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356-Pos
isenND: a fluorescent sensor for membrane binding and remodeling reactions
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Nonadiscs (NDs) are emerging as an excellent platform for structural and functional characterizations of membrane proteins. We herein further engineered nonadisc as a robust fluorescent sensor to monitor membrane biochemical reactions. Specifically, we circularized nonadiscs via split GFP, and thereby created an intensity-based fluorescent sensor for detecting membrane binding and remodeling events in NDs (isenND). We demonstrated the use of isenND to study the action of several bacterial and eukaryotic membrane proteins on lipids bilayers. Together, isenND could serve as a versatile biochemical reagent useful for basic and translational research of membrane biology.

357-Pos
Controlled membrane interactions by lipid coated quantum dots
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Quantum Dots (QDs) are being employed in a wide range of biological application due to their superior fluorescent characteristics. Bio-compatibility of QDs is usually achieved by exchange of as-synthesized surface ligands with ligands that impart the particle with water solubility properties. An alternative approach for surface functionalization is ligand adsorption. This approach is based on weak interactions between the alkane chains of the as-synthesized surface ligands and a hydrophilic element of an adsorbed ligand with a functional head group/s. There are several advantages for this approach: (i) The photophysical properties stay intact and (ii) the weak association allows for potential adaptive re-distribution of the ligands in response to environment changes. Membrane targeting introduces another layer of complexity and requires precise control of QD surface properties to control the mode of interaction with the membrane (adsorption, insertion, and uptake). The interplay between the hydrophobic, hydrophilic and electrostatic properties of a particle surface is crucial for controlling the mode of membrane interaction. Here we demonstrate that precise control of lipid mixture composition can modulate QDs mode of interaction with the membrane. We show compositions that favor membrane insertion and compositions that favor surface-charge dependent adsorption. We also show that the latter could be used to detect suspended malignant cells (that have different surface charge than healthy cells).

358-Pos
Long chain lipids facilitate insertion of large nanoparticles into membranes of small unilamellar vesicles
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Quantum Dots (QDs) and Nanorods (NRs) have found a vast array of applications in optoelectronics and bio-labeling: Incorporation of such NPs into the cell membrane holds great potential for many novel applications ranging from single molecule membrane potential sensors and actuators, to light harvesting, therapeutics and diagnostics. However, research aimed at deciphering the underlying design rules, which would allow for robust delivery, targeting, insertion and retention in the membrane for long durations is in its early stages. Previous studies have shown that without any surface modification, only small spherical QDs can be fused into Small Unilamellar Vesicles (SUVs) bilayers in between the two leaflets. Because the thickness of the hydrophobic bilayer of the SUVs is limited to 4-5 nm thick, the inclusion of hydrophilic QDs within the bilayer is size limited to ~5 nm in diameter. Incorporation of nanoparticles above this size limit requires development of challenging surface engineering methodologies. To overcome this limitation and facilitate particle insertion, we developed the capability to incorporate large NPs into the membrane of SUVs by optimization of lipid composition, NP/lipid ratio, type of detergent, and specifically by using very long phospholipids.

Here we explore the effect of very long phospholipids (C24:1) in SUVs, on the membrane insertion efficiency of nanoparticles in the range of 5-13 nm in diameter. To this end, we improved an existing vesicle preparation protocol and utilized cryogenic electron microscopy imaging to examine the mode of interaction and to evaluate the membrane insertion efficiency of membrane-inserted nanoparticles.

359-Pos
The role of virus geometry and matrix proteins in envelope and host membrane fusion
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Many medically important viruses, including influenza, Ebola, and SARS-CoV-2, are enveloped by a lipid membrane. Therefore, a crucial step in the infection involves the fusion of the viral and cellular membranes. Membrane fusion consists of a series of non-bilayer intermediate configurations with two significant energy barriers, each with a magnitude of dozens of kT. The first energy barrier is the merger of the proximal monolayers, a well-studied process requiring the mechanical work of the viral fusion proteins. The second barrier is the merger of the distal monolayers and the subsequent expansion of the fusion pore. Fusion pore expansion is driven by the membrane stress within the non-bilayer intermediate and is less well understood. Here, we use the theory of membrane elasticity to compute both energy barriers in the context of viral membrane fusion. We find that the virus geometry primarily affects the energy barrier for fusion pore expansion. Furthermore, we analyze the effect of virus shape and membrane-matrix interaction on the fusion rate. We suggest that morphological changes of the virus and the coordinated disassembly of its matrix layer in the acidified environment of the endosome reduces the energy barrier of pore expansion and thus accelerates fusion. Finally, we discuss how interferon-induced transmembrane protein 3 (IFITM3) prevents viral membrane fusion.

360-Pos
Why are SNARE complexes rod-shaped?
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SNARE proteins constitute the core of a cellular machinery that fuses membranes for vital processes such as exocytotic release of neurotransmitters or hormones and intracellular trafficking. Despite years of study, the mechanism remains highly controversial. Here we developed molecularly explicit simulations that fused synthetic-sized vesicle membranes on physiological millisecond timescales for the first time, and demonstrated that membrane fusion is driven by entropic forces among the rodlike SNARE complexes (SNAREpins) and membranes. Entropic force mediated SNAREpin formation and spherical-vesicle membranes together into an extended contact zone (ECZ). The entropic forces maintained the SNAREpins at the outer edge of the ECZ, catalyzed a hemifusion stalk at the edge, and expanded the stalk into a hemifusion diaphragm (HD) large enough to allow tension to complete the fusion pathway by nucleating an extended hydrophilic simple pore in the HD. Corroborating this pathway, ECZ and HD intermediates were experimentally observed in reconstituted exocytic systems (Diao et al., 2012; Hernandez et al., 2012). This mechanism radically differs from a common view, that fusion is driven by the ~60 kT zipperping energy of SNARE complexation. We find no support for this view; complexation occurs after microseconds (Gao et al., 2012; Kubekla et al., 2004; Xi et al., 2012), much faster than fusion. Additional corroboration of the entropic mechanism is that fusion required SNARE complexation zipperping forces to equal the experimentally measured ~18 pN (Gao et al., 2012). These entropic forces originate in the bulky rodlike SNAREPin shape, shared by refolded fusion glycoproteins of influenza, CoV-2 and other viruses. Therefore, we propose that the energy barrier for fusion pore expansion is driven by an entropic force that is mediated by the SNARE complexation.

361-Pos
Modeling simultaneous two-wavelength axial ratio imaging of clathrin mediated endocytosis
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Clathrin-mediated endocytosis (CME) facilitates the internalization of extracellular cargoes. However, how clathrin-coated vesicles (CCVs) form remains unclear due to the limited resolution of live-cell fluorescence microscopy and the need for sample fixation in electron microscopy. To bridge this gap, our lab developed Simultaneous Two-wavelength Axial Ratio Imaging (STAR) that...