High-Pressure Response of the Coupled Dynamics of Lipids and Membrane Proteins

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Cell membranes consist of a complex assembly of lipids and proteins that are essential to normal cellular function through their role as physical barrier, chemical filter or signal converter. The understanding of the interplay between the lipid properties, the collective physical properties of the membrane and the protein conformational landscape is key in order to explain the membrane protein function. Experimentally, high hydrostatic pressure can be used as a tool to modulate the lipids dynamics as well as a way to smoothly modulate the protein dynamics without denaturation. By combining high resolution liquid-state NMR and molecular dynamics (MD) simulation, we are characterizing the coupled dynamics of lipids and proteins in response to high pressures at the molecular level. We first demonstrate that state-of-the-art lipid forcefields enable to quantitatively reproduce the membrane phase transition at increasing pressure. As observed experimentally, the presence of a membrane protein such as OmpX shifts the phase transition to higher pressures. The MD simulations are then instrumental in providing a molecular picture of the protein's effect on the membrane lipids, in particular by providing a spatial resolution (that is, how lipids in contact with the protein are affected differently from those that are further away) that is not accessible in the experiments. In turn, we also characterize the lipid effect on the protein, and show that protein side-chains facing toward the membrane are very sensitive to the lipid phase transition, whereas groups pointing toward the protein core are much less affected, as suggested by the experimental results.

Keywords: Biological membranes, Hydrostatic Pressure, Membrane proteins, Lipids, Molecular dynamic simulations.