We aim to develop high-performance computer simulation, model membrane platforms and neutron scattering experiment to address a key outstanding question in membrane biology namely, how are lipid domains on opposite sides of an asymmetric bilayer coupled? We will perform all-atom molecular dynamics simulations of the experimental system (a 100 nm lipid vesicle) on ORNL’s supercomputers at biologically relevant time and length scales.

Cell membranes, once thought to be homogeneous assemblies of lipids and proteins, are now believed to contain nanoscopic domains (“lipid rafts”) critical to their function, particularly in transducing signals across the membrane. One persistent mystery in this regard is whether rafts bridge the two bilayer halves (leaflets), and how they could do so despite strong asymmetry in the composition, i.e., the presence of different lipids with distinct physical properties in the two bilayer leaflets. Resolving this mystery requires detailed structural information that has heretofore been unattainable, because rafts are disordered and transient entities, and their size is below the detection limits of commonly-used biophysical characterization techniques.

For biomolecular simulations, the messages to be sent and their associated latency dominate the FFT computation time.

A. Particle Mesh Ewald (PME) reduces the complexity in treating the Coulomb interaction to NlogN.

B. Fast Multipole Method (FMM) reduces the complexity in treating the Coulomb interaction to N. It allows non-periodic or periodic boundaries and avoids 3D FFTs, which could be potentially better suited for scaling on future parallel and heterogeneous computing architectures.

C. Reaction field (RF) is essentially a local electrostatic method, having excellent strong scaling performance on Titan.

D. Image Charge Method (IC) the reaction potential due to a source charge inside the spheres is represented in terms of a one dimensional distribution of image charges.

E. Advanced Sampling Techniques Methodological advances are required to reach the desired time scales with MD simulation. Our work is built upon a very promising enhanced sampling method - the orthogonal space generalized ensemble (OSGE) method.

F. Membrane Domains We combined neutron scattering and computer simulation to determine the structure and dynamics of nanoscopic lipid domains (~12 nm diameter) within unilamellar vesicles mimicking the mammalian plasma membrane outer leaflet. All-atom simulations qualitatively reproduce the experimental findings and add a molecular description of lipid organization at the nanodomain interface.

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