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A discrete simulation of protein movement and protein-protein interactions in a biological membrane

The membrane is a complex and dynamic system that plays a major role in the metabolic processes of organisms. The lateral organization and dynamics of proteins in the membrane are important factors in controlling membrane bioactivity. Simulations of the membrane, which strive to maintain biological realism, enable us to investigate these processes. The purpose of this work is to explore time and length scales that are not accessible to all-atom, or even coarse-grained, molecular dynamics (MD) simulations that are currently undertaken. Here we present a novel simulation method for a system of synthetic membrane peptides, WALP-23, in a DPPC phospholipid bilayer.

We are able to investigate many of the features that are observable in MD simulations, but at a fraction of the computational cost. The ability to simulate longer time and length scales also enables us to investigate aspects of the simulated system that we would be unable to investigate with MD. We can look at the longer-term evolution of protein clusters, investigating their mobility, lifetime and rates of coalescence. We are also able to look at the larger-scale structures that form, allowing us to make comparisons with experimental data from techniques like atomic force microscopy.

We employ an off-lattice model, with the membrane represented as a two dimensional sheet and the proteins described by the position of their centre of mass. The simulation uses stochastic Brownian dynamics to model the motion of the proteins through a lipid continuum. Forces between proteins, mostly a result of the hydrophobic mismatch between the protein and the bilayer, act along the line of centres. The influence of the surrounding lipids on each protein is manifested both in the stochastic nature of the Brownian motion, and in their contribution to the inter-protein forces.

We use MD simulations to characterise the force between proteins. The inter-protein force for a pair of WALP-23 proteins in a DPPC bilayer can be measured whilst varying the separation of their centres of mass. The benefit of this approach is that the inter-protein force includes contributions from different sources. Some of these, such as the hydrophobic mismatch, would be difficult to characterise without such a calculation. By improving the parameterization process and looking at more protein species we can work towards a more varied and realistic membrane simulation.