



Internal configuration and electric potential in planar negatively charged lipid head group region in contact with ionic solution



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ABSTRACT

The lipid bilayer composed of negatively charged lipid 1-palmitoyl-3-oleoyl-*sn*-glycero-3-phosphatidylserine (POPS) in contact with an aqueous solution of monovalent salt ions was studied theoretically by using the mean-field modified Langevin–Poisson–Boltzmann (MLPB) model. The MLPB results were tested by using molecular dynamic (MD) simulations. In the MLPB model the charge distribution of POPS head groups is theoretically described by the negatively charged surface which accounts for negatively charged phosphate groups, while the positively charged amino groups and negatively charged carboxylate groups are assumed to be fixed on the rod-like structures with rotational degree of freedom.

The spatial variation of relative permittivity, which is not considered in the well-known Gouy–Chapman (GC) model or in MD simulations, is thoroughly derived within a strict statistical mechanical approach. Therefore, the spatial dependence and magnitude of electric potential within the lipid head group region and its close vicinity are considerably different in the MLPB model from the GC model.

The influence of the bulk salt concentration and temperature on the number density profiles of counter-ions and co-ions in the lipid head group region and aqueous solution along with the probability density function for the lipid head group orientation angle was compared and found to be in qualitative agreement in the MLPB and MD models.

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1. Introduction

Accumulation of opposite charged ions (counter-ions) and depletion of the ions with the charge of the same sign (co-ions) in the vicinity of a charged surface in contact with electrolyte solution results in the creation of an electric double layer (EDL) [1,2,3,4,5,6,7,8,9]. In biological system EDL plays an important role in cell membrane functions, like transmembrane transport and protein binding [10,11,12,13]. In the past, many different EDL theories have been proposed to describe the electrostatics of the cell membrane or artificial lipid membranes in contact with electrolyte solution [3,8,11]. Hermann von Helmholtz was the first who started to investigate EDL properties in the middle of 19th century [14,15]. Although Helmholtz's model qualitatively predicts some important properties of EDL, such as for example the order of magnitude of the potential near the charged surface, it is based on a few incorrect assumptions. Among others in the Helmholtz model the ion number density is considered to be constant and the thermal motion of the ions is not taken into account [10]. In the beginning of the 20th century

Louis Gouy and Leonard Chapman, independently of each other, upgraded the Helmholtz's model of EDL within so-called Gouy–Chapman's (GC) model by considering the Boltzmann space distribution of the counter-ions and co-ions in Poisson equation [1,16,17,18]. A decade later Peter Joseph William Debye and Erich Hückel generalized GC model [1,18,19].

Stern [20] was the first who incorporated the finite size of ions in the EDL model by assuming the distance of the closest approach of counter-ions to the charged surface [13,21]. A more sophisticated approach to take into account the finite size of ions in the EDL (Wicke–Eigen model) was first discussed by Bikerman in [2] and then actually derived by Wicke and Eigen [22]. Since then many other generalized EDL models appeared which took into account the finite-size of ions by using different theoretical approaches [4,5,7,23,24,25,26,27,28,29,30,31,32,33].

Most of the mean-field theoretical models of EDL assume space independent relative permittivity throughout the whole electrolyte solution, accordingly the relative permittivity is considered as a constant in the Poisson–Boltzmann (PB) equation (for review see [1,3,7,8,11]). A constant relative permittivity is a relatively good approximation for small magnitudes of surface charge density, but not for higher magnitudes of surface charge density where a substantial decrease of relative permittivity in the vicinity of the charged surface in contact with electrolyte solution was predicted [8,9,13,34,35,36,37,38,39].

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Recently, a simple mean-field generalised Langevin–Bikerman model of the EDL was developed by Gongadze and Iglič [40] (GI model) which encapsulate both the excluded volume effect (finite size of ions) and the orientational ordering of water dipoles, considered as point-like dipoles at the centres of the spheres with permittivity equal to the square of the optical refractive index of water. Within the GI model, the mutual influence of the water molecules was taken into account by means of the cavity field [40]. The GI model predicts the space dependence of relative permittivity [8,40] and can be considered as a generalization of the previous Langevin–Poisson–Boltzmann's (LPB) model for point-like ions [38].

Electrostatic fields that are associated with the cell membrane arise mainly from charged phospholipid head groups and proteins. In the hydrophobic core of the membrane the net charge density is essentially zero. The net charge on the membrane is dependent on the pH and ionic composition of the adjacent solution phase. In physiological conditions, virtually all cells possess a negative membrane potential resulting from the predominance of negatively charged lipids. The negative charge on the membranes of mammalian cells is mainly a contribution of phosphatidylserines (PS), that typically constitute 2–10% of total phospholipids in most membranes [41]. Due to their important role in various cellular functions and in raft formation glycolipids, in particular gangliosides as for example GM1 [42], that contain one or more negatively charged sialic acid groups, also cannot be neglected [42,43,44], although they are present in much smaller proportion, only about 2% of the lipid in most plasma membranes. Lipid, glycolipids, protein, and ion contributions together result in electric potentials of -8 mV to -30 mV as found from electrophoretic mobility [45] and other types of measurements [46].

Additionally to the regulation of cell membrane surface charge, PS have been found to act as an important cofactor for virus infection, promoting vesicle endocytosis and fusion events, and are required for optimal protein targeting and activation during cell division and initiate the pathway of programmed cell death [47,48,49,50]. The understanding of the interactions of PS with cations and anions in ionic solution, therefore, contributes to better understanding of many membrane-mediated processes. Mostly, these interactions are studied by molecular dynamics (MD) computer simulation, which is an efficacious, but computational power demanding technique. The importance, prevalence and precision of MD simulations are growing, but the ion/lipid interactions for anionic lipids are still not fully understand. The reason might be in the ambiguous parameters and rules that are used for describing and calculating electrostatic interactions [51,52]. Therefore, theoretical models, like the MLPB model, can be useful in elucidating certain basic physical mechanisms that govern the interactions between anionic lipids and ions. Although the MLPB model presents a considerable simplification of the 3-D configuration of the lipid bilayer head group region in contact with ionic solution, it explicitly takes into account the spatial dependence of permittivity in the lipid bilayer head group region and its vicinity, derived within a self-consistent statistical mechanical approach, which is not the case in MD model.

In the present work we focused on the 1-palmitoyl-3-oleoyl-*sn*-glycero-3-phosphatidylserine (POPS) lipid (bi)layer in contact with electrolyte solution containing monovalent co-ions and monovalent counter-ions (e.g. NaCl). The POPS lipid molecule possesses a negatively charged PS head group. We included the charged structure of the PS lipid head groups in the modified LPB (MLPB) model [8,53] and compared the ion/lipid interactions obtained by this model with the results of MD simulations.

2. Methods

2.1. Theoretical model

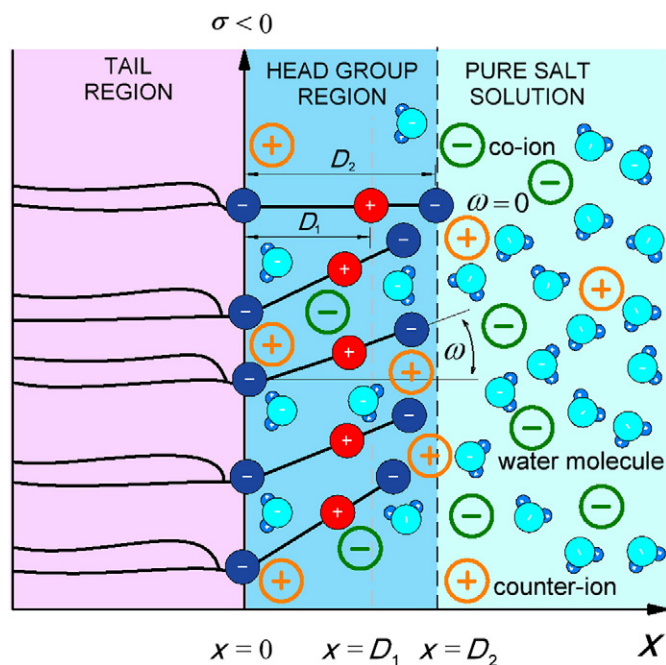
The POPS lipid bilayer in contact with an ionic solution is theoretically described by using the modified Langevin–Poisson–Boltzmann (MLPB) model [38,53]. The MLPB model takes into account the cavity

field in the saturation regimen, electronic polarization of water dipoles [38,40,54,55] and finite volumes of the amino (N) and carboxylate (O) parts of the lipid head groups. The finite volumes of other particles are not taken into account. Schematic presentation of the model is given in Schematic 1. The negatively charged phosphate (P) groups of the POPS molecules are described by the negative surface charge density $\sigma = -\frac{e_0}{a_0}$ at $x=0$, where a_0 is area per lipid molecule and e_0 is an elementary charge. Within our model the Poisson equation can be written as [56]:

$$\frac{d}{dx} \left[\varepsilon_0 \varepsilon_r(x) \frac{d\phi(x)}{dx} \right] = 2e_0 n_0 \sinh(e_0 \phi(x) \beta) - \frac{e_0 \mathcal{P}_1(x)}{D_1 a_0} + \frac{e_0 \mathcal{P}_2(x)}{D_2 a_0}. \quad (1)$$

On the left side of Eq. (1), $\phi(x)$ denotes the electric potential, ε_0 is permittivity of free space and $\varepsilon_r(x)$ is spatial depended relative permittivity of ionic solution. The first summand on the right side of the equation describes the macroscopic volume charge density of co-ions and counter-ions in ionic solution, which are assumed to be distributed according to Boltzmann distribution function; n_0 is bulk number density of salt co-ions and counter-ions and $\beta = 1/kT$, and kT is the thermal energy. By the second two terms we described the macroscopic volume charge density of positively charged N groups and negatively charged O groups; $\mathcal{P}_1(x)$ is probability density function indicating the probability that the positive charge is located at the distance x from the negatively charged surface at $x=0$ in the region $0 < x \leq D_1$ and $\mathcal{P}_2(x)$ is probability density function indicating the probability that the negative charge is located at the distance x from the negatively charged surface at $x=0$ in the region $0 < x \leq D_2$:

$$\mathcal{P}_i(x) = \Lambda_i \frac{\alpha \exp\left(e_0 \left(1 - \frac{D_1}{D_2}\right) \beta x d\phi/dx\right)}{\alpha \exp\left(e_0 \left(1 - \frac{D_1}{D_2}\right) \beta x d\phi/dx\right) + 1}, i = 1, 2, \quad (2)$$



Schematic 1. Schematic presentation of the MLPB model of POPS layer in contact with ionic solution containing monovalent co-ions and monovalent counter-ions. Phosphate groups at $x=0$ represent negatively charged surface described by the negative surface charge density σ . Other two groups of the lipid head groups, i.e. amino (positive) group and carboxylate (negative) group, penetrate into ionic solution. D_1 and D_2 are the distances to the amino and carboxylate groups from the negatively charged surface at $x=0$, respectively. ω is the lipid head group orientation angle measured relative to the normal to the plane $x=0$.

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