Molecular simulations of membrane dynamics, remodeling, and sensing

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Living cells use lipid membranes to maintain their internal structure, to guard their outside boundary, to establish potential and concentration gradients, and to transmit signals between their compartments and to the outside. As a consequence, the dynamics within the membrane, the sensing of the physical state of membranes, and the remodeling of membrane structures play vital roles in biology. To study these problems, we performed molecular dynamics simulations (primarily) using the coarse-grained MARTINI lipid membrane model.

We used molecular simulations to study the diffusive transport of lipids and membrane-spanning pores within membranes [1]. Remarkably, we found that the apparent diffusion coefficient diverges logarithmically as the size of the simulation box is increased, seemingly without bound. This divergence is consistent with hydrodynamic theory, which also suggests possible solutions to the problem of relating (divergent!) simulation results to experiment.

We also simulated the spontaneous fusion of small lipid vesicles [2]. Inspired by cryo-electron micrographs (Geng et al., Nature 2014) of membrane-embedded carbon nanotubes (CNTs), we set up lipid vesicles stapled together by CNTs. We found that CNTs act as powerful fusogens, inducing vesicle fusion on a (sub)microsecond timescale, with distinct mechanisms of merging first the outer and then the inner leaflets.

Molecular simulations combined with experiments helped us to identify a mechanism used by eukaryotic cells to sense the fluidity of lipid membranes [3]. From millisecond-long simulations, a unique sensory mechanism emerged. In essence, the relative rotation of two interacting transmembrane helices appears to report on the membrane state, probing quite directly the packing density as a key physical variable.

Overall, molecular simulations give us a detailed picture of the dynamic processes within lipid membranes. In particular, they helped us tackle the challenges of relating the observed lipid diffusion dynamics to experiment, of studying lipid membrane fusion at a molecular scale, and of identifying physical mechanisms in membrane sensing.

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