the local membrane curvatures. To understand the underlying mechanisms, we measure the monolayer spontaneous curvatures (C_0) of three phospholipids, including one zwitterionic phospholipid and two anionic phospholipids, under the perturbations induced by changes in phospholipid composition and calcium ion concentration ([Ca^{2+}]). With the X-ray diffraction techniques and the reconstruction of electron density profiles, the C_0 of the phospholipids and their mixtures were determined when the samples were affected by the biomimetic perturbations and at different temperatures. It is not surprising to see that while the C_0 of the zwitterionic phospholipid demonstrates nearly negligible dependence on [Ca^{2+}], those of the anionic phospholipids react strongly to the changes in [Ca^{2+}], with the strength of the response correlated with the charge density. Interestingly, the situation is completely reversed when the temperature perturbation is concerned: Whereas the C_0 of the zwitterionic phospholipid increases with temperature, as seen for most phospholipids, the modulation in temperature causes visually no effect on the C_0 of the anionic phospholipids. The discrepancies in the reactions to the two perturbations are expected to involve the differential binding affinities of Ca^{2+} and the contributions of the electrostatic interactions. Based on these observations and energetic considerations, we explore the likely mechanisms underlying the calcium-induced phase transitions of zwitterionic phospholipids and the thermal induced phase transitions of anionic phospholipids from the lamellar phase to the inverted nonlamellar structures. The biological implications of these proposed mechanisms are discussed.

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Investigating the Role of Bilayer Size and Composition on Membrane Fluctuations using Large Coarse-Grained Simulations

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Local curvature of membranes is suggested to play a role in the regulation of cell signalling pathways. Previous computational studies of membrane fluctuations were restricted to simulating the collective behaviour of ~1,000 lipids for tens of nanoseconds [1]. With the advent of coarse-grained forcefields, such as MARTINI and the continued advance of computational power we are now able to simulate complex lipid mixtures containing ~50,000 lipids for several microseconds. Here, we shall examine how the fluctuation modes exhibited by several different ternary lipid mixtures changes as both the size of the bilayer is increased and the amount of cholesterol is altered. Spectral decomposition of the observed fluctuations suggests that large simulations will be essential for dissecting the role of membrane dynamics in the clustering of cell signalling proteins, such as Ras.

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1210-Pos Board B161

Light-Induced Transformations in Lipid Membranes

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Cellular membranes perform key functions including regulation of transmembrane exchange, transport of nutrients and information that are determinant for cell survival. Regulation of the lipid membrane structure and morphology are critical for many cellular processes such as the fission-fusion sequence in vesicular transport or endo- and exocytosis. We studied the behaviour of giant unilamellar vesicles (GUVs) made of dipalmitoylphosphatidylcholine in the presence of photosensitive molecules, i.e., two tetrafluoroazobenzene derivatives (F-azo, and a more hydrophobic equivalent F-azo-ISE) and azobenzene trimethylammonium bromide (azoTAB). Uponirradiation with visible light (green and blue), the F-azo molecules undergo reversible trans-cis isomerzation [Bléger et al. J. Am. Chem. Soc. 134:20597, 2012]. This in turn was found to induce reversible morphological transformations such as budding and bud readsorption in the GUVs. The changes in the vesicle shape are detected already at sub millimolar F-azo concentrations. The molecule partitioning and orientation in the membrane was probed with molecular dynamics simulations. Correlation between the preferential partitioning and GUV morphological transitions suggest that both membrane area change and spontaneous curvature effects come into play. Differently from the F-azo molecules, azoTAB requires UV irradiation to change the molecular conformation. In this case, we observe GUV rupture. These results suggest that the photosensitive molecules provide us with a handle to modulate the membrane curvature, mechanical properties and stability. Another potential application could be the development of drug delivery systems with light-triggered release of solutes.

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1211-Pos Board B162

Measurement of Interleaflet Coupling in Phase Separated Bilayers using High Shear

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Lipid membranes composed of at least three lipid types can phase separate into micron-scale, coexisting liquid phases. Domains in each leaflet are never observed to move out of registration, which indicates a strong interleaflet coupling. For membranes that lack transmembrane proteins or gel phases, the origin of this strong coupling is not intuitive [1]. Our group previously found that this strong coupling persists in asymmetric membranes, in which lipid ratios are different in each leaflet [2]. Here, we use microfluidic techniques to apply high shear to supported bilayers in order to overcome coupling by moving the membrane's upper leaflet with respect to the lower leaflet. We use a flow cell design by Jönsson, which was previously used to move bilayers across a substrate [3]. In this system, the leaflet proximal to the substrate flows much slower than the leaflet proximal to the solution, leading to a macroscopic spatial shift between initially apposed regions. Our measurements of the applied shear and size of deregistered domains yields, via a simple theoretical model, quantitative measurements of the interleaflet coupling.

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1212-Pos Board B163

Coarse Grained Molecular Dynamics Simulations to Study Asymmetric Membranes

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Eukaryotic plasma membranes have different lipid composition of their cytosolic and their exoplasmic leaflets, but many studies have been performed on symmetric lipid compositions. We use Molecular Dynamics (MD) simulations to study these asymmetric systems. We built single-phase leaflets in order to compare results between coarse-grained and atomistic simulations, as atomistic simulations will not phase separate during simulated time scales. We have set up systems for the outer leaflet mimicking a liquid disordered (Ld) phase or a liquid ordered (Lo) phase, while the inner leaflet is represented by a composition rich in either phosphatidylethanolamine or phosphatidylserine. We also performed coarse-grained simulations on an initially mixed bilayer to observe the effects of phase separation in the outer leaflet on the coupling between leaflets, as phase separation over simulation time scales can be observed in coarse-grained models.

1213-Pos Board B164

Electrical Asymmetries in Polarized Membranes

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Lipid membranes behave like nonlinear capacitors which can display a net electrical polarization even in the absence of an electric field. Since they are made of polar molecules, this is achieved through different mechanisms that act by breaking the symmetry of the membrane, either chemically or geometrically. Polarized membranes display interesting electromechanical properties when electric fields are present. In particular, the spontaneous polarization is responsible for voltage offsets in the electrostrictive free energy. These offsets are able to explain asymmetric I-V relationships due to lipid ion channels observed in lipid membrane patches formed at the tip of glass pipettes, which are very similar to those found in biological membranes. Therefore, asymmetries in the I-V curve cannot be used to distinguish between protein and lipid ion channels.

1214-Pos Board B165

Charge Asymmetry in Outer Membrane Proteins

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Outer membrane proteins are the proteins found in the outer membranes of bacteria, mitochondria and chloroplasts. These proteins adopt a beta barrel structure. There are thousands of outer membrane beta barrels reported in genomic databases with approximately 2-3% of the genes in gram-negative bacteria encoding these proteins. Of the non-redundant outer membrane protein structures in the Protein Data Bank, half have been solved over the past 5 years.