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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.

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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.

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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.

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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.

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Role of Phospholipid Asymmetry in Stability of Inverted Hexagonal Mesoscopic Phases
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