hydrophobic lateral blocks promote adhesion between bilayers via bridging interaction controlled by the concentration and segments chain length of the polymer. The results pave a new route to the development of treatments for this debilitating disease and shed a new light on the relationship between polymer structure, self assembly and interactions with complex biomembranes.

Membrane Structure I

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Temperature Behavior of Nanometer-Size Lipid Domains in DPPC:DLPC Model Membranes Studied by Small Angle Neutron Scattering

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Cellular membranes are no longer viewed as a heterogeneous mix of lipids and proteins, but rather as having distinct lipid domains which are key for many biological processes. Much work devoted to understanding the mechanisms that drives lateral organization in cell membranes has been done on model membrane systems. The study of lipid-lipid phase separation contributes to our understanding of the structure-function relation in the cell membrane. Phase behavior of lipid mixtures has been studied extensively in model lipid membranes using microscopy and spectroscopy techniques. By microscopy, the domains are found to be microns in size. A hypothesis to explain small domains in real cell membranes is that the cytoskeleton generates boundaries, generating small membrane regions with access to only a small amount of lipids and other components. Therefore, to be able to correlate studies of model membranes to the actual plasma membrane, there is a need to characterize lipids domains in a system where they cannot grow more than few nanometers in size. To achieve such a goal, we use Small Unilamellar Vesicles made of a 1:1 ratio of deuterated DPPC and DLPC for which phase separation in large vesicles has been observed. Small Angle Neutron Scattering was used to characterize the size and composition of the domains, which appeared as the temperature was lowered below the Tm of the system (which lies between the two Tm values of each lipid depending on the composition). The scattering was fitted using an ab initio method developed by Svergun and colleagues to analyze scattering data from biological macromolecules. The results show that domains in these systems do not coalesce to form a single stable domain but rather break-up into smaller domains as the temperature lowers.

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Physical Properties of Lipid Membranes Containing Sterol Studied by Deuterium NMR and Fluorescence Microscopy

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We study the physical properties of model membranes composed of phosphatidylcholines and sterol. The morphology and phase behavior of membranes were investigated by deuterium NMR and fluorescence microscopy. In binary mixtures, coexistence of solid-ordered and liquid-disordered phases was observed in a wide temperature and composition range. The results for ternary mixtures containing sterol show that addition of sterol promotes the formation of the liquid-ordered phase. Sterol has strong influence on the morphology and the phase behavior of membranes. A partial phase diagram of will be presented.

1497-Pos Board B267

Role of Curvature to Produce Modulated Patterns of Lo + Ld Phases on GUV Surfaces

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GUV studies of the three component lipid system DSPC/DOPC/CHOL show macroscopic phase separation of Ld + Lo phase domains. In contrast, GUVs of DSPC/POPC/CHOL appear uniform in the Ld + Lo region, but show nanometer-scale phase separation in FRET and ESR studies. Examination of the four component system DSPC/DOPC/POPC/CHOL enables study of macroscopic-to-nanoscopic transition as composition (DOPC/POPC ratio) is changed. The transition is observed to be rather abrupt, and reveals ''modulated phase'' patterning on the GUV in a small window of compositions. The patterns show stripe, bubble, and honeycomb structures. Following Helfrich, we attempt to explain these patterns through the energetics of curvature. We perform calculations and simulations to determine whether a heterogeneous membrane can stabilize modulated phases, subject only to a line tension and a bending rigidity. We also explore the energetic stability, shape, and size scales of these patterns.

1498-Pos Board B268

Cholesterol Mediates Membrane Curvature during Fusion Events

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Biomembranes undergo extensive shape changes as they perform vital cellular functions. The molecular mechanisms by which lipids and proteins generate and control membrane curvature remain largely unclear. Membrane curvature can be generated by a protein that embeds its amphipathic domains into the lipid matrix. Shallowly embedded domains expand, mainly, the lipid polar heads, while the hydrocarbon chains remain undisturbed. This leads to a strong asymmetry in spacing between the tails and headgroups of the membrane lipids and, consequently, to generation of a positive membrane curvature. In contrast, when a protein's domain expands the polar and hydrocarbon regions of the membrane lipids evenly, only negligible curvature is produced. We present evidence that cholesterol could directly control the embedding depth and occupied surface area of protein's amphipathic domains, and thus induced membrane curvature on the example of fusion between HIV-1 viral envelope and host cell membranes. Bending of the host cell membrane in this process is mediated by the N-terminal fusion domain of the viral glycoprotein gp41. DPPC/cholesterol monolayers at the air/liquid interface with different ratios of cholesterol were used to mimic the host cell membrane. The membrane binding properties of the fusion domain were assessed with the constant-pressure insertion assays and X-ray reflectivity. When the concentration of cholesterol is low, the gp41 protein's domain embeds shallowly into the lipid matrix, causing significant surface area perturbations and generating positive membrane curvature. In contrast, deep insertion of the fusion domain implies that it produces negligible curvature in membranes with high cholesterol content. Taken together, previous reports and our data offer a new mechanism of how lipids and proteins could regulate membrane curvature - in response to the protein domains' binding cholesterol may rearrange locally thereby altering membrane-binding properties of these domains and curvature they produce.

1499-Pos Board B269

Calculating Elastic Constants and the Effects of Curvature on the Binding of Lipid Chain Anchors to DPPC/DOPC/Cholesterol Model Lipid Bilayers

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Using a theoretical model of a bilayer membrane containing cholesterol, dipalmitoyl-phophatidylcholine (DPPC), and dioleoylphosphatidylcholine (DOPC) that qualitatively reproduces phase diagrams of giant unilaminar vesicles (GUVs) of the same three components [R. Elliott, I. Szleifer, and M. Schick, Phys. Rev. Lett., 96, p.098101 (2006)], we calculate the bending and saddle-splay force constants in Gel, liquid-ordered (lo), and liquid-disordered (ld) phases. The molecular theory employed in our study allows us to determine the effects of the mode of membrane bending deformation on the value of the elastic constants for different phases. The effect of ''blocked'' vs ''free'' exchange of lipids across the two monolayers on the values of the bending constant is as high as 50 kbT in the ld phase to as high as 200 kbT in the lo phase. These results show that one must strongly consider the mode of deformation in regard to the mechanical properties of lipid bilayers. For example, if cholesterol is allowed to flip-flop and the other lipid species are ''blocked'', then the bending elastic constant is 20-40 kbT larger then the case where all of the lipid species are allowed to be exchanged from leaflet to leaflet.
We will also present results on how the curvature of lipid vesicles determines the amount of binding of molecules with lipid tail anchors. By explicitly determining the chemical potential difference of species across a curved bilayer under different modes of deformation, we are able to calculate the equilibrium binding concentrations of lipid tail anchors as a function of membrane curvature, concentration of lipids, and local electrostatic environment.

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Cholesterol-Lipid Affinity Determined by EPR

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Cholesterol-lipid interactions are thought to play an intrinsic role in determining lateral organization within cellular membranes. Rafts enriched in cholesterol are ''glued'' together by the high affinity that the sterol has for sphingolipids, whereas poor affinity for cholesterol is hypothesized to drive the formation of polyunsaturated fatty acid (PUFA)-containing phospholipid domains depleted in the sterol. Here we describe a novel method using electron paramagnetic resonance (EPR) to measure the affinity of cholesterol for model membranes. Our method determines the relative amount of cholesterol that partitions between large unilamellar vesicles (LUV) and cyclodextrin by analyzing