The preferred conformations of the glycerol region of a phospholipid have been explored using replica exchange molecular dynamics (MD) simulations and compared with the results of standard molecular dynamics approaches and with experiment. We find that due to isomerization rates in key torsions that are slow on the timescale of atomistic molecular dynamics simulations, standard MD is not able to produce accurate equilibrium conformer distributions from reasonable trajectory lengths (~ 100 ns). Replica exchange MD, however, results in quite efficient sampling due to the rapid increase in isomerization rate with temperature. The equilibrium distributions obtained from the replica exchange MD have been compared with the results of experimental nuclear magnetic resonance (NMR) observables providing a valuable tool in the refinement of force fields for membrane simulation.

2372-Pos Board B342
Self-assembly and Equilibration of Bolalipid Membranes Studied by Molecular Dynamics Simulations
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Bolalipids are bi-polar lipids, consisting of two mono-polar lipids chemically linked together at either one or both of the lipid tails. Membranes formed by these lipids or by their mixtures with mono-polar lipids are known to have additional mechanical stability while retaining membrane fluidity. This is traditionally attributed to the fact that bolalipids can span the bilayer with their two polar heads positioned at opposite membrane-water interfaces. Our primary interest is to confirm this hypothesis by studying the relation between bolalipid configurations inside the membrane and the structural and mechanical properties of the membrane.
To this end, we performed molecular dynamics simulations using the coarse grained MARTINI force field [1]. We start with self-assembly simulations of bolalipids in mixtures with mono-polar lipids, to elucidate the preferred orientation of the bolalipids, i.e. spanning versus a looping configuration in which both head groups reside in the same monolayer. To assure proper equilibration between the spanning and looping conformations, we introduce artificial pores in the membrane to allow lipid flip-flops. We consider different types of linkage, including also bi-polar lipids attached at head group level for which spanning configurations are inaccessible.
After equilibration, the membrane properties are characterized in terms of a variety of structural properties and the lateral pressure profile. The resistance of the membrane to mechanical rupture is also investigated. We find that both the spanning/looping ratio and the stability of the membrane depend strongly on the type of crosslink, as well as on the concentration of bolalipids and length of the lipid tails. Our study can help designing new artificial membranes, with higher stability under a variety of extreme conditions.
[1] S.J. Marrink, H.J. Risselada, S. Yefimov, D.P. Tieleman, A.H. de Vries, J. Phys. Chem. B 111 (2007) 7812-7824.

2373-Pos Board B343
Mean Field Based Coarse-Grained Simulations of Ternary Mixtures
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Traditional methods of bilayer simulation at an atomistic level fail to capture length and time scales of biological interest. For example, the formation of lipid rafts in ternary mixtures is not observable with Molecular Dynamics (MD) simulations. To address this fundamental problem we have developed a coarse-grained model to simulate lipid bilayers based on self-consistent mean-field theory (SCMFT) that uses MD trajectories to extract simulation parameters, and a library of chain states that is used for statistical mechanical calculations. We have applied this model to two ternary mixtures: DOPC, SM and Cholesterol and POPC, SM and cholesterol. The thermodynamic behavior of these two systems is of interest because they are known from experiment to exhibit coexisting regions of lipid order and disorder, related to lipid rafts, at certain temperatures and concentrations. In this poster we describe predictions of the SCMFT model for both ternary mixtures, over a range of mixture concentrations, and over microsecond time scales. The existence of the single double bond in POPC influences packing among neighboring lipids differently from two double bonds of DOPC, and this has an effect on the system-wide level of lateral organization. The two systems are compared with experiments conducted with these mixtures.

2374-Pos Board B344
Molecular Dynamics simulations of mixture of POPC and PIP2 bilayer
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PI(4,5)P2 is a phospholipid that plays a role in a wide variety of cellular signaling processes. We have developed force field parameters for the molecular dynamics simulations of PI(4,5)P2 that are consistent with the modified GROMACS parameters 43A1-S3. Furthermore, we performed a long time simulation of hydrated bilayers of mixtures of POPC and 5 mol% PIP2 lipids. The simulated system consists of 800 POPC molecules. This is system is large enough to demonstrate the effect of small quantities of PIP2 and yet small enough to be trackable for molecular dynamics techniques. In this simulation we study the structural properties of poly-unsaturated chains of PIP2 molecules and electrostatic interactions at the bilayer-water interface that enable PIP2 to play significant roles in singling processes.

2375-Pos Board B345
Coarse-Grained Molecular Dynamics Simulations of an Inhomogeneous Ternary Lipid Bilayer
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Lateral, phase-separated microdomains form in model membranes composed of multi-component lipid mixtures. Similar structures are hypothesized to be of significant functional relevance in biological membranes. Though intensely studied, the molecular-level structures of these domains as yet remain unclear. We present coarse-grained molecular dynamics simulations (employing the MARTINI force-field) of a bilayer containing a ternary mixture of glycerophospholipids (saturated DPPC and unsaturated DOPC) and cholesterol. On the microsecond timescale we observe inhomogeneous mixing, with the saturated and unsaturated lipids showing preferential self-interaction. This simulation of the early stages of domain formation provides insight into the interactions that favor lateral domains, the dynamics of lateral separation, and the molecular-level structure and biophysical properties of the lateral domain.

2376-Pos Board B346
Molecular Dynamics simulation of a large asymmetric lipid bilayer
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Many factors are responsible for the curvature of lipid membranes. In this work we use very large scale Molecular Dynamics (MD) to investigate asymmetry in lipid composition as one of the factors that can induce curvature in bilayers. A very large MD simulation can begin to address this issue since larger boundaries permits longer wavelength undulation fluctuations. The simulation we describe on this poster consists of a hydrated bilayer with lipids of composition that mimics inner and outer leaflet compositions of biological membranes, viz, a 20 mol% mixture of cholesterol in 1500 POPE molecules in one leaflet and a 20 mol% mixture of cholesterol in 1500 POPC lipids in the second leaflet. The simulated system is large enough and compositionally heterogeneous enough to demonstrate undulation and curvature within the periodic boundaries. We study the bending modulus and compressibility of the system along with structural properties such as fluctuations in head group areas and order parameters. Other structural properties and in-plane radial distribution function data will also be presented. In this poster we present re simulation results and compare the model predictions with experimental structural and mechanical data.

2377-Pos Board B347
Critical Instability Leads To Labyrinthine Transition In Binary Lipid/ Polymer Monolayers
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Near critical points, the microscopic structures of fluid mixtures become unimportant and systems are characterized by strong susceptibility to small perturbations, large fluctuations and mesoscopic ordering. In biological membranes, these fluctuations in physical properties (composition, density, and curvature) may provide a spatially and temporally defined structural means to organize important functions such as formation of lipid rafts, caveolar invaginations or molecular colocalization. We report an observation of characteristic critical fluctuations in lipid monolayers composed of binary mixtures of 1,2 dipalmitoyl-sn-glycerol-3-phosphocholine (DPPC) and polyoxyethylene stearate (PegxS of varying PEG chain length) confined to an air/water interface. Using fluorescence and Brewster angle microscopy, compositional changes that occur during the expansion of an initially phase-separated binary monolayer reveal a passage through a critical composition at vanishing lateral surface pressure. The corresponding morphological transformation from an optically homogeneous liquid expanded state to a gas bubble phase via a striped, labyrinthine phase reflects the competition between long-range electrostatic repulsion and line tension forces caused by interactions between DPPC and PegxS.