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Strain, stress and energy in lipid bilayer induced by electrostatic/electrokinetic forces

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ABSTRACT

Lipid bilayer was deformed by the electrostatic/electrokinetic forces induced by the fixed charges on the top monolayer–solution interface. The strains, stresses and energy were simulated using finite element method. The elastic moduli of the heads were four times greater than those of tails sections, but were individually isotropic. The physics of the situation was evaluated using a coupled system of linear elastic equations and electrostatic–electrokinetic (Poisson–Nernst–Planck) equations. The Coulomb force (due to fixed charges in the electric field), and the dielectric force (due to uneven electric field and the solution-membrane permittivity mismatch) bend the membrane, but unevenly. Whereas the bottom monolayer extends vertically (towards charged surface), the top monolayer compresses. In contrast the top monolayer extends horizontally, but the bottom monolayer compresses. The horizontal normal stress is higher in the heads than in the tails sections, but is similar in two monolayers, whereas the vertical normal stress is small. The horizontal normal stress is associated with horizontal normal strain, and vertical with both vertical and horizontal strain. Surprisingly, the shear stress (an indicator where the membrane will deform), is greater in the tails sections. Finally, the elastic energy (which is clearly greater in the heads sections) is dominated by its horizontal component and peaks in the middle of the membrane. The shear component dominates in the tails sections, and is minimal in the membrane center. Even spatially uniform external force thus leads to complex membrane deformation and generates complex profiles of stress and elastic energy.

1. Introduction

The membrane plays numerous roles and influences or critically determines the functioning of the cells or cellular organelles. The membrane delineates the boundaries of cells and compartmentalizes cellular organelles, and modulates the functioning of a variety of biological processes, and this often depends on the membrane shape. The shape, which is often intricate, thus has to be regulated precisely [1,2]. As argued persuasively in several studies the membrane curvature is to a significant extent determined by the elastic interactions between embedded proteins and the membrane [3,4,2]. Such interactions may in turn influence the spatial distribution of membrane proteins [5] and their function [6]. Finally, if the individual membrane proteins undergo conformational changes, this can also be communicated via deformations they cause in the elastic bilayer to the surrounding membrane proteins, and may further influence how the membrane proteins are spatially organized, and how they function. Individually, bilayer thickness, spontaneous curvature and bending stiffness can each modulate the function of membrane proteins [7,8].

For example the gating properties of mechano-sensitive (MS) channels, whose role is to respond to membrane mechanical stress, and which are influenced by the mechanical conditions of the membrane, depend on membrane curvature [9]. In prokaryotic cells [10,11,12] and in some eukaryotic MS channels [13], the transduction mechanism of MS channels responds directly to bilayer deformations and occurs at the protein–lipid interface. In contrast MS channels of other eukaryotic cells respond to mechanical deformations through the cytoskeletal network [14]. The membrane stresses probably influence not only the functions of MS channels, but also other channels and other proteins and lipids embedded in the biological membrane by modifying the “working” condition for their activity [15,16]. The membrane stress can alter the dimerization kinetics of the channel-forming peptide gramicidin A [17]. Hyposmotic swelling in pituitary cells directly modulates calcium influx through L-type channels, which plays a critical role in regulating basal and evoked transmitter or hormone secretion in a variety of secretory cells [18,19], and alters the hormone secretion [20]. Given that swelling leads to a higher membrane tension, the calcium channels probably directly sense change in membrane tension [21,22], which influences their gating. The mechanical state of the membrane can also have a large effect on the function of a voltage dependent K channel [23]. Finally, the membrane tension may also directly modulate exocytosis and endocytosis, with greater membrane tension stimulating the exocytosis, but suppressing the endocytosis [24].

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Given that membrane stresses may be influencing the function and spatial distribution of a variety of membrane proteins and the fact that the reshaping of the membrane bilayer occurs on a wide length scale (ranging from the micrometer to nanometer), better understanding of the stresses and their spatial distribution is needed. We evaluated the strains, stresses and elastic energy within the membrane bilayer bent by a spatially uniform and constant electrostatic force induced by an asymmetrically charged membrane placed in a liquid electrolyte [25]. The electrostatic/electrokinetic forces were estimated by evaluating a coupled system of electrostatic/electrokinetic (Poisson–Nernst–Planck) equations [26,27,28], and strains, stresses and elastic energy within the membrane were evaluated using linear elastic equations [29,30,31]. The ionic concentrations and composition were as encountered physiologically [25].

Although the basic aspects of membrane bending can be studied by considering the membrane as an elastic surface [1,32], the focus of this study is in determining what the strains and stresses are within the membrane. We thus took into account its finite thickness and different elastic properties of heads and tails sections [2]. The elastic moduli of the heads and tails sections were different, but were individually both homogeneous and isotropic [25]. The simulations demonstrate that the stresses are distributed very unevenly in the bilayer. Briefly, the horizontal normal stress dominates in the heads sections, the shear stress in the tails sections, and the vertical normal stress is small everywhere.

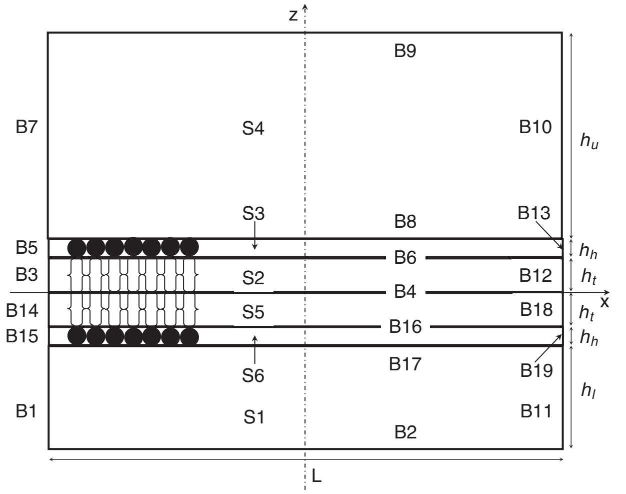

Fig. 1. Schematic representation of the lipid bilayer in the *x*–*z* plane. The membrane height *h* is divided into the hydrophilic heads (closed circles) with the height h_h and the hydrophobic tails (h_t) sections. *L* is the membrane length, and h_u and h_l are the heights of the upper and lower compartments with the electrolyte solution. The membrane plane is centered at the origin, and its thickness t_m is 100 nm. *L* is 20 nm, *h* is 2 nm, $h_h = 0.7$ nm, $h_u = 8$ nm, and $h_l = 4$ nm. S_i (i = 1–6) and B_j (j = 1–19) stand for the subdomains and boundaries of the lipid bilayer, respectively, and are defined in Table 1.

2. Methods

We evaluated numerically the deformation of a segment of the membrane lipid bilayer due to the presence of fixed charges on the internal side of the bilayer, but also due to the potential difference between two compartments bathing the membrane containing an electrolyte solution made of K^+, Cl^- (intracellular or upper compartment) or Na^+ and Cl^- (extracellular or lower compartment). The flat lipid membrane is considered as a two-dimensional (2-D) sheet in the *x*–*y* plane of the Cartesian coordinate system (*x*, *y*, *z*) with the center of the lipid bilayer in the origin. Fig. 1 depicts the schematic representations of the lipid bilayer. To account for the amphiphilic, and in turn anisotropic, nature of each lipid monolayer, we divide it into two sections — a hydrophilic heads section and a hydrophobic tails section. The height of the lipid monolayer *h* is 2 nm, its heads section h_h is 0.7 nm, whereas the tails section h_t is 1.3 nm (or as otherwise specified). The length of the membrane $L = 20$ nm (or in some simulations 40 nm or 80 nm), and its thickness t_m is 100 nm. h_u (= 8 nm) and h_l (= 4 nm) denote the heights of the upper and lower compartment, respectively. The subdomains and boundaries of the lipid bilayer are S_i and B_j respectively, where i = 1–6 and j = 1–19.

To analyze the structural deformation of the lipid membrane we consider the plane-stress model in the associated subdomains (i.e., 2, 3, 5, and 6). In contrast, the Poisson equation describing the electrostatics is defined in all the subdomains. The Nernst–Planck equation describes the electrokinetic flow and accounts for the movement (i.e., diffusion and migration) of ions in the electrolyte media and is active in subdomains 1 and 4. The membrane is assumed to be impermeable to movement of ions. Table 1 gives all boundary conditions and Table 2 details the model parameters and constants. In the companion paper we described in detail how to calculate all electrostatic (potential, electric field, space charge density), electrokinetic variables (concentrations), but also electrostatic forces (Coulomb and dielectric) and stresses (Maxwell stress). In the Appendix of the same paper we gave all equations for the structural analysis and showed how to evaluate the elastic strains, stresses, surface traction and elastic energy for an isotropic and an anisotropic membrane bilayer [25]. Finally, the numerical evaluation of the system of coupled equations given by the Poisson–Nernst–Planck and elastic equations was done using finite element method and a commercial software package program Comsol 3.5 (Comsol, Burlington, MA, USA), whereas the postprocessing was performed using a software package for scientific and engineering computing Matlab (MathWorks, Natick, MA, USA).

3. Results

3.1. Membrane deformation

How does the membrane deform as it is pulled up by the electrostatic (Coulomb and dielectric) forces? Fig. 2A gives the horizontal plot of the vertical displacement of the top and bottom membrane surface, and it is clear that even when the vertical displacement is significant, the difference in displacement is small. Nevertheless, it is of interest to

Table 1
Boundary conditions.

Boundary	Plane Stress	Electrostatics	Electro-kinetics
B1, B7, B10, B11	NA	Zero charge symmetry	Insulation symmetry
B2	NA	Electric potential V_d	Concentration C_{i0d}
B3, B5, B12, B13, B14, B15, B18, B19	*x*–*y* symmetry plane	Zero charge symmetry	NA
B4, B6, B16	Continuity	Continuity	NA
B8	Prescribed displacement: *u* and *w* in *x* and *z* directions, respectively; applied total force due to Maxwell stress tensor and charged surface (F_{e8})	Surface charge density σ_{e8}	Insulation symmetry
B9	NA	Electric potential V_u	Concentration C_{i0u}
B17	Prescribed displacement: *u* and *w* in *x* and *z* directions, respectively; Applied force due to Maxwell stress tensor (F_{e17})	Surface charge density σ_{e17}	Insulation symmetry