result in both the partial loss of α-helical structure, as well as differences in peptide positioning with respect to the lipids.

1469-Pos
Antimicrobial Peptides in Toroidal and Cylindrical Pores
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Antimicrobial peptides (AMPs) are small, usually cationic peptides, which permeabilize biological membranes. Understanding their mechanism of action might help design better antibiotics. Using molecular dynamics (MD) simulations, we investigate the preference of alamethicin and melittin for pores of different shapes. In the simulations, an alamethicin hexamer initially embedded in a pre-formed cylindrical pore preserves the pore shape or closes the pore if glutamines in the N-terminus are not located within the pore. On the other hand, when a melittin tetramer is embedded in a toroidal pore or in a cylindrical pore, at the end of the simulations the pore is lined both with peptides and lipid headgroups, and, thus, can be classified as a toroidal pore. These observations agree with the prevailing views that alamethicin forms barrel-stave pores whereas melittin forms toroidal pores. The melittin tetramer interacts more strongly with lipids in the toroidal pore than in the cylindrical one, due to more favorable electrostatic interactions. Using an implicit membrane model, modified to include pores of different shapes, we show that melittin is better solvated in toroidal pores than in cylindrical ones.

Membrane Structure I

1470-Pos
Hybrid Lipids as a Biological Line-Active Component
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The lipid raft hypothesis posits that certain cellular functions are mediated by small (nanometric to tens of nanometers) domains rich in sphingolipids and cholesterol. These sphingolipids have two completely saturated hydrocarbon tails that show good orientational order in the membrane. The surrounding phase consists mostly of lipids with at least one unsaturated bond in the hydrocarbon tails which forces a ''kink'' in the chain and inhibits ordering. In vitro, this phase separation can be replicated; however, the finite domains coarsen into macroscopic domains with time. We have extended a model for the interactions of lipids in the membrane, motivated by the work in (Elliott et al., PRL 2006 and Garbes Putzel and Schick, Biophys. J. 2008), which depends entirely on the local ordering of hydrocarbon tails. We generalize this model to INCLUDE an additional species THAT IS LINE ACTIVE and identify a biologically relevant component, a hybrid lipid with one fully saturated hydrocarbon chain and one chain with at least one unsaturated bond, that may serve as a line-active component. we show that in some cases, the hybrid is capable of reducing the line tension between the saturated and unsaturated domains to zero, thus stabilizing finite sized domains in equilibrium. We then present simple packing arguments that predict the expected size of such domains as a function of the molecular volume and area per headgroup of the composing lipids which is dictated by parameters such as cholesterol concentration, chain length and degree of unsaturation.

1471-Pos
Characterization of Horizontal Lipid Bilayers as a Model System to Study Lipid Phase Separation
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Black lipid membranes are widely used as a model system to study ion channel activity with electrophysiological techniques. In this study we characterize the properties of the bilayer system with respect to its dynamics of lipid phase separation using single molecule fluorescence fluctuation and electrophysiological techniques. On the nanosecond time scale we determined the rotational motions of fluorescently labeled lipids using confocal time resolved anisotropy to probe the microscopic viscosity of the membrane. Simultaneously long range mobility was investigated by the lateral diffusion of the lipids through the laser focus with fluorescence correlation spectroscopy. Depending on the solvent used for membrane preparation, lateral diffusion coefficients between $D_{lat} = 10$ - 25 $\mu m^2/s$ and rotational diffusion coefficients of $D_{rot} = 2.8\ 10^7\ s^{-1}$ - $1.4\ 10^7\ s^{-1}$ were measured in pure liquid disordered (Ld) membranes. In ternary mixtures containing saturated, unsaturated phospholipids and cholesterol, liquid ordered (Lo) domains segregated from the Ld phase at 23°C. The lateral mobility of lipids in Lo domains was ~8-fold lower compared to the Ld phase while the rotational mobility decreased by a factor of 1.5. Burst integrated steady state anisotropy histograms as well as anisotropy imaging were used to visualize the rotational mobility of lipid probes in phase separated bilayers. The electrical conductance of pure Ld and ternary bilayers was linearly dependent on the temperature. No discrete current fluctuations were found near the phase transition between coexisting Ld and Lo domains. Our results demonstrate that horizontal bilayers can be used as an alternative model system for lipid phase separation (taking solvent partitioning into account) favorably when electrical properties of the membrane want to be studied in parallel

1472-Pos
Phase-Field Modeling and Simulations of Lipid Membranes Coupling Composition with Membrane Mechanical Properties
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The plasma membrane, a lipid bilayer membrane surrounding all mammalian cells, is not homogeneous, but rather contains domains termed 'rafts,' defined as regions enriched with cholesterol and saturated lipids. Understanding how and why these rafts form is of great importance to cell biologists and immunologists, since they are involved in many important cell functions and processes including endocytosis, cell adhesion, signaling, protein organization, lipid regulation, and infection by pathogens. These raft structures also show great potential for technological applications, especially in connection with biosensors and drug delivery systems. We examine the formation and evolution of lipid raft-like domains in multicomponent lipid membrane vesicles using a continuum-level simulation method. Our objective is to investigate how various physical parameters input into the model, such as spontaneous curvature, bending rigidity, and phase fraction, affect the dynamics and equilibrium morphological phases formed in two-phase lipid membrane systems. This model is applied to membranes with spherical background geometries, simulating the compositional and shape evolution of lipid vesicles, coupled using a modified Helfrich free energy. The compositional evolution is modeled using a phase-field method and is described by a Cahn-Hilliard-type equation, while the shape changes are described by relaxation dynamics in which the vesicle surface area is conserved. We find that the compositional and morphological evolution are significantly altered when the mechanical coupling is present by comparing the results with those of systems where this coupling is absent. More specifically, we find that the evolution is significantly slowed when the phases have equal and opposite spontaneous curvatures and are present in roughly equal amounts. We also investigate equilibrium shapes formed by completely phase-separated vesicles as a function of spontaneous curvature, bending rigidity, and phase fraction.

1473-Pos
Computation of Lipid Headgroup Interactions
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The equilibrium structure of lipid aggregates is determined by the balance of numerous forces between hydrophobic acyl chains, hydrophilic lipid headgroups, and the lipid's environment. Among these forces, lipid headgroup interactions are both important to the stability of lipid structures and responsible for many of the interactions between biological membranes and aqueous solutes including ions and soluble peptides. In order to model these headgroup interactions, we consider the electrical properties of the headgroup molecules via the multipole expansion. While common lipid headgroups such as phosphatidylcholine are electrically neutral, they are characterized by non-zero higher order terms in the multipole expansion. Making a dipole approximation, we employ a two dimensional lattice of classical dipoles to model the headgroup networks of lipid aggregates. Restrictions to each dipole's position and orientation are imposed to account for the effect of hydrocarbon chains which are not included in the model. A Monte Carlo algorithm is used to calculate headgroup-headgroup interactions and network energies in both dipole and point-charge approximations.

1474-Pos
X-Ray Scattering from Gold Labeled Supported Membranes
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X-ray scattering is a promising tool with which to characterize systems of solid-supported membranes. There are many different scattering techniques used in the characterization, but all suffer from a necessarily low electron density contrast between the membrane and the water medium in which it must exist. Labeling membranes with a high-contrast scatterer such as gold is a promising avenue to solve this problem. In this work, silicon-supported membranes of 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) were prepared by both standard Langmuir-Blodgett deposition and fusion of vesicles onto the substrate surface. Membranes are characterized using specular x-ray reflectometry, and modeled to fit physical systems. One percent by count 1,2-dipalmitoyl-sn-glycero-phosphoethanolamine (DPPE) with a gold tag attached was then added to both systems. Gold labeled membranes were then characterized and modeled. The effect of gold labeling is shown to characteristically change the membrane density profile in addition to enhancing density contrast between the membrane and the water medium.

1475-Pos

Analysis of the Structure and Interaction in Two-Dimensional Assemblies of Tobacco Mosaic Viruses on Model Lipid Membranes

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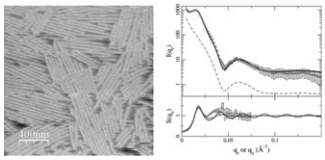
We created two-dimensional (2D) assemblies of tobacco mosaic viruses (TMVs) and characterized their structures using Atomic Force Microscopy (AFM) and X-ray scattering. The TMVs were adsorbed on an oppositely charged, fluid lipid monolayer supported by a solid substrate and submerged in a buffer solution. The lipid monolayer confined the viral particles within a plane, while providing them with lateral mobility so that overall the TMV assembly behaved like a 2D liquid. The inter-particle interaction is controlled by the chemical condition in the buffer. The degree of structural orders observed varied, depending on both the inter-particle interaction and the lateral mobility of the particles. Quantitative analysis of the X-ray scattering data provides information on the nature of the interaction between TMVs as well as possible membrane deformation due to the contact with TMVs. This study provides the proof-of-concept that X-ray scattering may be used to study the structure of membrane associated proteins in substrate-supported single bilayer under near-native conditions.



1476-Pos

Structure and Water Permeability of Fully Hydrated Diphytanoylpc

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Diphytanoylphosphatidylcholine (DPhPC) is a branched chain lipid often used for model membrane studies, including peptide/lipid interactions, model ion channels and lipid raft studies. This work reports results of volume measurements, water permeability measurements P_f, X-ray scattering from oriented samples, and x-ray and neutron scattering from unilamellar vesicles at T=30 °C. The volume/lipid was $V_L = 1427 \pm 1$ Å^3. The area/lipid was found to be 83 ± 1 Å^2 when only x-ray data were used in the H2 model analysis (Klauda et al., Biophys. J. 2006) and $A = 80.3 \pm 1$ Å^2 when both x-ray and neutron data were combined with the SDP model analysis (Kucerka et al., Biophys. J. 2008). P_f was measured to be $7.04 \pm 0.97 \times 10^{-3}$ cm/sec, which is considerably smaller than predicted by the recently proposed 3-slab model (Nagle et al., J. Gen. Physiol. 2008). This suggests that water flow through the branched chain region becomes the rate limiting step instead of the entry of water through the interfacial region when the chains are not branched. The DPhPC head-head thickness (D_{HH}= 36.1 Å), the bending modulus (K_C=$6.4 \pm 1.5 \times 10^{-21}$J) and the Hamaker parameter (H=4.5×10^{-21}J) were similar to the linear chain lipid DOPC. Even though DPhPC does not occur in mammalian cell membranes, these similarities are consistent with DPhPC bilayers being an appropriate model for many cell membrane studies. This work was supported by grants from National Institutes of Health (GM44976, JFN,STN,) and (DK43944,JCM,MZ).

1477-Pos

Osmotic Membrane Deformation Revealed by Solid-State ^{2}H NMR and Small-Angle X-Ray Scattering

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Phospholipid membranes are implicated in cellular homeostasis together with a multitude of key biological functions. Many regulatory functions are known to be mediated through protein-lipid interactions. An important feature of pressure-sensitive membrane proteins (mechanosensitive channels, rhodopsin) is that their activation is coupled to membrane tension and curvature elastic stress [1,2]. Solid-state ^{2}H NMR and small-angle X-ray scattering (SAXS) studies of bilayer ensembles of phospholipids under osmotic stress enable membrane structural deformation to be determined. Here we highlight the results from a combined NMR and SAXS approach utilizing pressure-based force techniques that control membrane structure [3] and tension [1].Our ^{2}H NMR results using both osmotic pressure (PEG osmolyte) and gravimetric pressure (low water concentration) techniques show that the segmental order parameters (S_{CD}) of liquid-crystalline DMPC approach very large values $\approx$0.35 at $\approx$30 °C. These correspond to $\approx$20% change in bilayer structural properties (cross-sectional area per lipid and acyl chain thickness) versusthefully hydrated membrane. The two stresses are thermodynamically equivalent because the change in chemical potential when transferring water from the interlamellar space to the bulk water phase corresponds to the induced pressure. A simple theoretical framework based on a unified thermodynamic description is developed. It is shown that the gating threshold for mechanosensitive channels may be shifted to higher or lower values due to lipid-mediated control of channel properties. These findings demonstrate the applicability of solid-state ^{2}H NMR spectroscopy and SAXS together with membrane stress techniques for investigating the mechanism of pressure sensitivity of membrane proteins. [1] S.I. Sukharev *et al*. (2001) *Biophys. J.***81**, 917-936. [2] A.V. Botelho *et al*. (2006) *Biophys. J.***91**, 4464-4477. [3] H.I. Petrache, M.F. Brown. (2007) *Methods in Membrane Lipids*, Humana Press, 339-351.

1478-Pos

A Modified Lipid Force Field for Charmm: Development and Application to Single-Celled Organism Membranes

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Biological membranes form a barrier to protect the cell from its environment and selectively control the entrance/exit of small molecules. Molecular simulations of these biological membranes require an accurate lipid force field (a major component of the membrane). Previously, extensive *ab initio* quantum mechanical (QM) calculations have been used to improve the aliphatic portion of the CHARMM27 lipid force field. Although this was a significant improvement, the lipid head group required additional modifications to agree with experimental lipid bilayer deuterium order parameters (S_{CD}) and solvation free energies. Therefore, we modified the atomic charges in the carbonyl-glycerol region and fit dihedral energy terms to high-level QM calculations and/or experiment. Molecular dynamics (MD) simulations with this new force field, referred to as CHARMM36 (C36), resulted in a significant improvement to the S_{CD}'s and water hydration for DPPC lipid bilayers. The calculated electrostatic profile and lipid bilayer surface tension decreased significantly. Consequently, the C36 force field resulted in excellent surface areas per lipid (and other properties) with NPT simulations, which is a significant improvement from the C27r force field that required constant area simulations (NPAT) to prevent some bilayers from laterally condensing. MD simulations of other pure lipid bilayers and monolayers also agreed favorably with experimental densities, monolayer surface tensions, and S_{CD}'s. The success of the C36 force field allowed for the study of complex lipid membranes in single-celled organisms. Model membranes were developed and simulated for yeast (six phospholipids, cholesterol, and 25-hydroxysterol) and Chlamydia (five unbranched lipids, a branced lipid, and cholesterol). These membranes are currently being used to study intracellular sterol transport and a porin protein that induces an immune response.

1479-Pos

Calculation of Partition Coefficients of Chain Anchors in Liquid-Ordered and Liquid-Disordered Phases in Model Lipid Bilayers

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We calculate partition coefficients of various chain anchors in liquid-ordered and liquid-disordered phases utilizing a theoretical model of a bilayer membrane containing cholesterol, dipalmitoylphophatidylcholine (DPPC), and dioleoylphosphatidylcholine (DOPC). The model qualitatively reproduces experimentally observed phase diagrams of this ternary system [R. Elliott,