(62%), but the remaining 38% of digestion occurred in the course of the subsequent intermittent encounters. The complex formation was maintained after the DNA break. This is suggestive of an intrinsic behaviour in which the DNA and protein molecules are continuously held together by switching their binding positions with short-range interactions. It also provides a clue to understanding an efficient and effective reaction by the DNA-binding proteins in bacterial cells.

Membrane Physical Chemistry III

3546-Pos Board B274

Rapid Determination of Geometry and Elastic Constants of Lipid Nanotubes

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Membrane nanotubes (NT) are cylinders made of a lipid bilayer. They are widely used to study the effects of curvature on the mechanics of lipid bilayers and proteo-lipid interactions. Fast and accurate determination of the size (length and radius) and the elastic parameters (membrane tension and bending rigidity) of the tube is imperative to quantify its interaction with proteins. Here we describe how measurements of electrical conductivity of the NT interior under different voltage protocols allows for simultaneous real time measurements of its geometry and mechanical properties. We present the correlative analysis of conductance and fluorescence microscopy measurements performed on a single microns-long nanotube. For submicron nanotubes we discuss the precision of the method (which approaches 0.5 nm for the measurements of the NT radius) and demonstrate that bending moduli obtained here for the nanoconfined NTs of different lipid compositions correspond to those obtained from the bulk measurements.

3547-Pos Board B275

Interaction of Digitonin and Cholate with Complex Membranes

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The non-ionic detergent digitonin, extracted from purple foxglove, is widely used in the solubilization and reconstitution of membrane proteins. Its physical-chemical properties are not well characterized, however, and literature on its aggregation behavior is limited. In contrast, the bile salt sodium cholate which also is commonly used in the solubilization of membrane proteins, has been studied extensively. In order to understand the role of digitonin-lipid interactions in the reconstitution of G protein-coupled receptors, we have studied the interactions between a particular digitonin-cholate mixture and a mixed membrane composed of phosphatidylcholine, phosphatidylserine and cholesterol. Isothermal titration calorimetry was used, along with time-resolved fluorescence leakage assays and light scattering, to study the self-assembly of the mixed-surfactant system and its interactions with lipid membranes. The mechanism by which the digitonin-cholate surfactant mixture aids in the reconstitution of membrane proteins will be discussed. The insights gained from this work will facilitate the selection of detergents in future studies on the solubilization of membrane proteins.

3548-Pos Board B276

Membrane Leakage and Antimicrobial Action of Polymers and Surfactants

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Surfactants and nylon-type polymers have been found to induce leakage of lipid membranes as detected by dye efflux from liposomes. They also show inhibitory or cytotoxic activity against living cells. We aim at better understanding the quantitative correlation between these two activities. We hypothesize that this correlation depends crucially on the mechanism of membrane leakage. The graded mechanism involves partial efflux of entrapped dye from all vesicles, suggesting that it is based on frequent yet very small and short-lived defects distributed over all liposomes. Partial efflux by the "all-or-none" mechanism means that some liposomes leaked out all entrapped dye whereas others remained fully intact. This scenario implies the existence of distinct pores that develop in some of the liposomes and remain there during the incubation time of the experiment. The experiments are done using the fluorescence lifetime-based leakage assay.

3549-Pos Board B277

Influence of Cholesterol Microstructures on Fluctuation Spikes in Nystatin Channel Currents in Phospholipid/Cholesterol Bilayers

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Nystatin (NYS) is an antifungal agent that preferentially forms ion channels in membranes containing ergosterol (ERG) or cholesterol (CHOL). In phospholipid bilayers ERG or CHOL segregate into ordered (L_o) and disordered (L_d) domains. We prepared POPC bilayers containing CHOL mol fraction $0.18 \leq \chi_{ERG} \leq 0.50$ separating two chambers containing KCl solutions. The concentration gradient between chambers was 435/150 mM KCl. We allowed the CHOL/POPC bilayer to settle 15 min then added 19 or 38 microM NYS to the reference (Cis) chamber, imposed 50 mV across the bilayer, and stirred the Cis chamber at 4 Hz. The NYS molecules adhered to the bilayer forming channels on the boundaries of the L_o domains. [1] The resultant bilayer current exhibited prominent spikes of very short duration. A plot of the frequency of these spikes against χ_{ERG} revealed prominent spikes at $\chi_{ERG} = 0.19$, 0.25 and 0.40. These correspond well to the dips in dehydroergosterol fluorescence observed by Chong [2], which he understood in terms of a superlattice. We conclude that fluctuations in NYS channels on the perimeter of the L_o CHOL domains depend strongly on L_o domain structure.

1. Helrich, C. S., J. A. Schmucker, and D. J. Woodbury 2006. Evidence that Nystatin Channels Form at the Boundaries, Not the Interiors of Lipid Domains. Biophys. J. 91: 1116-1127.
2. Chong, P.L-G. 1994. Evidence for regular distribution of sterols in liquid crystalline phosphatidylcholine bilayers, Proc. Nati. Acad. Sci. USA 91:10069-10073.

3550-Pos Board B278

Optimizing Drug Release: Bilayer to Inverted Hexagonal Phase Transition of Cationic XTC2 and Anionic DSPS Lipid System is Influenced by pH, Temperature, and Salt Concentration

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The effectiveness of a macromolecular drug delivered in lipid nanoparticles (LNP) depends upon the biophysical properties of the delivery vehicle. Recent research has shown that the design of the cationic lipid component of LNPs improves the intracellular delivery of therapeutic siRNA[1]. Even in these optimized LNPs, only 1% of the siRNA taken up by the cell via endocytosis is actually released into the cell cytosol. We proposed a mechanism of endosome disruption that relies on the formation of non-bilayer phases in the presence of anionic endosomal lipid and synthetic cationic lipids. A model system using prototypical anionic lipid 1,2-distearoyl(d70)-*sn*-glycero-3-[phospho-L-serine] (DSPS-d70) in 1:1 molar ratio to the cationic lipid DLin-KC2-DMA (XTC2) (pKa~6.7) was characterized by ^2H and ^{31}P NMR spectroscopy. Through spectral analysis, we determined that at physiological pH (~7.4) the XTC2/DSPS system exhibits a stable gel phase for temperatures below 45°C while an isotropic signal emerges at higher temperatures - no inverted hexagonal (H_{II}) phase is observed. At low pH (~4.75), the XTC2/DSPS system is principally in a bilayer gel phase at low temperatures with a non-bilayer H_{II} phase predominating at higher temperatures. The transition from gel to H_{II} phase is dependent on salt concentration and is most evident in the range of 15-25°C for 0.25M [Na^+], 20-30°C for 0.5M [Na^+] and 35-45°C for 1M [Na^+]. Through depaking the spectra, order parameter profiles S_{CD} have been obtained and compared for DSPS-d70 chains in bilayer and H_{II} phases. These will be useful for computational simulation and eventually to design *in vivo* animal model experiments.

[1] Semple, S.C., et al., *Rational design of cationic lipids for siRNA delivery.* Nat Biotechnol, 2010. **28**(2): p. 172-6.

3551-Pos Board B279

Modelling of the Interaction between Cationic Lipid Dlin-Kc2-Dma (XTC2) and Anionic Lipid Distearoylphosphatidylserine (DSPS)

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Short pieces of double stranded small interfering RNA (siRNA) could be used as a potential drug to cure cancer by binding to cancer gene's messenger RNA. However, the siRNA is not stable in the blood stream, and tends not to penetrate target cell membrane. So, it must be encapsulated in a lipid nanoparticle. LNPs have been shown to be strong candidates for drug delivery [1]. Lipid