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Model cellular membranes: From flat to strongly curved structures

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Cellular membranes are essential components of cells that compartmentalize cellular events, control communication between compartments and with the exterior, enable the formation of gradients of ions and other solutes, and provide a proper environment for the large percentage of proteins that are membrane bound or associated to it1. The ability to carry out this diverse array of essential functions requires a high degree of dynamic organization at the nanoscale. It is proposed that the different functions are compartmentalized into different domains by lipid-lipid and/or lipid-protein interactions, but studying these systems have proved difficult due to the nature of cellular membranes and the requirement of sophisticated techniques to analyze them at the molecular level. The current state of the art on membrane organizations heavily focusses on planar membranes2 despite these membranes often being highly curved as in dynamic processes such as invagination and vesiculation, but also in organelles such as the endoplasmic reticulum and the mitochondria. Neutron scattering combined with deuteration is an ideal technique to study the structure and dynamics of multicomponent systems where different parts of the system can be highlighted individually3–5. For example, Neutron Reflection (NR) allows to extract depth profiles of rather complex biointerfaces2 and revealed the overall structure of lipid bilayers as a function of composition6,7, the dependency of the core thickness on acyl chain type7, and the position of cholesterol in the bilayer 8,9, the flip/flop 10, and the ability of membranes to exchange lipids across bilayers3, among other parameters such as fluctuations on floating bilayers11. Similar depth profile information can be extracted for lipid vesicles from small angle neutron scattering (SANS) but the accuracy is lower as compared to NR due to the smearing by the inherent orientational averaging and lower dQ/Q. For example, using SANS the membrane thickness of photolipid vesicles was shown to be tuned in response to illumination by UV and blue light12. Both NR and SANS lack the possibility to extract lateral correlations, which is accessible to GISANS, such as local adhesion points, clustering of adhesion anchors13 as well as lipid rafts14.
In this talk I will present a range of examples that demonstrate the power of neutron scattering and selective deuteration for studying the structure and composition of model cellular membranes. I will then finally present a new approach based on diffracting scaffolds to study membrane structure as a function of curvature suited for a range of surface sensitive techniques. I will also show fluorescence microscopy data for lipid diffusion on curved membranes among others.

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Primary author: Prof. CARDENAS, Marite (Biofisika Institute)

Presenter: Prof. CARDENAS, Marite (Biofisika Institute)

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