

in the tube should adjust in order to minimize the bending free energy in the curved structures like tubes or small vesicles. Here we have systematically studied lipid sorting in membrane nanotubes of controlled diameter.

We designed an assay where nanotubes are pulled out of Giant Unilamellar vesicles made of Sphingomyelin (BSM), Cholesterol (Chol) and DOPC using optical tweezers. The tube radius is set via micropipette aspiration. The composition in the tube's membrane is measured by recording the fluorescence intensity of labeled lipids under a confocal microscope; simultaneously the force necessary to hold the tube is measured with optical tweezers.

We will show that curvature induced lipid sorting can occur, but only near a phase transition of the ternary system BSM:Chol:DOPC. We will show that the physical origin of sorting by curvature in pure lipid system is a reduction of the free energy of curvature of the membrane in the tube. We will present theoretical considerations supporting these observations.

Finally we will show that protein binding a specific lipid in the membrane can enhance sorting.

References

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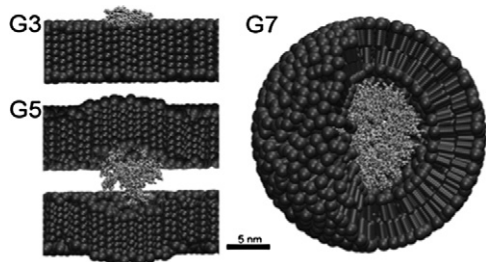
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Stoichiometries and Energetics of Cationic Nanoparticle-Membrane Complexes

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The nanoparticle-membrane interaction is essential to nanotherapeutic design and nanotoxicity concerns. The equilibrium structure was determined for phospholipid membranes interacting with one type of nanoparticle, poly(amidoamine) dendrimers, at the atomistic and molecular scale via both experimental and theoretical approaches. The resulting dendrimer-phospholipid complex depends on both the number of primary amines per dendrimer and the dendrimer size. Large dendrimers (> 7 nm diameter) induce vesicle-encased dendrimers and significant membrane disruption. In contrast, small dendrimers (< 5 nm diameter) bind to the membrane surface without individually inducing significant membrane disruption. Techniques such as isothermal titration calorimetry (ITC), molecular dynamics (MD), and differential scanning calorimetry (DSC) were used for examination of the equilibrium structures and identifying the mechanisms of nanoparticle-induced membrane disruption.

Third-, fifth-, and seventh-generation poly(amidoamine) dendrimers (G3, G5, and G7, respectively) are shown here in complexes with phospholipids. The stoichiometries and dimensions of the dendrimer-lipid complexes indicate small dendrimers (G3) saturate with lipids on a planar membrane, medium-sized dendrimers (G5) induces local membrane curvature and/or binds to multiple bilayer surfaces, and each larger dendrimer (G7) becomes encased by a lipid vesicle. These understandings will guide nanoparticle design in both medical and industrial applications.



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The Delivery of Lipidic Compounds to Model Membrane Interfaces by Non-lamellar Liquid Crystalline Nano-particles

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There is an increasing demand for methods to study processes at the lipid-aqueous solution interface, due to the importance of lipids and lipid self-assembly structures as regulators both for biological activity and for drug

delivery vehicles. The biological membrane is one of the most important interfaces that the drug delivery vehicles encounter. The potential use of non-lamellar lipid structures delivery systems in pharmaceutical, food and cosmetic applications has invoked a number of studies of the assembly and interactions of cubic phases of these materials. One such system is a colloidal dispersion of the cubic liquid crystalline phase of glycerol monooleate. We will discuss some aspects of what happens when these liquid crystalline lipid nanoparticle encounters a lipid bilayer, consisting dioleoylphosphatidylcholine, either as supported bilayer or as a vesicle. Null ellipsometry and QCM-D provides kinetic information about the adsorption and triggerable release of the nanoparticles. Using contrast matching of the supported lipid bilayer, neutron reflectivity makes it possible to assess the exchange of material from one ordered lipid phase to another. Synchrotron Small Angle X-Ray Diffraction allowed us to in detail study the phase transition when non-lamellar glycerol monooleate based nanoparticle interact with phospholipid vesicles. Together the four techniques provide insight into the interaction mechanism and shows that the release of the particles are likely to be caused by phase transition of the lipid self-assembled structures.

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Construction Of A Tethered-bilayer Lipid Membrane By Physiosorption Of Glycolipid GM₁ To A Hydrophilically Modified Gold Surface

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Interactions of membrane-bound molecules with their environment are difficult to study due to the complex and dynamic nature of biological membranes. The development of model membranes can provide insight into the function of membrane proteins in their natural environment. A phospholipid bilayer deposited at a gold surface offers a unique opportunity to investigate the mechanism of voltage-gated ion channel formation induced by surface-active proteins such as Colicin E1. Studies of voltage-gated phenomena involving transmembrane proteins require a model membrane that is supported at a gold electrode and has a water layer on either side of the bilayer. This can be achieved by creating a tethered lipid bilayer membrane (tBLM) with a hydrophilic spacer region separating the gold surface from the bilayer. We describe here the construction of a lipid bilayer membrane which is tethered from the gold surface using glycolipid, GM₁. The bilayer is composed of 1,2-dimyristoyl-sn-glycerol-3-phosphocholine (DMPC) and cholesterol. GM₁ is physiosorbed to gold by modifying the gold surface with a hydrophilic thiol, 1-thio-D-glucose. Due to the amphiphilic nature of GM₁ this is performed at the air/water interface using the Langmuir-Blodgett technique. The outer leaflet of the bilayer is deposited using the Langmuir-Schafer method. The quality of the bilayer formed at the gold surface was characterized using electrochemical methods, in which the capacitance of the tether bilayer is measured on a single crystal gold electrode (Au(111)). The tBLM was further characterized using Atomic Force Microscopy (AFM). The tBLM was deposited on a substrate composed of Au(111) terraces, force-distance curves were measured using AFM, the thickness of the bilayer was then extracted from these curves. These results will be presented for tBLMs constructed with varying GM₁ content (10, 20, and 30 mole percent).

Platform I: DNA, RNA Structure & Conformation

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Computational and Experimental Determination of the tRNA-like Structure in the 3'UTR of the Turnip Crinkle Virus (TCV)

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Turnip crinkle virus (TCV) is a plant virus, which is not capped or polyadenylated. Being one of the smallest plus strand viruses makes it a useful system for studying translation and transcription. Its 3' proximal region, together with the 5' UTR, enhances translation. We have employed our massively parallel genetic algorithm, MPGAfold, to predict the secondary structure of the 3' terminal 195 nt region. Compensatory mutagenesis analyses in vivo and in-line structure probing confirmed the existence of the key predicted features (stem-loop motifs an one H-type pseudoknot) and added another pseudoknot to the model. Based on this information, we employed our 3D molecular modeling software, RNA2D3D, to predict the 3D structure of the core three hairpins and two pseudoknots. Our model structurally resembled a tRNA. Experimental