predicted to be 1/3 [Gomez et al., Saeki et al.] or 1/4 [Yanagisawa et al.]. The power law exponent has been measured previously for liquid domains in vesicle membranes as 0.15 [Saeki et al.] and 2/3 [Yanagisawa et al.]. Here we present an independent measurement of the power law exponent.

Gomez, J., Sagues, F., & Reigada, R. (2008). Use of an enhanced bulk diffusion-based algorithm for phase separation of ternary mixture. The Journal of Chemical Physics , 184115-1-184115-9.

Saeki, D., Hamada, T., & Yoshikawa, K. (2006). Domain-Growth Kinetics in a Cell-Sized Liposome. Journal of the Physical Society of Japan, 013602-1-013602-3.

Yanagisawa, M., Imai, M., Masui, T., Komura, S., & Ohta, T. (2007). Growth Dynamics of Domains in Ternary Fluid Vesicles. Biophysical Journal , 115-125.

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Molecular Interactions in Phase Separation of DOPC/DSPC/cholesterol Ternary Mixtures

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With the aim of investigating molecular interactions between lipids involved in lipid-raft formation, the experimental phase diagram of a DOPC/DSPC/cholesterol ternary system was simulated using Monte Carlo simulation. Both pairwise (Ising-like) and multibody interactions were used to simulate the phase boundary of liquid-ordered phase and liquid-disordered (Lo-Ld) phase coexistence regions. The ''Composition Histogram Method'' (CHM) was specifically developed to quickly determine the compositions of coexisting phases as well as the thermodynamic tie-lines. The simulation demonstrated that the phase boundaries produced by pairwise (Ising-like) interactions alone generally do not agree with the experimental phase boundary. A much better fit for the experimental phase boundary was obtained by including a ''domain edge energy'' term, which is expressed in a form ofssmultibody interaction. Our result shows that the ''domain edge energy'' is essential for creating phase separation in lipid raft mixtures. The magnitude of this interaction energy determines the location of the critical point, the shape the phase boundary, and the size distribution of lipid domains in lipid raft mixtures. Any experimental condition that alters the domain edge energy, could significantly change the shape and location of the Lo-Ld phase boundary.

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Molecular Dynamics Simulations of Ceramide Flip-Flop and Desorption in Lipid Rafts

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Ceramides are important signaling lipids, involved in processes such as apoptosis and cell differentiation. Upon stimulus acid sphingomyelinase hydrolyses sphingomyelin into ceramide on the extracellular leaflet. How ceramide generated on the extracellular leaflet induces an intracellular response remains unknown. Ceramide has been shown to associate and stabilize lipid rafts, which could create a signaling platform. We have undertaken molecular dynamics computer simulations (MD) of ceramide in both putative raft and non-raft bilayers. Using umbrella sampling we determined free energy profiles for moving ceramide and cholesterol from water to the center of raft and non-raft bilayers. The free energy barrier for ceramide flip-flop is 49 kJ/mol and 62 kJ/mol in the non-raft and raft bilayers. From these barriers, we estimate the rate of ceramide flip-flop is 0.3 s-1 and 0.003 s-1 in the non-raft and raft bilayers. The free energy for desorption can be equated to the excess chemical potential of ceramide in the bilayer compared to water. By comparing the chemical potentials, we can infer the relative affinity of ceramide and cholesterol for the raft and non-raft bilayers. Cholesterol has a large affinity for the raft bilayer compared to the non-raft bilayer, while ceramide has only a slight preference for the raft bilayer. These results provide a thermodynamic molecular-level description of the interactions of ceramide with lipid rafts, and the rate of translocation.

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Dna Lipoplexes: Prediction of Phase Architectures Using Cg Simulations and Experimental Validation

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DNA lipoplexes are important mediators of transfection that offer a safer, although less efficient alternative to their viral counterparts. Thus improving the efficacy of DNA lipoplexes is essential for their exploitation in nanomedicine. Experimentally, it has been shown that the architecture of DNA lipoplexes is linked to their biological efficacy. Therefore the ability to predict the architectures of compositions of DNA lipoplexes would be highly desirable. However, prediction of the phase behaviour of such systems is difficult, largely owing to a complex interplay of intermolecular forces. Molecular dynamics simulations provide a potential strategy for predicting phase behaviour, but traditional, atomistic methods are not applicable to large DNA-lipid systems. Here, we present coarse-grained simulations of the lyotropic phase transitions of DNA lipoplexes as a function of lipid composition and water content. Our coarse-grained model of DNA uses a ~ 4 to 1 mapping of atoms to particles and is compatible with existing coarse-grained models of biomolecules. With the appropriate balance of water content and lipid composition, we are able to capture the transition from the originally lamellar phase to the inverse hexagonal phase. Our simulation results show an inverse hexagonal phase with a calculated d-spacing of 6.2 nm for a DOPE-DNA system. Together with the disorder of the hexagonal phase, this d-spacing increases with increasing cationic lipid (DOTAP) content, in agreement with experimental data obtained by SAXS and polarizing light microscopy. Our simulations have provide insights into the rearrangements that occur to effect the transition to the inverse hexagonal phase; this level of detail is difficult to obtain using experimental methods alone. Furthermore, our simulations have highlighted the increasingly important role of coarse-grained simulation methods for the design of novel DNA lipoplexes and applications in synthetic biology, in general.

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Microrheology of Freestanding Lipid Bilayers

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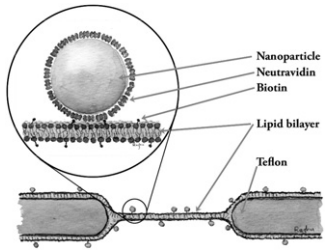
The macroscopic material properties of cellular membranes, determined by the composition and interactions of their constituent lipids, are important factors in the structure and function of all living cells. Fluidity is a key material property of membranes, yet the underlying lipid bilayer viscosity and other rheological parameters remain poorly quantified.

We adopt recently developed microrheological methods to study multiple composite freestanding ''black'' lipid membranes. Using high speed video particle tracking, we monitor dynamics of membrane-anchored nano- and micro-particles across a range of temperatures that span bilayer phase transitions. Two particle spatial correlation functions and the complex shear modulus are extracted from such measurements and provide information about fundamental membrane material properties. We find striking and previously unreported signatures of viscoelasticity in these lipid bilayers whose properties are sensitive to the bilayers' temperature dependent liquid ordered to liquid disordered phase transitions.



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Coping With the Cold: Effect of Hibernation on Pulmonary Surfactant in the Thirteen-Lined Ground Squirrel

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Pulmonary surfactant, a mixture of phospholipids, cholesterol, and proteins, stabilizes the lung by reducing surface tension at the air-water interface of the alveoli. We hypothesized that lowering body temperature to approximately 5°C during hibernation would require compositional changes in surfactant lipids and perhaps proteins in order to maintain lung function. Large aggregate (LA) fractions were obtained by centrifuging lung lavage at 40,000 g for 15 min, with small aggregates (SA) remaining in the supernatant. Because hibernating animals have lower body masses, surfactant levels per animal were compared. Hibernation resulted in an increase in total surfactant due to increased LA with little change in SA. Cholesterol at 8 wt% PL was not altered. Hibernation was accompanied by a small (~15%) decrease in disaturated phosphatidylcholine and phosphatidylglycerol. Decreases were observed in the mRNAs for the surfactant proteins (SP-). Western analysis revealed levels of all SP-s decreased to approximately 10% (SP-A), 50% (SP-B), 90% (SP-C), and 50% (SP-D) of warm active levels. We speculate that the changes in surfactant LA levels might reflect the much lower breathing rate during hibernation. Furthermore, the compositional changes could arise, in part, from a slowing of metabolism. The decrease in disaturated phospholipid levels could lead to enhanced adsorption due to increased fluidity, but this suggestion will have to be confirmed experimentally.