterate beforehand that our result relies on the existence of a regular lattice with lattice constant \( a \) superposed on the surface, and that it is thus valid only if one can assume that all membrane components are of the same size and arrangeable on such a lattice. In both Eqs. 7 and 8, \( a^2 \) appears in conjunction with surface densities \( c_i \) (or \( \rho_i \)), and the product \( c_i a^2 (\rho_i a^2) \) can be understood just as the surface fraction of species \( i \). Because the surface is closely packed with groups, \( \sum_{i=1}^{M_k} c_i a^2 = 1 \).

The simplest case is that the potential does not depend on the surface position vector \( \mathbf{r}_s \), either because the charged surface is well separated from other charged objects in the solution, or because of symmetry reasons (e.g., two parallel planar walls). Then \( \Delta \phi(\mathbf{r}_s) = 0 \) and Eqs. 7 and 8 reduce to
with a surface composed of two sorts of fully dissociated surface groups ($\alpha_1 = \alpha_2 = 1$) of opposite charge, $q_1 = -q_2 = q$. Eq. 7 then leads to

$$\rho_c(r_S) a^2 = q a^2 (\rho_1(r_S) - \rho_2(r_S))$$

$$= q \frac{c_1 a^2 e^{-q_1 \Delta \phi(r_S)}}{c_1 a^2 e^{-q_1 \Delta \phi(r_S)} + (1 - c_1 a^2)}$$

which becomes

$$\rho_c(r_S) a^2 = -q \tanh q \Delta \phi(r_S),$$

if $c_1 a^2 = c_2 a^2 = \frac{1}{2}$. If $\Delta \phi(r_S) = 0$, the surface-charge density in Eq. 43 becomes zero. If, however, there is a perturbation of the surface potential due to the presence of another charged object, then the surface ions are taking part in a 2D screening of the object and escape from, or assemble in,
regions where $\Delta \phi(r_s)$ departs from zero. The surface is then locally charged.

To give an alternative access to our results, let us reformulate Eqs. 7 and 8 in terms of chemical potentials. With $\alpha_i = p_i^w/c_i$, Eq. 30 becomes

$$e^{\beta \mu_i} = \lambda_i^D = \frac{p_i^w e^{\phi_i^+ \epsilon}}{c_i - \rho_i^w},$$

(44)

which we insert in Eq. 29 to find the chemical potentials of the associated surface groups,

$$\frac{e^{\beta \mu_i}}{e^{\beta \mu_{i,M}}} = \frac{c_i - \rho_i^w}{c_M - \rho_M^w}.$$  

(45)

The charged groups are sensitive to the surface potential, and we thus have to consider the electrochemical potential,

$$\beta \mu_{i,M}(r_s) = \beta \mu_i + \beta \mu_i^D - q_i \phi(r_s),$$

(46)

which is $r_s$-dependent if $\Delta \phi(r_s) \neq 0$. Inserting Eqs. 45 and 46 in Eq. 44, one obtains

$$\frac{e^{\beta \mu_{i,M}}}{e^{\beta \mu_{i,M}}} = \frac{\rho_i^w}{\rho_M^w}.$$  

(47)

These equations provide us with an expression for $c_i/c_j$ in terms of the chemical/electrochemical potentials, and Eqs. 7 and 8 can then be brought into the form,

$$\rho_i(r_s) a^2 = \frac{q e^{\beta \mu_{i,M}(r_s)}}{\sum_{j=1}^M (e^{\beta \mu_{i,M}(r_s)} + e^{\beta \mu_{j,M}(r_s)})},$$

(48)

and

$$\rho_i^M(r_s) a^2 = \frac{q e^{\beta \mu_{i,M}(r_s)}}{\sum_{j=1}^M (e^{\beta \mu_{i,M}(r_s)} + e^{\beta \mu_{j,M}(r_s)})}.$$  

(49)

These two expressions lead us to a simple statistical explanation of our result, suggested by the fact that the denominators in both expressions have the appearance of partition functions. Changing from the continuous description to a discrete counting of surface groups, $r_s \rightarrow r_n$, one may regard every single surface group at $r_n$ as an independent subsystem. Each surface site $r_n$ is occupied by a group which can be in one of $2M$ possible energy states, $\mu_{i,1}(r_n) \ldots \mu_{i,M}(r_n)$, $\mu_1 \ldots , \mu_M$. The partition function of this subsystem then is

$$Z_n = \sum_{i=1}^M (e^{\beta \mu_{i}} + e^{\beta \mu_{i,M}(r_n)}),$$

(50)

from which the probability $P$ of finding the particle in state $\mu_{i,1}(r_n)$ follows according to the basic rules of statistical mechanics,

$$P(\mu_{i,1}(r_n)) = \frac{e^{\beta \mu_{i,1}(r_n)}}{Z_n}.$$  

(51)

This is Eq. 48, which is thus understood as the probability that the surface group is in one specific discrete energy state out of $2M$ possible, namely in the state $\mu_{i,1}(r_n)$. Accordingly, Eq. 49 is interpreted as the probability of finding the surface group in one of the energy states $\mu_i$ corresponding to an associated group. Regarding the surface as a collection of independent subsystems, one at each lattice site, the partition sum of the whole system can be obtained as a product of Eq. 50 over all lattice sites. This leads us back to Eq. 34. Allowing in the sums of Eqs. 48 and 49 only the term $j = i$ gives us the equivalent expressions for the case of immobile ions. The basic difference between immobile and mobile ions, then, is that, for immobile ions, we have $M$ noninteracting sublattices with two possible states on each site, whereas, for mobile groups, we have just one lattice with $2M$ states on each site.

This interpretation is very intriguing because it allows a direct generalization of our result to the three-dimensional (3D) case. Consider an aqueous $q_+\cdot q_-\cdot$ electrolyte solution in bulk. Suppose the volume of the solution is divided into small cells, with each cell of volume $a^3$ being occupied by either a water molecule or a negative ion or a positive ion. The concentration (volume fraction) of either ion type is $c_b$ ($c_b a^3$). In each cell, there is thus either a water molecule having the chemical potential $\beta \mu_w$ or a positive (negative) ion having the electrochemical potential $\beta \mu_{i} - q \cdot \phi(r)$. As in Eqs. 45 and 47, the chemical potentials are given by the ratio between the volume fraction of water $(1 - 2c_b a^3)$ and the volume fraction of one ion type, $\exp(\beta(\mu_w - \mu_{i})) = c_b a^3(1 - 2c_b a^3)$. The probability $P(\pm)$ of finding the cell at position $r$ being occupied by a particle in state $\mu_{i} - q \cdot \phi(r)$, i.e., by a positive or negative ion, is

$$P(\pm) = \frac{e^{\beta \mu_{i} - q \cdot \phi(r)}}{e^{\beta \mu_{i} - q \cdot \phi(r)} + e^{\beta \mu_{i} - q \cdot \phi(r)} + e^{\beta \mu_w}} = c_b a^3 e^{-q \cdot \phi(r)} e^{-q \cdot \phi(r)} + 1 - 2c_b a^3,$$  

(52)

which is obviously the generalization to 3D of Eq. 51. For $q_+ = -q_-=1$, this leads to a density

$$\rho(r) a^3 = P(+) - P(-) = -2c_b a^3 \sinh \phi(r) + 2c_b a^3 \cosh \phi(r) + 1 - 2c_b a^3,$$  

(53)

which, when placed into the Poisson equation $\nabla^2 \phi = -4\pi \lambda_{bp} \rho$, yields the modified PB equation suggested by Borukhov et al. (Borukhov et al., 1997, 2000; Kralj-Iglic and Iglic, 1996). It takes account of steric effects in electrolytes, and is thus an attempt to overcome one of the major deficiency of standard PB theory, the point-charge approximation, which leads to an unphysically high charge density near charged surfaces, (see Borukhov et al., 1997). Having thus shown the close relationship between our 2D result and the 3D calculation of Borukhov et al. (1997) we now want to set up and solve a full PB BVP.

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The density distribution of the dissociated and associated surface groups, Eqs. 7 and 8, depends on the potential at the surface that has a spatial dependence due to the presence of a charged object near the surface. We now formulate a PB BVP where Eqs. 7 and 8 appear as boundary conditions, and calculate the effective interaction between the object and the surface. As an example, we choose the model system of an infinitely long charged rod interacting with an oppositely charged plate that is densely packed with mobile surface groups. Such a system is realized, for example, by an anionic DNA strand interacting with a supported cationic lipid bilayer, something that has been studied extensively in recent years (Fang and Yang, 1997; Lasic et al., 1997; Maier and Rädler, 1999; Gelbart et al., 2000). Stable multilamellar aggregates of DNA with cationic liposomes have been identified (Lasic et al., 1997; Rädler et al., 1997; Koltsov et al., 1998, 1999; Salditt et al., 1997), which are of special interest because they are possible candidates for nonviral gene-therapy strategies and can serve as vehicles to transport DNA into cells (Firshein, 1989; Behr, 1994; Verma and Somia, 1997; Felgner et al., 1987, 1994; Templeton et al., 1997). Theoretical studies on the stability and organization of such complexes have appeared in literature (Dan, 1997; Harries et al., 2000; Bruinsma and Mashl, 1998), focusing in particular on such issues as the counterion release force (Fleck and von Grünberg, 2001; Sens and Joanny, 2000; Bruinsma and Mashl, 1998; Wagner et al., 2000), the evolution of phases of these complexes (May et al., 2000b; Harries et al., 2000), salt effects on effective interactions (Parsegian and Gingell, 1972; Mashl et al., 1999), and the effect of surface ion mobility on screening (Menes et al., 1998). Numerous other theoretical and experimental adsorption studies of polyelectrolytes other than DNA can be found in Fleck et al. (1993).

In particular, it has been shown that spatial inhomogeneities in the membrane surface-charge density in response to interactions with the DNA can have a significant effect on the phase behavior and stability of DNA/cationic lipid complexes (Harries et al., 2000). However, only whole complexes of DNA plus membranes have been studied theoretically, but never the problem of a single DNA molecule in interaction with a membrane. Against this background, the example considered in this section is certainly useful not only to clarify the usage of Eqs. 7 and 8 in an effective-interaction calculation, but also to study exemplarily the effect of surface-group mobility for a single DNA interacting with a lipid membrane. Important in the following is the pH-dependent charge fraction parameter \( \alpha_i = \rho_i^0/c_i \), which, for simplicity, we take as an independent input parameter in the following calculations. If one wishes to apply our results to a specific membrane, one first has to formulate the specific charge-regulating chemical reaction at the membrane’s surface (which need not be our Eq. 1), then write down the law of mass action as in Eq. 2, and use this to define \( \alpha_i \) in the same way as we have done in Eq. 3 for our reaction in Eq. 1. The inset of Fig. 6 shows the degree of dissociation \( \alpha_i \) as a function of the difference \( pK_a = \text{pH for a specific choice of parameters.} \)

We now assume that the surface \( S \) in the Theory section is the \( x-y \) plane at \( z = 0 \), which divides the configuration space into two parts, an aqueous 1:1 electrolyte solution of salt concentration \( c_i \) in \( G_> = \{ r | z > 0 \} \), \( G_z \) (region of the cylinder) with a dielectric constant \( e_> \), and a dielectric medium with a dielectric constant \( e_< \) at \( z < 0 \) \((G_<)\). A cylinder, having a radius \( r_0 \), a line charge density \( \tau \), and being made of a material with a dielectric constant \( e_r \), is located at \((x = 0, z = h)\), with its axis parallel to the \( y \)-axis. The dielectric field is thus given by,

\[
\begin{align*}
\epsilon(r) = e_\tau \theta(z) + e_\tau \theta(-z) + e_i \theta(c(r) - c),
\end{align*}
\]

with \( c = -c(r) \) and \( c(r) = \sqrt{x^2 + (z - h)^2 - r_0^2} \) determining the region \( G_z \) of the cylinder. Eq. 22 then gives, with Eqs. 29 and 30,

\[
0 = -\frac{k_B T}{4 \pi \epsilon^2} \nabla (\epsilon(r) \nabla \psi(r)) + i \sigma(r)
+ i c_i \theta(z) e^{i(\epsilon(r))}
+ i c_i \theta(-z) e^{-i(\epsilon(r))}
+ \frac{i \delta(z)}{\epsilon^2} \sum_{i=1}^M q_i \epsilon_i \alpha_i e^{-i q_i \Delta \phi(r)}
+ i \frac{\delta(z)}{\epsilon^2} \sum_{i=1}^M q_i \epsilon_i \alpha_i e^{i q_i \Delta \phi(r)}
+ (1 - \alpha_i),
\]

where \( \sigma = \partial \psi / \partial n \). The charge distribution of fixed charges is now given by the charges on the cylinder surface, \( \sigma = e_i / 2 \pi r_0 \). We furthermore assume \( e_\tau \to e_\tau = 0 \) and \( e_i / e_\tau \to 0 \), because water has an extraordinarily high dielectric constant compared to most other materials. Writing \( \psi = i \psi_{sp} \), with \( \psi_{sp} \) satisfying Eq. 55, and using the definition of \( \epsilon(r) \) (Eq. 54), we arrive at the following PB BVP:

\[
\begin{align*}
\Delta \phi(r) &= \kappa \sinh \phi(r) \quad r \in G_>
\quad \n_\tau \nabla \phi(r) = 2 \lambda_{Bz}/r_0 \quad r \in \partial G_z
\quad \n_\tau \nabla \phi(r) = -4 \pi \lambda_B \rho_c(r) \quad r \in S,
\end{align*}
\]

with

\[
\rho_c(r) = \frac{\sum_{i=1}^M q_i \epsilon_i \alpha_i e^{-q_i \Delta \phi(r)}}{\sum_{i=1}^M q_i \epsilon_i \alpha_i e^{-q_i \Delta \phi(r)} + (1 - \alpha_i)},
\]

and \( \lambda_B := e^2 / e_\tau \), \( \partial G_z \) for the cylinder surface and \( \kappa^2 = 8 \pi \lambda_B \epsilon_i \). \( \n_\tau \) and \( \n_\tau \) are two unit vectors, normal to the surfaces \( \partial G_z \) and \( S \), respectively, and pointing both into the region \( G_\tau \). Note that Eq. 57 is the membrane surface-charge density \( \rho_c(r) \) of Eq. 9 with the partial surface-charge den-
sity $\rho(r_s)$ given in Eq. 7. The grand potential, Eq. 32, now becomes

$$\beta \Omega = -\frac{1}{8\pi\lambda_B} \int_{G_\perp} dr (\nabla \phi(r))^2$$

$$- \frac{\tau}{2\pi r_0} \int_{\partial G_\perp} dr \phi(r) - 2c_s \int_{G_\perp} dr \cosh \phi(r)$$

$$- \frac{1}{a} \int_S dr \ln \left( \sum_{i=1}^M c_i a^2 (\alpha_i e^{-q_i \Delta \phi(r)} + (1 - \alpha_i)) \right),$$

which can be transformed into

$$\beta \Omega = \frac{1}{8\pi\lambda_B} \int_{G_\perp} dr (\nabla \phi(r))^2$$

$$+ 2c_s \int_{G_\perp} dr [\phi(r) \sinh \phi(r) - \cosh \phi(r)]$$

$$- \frac{1}{a} \int_S dr \ln \left( \sum_{i=1}^M c_i a^2 (\alpha_i e^{-q_i \Delta \phi(r)} + (1 - \alpha_i)) \right).$$

(58)

(59)

We solve the BVP in Eq. 56 numerically with a commercial finite-element program. To improve the resolution, we have first transformed the region $G_\perp$ onto a rectangular domain by using bicylindrical coordinates. Calculating $\phi(r)$ for a sequence of rod-membrane distances $h$, inserting it each time into Eq. 59, one obtains $\beta \Omega$ as a function of $h$, which is nothing but the effective rod-membrane interaction potential. To calculate the distribution of surface ions in the plane of the membrane, the solution $\phi$ must be placed into Eq. 7 or Eq. 9.

The input parameters of our calculation are $\tau$, $r_0$ for the cylinder, and $\lambda_B$ and $c_s$ (or $\kappa$) for the electrolyte solution. Fixed throughout are $\lambda_B = 0.714$ nm, and $\tau$ and $r_0$, which are both chosen to simulate a DNA molecule, $\lambda_B \tau = 4$ and $r_0 = 1$ nm. The salt concentration is varied. We first assume that the surface is composed of only two types of lipids, $M = 2$, with valencies $q_1$ and $q_2$ and charge ratios $\alpha_1$ and $\alpha_2$, but with the same head group size $a^2$. The mixture is characterized by specifying the surface fraction of species one, $c_1 a^2$, which we choose to be either 0.1 (as in Rädel et al., 1997; Wagner et al., 2000; Kennedy et al., 2000) or 0.5 or 1.0. The homogeneous surface-charge density far away from the rod, then, is $\rho_s a^2 = q_1 c_1 a^2 \alpha_1 + q_2 (1 - c_1 a^2) \alpha_2$. The head group size of lipids is ranging between 0.4 and 0.8 nm$^2$ (Shinitzky, 1993; Silver, 1985). In addition to these values, we consider the extreme size of 2 nm$^2$ for a head-group to obtain more pronounced finite size effects.

**In-plane distribution of mobile surface groups for an almost adsorbed DNA molecule**

We first concentrate on the mobility of the surface groups; effects arising from the additional dissociation are discussed later. Let us start by considering a rod that almost touches the $x$-$y$ plane, i.e., $h = r_0 + 0.1$ nm. The plane is composed of a mixture of positively charged ($\alpha_1 = 1$, $q_1 = 1$) and neutral ($\alpha_2 = 0$, $q_2 = 0$) mobile surface groups, and we calculate from Eqs. 56 and 39 the distribution of the charged surface groups in the plane of the membrane.

This distribution is translationally invariant along the axis of the cylinder and has a mirror symmetry with respect to the $x$-$z$ plane, so that it suffices to plot the distribution in the direction of the positive $x$ axis. Figure 1 shows the in-plane distribution of the charged surface groups $\rho_i(x)/c_1$ for different salt concentrations ($\kappa^{-1} = 0.3, 1, 10, and 100$ nm) and different head-group sizes ($a^2 = 0.4$ nm$^2$ and $a^2 = 2$ nm$^2$). The surface fractions are $c_1 a^2 = 0.1$ (Fig. 1 $A$ and $B$) and $c_1 a^2 = 0.5$ (Fig. 1 $C$ and $D$). $\kappa^{-1} = 1$ nm corresponds to the physiological salt concentration of 0.1 M, whereas $\kappa^{-1} = 100$ nm is about the degree of de-ionization that can be achieved with modern ion-exchangers.

Due to their mobility, the positively charged surface groups can move to the negatively charged cylinder adsorbed at $x = 0$. As in a perfect bulk environment, the cylinder is screened by oppositely charged ions, but now this is a screening of ions that are confined to the plane. Clearly, such a 2D screening cannot be perfect, and the total numbers of screening surface groups is smaller than the total number of charges on the cylinder. In other words, there are still mobile ions of the electrolyte solution involved in the screening of the cylinder. The distributions in Fig. 1 reveal that the ratio of screening electrolyte ions to screening surface ions is not a fixed quantity, but changes with $a^2$ and $\kappa^{-1}$. For example, if the concentration of salt in bulk is reduced, the number of screening surface ions increases.

Mobility allows an inhomogeneous surface ion distribution, and, locally, the surface density of ions can become much larger than it is at infinite $x$. Mobility actually means that neutral surface groups are replaced by charged groups, or vice versa. This process naturally ends if all possible replacements are made. In the case of $c_1 a^2 = 0.1$, this happens at a density of $\rho_i/c_1 = 10 = 1/(c_1 a^2)$ when all neutral groups are replaced by charged groups. This limit, as we can see from Fig. 1 $B$, is reached for $a^2 = 2$ nm$^2$, $\kappa^{-1} = 100$ nm, i.e., only for very large surface groups or low salt concentration. If this packing effect sets in, it has a pronounced impact on the whole distribution, which we see is spread over a much larger $x$ range now. This can be attributed to the fact that, due to the packing effect, the surface
ions can no longer screen the fixed cylinder charges in the best way possible so that the Coulomb field becomes longer ranged now.

Another interesting feature of the curves in Fig. 1 is the peak in the density distribution at $x/r_0 = 0.1$ for $\kappa^{-1} = 100$ nm and $a^2 = 0.4$ nm$^2$. Because the electrolyte ions are hardly taking part in the screening of the cylinder and the surface ions are too small for any packing effect to occur, the distribution can accurately trace the 2D projection of the electric field of the cylinder; the peak occurs at $x = r_0$. The distribution for $x < 1$ nm follows just the curvature of the cylinder. Increasing the salt concentration in the electrolyte destroys this effect, because the 3D screening of the electrolyte ions between the rod and the membrane now prevents that the shape of the rod can be seen by the surface ions.

What determines the density value at $x = 0$? To understand this value, we consider the dimensionless quantity $\lambda_B(x) := 2\pi r_0 \lambda_B \rho_1(x)$ by means of which $\rho_1$ becomes directly comparable to the line charge density $\lambda_B \tau$ on the cylinder. Figure 2 shows $\lambda_B(x)$ for $a^2 = 0.4, 0.8, 2$ nm$^2$ at an intermediate salt concentration of $\kappa^{-1} = 50$ nm ($c_1a^2 = 0.1$). The plot reveals that the surface-charge density distribution $\rho_1(x)c_1$ at $x = 0$ reaches a value such that $\lambda_B(x)$ becomes equal to the line-charge density $\lambda_B \tau = 4$ of the cylinder, which clearly means optimal screening of the cylinder.

**FIGURE 1** Surface-charge density distribution $\rho_1(x)c_1$ of mobile, positively charged surface groups in a membrane, for a negatively charged rod (DNA molecule), which almost touches the membrane ($h = r_0 + 0.1$ nm) at $x = 0$. The surface fractions of positively charged surface groups are $c_1a^2 = 0.1$ in (A) and (B) and $c_1a^2 = 0.5$ in (C) and (D). For each surface fraction, we consider surface groups of size $a^2 = 0.4$ nm$^2$ and $a^2 = 2$ nm$^2$. The numbers at the curves specify the salt concentration $\kappa^{-1}$. For low salt concentration ($\kappa^{-1} = 10$ and 100 nm), one can clearly recognize the effect due to the packing of the surface groups (Panels B and D). The packing effect results in a spread of the distribution over a much larger $x$ range.
charges. A prerequisite for this optimal screening however is that the surface ions are small enough to be packed so closely. For example, the \( a^2 = 2 \text{ nm}^2 \) curve, with \( \lambda\varphi(0) \) remaining well below 4, demonstrates that packing effects can prevent optimal screening.

With this result, we can derive a criterion beyond which value of \( a^2 \), the finite size of the surface groups becomes effective. Using \( \lambda\varphi(0) \) and \( \lambda\varphi(0) = 2\pi r_0 \lambda\varphi(0) \), plus the fact that the maximum density of ions in the surface is \( a^{-2} \), we find that \( a^2 \) must be greater than \( 2\pi r_0 \tau^{-1} \) for packing effects to occur, something that we have successfully checked by explicit calculations for other values of \( r_0 \) and \( \tau \). The critical value for \( a^2 \) is 1.12 nm\(^2\) for a DNA molecule with \( \lambda\varphi = 4 \) and a radius of \( r_0 = 1 \text{ nm} \), and is thus much larger than the head groups of typical lipids. A saturation effect like that shown by the curve for \( a^2 = 2 \text{ nm}^2 \) in Fig. 2 is therefore not to be expected in real DNA/membrane systems. Other finite size effects, however, are possible; for instance, the disappearance of the peak at \( x = r_0 \) in going from \( a^2 = 0.4 \text{ nm}^2 \) to \( a^2 = 0.8 \text{ nm}^2 \) in Fig. 2.

**Effective interaction for variable rod-membrane distances**

We now vary the rod-wall distance \( h \). In the following, we present all quantities per unit charge on the cylinder. In Fig. 3, we show the grand potential as a function of \( h \), for \( \kappa^{-1} = 50 \text{ nm} \), \( c_1 a^2 = 0.1 \), \( a^2 = 0.4 \), 0.8, and 2 nm\(^2\). This is the set of parameters already used before and the in-plane ion distribution corresponding to the point \( h = r_0 \) in Fig. 2.

**FIGURE 2** In-plane density distribution as in Fig. 1, but now plotted using the dimensionless quantity \( \lambda\varphi(x) = 2\pi r_0 \lambda\varphi(0) \). The salt concentration is \( \kappa^{-1} = 50 \text{ nm} \). If the size of the surface group is small enough, the surface charge density in the vicinity of the cylinder matches the charge density on the cylinder.

**FIGURE 3** Effective DNA–membrane interaction potentials per unit charge on the cylinder for (A) mobile and (B) immobile surface ions (\( L \) denotes the length of the cylinder). Three different homogeneous charge densities \( \beta\varphi = 2\pi r_0 \lambda\varphi c_1 \) are considered (specified by the numbers at the curves), which, in the case of mobile ions, correspond to a head group size of \( a^2 = 0.4, 0.8, \) and 2 nm\(^2\) and a surface fraction of \( c_1 a^2 = 0.1 \). The salt concentration is again \( \kappa^{-1} = 50 \text{ nm} \). The mobility of the surface groups leads to an increased rod–membrane Coulomb attraction (A) in comparison to the immobile case (B).

Given in Fig. 2. The interaction energy at infinite distance from the membrane, \( \beta\Omega(h = \infty) \), is subtracted. The surface charge density at infinity is conveniently characterized by \( \lambda\varphi^\infty = 2\pi r_0 \lambda\varphi c_1 \) which is 0.22, 0.56, and 1.12 for \( a^2 = 2, 0.8, \) and 0.4 nm\(^2\). In Fig. 3 B, we calculate the effective interaction for the same surface-charge densities \( \lambda\varphi^\infty = 0.22, 0.56, \) and 1.12, but now for immobile ions. For that, we have to solve Eq. 56 with \( \rho_\text{c} = c_1 \).
Let us first discuss Fig. 3 B. If there were no interfacial charges and no screening ions at all, the boundary condition at \( S \) in Eq. 56 would reduce to \( \mathbf{n}_n \nabla \phi(\mathbf{r}) = 0 \), which can be satisfied with the auxiliary construction of image charges, i.e., by the assumption that, at \( z < 0 \), there is a perfect mirror image of all charges at \( z > 0 \). Then the \( x\text{-}y \) plane is a symmetry plane and \( \mathbf{n}_n \nabla \phi(\mathbf{r}) \) must vanish. Clearly, a rod approaching the plane will, at some stage, become aware of its own image, which must result in an repulsive interaction. The interplay of this image–charge repulsion and the direct (screened) Coulomb attraction between the membrane and the rod charges leads to the minimum in the effective interaction potentials of Fig. 3 B. Increasing \( \lambda_B \xi^0 \), while leaving \( \lambda_B \tau \) constant, enhances the direct Coulomb attraction, but leaves the indirect repulsive image–charge interaction unchanged. As is evident from the three curves of Fig. 3 B, the minimum then becomes deeper and its position moves toward the plane. For even larger surface-charge densities (\( \lambda_B \xi^0 > 1.9 \)), the minimum will be directly at the membrane.

Comparison of Fig. 3, A and B, now shows that surface-group mobility considerably increases the effective DNA–membrane attraction. The positions of the energy minima of all three curves in Fig. 3 B are shifted toward the contact value in Fig. 3 A, and their depth is a factor 1.5–3 times larger than before. The reason for this follows from an observation made in Fig. 1: locally, the surface density of mobile surface ions can become much larger than it is at infinite \( x \) (and thus for immobile surface groups) and this leads, globally, to an increased rod–membrane Coulomb attraction.

Figure 4 shows the result of our numerical PB solution for the effective rod–membrane interaction in the case of a membrane with immobile charged lipids and a surface charge density \( c_1 = 0.1 \text{ nm}^{-2} \) \( \text{(broken line)} \). The screening length in this case is fixed at \( \kappa^{-1} = 10 \text{ nm} \). Here, we compare this curve with various approximations that can be made. On the linear level, the electrostatic interaction energy between a negatively charged line and charged wall that is impenetrable to salt ions is given per unit charge on the line by

\[
\frac{\beta \Omega_{\text{DH}}}{L_T} = -\frac{4\pi \lambda_B c_1}{\kappa} \exp(-h\kappa), \tag{60}
\]

where \( h \) denotes the distance of the charged line from the charged wall and \( L_T \) the length of the line. This function is denoted by \( \text{DH} \) in the Fig. 4. The self-energy of a charged line close to a wall that is impenetrable to salt ions has been calculated in Netz (1999) and is given by

\[
\frac{\beta \Omega_{\text{DH}}}{L_T} = \lambda_B \tau K_0(2\kappa h), \tag{61}
\]

and denoted by \( K_0 \) in Fig. 4. On the linear level, it is permitted to add Eqs. 60 and 61, and the result is denoted by \( \text{DH} + K_0 \) in Fig. 4. All these approximations neglect nonlinear effects, but also the fact that the cylinder is impenetrable to ions. Nonlinear effects can be taken into account by using the PB potential of a charged wall. The interaction of a line charge with the unperturbed double layer of a charged wall reads

\[
\frac{\beta \Omega_{\text{PB}}}{L_T} = -2 \ln \left[ \frac{1 + \tanh(\phi_0/4)e^{-h\kappa}}{1 - \tanh(\phi_0/4)e^{-h\kappa}} \right], \tag{62}
\]

which is labeled by surface \( \text{PB} \) in Fig. 4. Here, \( \phi_0 \) denotes the surface potential on the membrane. We also show the sum of the PB potential and the DH self-energy of a line, denoted by \( \text{PB} + K_0 \). The PB curve describes the true nonlinear free energy, which includes ion-exclusion effects \( \text{(broken line)} \) best, as one would expect. Despite the fact that the charge density on the wall is very small, the linear approximation for the electrostatic interaction energy \( \Omega_{\text{DH}} \) differs clearly from the nonlinear expression \( \Omega_{\text{PB}} \), as can be seen by comparison of the curves \( \text{DH} \) and \( \text{PB} \) in Fig. 4. The linear solution overestimates the interaction between rod and wall. This demonstrates that nonlinear effects are important and a linearization is not allowed for the parameters used here. The linear approximation becomes better if one increases the salt concentration \( \kappa^{-1} \).

Because rod and plane, and thus their associated double layers are oppositely charged, the two double layers will start to dissolve each other when the rod–plane distance
becomes small enough for the two double layers to overlap. Because the fixed charges of rod and plane then begin to screen each other, mobile electrolyte ions of these double layers are no longer needed to screen the fixed charges and can disappear into the reservoir. This release of ions can be seen in Fig. 5, where we plotted the change in the total number of screening electrolyte ions per unit charge on the cylinder, given by

$$
\frac{N}{L_T} = \frac{1}{L_T} \int_{c_1} \text{d}r [\rho^+_i(r) + \rho^-_i(r) - 2c_i],
$$

(63)

as a function of the distance \( h \). This is a negative number for all distances, but with a minimum at some finite value of \( h \) due to the image-charge effect. Connected with this release of counterions, there is an enthalpy gain of the whole system, which leads to an additional attractive rod–membrane force, the counterion release force (Fleck and von Grünberg, 2001). In addition, we show, in Fig. 5, the change,

$$
\frac{N_1}{L_T} = \frac{1}{L_T} \int_{S} \text{d}r [\rho_i(r) - c_1],
$$

(64)

in the total number of surface ions (integral over ion distributions like in Fig. 1) as a function of \( h \). These are positive numbers; surface ions flow in from the reservoir to help screen the cylinder. The cylinder becomes visible for the surface ions only after the 3D screening of the rod is sufficiently reduced; that explains why the disappearance of electrolyte ions sets in earlier than the appearance of additional surface ions. Closer inspection shows that the two curves \( N_i(h) \) and \( N(h) \) are, in fact, intimately related to each other, any change in one quantity affects the other. In essence, Fig. 5 describes the transition from the 3D bulk ion screening to the 2D surface ion screening.

Up to now we have completely ignored the dissociation as a competing charge-regulating mechanism. Let us now consider the effect of the variables \( \alpha_i \), a quantity that, in an experiment, can be regulated by changing the pH value of the solution (see Eqs. 2 and 3). Figure 6 displays the effective interaction when \( \alpha_1 \) is varied from 0.1 to 1.0. In this calculation, Eq. 39 is used for \( \rho_c \) in Eq. 56, and \( \alpha^2 \) is fixed to 0.8 nm\(^2\) in a mixture of neutral (\( \alpha_2 = 0 \)) and positively charged surface groups (\( \alpha_1 \alpha^2 = 0.1 \), \( \kappa^{-1} = 50 \) nm). The curve for \( \alpha_1 = 1.0 \) is the same as the curve for \( \alpha^2 = 0.8 \) nm\(^2\) (\( \lambda_{B_\alpha^{\infty}} = 0.56 \)) in Fig. 3 A. The inset of Fig. 6 shows \( \alpha_1 \) as a function of the difference \( pK_a - \text{pH} \) to render this graph useful to experimentalists. (Looking at Eq. 3, it becomes obvious that, to calculate \( \alpha_1 \) as a function of \( pK_a - \text{pH} \), it is necessary to determine \( \phi^{\infty} \). This can be done by solving the Graham equation: \( 2 \kappa \sinh(\phi^{\infty}/2) = 4 \pi \lambda_B / (e^{10(pK_a-\text{pH})} + 1) \) for \( \phi^{\infty} \).) We have already noted in the discussion of Eq. 39 that, in such a two-component mixture with one group type being neutral, variations of \( \alpha \) are equivalent to changes in \( \alpha_1 \alpha^2 \). Thus, Fig. 6 can also be understood as the variation of the effective interaction in response to changes of the surface fraction \( \alpha_1 \alpha^2 \). The message of the plot is that increasing \( \alpha \) (or increasing \( \alpha_1 \alpha^2 \)) makes the interaction more attractive because any increase of the homogeneous surface charge density \( \lambda_{B_\alpha^{\infty}} \) causes an increase of the direct Coulomb interaction between the rod

![Figure 5](image1)

FIGURE 5 Change of total number of screening salt ions per unit charge on the cylinder (lower curve, left scale) and of screening surface ions (upper curve, right scale) as a function of the DNA–membrane distance \( h \) \((c_1\alpha^2 = 0.1, \alpha^2 = 0.8 \text{ nm}^2, \kappa^{-1} = 50 \text{ nm})\).

![Figure 6](image2)

FIGURE 6 Effect of varying the degree of dissociation \( \alpha \) on the effective DNA–membrane interaction per unit charge on the cylinder. \( \alpha_1 \) is 0.1, 0.3, 0.5, 0.7, and 1 from top to bottom. The inset shows \( \alpha_1 \) as a function of the difference \( pK_a - \text{pH} \) \((c_1\alpha^2 = 0.1, \alpha^2 = 0.8 \text{ nm}^2, \kappa^{-1} = 50 \text{ nm})\).
and the membrane, something we have already learned from Fig. 3 A, where $\lambda_{\text{diff}}^{\text{eff}}$ was varied by changing $a^2$.

We still need to show that, allowing for both charge-regulating mechanisms, mobility plus dissociation (case I), makes an effect and leads to an interaction potential that is different from the one based on only one such mechanism, for instance, dissociation (case II). The latter is realized by using Eqs. 4 and 9 in the boundary condition at $5$ in Eq. 56, a trivial generalization of Eq. 41 used first by Ninham and Parsegian (1971). We now take a membrane made of three different components, with surface fractions $c_1 a^2 = c_2 a^2 = c_3 a^2 = 0.33$, valencies $q_3 = -q_2 = 1$, $q_1 = 0$, and $a^2 = 0.8$ nm$^2$ ($\kappa^{-1} = 50$ nm). The components are neutral, fully, and only partially charged ($\alpha_1 = 0$, $\alpha_2 = 1.0$, $\alpha_3 = 0.5$). Thus the membrane is (on average) negatively charged. The same values for $\alpha_i$ are taken in Eq. 4 where the $c_i$ are chosen such that the homogeneous surface-charge density $\lambda_{\text{diff}}^{\text{eff}}$ is identical in case I and II. As a third case, we calculate the effective interaction between the DNA and a homogeneously charged membrane composed of immobile surface groups, that is, we used $\rho_s = -\zeta/(2\pi\rho_0)$ in Eq. 56, with $\zeta^-$ being the same as in case I and II.

As we noticed already, in Fig. 7, surface-group mobility takes effect at short distances, that is, long after the rod has started to interact with the membrane. For larger distances, the specific properties of the membrane are obviously unimportant; only the characteristic of the double-layer in front of the membrane is essential. But, because the double-layers are determined by nothing but the homogeneous surface-charge densities that are the same in all three cases, the interaction potentials in Fig. 7 must coincide for larger distances. However, for smaller distances a drastic change sets in: positively charged, mobile ions ($q_3 = +1$) flow into that region of the interface where $\Delta\phi(r_s) \neq 0$ and replace the neutral groups, while ions of the second type ($q_2 = -1$) escape from this region. The surface, though, on average, still negatively charged, becomes locally positively charged so that the DNA–membrane interaction becomes attractive. This change from repulsion to attraction is a remarkable result and underlines the importance of surface-group mobility: ignoring the ion’s ability to move within the plane of the membrane as done in case II and III, one comes to the wrong conclusion that the interaction is repulsive. In case II, the Ninham–Parsegian case, the in-plane ion distribution adapts to the electric field of the DNA rod, with a strongly enhanced dissociation in regions where $\Delta\phi(r_s) \neq 0$. The membrane becomes locally neutral, and the resulting effective interaction is repulsive at all distances. The spatially dependent dissociation rate does not lead to a change of sign of the effective force, but just, for very short distances, to a small reduction of the interaction potential in comparison to the homogeneously charged membrane.

CONCLUSION

Charges on membranes arise from a pH-dependent chemical reaction on the headgroups of phospholipids. If another charged object approaches the membrane, a local adaption of the degree of dissociation of the surface groups is an effective way for the system to lower its total energy. Theoretically, this case is treated by solving the PB equation with the traditional charge-regulation boundary condition first introduced by Ninham and Parsegian (1971). However, a realistic model of a membrane must also take account of the fluidity of membranes. The in-plane mobility of membrane components represent a second and additional charge-regulating mechanism. The appropriate boundary condition dealing with this case is derived and discussed in this work.

Using this boundary condition, we have numerically calculated the interaction of a stiff DNA molecule with a model membrane consisting of mobile surface groups whose state of charge depends on the pH of the solution. Figure 7 represents perhaps the best summary of our results: it shows that modeling the membrane by a homogeneously charged surface is adequate only if one is interested in the interaction at larger distances where the particulars of the membrane can be ignored. However, at short distances, membrane fluidity can have a considerable impact on the DNA adsorption behavior. Figure 7 shows that, in this distance regime, the interaction of the DNA with a membrane composed of mobile surface groups differs appreciably from the interaction of a DNA with membranes having
imobile surface charges. We thus see that surface-group mobility can lead to such counterintuitive phenomena as the adsorption of a negatively charged DNA onto a like-charged membrane.

Neither the idea of taking account of the lipid’s ability to move, nor the idea of including the charge-regulating chemical reactions at the membrane’s surface, are new, but have appeared in literature before as we have repeatedly stressed in the text. New is, and that is the contribution of this work, the combination of both aspects: surface group mobility and dissociation as two competing mechanisms to regulate the surface charge density of the membrane.

In this paper, we assumed implicitly as in the DLVO-Theory that van der Waals forces and electrical double-layer forces are additive and can be treated independently. This is generally not true as pointed out by (Ninham and Yaminsky, 1997; Ninham, 1999). A more detailed description should take into account the intimate relation between electrostatic and van der Waals forces. For a discussion of van der Waals forces in bilayer systems, see Kékicheff and Ninham (1990), Nylander et al. (1994), and Attard et al. (1988b). A complete theory should also include the effect of ion specificity, dissolved gas, and the role of the buffer as discussed in Kim et al. (2001). Nevertheless, we believe that, within the known limitations of DLVO theory, our results, in particular the derived boundary condition, should be useful in more elaborate PB calculations of proteins, DNA, and cell membranes.

Acknowledgments

Financial support from the Deutsche Forschungsgemeinschaft (SFB 513) is gratefully acknowledged. C.F. thanks Reinhard Sipowsky for his kind hospitality at the Max-Planck-Institut für Kolloid-und Grenzflächenforschung.

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