Laurdan and di-4-ANEPPDHQ are membrane order reporting probes whose peak emission wavelengths depend on the lipid environment. The probes report membrane order through different mechanisms, laurdan by sensing changes in the level of water penetration into the lipid bilayer and Di-4-ANEPPDHQ by sensing dipole potential changes in the membrane. Laurdan and di-4-ANEPPDHQ are excited by UV and blue light, respectively, and both show an ~50 nm blue shift in emission for membranes in liquid-ordered (l_o) phase versus membranes in liquid-disordered (l_d) phase.
Large unilamelar vesicles (LUVs) in l_o phase were created by mixing sphingomyelin, DOPC spiked with 5% DPPG and cholesterol in 1:1:2 ratio. LUVs in l_d phase were created only using DOPC spiked with 5% DPPG. Transmembrane polypeptides, mastoparan (a 14-residue peptide toxin isolated from wasp venom) or bovine prion protein (N-terminal residues 1-30), were added to 100 nm LUVs stained with 1μM laurdan or di-4-ANEPPDHQ in up to 1:10 protein/total lipid ratio. The laurdan and the di-4-ANEPPDHQ emission spectra were measured for both l_o and l_d phase LUVs before and after the addition of polypeptides and remained unchanged for all conditions. The integrity and size distribution of the LUVs upon addition of the polypeptides were determined by dynamic laser light scattering and no changes were detected. The insertion efficiency of the polypeptides into LUVs was determined by measuring their 3D polypeptide structure by circular dichroism. Both polypeptides had an alpha helical conformation compatible with them being inserted into the lipid bilayer. Our results suggest that the presence of proteins in biological membranes does not influence the spectra of laurdan and di-4-ANEPPDHQ showing that the dyes report solely on lipid order.

2491-Pos
Thermodynamics and Dynamics of the Formation of Spherical Lipid Vesicles
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We propose a free energy expression accounting for the formation of spherical vesicles from planar lipid membranes and derive a Fokker-Planck equation for the probability distribution describing the dynamics of vesicle formation. We found that formation may occur as an activated process for small membranes and as a transport process for sufficiently large membranes. We give explicit expressions for the transition rates and the characteristic time of vesicle formation in terms of the relevant physical parameters.

2492-Pos
Permeability of Model Stratum Corneum Lipid Membrane Measured using Quartz Crystal Microbalance: Non-Fickian Diffusion and Transient Membrane Swelling
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The stratum corneum (SC) is the outermost layer of the epidermis. Stacked intercellular lipid membranes found in the SC play a crucial role in regulating transport of water through the skin. In this work, we present a new method to determine the water permeability of a model SC lipid membrane using a quartz crystal microbalance (QCM) [*Langmuir*, **2009**, 25 (10), 5762-5766]. We investigate a model SC lipid membrane comprising an equimolar mixture of brain ceramide (CER), cholesterol (CHO) and palmitic acid (PA), and use QCM to determine the diffusivity (*D*), solubility (*S*) and permeability (*P*) of water vapor. We have found that the water transport in model skin lipid membranes can not be described in terms of *Fickian* process as the effective diffusion constant depends on the thickness of the lipid bilayer stacks. This may be due to slow equilibration process related to the membrane hydration. Using polarity-sensitive probe, PRODAN, we have found that the time scale of slow equilibration process is ~ 10 hrs, which may explain the non-Fickian behavior of a skin lipid membrane.

2493-Pos
Photophysical Studies of Novel Ruthenium Metal-Ligand Complexes Incorporated in Model Lipid-Membrane Bilayers
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We have designed and synthesized ruthenium metal-ligand complexes (MLCs) with amine- or acyl-reactive functional groups. The MLCs have potential as luminescent probes to investigate bio-macromolecular dynamics on the sub-microsecond-to-microsecond timescale. This timescale is of interest, for example, for analysis of the motions associated with macro-molecular assemblies and interactions of membrane-bound proteins. Here we report the photophysical and structural properties of MLCs (1) $[HRu(CO)(4,4'\text{-dicarboxybipyridyl})(PPh3)_2]^+$ $[PF_6]^-$ conjugated to dipalmitoyl-phosphatidyl-ethanolamine (DPPE), (2) $[HRu(CO)(bpy)(PPh_2C_2H_4COOH)_2]^+$ $[PF_6]^-$ conjugated to dimyristoyl-phosphatidyl-ethanolamine (DMPE) and (3) $[(CF_3CO_2)Ru(CO)(5\text{-aminophen})(Ph_2PC_2H_2PPh_2)]^+$ $[PF_6]^-$ conjugated to DPPE and cholesterol. These conjugates were incorporated in 100nm-diameter-unilamellar lipid-membrane vesicles to investigate the photophysical properties of the probes in a model membrane environment and to evaluate the utility of these probes for investigating the physical properties of lipid membranes. We are also investigating the photophysical behavior of MLCs in Nanodiscs, which are ~10nm-diameter phospholipid bilayers surrounded by a recombinant scaffold protein. We are using Nanodiscs as a platform for investigating the dynamics of transporter proteins, and we are using the MLCs as tools to characterize the physical properties of the Nanodisc-transporter assembly.

2494-Pos
Theoretical Design of Model Nanoparticles for Targeted Cell-Surface Binding
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Targeting therapeutic nanoparticles to circulating tumor cells is a crucial step in eradicating cancer from the body. The efficiency of this treatment relies on optimally binding surface ligands of the nanoparticles to the specific patterns of receptors uniquely displayed by the target cells prior to cellular uptake. We present a theoretical study that identifies the key characteristics of nanoparticles for binding to different types of afflicted cells, enabling enhanced detection and targeting capabilities.
Dynamic behavior of nanoparticle ligands and cell surface receptors are influenced by the properties of the surfaces on which they are attached. Thermal fluctuations enable the ligands and receptors to bind securely by probing varied conformations, but these systems are also subject to forces from elastic deformation of the surfaces and local tethering at receptor-ligand complexes. We introduce a novel simulation methodology that enables the coupling of particles' motion and the motion of their associated surface, which improves upon existing techniques that neglect the influence of particle dynamics on membrane motion. We explore how properties such as size, elasticity, and ligand mobility of a nanoparticle influence its ability to effectively associate with various target cells displaying unique receptor profiles. Our results elucidate the physical consequences of certain properties on receptor-ligand interactions, allowing systematic design of nanoparticles with improved abilities to bind specifically to a large array of tumor cells.

2495-Pos
PH.D Student
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Manipulations that alter the energetics of a chemical reaction often alter the activation free energy in linear correlation with the equilibrium free energy change. Such linear free energy relationship (LFERs) have been widely used to probe the energetics of transition states associated with protein folding and enzymatic catalysis. Nevertheless, the physical basis that underlie LFERs in such systems are not well understood, and it is not obvious how the slope of the linear relation should be interpreted. We show that the effects of amphiphiles on gramicidin A(gA) channel gating in lipid bilayers obeys a LFER and have studied the underlying mechanisms. The channel gating process provides a unique chemical reaction, in which structural changes in a model protein can be studied at the level of single molecules, while offering quantitative information about the energetics of a reaction transition state and its position on a spatial coordinate. We show that the LFER can be understood - and that the slope of the linear relation between changes in activation energy and equilibrium free energy for channel formation can be interpreted - by considering the effects of amphiphiles on the changes in bilayer elastic energy associated with channel gating. The use of amphiphile-induced changes in bilayer elastic properties provide a tool for studying LFERs associated with membrane protein function and folding.