

peptide-lipid interactions. As opposed to most natural lipids, DPhPC is more chemically stable, and therefore, it can provide for a more robust model of lipid membranes. However, despite its frequent use, DPhPC has been less investigated than other PC lipids. To measure the physical properties of DPhPC membranes we employ a combination of complementary methods that include x-ray scattering, Nuclear Magnetic Resonance (NMR), and osmotic stress. By X-ray scattering, we obtain the repeat distances (D-spacings) of multilamellar structures formed by DPhPC in solution. By applying osmotic stress, we are able to modify and control intermembrane spacings and molecular conformations, the latter measured by NMR. These structural measurements together with ion channel activity measurements using the standard gramicidin A channels allow us to compare DPhPC with more common and better studied PC lipids. In this way, we can help rationalize the use of DPhPC as a model membrane for studies of membrane function.

3480-Pos

Protein-Lipid Interaction and Domain Formation in Asymmetric Membranes

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The lateral organization of lipids and receptors in cellular membranes is connected to a multitude of biological and pathological processes. The role of sphingolipid- and cholesterol-rich lipid "rafts" as membrane domains that control protein-protein interaction has recently attracted much attention. While the model membrane approach has yielded fundamental insights into cell membrane structure and function, the majority of these studies did not take into account the very important asymmetry between the composition of the inner and the outer leaflets of cell membranes. Therefore, certain key questions remain still unanswered: for example, how is the partition of membrane components in raft domains affected by the presence of non-raft lipids in the inner leaflet? To answer questions of this type we have developed a new method based upon cyclodextrin-induced lipid exchange to create giant unilamellar vesicles (GUVs) featuring the same type of asymmetry encountered in biological membranes. These vesicles can be produced with a very large yield, while avoiding use of organic solvents. The asymmetry of the bilayer can be confirmed by leaflet-targeted Fluorescence Correlation Spectroscopy (FCS). The use of asymmetric GUVs as novel model bilayers should allow the investigation of the principles underlying communication between raft-like domains in opposite leaflets of the bilayer, as well as investigation of the origin of lipid and membrane protein affinity for rafts.

3481-Pos

Thermal Energies and Invariant Lipid Structures

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Indiana University Purdue University Indianapolis, Indianapolis, IN, USA. Biological membranes pose many interesting problems amenable to a physicist's perspective. A central effort of a physicist is to discover invariant properties as conditions and systems change. As an example, for a lipid bilayer system one can vary the type and length of the hydrocarbon chains, in addition to the specific lipid headgroup. Furthermore, lipid bilayers in solution exhibit a range of molecular motions with amplitudes determined by the available thermal energy. How will membrane properties behave under these changes? The theoretical framework to answer this question is within classical equilibrium thermodynamics. We use a mean-torque potential model [1] to analyze order parameter data from solid-state NMR measurements on lipid bilayers to describe how bilayer properties scale with temperature and acyl chain length. We find an invariant description of acyl chain packing, which allows us to address the correspondence between changes in acyl length and changes in temperature. We present the functional form of this scaling relationship, the conclusions that can be drawn from such a temperature study, and how this invariance is ultimately a step in determining the guiding principles of lipid mixture organization in biological membranes. [1] **H. I. Petrache**, S. W. Dodd, and M. F. Brown. *Biophys. J.* **2000**, 79:3172-3192.

3482-Pos

Specific Spatial and Orientational Order in Phospholipid Membranes Induced by Cholesterol

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¹Tampere University of Technology, Tampere, Finland, ²The University of Western Ontario, London, ON, Canada, ³Barcelona University, Barcelona, Spain, ⁴Helsinki University of Technology, Helsinki, Finland. Cholesterol plays a major role in formation of laterally ordered membrane structures such as lipid rafts. These domains have been found to be involved in a variety of cellular functions, implying that there is immediate interest to understand the structure as well as the dynamics of rafts, and in particular the role of cholesterol in promoting order in rafts. Nonetheless, due to the molecular scales asso-

ciated with lipid rafts and the soft nature of membrane domains overall, the atomic-level mechanisms responsible for cholesterol's specific ordering capability have remained unresolved. Our atomistic simulations [1] reveal that this ordering and the associated packing effects in membranes largely result from cholesterol's molecular structure, which differentiates cholesterol from other sterols. Cholesterol molecules are found to prefer a specific spatial and orientational molecular in-plane organization, where cholesterol molecules are located in the second coordination shell, avoiding direct cholesterol-cholesterol contacts, and forming a three-fold symmetric arrangement with proximal cholesterol molecules. At larger distances, the lateral three-fold organization is broken by thermal fluctuations. Other sterols having less structural asymmetry are found to lack the three-fold arrangement that is characteristic to cholesterol.

[1] **H. Martinez-Seara**, T. Róg, M. Karttunen, I. Vattulainen, and R. Reigada. Manuscript under review (2009).

3483-Pos

Near-Field Structural Studies of Lipid Bilayers

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We use a Near-field Scanning Optical Microscope (NSOM) in conjunction with a Photo Elastic Modulator (PEM) to conduct birefringence (ne-no) measurements with a spatial resolution of ~80nm. With our current setup we are able to distinguish changes in retardance S on the order of 10-4 radians. Simultaneously while gathering information about S we extract information about the samples optical orientation θ referenced to the system's axis, with an accuracy of ~7.24x10-4 radians. We use our system on 1,2-dipalmitoylphosphatidylcholine (DPPC) bilayers, which at room temperature are in the gel state, (i.e.: their acyl chains have a ~32o degree azimuthal tilt with respect to the membranes normal). Modeling the membrane as a uniaxial crystal we are able determine the position of the acyl chains by measuring the birefringence and optical orientation. By controlling the temperature of our sample we hope to better study the structural changes that occur during phase transitions from gel to liquid states. The investigation of other lipid mixtures and the transformations they undergo during different phases will also be discussed.

3484-Pos

Calgary Lipids: A Lipid Force Field for Molecular Simulations

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Lipid bilayers are fundamental components of biological membranes. The most biologically relevant state of lipid bilayers is the fully hydrated fluid phase (fluid-disordered or liquid-ordered). Due to their fluidity, it is not possible to obtain experimentally atomic level structures of single bilayers. Computer simulations have been widely used to study lipid bilayers, providing detailed structural information that can aid the interpretation of experimental results. A large body of literature is available on simulations of lipid bilayers, but different studies used different simulation conditions and different force fields, which makes it difficult to compare results for different lipids.

We present here a new united-atoms force fields for lipids, compatible with common protein force fields. Partial charges and dihedral angle profiles were derived from quantum mechanics calculations on lipid fragments, while Lennard-Jones parameters were tuned by fitting thermodynamic data for simple molecular building blocks. We built a library of structures of 60 different lipid bilayers, generated using molecular dynamics simulations in identical conditions. The library provides comparable structural data for bilayers with 4 different head groups and 15 pairs of acyl chains, including the most common lipid molecules. Structural parameters (such as the area per lipid and the electron density profiles) as well as dynamic properties (diffusion coefficients, deuterium order parameters) have been calculated for each bilayer, allowing for a systematic analysis of the effect of chain length, chain unsaturation and the chemical nature of the head group.

3485-Pos

Viscoelastic Properties of Plasma Membranes Varies with Cholesterol Level

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Cholesterol is an important lipid component of mammalian cell plasma membranes. It contributes to the biophysical properties of the membrane, and plays an important role in the regulation of the membrane protein function.