1788-Pos Board B632
The Role of Bilayer Edges in Supported Lipid Bilayer Formation at Low Lipid Concentrations
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We resolve new aspects of supported lipid bilayer (SLB) formation by temperature-controlled time-resolved fluorescence microscopy at low lipid concentrations (<40μM DMPC). The deposition rate *increases* after lipid has steadily accumulated on the surface to a density of ~80% of that required for a complete bilayer. Around this time, resolvable patches of bilayer appear. After reaching a density of ~150% bilayer, excess lipid is ejected back into solution while patches continue to nucleate and spread, rapidly merging into a continuous SLB. Measurements of lipid density at and around patch nucleation sites argue against the existence of a critical vesicle density necessary for rupture. We associate the increased rate of adhesion and subsequent loss of lipid with the emergence and disappearance of bilayer edges. We conclude that bilayer edges play a key role in the formation of SLBs, anchoring vesicles to the surface and inducing rupture.

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Dynamics Of Concentration Fluctuations In Lipid Bilayers Near A Critical Point
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Membranes produced from appropriate mixtures of lipids separate into coexisting liquid phases. I previously presented correlation lengths and line tensions for liquid domains in membranes near a miscibility critical point. I found that the static critical exponents for correlation length and order parameter were consistent with the universality class of the two-dimensional Ising model [1]. By applying scaling laws, I predicted the size distribution of composition fluctuations in model membranes above their critical temperature. Here I analyze the dynamics governing the lifetimes of these composition fluctuations. Fits of the dynamic structure function to a theoretical model are relevant to predictions of how long fluctuations of a certain size persist in the membrane. This information is important for thinking about how distributions of membrane proteins may be affected by the dynamic heterogeneity of lipids.
[1] A.R. Honerkamp-Smith et al., Biophys J. 2008 95(1): 236-46.

1790-Pos Board B634
Shedding (UV) Light On The Interactions Of Paclitaxel With Liposomes
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The interactions of paclitaxel (PTX), a hydrophobic anti-cancer drug, with liposomes and other delivery vehicles can be very favorably studied using fluorescence spectroscopy. PTX can be excited at 260 - 280 nm to emit fluorescence at a maximum wavelength of about 300 nm and with a fluorescence lifetime of ~3 ns. Time-resolved emission spectra (TRES) show an excited state reaction relaxing the fluorescence maximum from 298 nm to 355 nm within ~10 - 20 ns if the drug is in a hydrophobic environment, whereas little relaxation is seen in water. The relaxation is a two-state process, likely involving two specific molecular conformations of PTX. The relaxation causes a slight yet detectable shape change of the steady-state emission spectra that is quantified as a generalized polarization (GP); a much more sensitive detection and characterization of the molecular environment of PTX is however obtained by time-resolved GP and TRES measurements.

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Interaction of Fullerenes with Model Membranes
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Fullerenes (C_{60}) and fullerene-based molecules are present in a broad spectrum of applications including semi-conductors, microelectronics and potentially biomedicine. Their use is however limited by their toxicity which has been evidenced but not unambiguously understood, particularly on a molecular level. Their potential presence in the organism raises the question of their interaction with biological membranes.
In this work, we intend to elucidate the molecular details of fullerene-membrane interactions by Fourier transform infrared (FTIR) spectroscopy and solid-state NMR (SS-NMR). Model membranes composed of dipalmitoylphosphatidylcholine (DPPC) or dimyristoylphosphatidylcholine (DMPC) were prepared in the presence of fullerenes, either by co-dissolution in organic solvents followed by evaporation and re-hydration, or, by a passive solubilisation technique in aqueous solution. Our FTIR results show a perturbation of the hydrophobic core of the bilayer at fullerene:lipid ratios as low as (1:1000). This effect augments with increasing fullerene concentration until a saturation is reached at (2:100) for DPPC and (5:1000) for DMPC. The effect of the presence of fullerenes on the lipid phase transition temperatures is however weak. Our results suggest an insertion of fullerenes into the membrane, and an interaction which depends on the hydrophobic length. A more precise localization of the fullerene within the membrane, based on ^{2}H NMR results, will be discussed. Finally, our ^{31}P SS-NMR results show the presence of a fullerene induced fast reorienting lipid phase in addition to the intact vesicles.

1792-Pos Board B636
Lipid Flip-flop: Influence Of The Bilayer Composition And The Presence Of Peptides
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Lipid bilayers are the core structure of cell membranes. Their lipid composition varies as a function of the cell or organelle type and many of them show an asymmetric composition between leaflets. In the case of the plasma membrane, this asymmetry is crucial to the cell; breaking the asymmetry can lead to severe dysfunctions or even apoptosis. Therefore, cells must maintain the composition of their plasma membrane by transferring lipids from leaflet to leaflet. This process is called lipid flip-flop.
Spontaneous lipid flip-flop in model membranes is a very slow process, with half-times on the order of hours. In contrast, rates measured in living cells or reconstituted membranes range from several seconds to several minutes. The cellular mechanisms controlling lipid flip-flop are still poorly understood. To date, no protein directly involved in this process has been firmly identified. In the case of the endoplasmic reticulum, it has been proposed that the mere presence of transmembrane segments could increase the flip-flop rate.
Here, we present a thorough investigation of lipid flip-flop as a function of the bilayer composition using molecular dynamics simulations. First, the influence of the acyl chain composition on phosphatidylcholine (PC) flip-flop was investigated. As expected, PC lipids with short acyl chains require less energy for flip-flop and desorption from the bilayer. In addition, the effect of cholesterol concentration on the dipalmitoylPC flip-flop was studied. The energy barrier for flip-flop increases with the amount of cholesterol, as expected. On the opposite, the energy barrier for desorption decreases with higher contents of cholesterol. Finally, we have simulated lipid flip-flop in the presence of WALP23 or KALP23 peptides. The peptides do not significantly modify the energy required for lipid flip-flop, in contrast with experimental results.

1793-Pos Board B637
Lipid Monolayer Experiments and Simulations to Extract Line Tension
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The physical chemistry of liquid-liquid phase separation is currently of interest to the study of lateral inhomogeneities or ''lipid rafts'' within lipid membranes. We present measurements of line tensions between immiscible phases in mixed monolayer systems of phospholipids and cholesterol. Data was collected in the form of fluorescence microscopy images and analyzed using custom software routines written in Matlab. Our analysis uses capillary wave theory and will explore the importance of electrostatic interactions. We will describe image analysis software routines which allow us to track and analyze hundreds of lipid domains from a single movie. Measurements for several compositions will be presented and compare the influence of phospholipid chain length on line tension measurements. In addition to experimental data we use model-convolution microscopy to generate images which convolve the point spread function of our microscope system with the expected location of fluorescently tagged lipids in our monolayer. This technique allows us to investigate experimental uncertainties inherent in the use of fluorescence microscopy.

1794-Pos Board B638
Role of Phospholipid Asymmetry in Stability of Inverted Hexagonal Mesoscopic Phases
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Academy of Sciences, Trieste, Austria, [6]Laboratory of Clinical Biophysics, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, [7]Laboratory of Physics, Faculty of Electrical Engineering, University of Ljubljana, Ljubljana, Slovenia.
The role of phospholipid asymmetry in the transition from the lamellar (L_α) to the in-verted hexagonal (H_{II}) phase upon the temperature increase was considered. The equilibrium configuration of the system was determined by the minimum of the free energy including the contribution of the isotropic and deviatoric bending and the interstitial energy of phos-phospholipid monolayers. The shape and local interactions of a single lipid molecule were taken into account. The minimization with respect to the configuration of the lipid layers was performed by a numerical solution of the system of the Euler-Lagrange differential equations and by the Monte Carlo simulated annealing method. At high enough temperature the lipid molecules attain a shape exhibiting higher intrinsic mean and deviatoric curvatures which fits better into the H_{II} phase than into the L_α phase. Furthermore, the orientational order-ing of lipid molecules in the curvature field expressed as the deviatoric bending provides a considerable negative contribution to the free energy which stabilizes the non-lamellar H_{II} phase. The nucleation configuration for the L_α - H_{II} phase transition is tuned by the isotropic and deviatoric bending energies and the interstitial energy. For the mathematical model the deviations from sphericity of inverted hexagonal phase cross-section were calculated, resulting in lower energy in non-spherical cross-section than in spherical cross-sectin.

1795-Pos Board B639
Phase Behavior And Domain Structures Of Lipid Membranes Under Tension
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The lateral domain structure of lipid membranes is mainly controlled by the thermodynamic characteristics, i.e. composition, temperature and tension. In this study we show experimentally by the combination of fluorescence microscopy and micropipette aspiration techniques and theoretically by phenomenological modeling that the lateral tension of the membrane provides a potent control parameter of the lateral phase behavior and domain structures in lipid membranes. The lateral tension can lead to significant distortions of the phase diagrams and modification of critical behavior, and hence enhancement or suppression of lateral domains.

1796-Pos Board B640
Phosphatidylinositol-4,5-bisphosphate Affects Ceramide 1-phosphate Phase Behavior
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Ceramide is a well-characterized sphingolipid metabolite and second messenger that participates in numerous biological processes. When ceramide is phosphorylated by ceramide kinase (CERK), ceramide-1-phosphate (Cer1P) is obtained. It has recently been proposed that Cer1P is involved in cell survival, cell proliferation, inflammation and phagocytosis. It has been observed that the CERK activity is dependent on the interaction with phosphatidyl inositol-4,5-bisphosphate ($PI(4,5)P_2$). In turn, Cer1P was found to affect the PI3K/AKT pathway. This suggests that $PI(4,5)P_2$ and Cer1P might co-localize and interact. To address this issue, giant unilamellar vesicles (GUVs) composed of POPC and 10% Cer1P were made with different concentrations of brain $PI(4,5)P_2$ (from 2%, 5%, 10% to 20 mol%), labeled with fluorescent lipids and analyzed by fluorescence microscopy. GUVs composed of POPC and 10% Cer1P showed irregular branch-shaped domains, which are characteristic for the Cer1P gel phase. In the presence of 2% brain $PI(4,5)P_2$, the irregularly branched domains took on a shape of beads on strings, i.e., the domains were round indicating increased fluidity. With increasing amount of $PI(4,5)P_2$ added, the bead region became larger and larger. In the presence of 10% $PI(4,5)P_2$; the gel type string regions can barely be seen. For 20% $PI(4,5)P_2$ only one fluid type region can be seen. Since the portion of Cer1P in the GUVs was fixed, (10% of the total lipids) the increasingly larger domains have to be the result of the incorporation of brain $PI(4,5)P_2$ in the Cer1P phase. This incorporation of $PI(4,5)P_2$ in the Cer1P phase leads to an increasing fluidity and increasing size of the domain. In conclusion, Cer1P and $PI(4,5)P_2$ co-localize into a domain when mixed with POPC and this domain exhibits fluid like properties at high $PI(4,5)P_2$ concentrations.

1797-Pos Board B641
Determination of Inter-Phase Line Tension in DMPC/D-Cholesterol mixed Langmuir Films
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The hydrodynamic response of a thin fluid film, whether a Langmuir monolayer at the air/water interface or a cell membrane, is difficult to model, since it involves the coupling of both bulk and surfaces phases. However, such hydrodynamic response is not only intrinsically critical for transport within the layer, it also provides a major available means to evaluate an important parameter for phase-separated layers such as rafts, the line tension. We have developed a line-integral formulation of the hydrodynamic response of phase-separated layers with short-ranged forces, and tested it by comparisons between numerical simulations based on this model and experiment. These experiments both validate the model and demonstrate that the line tension can be determined with unprecedented accuracy and precision. Long-range dipole-dipole interactions are introduced into the model. The method is applied to coexistence between phases in binary phospholipid/cholesterol mixed layers. Data is evaluated for both Brewster and microscopy and fluorescence microscopy and implications of the use of fluorescent probes are discussed.

1798-Pos Board B642
On The Properties Of Surfactant Monolayers At Low Surface Tensions
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The properties of surfactant monolayers at the air/water interface depend strongly on the monolayer surface density. As the density increases, the monolayers undergo transitions from gas to liquid and condensed phases, and transform from 2D to 3D geometry as their stability limit is reached. For a given surfactant, the higher the surface density, the smaller is the monolayer area, and lower is the resulting surface tension at the interface. We found that for selected lipid mixtures and lung surfactant extracts, the monolayer surface tension - area isotherms deviate from the expected dependence. For these mixtures, the captive bubble surfactometer measurements show that at low surface tensions (< 20 mN/m) the reduction of surface tension is accompanied by an increase rather than a decrease of monolayer area. We used a combination of experimental techniques, theoretical models and computer simulations to investigate the properties of monolayers of varying composition at low surface tensions. We hypothesize that the observed effect originates from monolayer 2D-3D transformations. Monolayer wrinkling in particular leads to a decrease of monolayer apparent area and lowers the total surface tension.

1799-Pos Board B643
Effect Of A Water-soluble Polymer On Lamellar Surfactant Phases
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We study the effect of a water-soluble polymer, PEG, on the lamellar phases of different surfactants (non-ionic and ionic). Different experimental techniques (Polarized Light Microscopy, Freeze-Fracture Electron Microscopy, Small-Angle X Ray Scattering, Dynamic Light Scattering, Rheology) show that the polymer strongly affects the structural and physical properties of the membranes. In some cases, the polymer induces a phase of highly packed multilamellar vesicles. We present the effect of polymer concentration and polymer molecular weight.

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Measuring The Energetic Cost Of Burying An Arginine Sidechain Into A Lipid Bilayer Using A Transmembrane Protein
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Arginine is not a hydrophobic amino acid. On its own, an arginine sidechain would face a large energetic barrier to entry into the apolar core of a lipid bilayer. But, would a similarly high barrier also exist for an arginine if it were part of a whole transmembrane protein? Whether or not that barrier is high, how would such an arginine interact with a lipid bilayer? The answers to these questions will likely have implications on the normal functioning of some ion channels and also on the abnormal mis-folding of some other membrane proteins. Here we attempt to experimentally measure the free energy cost of burying an arginine into the apolar core of a lipid bilayer when that arginine is on the otherwise hydrophobic surface of a transmembrane protein. We also attempt to uncover some molecular details about how the misplaced arginine and its neighboring lipids behave. The transmembrane protein we use is the Outer Membrane Pospholipase A (OmpLa) of *E. Coli*. We engineered OmpLa to have an arginine at each of several positions that, in the crystal structure of