Allosteric Coupling Between a Lipid Bilayer and a Membrane Protein

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Cell membranes are complex assemblies of lipids and proteins that are essential to normal cell function through their role as physical barrier, chemical filter, or signal converter [1]. The understanding of the interplay between the lipid properties of the membrane and the protein conformational landscape is key to explaining the function of membrane proteins. Experimentally, high-pressure NMR on lipid nanodiscs has recently been proposed as a method to probe the allosteric communication between the lipid bilayer and the bacterial model membrane protein OmpX [2]. Here, I will present our recent atomistic molecular dynamics (MD) simulations on periodic bilayer models, carried out in close collaboration with experimental groups [3], which provide unprecedented insight into the molecular details of lipid-protein interactions.
We show that, state-of-the-art lipid force field quantitatively capture the membrane phase transition under increasing pressure [4]. The presence of a membrane protein such as OmpX shifts this transition to higher pressures, in agreement with experimental observations. Simulations reveal that OmpX delays gelation by structurally liquefying the annular shell of lipids in its first solvation layers. We further compare infinite bilayer systems (proxies for liposomes) with lipid nanodiscs commonly used in experiments, highlighting the impact of the scaffold protein on the pressure response of both lipids and membrane proteins. I will present preliminary results in a G-protein-coupled receptor, which displays a more complex conformational landscape than OmpX.

Bibliography :

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