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13-Subg
Lipid Nanotubes as a Tool for Studying Nanoscale Proteo-Lipid Domains
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Membrane curvature can play a decisive role in demixing of membrane bound proteins, allowing for formation of fluid-like or gel-like proteo-lipid domains responsible of distinct shape (shape creators) and/or function (e.g. topological remodeling). We take advantage of the nanoconfinement offered by the lipid membrane tethers or lipid nanotubes to access such domains and reveal the fine details of their dynamic life. By combining conductance and fluorescence measurements on a lipid nanotube we are able to monitor the nucleation, stepwise growth and disassembly of individual dynamin1 nanodomains and observe reversible changes in membrane shape and topology produced by them. The sensitivity of this method relies on the nanoconfinement of the tube and the correlative analysis of the data, and gives the spatial and temporal resolution needed for the study of dynamic elasticity of non-homogeneous membranes at nanoscales.

14-Subg
How Cells Exploit Forces to Sense and Respond to their Environments
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Cells recognize physical features in their environments by exploiting mechanical forces generated by their motors which pull on distal extracellular anchoring points. Filopodia have been described previously as the ''sticky fingers'' that help cells to explore their environments and help immune cells to clear pathogens. Here we will ask how cells exploit the interplay between filopodia and lamellipodia to explore their environments, recognize surface properties and find their pray. Myosin-generated tensile forces acting on filopodia are utilized by cells to pull on external adhesive objects. If the external objects can be deflected, the filopodia adhesion will grow as filopodia and object align, but filopodia often peel off from flat surfaces. Tensile forces acting on filopodia are thus used by cells to distinguish between deflectable nanofibrillar environments and flat surfaces. Only if lamelliopdia are in contact with flat surfaces, the tensile forces acting on filopodia can steer the protrusion of lamellipodia. This synchronized movement is needed for the physical removal of surface adhering pathogens for example by macrophages. Membrane tension might play a still poorly understood role in the local coordination of events.

15-Subg
Determining the In-Plane and Out-of-Plane Structure of Model Membranes; Two Recent Examples
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With the exception of hydrogen, neutrons are found in all atomic nuclei. Importantly, unlike X-rays, neutrons are able to differentiate between the different isotopes of the same element. In biology, the classic example is the isotopic substitution of hydrogen for deuterium, allowing one to selectively tune the sample's contrast *in situ* with minimal or no change to its native structure. Biological membranes are believed to exist in a disordered state, a fact that presents unique challenges to elucidating their fine structure. In the case of model membranes, to overcome this difficulty we have developed the Scattering Density Profile (SDP) model, which combines neutron and x-ray scattering data, with molecular dynamics simulations to yield robust structural data, including the much sought after area per lipid needed by simulators to refine their force fields. In addition to one-dimensional structural data along the membrane, we have recently exploited the contrast variation offered by neutron scattering (exchange of hydrogen for deuterium), to study - with unprecedented accuracy - the lateral phase separation (in-plane structure) of so-called ''raft'' forming mixtures. We hope that in the near future we will apply this knowledge to address the question that has vexed biologists and confounded experimentalists for over 40 years: do membrane domains exist *in vivo*?

16-Subg
Membrane Fusion by X-Rays: From Model Membranes to Organelles
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Understanding the physical mechanisms underlying membrane fusion requires a multi winged approach, involving model systems as well as biological membranes. We study fusion intermediates occurring in form of ordered passages or stalks connecting neighbouring bilayers in multilamellar model membrane stacks. The stalks exhibit long range crystalline order with rhombohedral symmetry in a fluid 'host' membrane stack, which is studied by high resolution x-ray diffraction under grazing incidence angles. Information on membrane curvature, and hydration interaction can be revealed by analyzing the quantitative electron density maps, collected for controlled environmental parameters and membrane composition [1]. Phase diagrams can be analyzed in view of stabilizing or destabilizing agents for stalk formation.
While in these equilibrium phase, dehydration forces bring bilayers together favoring at some point the formation of stalks, it is specific membrane proteins and their interaction which set the local boundary conditions for membrane apposition in biological membrane fusion. In view of studying fusion in the presence of SNARE proteins, we have started a x-ray structural characterization of synaptic vesicles (SV) by small-angle x-ray scattering, and currently extent this work towards studies of SV dockled to and interaction with model bilayers [2].
Finally we present a novel high resolution x-ray imaging scheme capable of yielding a magnified hologram of a freely suspended lipid membrane illuminated by highly divergent and coherent x-ray beams. We propose this setup to image fusion trajectories at high resolution in future experiments [3].
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17-Subg
Some of my Greatest Mistakes
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Subgroup: Bioenergetics

18-Subg
FOF1-ATP Synthase Dimers and The Mitochondrial Permeability Transition Pore from Yeast to Mammals
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The mitochondrial permeability transition pore (PTP) is a voltage-dependent channel that allows solutes of molecular mass $\leq$ 1.5 kDa to equilibrate across the inner membrane. Matrix Ca^{2+} accumulation, together with Pi and a set of compounds collectively called ''inducers'', is necessary to induce PTP opening. In mammals cyclosporin (Cs) A desensitizes the PTP through its binding to cyclophilin D, a matrix protein that facilitates PTP opening. Yeast and Drosophila mitochondria also possess Ca^{2+}-activated channels which, at variance from the mammalian PTP, are insensitive to CsA and inhibited rather than activated by Pi. We show (i) that the permeability properties of the Drosophila channel, which displays selectivity toward Ca^{2+} and H^{+}, are not modified by expression of human cyclophilin D; and (ii) that, in keeping with our recent demonstration that the mammalian PTP forms from dimers of the FOF1-ATP synthase, Ca^{2+}-dependent currents can be elicited in reconstitution experiments with purified dimers of the yeast enzyme. We are currently investigating the effect of genetic ablation of FOF1-ATP synthase subunits that mediate dimerization on PTP opening in yeast, Drosophila and mammalian mitochondria. Our findings suggest that the PTP-forming ability of FOF1-ATP synthase has been conserved in evolution, and that the channels display species-specific features.

19-Subg
The C-Subunit of the ATP Synthase Forms the Pore of the PTP
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Mitochondria maintain tight regulation of inner mitochondrial membrane (IMM) permeability to sustain ATP production. Stressful events cause cell