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Translocation of Small Interfering RNA and Cholesterol Molecules in Biomembranes[1]

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This presentation will focus on all-atom molecular dynamics (MD) simulation studies of (1) structural and mechanical barriers to translocation of small interfering RNA (siRNA) across a phospholipid bilayer, and (2) flip-flop dynamics of cholesterol (CHOL) molecules across a phospholipid bilayer. In the first case, we find that the siRNA induces a liquid-to-gel phase transformation. In the gel phase we find large compressive lateral stresses in the hydrocarbon chains of lipid molecules, which present a considerable barrier to siRNA passage across the bilayer. In the second case, we study spontaneous CHOL inter-leaflet transport (flip-flop), the effect of this process on mechanical stresses across the bilayer, and the role of CHOL in inducing molecular order in bilayer leaflets. The simulation was run for 15 microseconds and we found 24 CHOL flip-flop events over that duration. On average, a CHOL molecule migrates across the lipid bilayer in about 73 ns after a flip-flop event is triggered. We have calculated diffusion maps and determined free energy surfaces and flip-flop mechanisms for CHOL molecules.

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