BLUE WATERS
SUSTAINED PETASCALE COMPUTING

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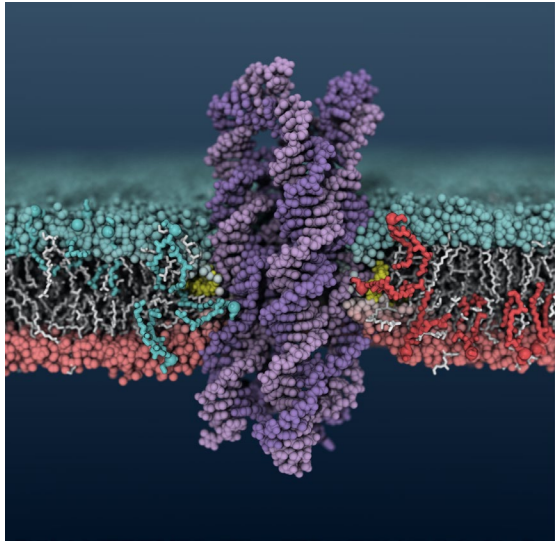
OUTPERFORMING NATURE: SYNTHETIC ENZYME BUILT FROM DNA FLIPS LIPIDS OF BIOLOGICAL MEMBRANES AT RECORD RATES

Research Challenge

Mimicking enzyme function and increasing the performance of naturally evolved proteins is one of the most challenging and intriguing aims of nanoscience. The team employs DNA nanotechnology to design a synthetic enzyme to substantially outperform the biological archetypes. Since the function of an enzyme sensitively depends on its atomic-scale structure and dynamics, this aspect of the studied system necessitates the use of all-atom molecular dynamics (MD) for prototyping the designer enzymes.



Lipid scrambling by a designer DNA enzyme. The DNA nanostructure (purple) is inserted via hydrophobic cholesterol anchors (yellow) into a lipid bilayer membrane (cut away for clarity). A toroidal pore that connects the upper (blue) and lower (red) leaflets of the bilayer allows lipids to pass between the leaflets.

Methods & Codes

This project employs the NAMD package to perform explicit-solvent all-atom MD simulations of a synthetic scramblase—an enzyme that transports lipids from one leaflet of a bilayer to the other. The studied system consists of eight DNA strands embedded in a lipid bilayer membrane through two covalently attached cholesterol anchors. Experimental work conducted in the Keyser Lab in Cambridge, UK complements the microsecond-timescale MD simulations.

Results & Impact

The conducted MD simulations provide a microscopic detail of the mechanism of lipid transport, and show that a membrane-spanning single DNA helix forms a toroidal pore that provides a pathway for lipid molecules to cross from one leaflet of the bilayer to the other leaflet. Computations predict very small ~2 k_BT barrier to lipid crossing at the toroidal pore indicating the diffusion-limited rate. The computed rate that exceeds 10^7 molecules per second matches the experiment, which confirms the enzyme activity in cancer cells.

Why Blue Waters

Accurate characterization of structural fluctuations and transport properties of DNA nanotechnology systems enhanced by the presence of nonstandard functional groups requires the use of explicit-solvent all-atom MD simulations. The massive size of DNA structures makes their MD simulations computationally demanding. The large number of GPU-accelerated nodes and fast Gemini interconnect available on Blue Waters significantly speed up the DNA nanotechnology simulations.