comparison to structural or thermodynamic data at ambient conditions or by comparison to the variation of structural data as a function of temperature. Here we compare these models on new grounds by using a computational version of differential scanning calorimetry, an experimental technique widely employed to observe phase transitions in model bilayer systems. The goal of such an endeavor is to gain insight into the driving forces behind phase changes in single component model lipid systems. The strong interest in the phase behavior of multi-component bilayers as simple models of cell membranes requires that we also more deeply understand the phase behavior of the pure lipid bilayer computational models first. This study yields progress in understand the driving forces of each model and the trade-offs in choosing various coarse-grained models.

1807-Pos Board B717

The Lateral Stress Profiles of Lipid Bilayers Compared with Spontaneous Lipid Curvature Using Computer Simulations

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For transmembrane protein folding, it is hypothesized that the lateral stress profile of the lipid bilayer is an important factor for comparing protein conformations, such as the open and closed states of a channel. For example, according to this theory, the positive pressure at the bilayer interior and negative pressure at the bilayer surface stabilize protein conformations with an hourglass shape. However, the lipid-dependent lateral stress profile of a lipid bilayer is not directly measurable by experiment, but rather is inferred, e.g., from the spontaneous curvature of its constituent lipids, a geometric parameter that may be measured by x-ray scattering of the hexagonal phase of lipid/water systems. The lateral stress profile of model bilayers may be measured by computer simulations, in this work using the latest all-atom lipid CHARMM forcefield. By simulating both the fluid bilayer and hexagonal phases of lipid systems with varied spontaneous curvature, we seek to bridge the gap between experimentally measured spontaneous curvature of lipids and their characteristic bilayer lateral stress profile.

1808-Pos Board B718

Molecular Dynamics Simulation Studies of Cardiolipin Bilayers

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Molecular dynamics (MD) simulations of tetramyristoyl cardiolipin (TMCL) and tetraoleoyl cardiolipin (TOCL) were carried out with the newly developed CHARMM lipid force field (FF), C36, and with head group charges q= −1 and −2. The surface areas per lipid, A_L, for q=-1 are 126 ± 0.1 Å^2 for TOCL and 111 ± .1 Å^2 for TMCL. These are 1.8 times than those of the diacyl equivalents: 63 Å^2 for dimyristoylphosphatidylcholine (DMPC) at 328K, and 69 Å^2 for dioleoylphosphatidylcholine (DOPC) at 310K. Area compressibility, K_a, of TOCL equals 340 ± 40 dyn/cm, approximately 50% higher than experimentally obtained for DOPC (and most diacyl lipids); an experimental value for K_a for cardiolipins is not presently available. The areas and compressibilities for TOCL from the present simulation differ substantially from those obtained by Dahlberg and Maliniak using the FF of Berger et al. under the same conditions (A_L= 99 Å^2; K_a = 1100 dyn/cm). The origin of the differences appears to be in the ion binding to the surfaces of the cardiolipin bilayer. Under FF of Berger et al., ions bind closer to the carbonyl group in the lipid chain region whereas C36 CHARMM FF results ion binding closer to the negatively charged phosphate groups of the head group. Deuterium order parameter measurements are underway to determine which FF yields areas more representative of the fluid state of cardiolipin bilayers.

1809-Pos Board B719

Effect of Extrinsic Constraints on Lipid Bilayers

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The structure, dynamics and organization of cell membranes are not passive consequences of lipid equilibration in a two-dimensional milieu. Instead, a rapidly advancing body of work now suggests that these physical properties are actively and spatiotemporally regulated by a variety of intrinsic and extrinsic constraints. Extrinsic constraints, or interfacial templating, involve dynamics and fluctuations in the underlying cytoskeleton and cytoskeleton-binding membrane proteins, which actively re-compartmentalize the membrane fluid, modulating molecular diffusion and organization in membrane bilayers. In addition, modulations in the polar environment surrounding the membrane, including pH, ionic strength and composition, also influence membrane equilibration and dynamics. Precisely how these constraints influence membrane properties remains incompletely understood. Here we introduce and employ three different types of model membrane configurations that resemble physical constraints offered by the cytoskeleton. By analyzing statistics from microsecond-long atomistic molecular dynamics simulations, we develop detailed correlations between the properties of the lipid bilayers and the interfacial constraints. Our main finding is that despite the presence of nanometer-thick water layers buffering the interaction between the cytoskeletal constraints and the lipid bilayers, the cytoskeletal constraints induce a striking asymmetry between the properties of the bilayer leaflets.

1810-Pos Board B720

Molecular Modeling of Domain Formation upon Protein Adsorption in Lipid Bilayers

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The mechanisms that govern domain formation in phospholipid bilayers are unclear. Understanding the underlying principles of domain formation in model lipid bilayers will provide with insights on how protein adsorption leads to domain formation and also will lead to the effective design of novel biotechnology applications that can take advantage of the structure to function relationship in biology. In this work, the thermodynamics and structural properties of domain formation upon protein adsorption in model lipid membranes are studied through the application of a three dimensional molecular theory that includes a complete description of the relevant interactions of the entire phospholipid molecules. This theoretical approach takes into account the electrostatic interactions of the hydrophilic phospholipid headgroups as well as the attractive packing interactions of the phospholipid acyl tails. The proposed theory considers in an explicit manner the molecular conformations, size, shape and charge density of each molecule within a mean-field level approximation for the intermolecular interactions. The results show how domain formation in lipid bilayers depends on several biologically relevant environments such as different salt concentrations, solution pH and phospholipid composition of the bilayer, i.e. , the chemical structure and number density of the different phospholipid molecules present in the bilayer. The molecular theory provides with the tools for understanding the fundamental principles of phospholipid domain formation by giving insights on how the membrane responds to changes in its chemical environment. Moreover, since the theory includes an explicit description of the phospholipid headgroups, the coupling between the physical states of the two leaflets of the bilayer as the result of protein adsorption onto one side of the bilayer is also described.

1811-Pos Board B721

External Electric Field in the Atomistic Simulation of Membrane Systems

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The relationship between the membrane voltage and the gating of voltage activated ion channels has been a problem of great current interest. Although the macroscopic representation of external potential is well-known, incorporation of external voltage in a consistent molecular model is not trivial. In the current work, the effect of external electric field as well as the effect of ionic strength is introduced into the Coarse-Grain molecular simulation approach. This simulation technique allows us to calculate effect of transmembrane potential in an atomistic simulation. The resulting model is validated with known results(Debye-Huckel, Gouy-Chapman, and membrane in electrolyte solution).Preliminary results for K channel and its gating process are discussed.

Membrane Active Peptides I

1812-Pos Board B722

The Molecular Basis for Antimicrobial Activity of Pore-Forming Cyclic Peptides

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The mechanism of action of antimicrobial peptides is still not understood in molecular detail. Here, we present a molecular-dynamics and biophysical study of a cyclic antimicrobial peptide, c(KKLKKWKKLQ), and its inactive linear analogue. We establish that, relative to the linear peptide, the cyclic one binds stronger to negatively-charged membranes, folds at the interface and subsequently penetrates deeper into the bilayer. In the simulations, the cyclic peptide caused large perturbations in the bilayer and cooperatively opened a disordered toroidal pore, 1-2 nm in diameter. Electrophysiology measurements confirm discrete poration events of size 1.5-2 nm by the cyclic peptide. By employing dual-color fluorescence burst analysis, we show that both peptides are able to fuse/aggregate liposomes but only the cyclic peptide is able to form pores with a size of ~2 nm. Fluorescence Resonance Energy Transfer (FRET) proved the fusiogenic activity of the cyclic versus the aggregation of vesicles caused by the linear peptide. The results provide detailed insight on the molecular basis of the activity of cyclic antimicrobial peptides.