

Simulating biologically relevant membranes: tackling lipid diversity in bacterial membranes

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Biological membranes regulate a myriad of critical cellular processes through the modulation of essential properties such as membrane elasticity, membrane fluidity and the formation of lipid microdomains. Such differences in turn affect the function of membranes and membrane proteins. While once biological membranes were thought of as simple bilayers composed of a just few simple lipids, they are now known to contain over a thousand unique lipid species. Many, if not most, are yet to be functionally characterized. Lipids are known to play a central role in determining the resilience of a cell to environmental stress and its sensitivity to toxic agents including antimicrobial peptides, antibiotics, disinfectants and organic pollutants. Examining the structure and function of biological membranes and membrane proteins using simulation methods therefore faces a number of challenges that are yet to be addressed, overcome or even identified. Modelling a biologically relevant membrane requires a system of known composition and an accurate and reliable model to describe interatomic interactions (the force field). The latter is essential to capture the individual and collective behaviour of lipids under a given set of conditions (*e.g.* temperature, hydration and compositional heterogeneity and stoichiometry) and is based on the comparison of properties calculated from simulations with reference data obtained experimentally. However, how reliable are experimental data? Can differences between experimental and simulation systems fundamentally flaw this approach? Furthermore, the chemical and structural diversity of lipids is only being uncovered. For example, the repertoire of lipids in bacterial membranes is much broader than in eukaryotic membranes and includes branched-chain fatty acids and hopanoids amongst others. Branched-chain fatty acids have been proposed to protect membranes against hostile conditions and hopanoids have long been hypothesized to be surrogates of sterols, but, in fact, little is known about the actual effect of those lipids on membranes. Simulations have shown that the different types of branching and hopanoids have specific effects on membrane fluidity that allow bacteria to finely tune the sensitivity of their membranes to the environment. The lipid composition is thus a critical parameter to consider when studying a biologically relevant model membrane.