Dealing with Divergent Diffusion Coefficients in Large-Scale Lipid Membrane Simulations

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We used molecular dynamics simulations to study the diffusive motions of lipids, membrane-spanning nanopores, and integral membrane proteins within lipid membranes. We found that their apparent diffusion coefficients diverge logarithmically as the width of the simulation box is increased, seemingly without bound. This divergence would appear to preclude the calculation of proper size-independent diffusion coefficients that can be compared to experiment. However, in simulations with systems of more than 100 million particles, we show that a hydrodynamic model not only explains the divergence, but can also be used to obtain both proper diffusion coefficients and difficult-to-calculate membrane properties.

Hydrodynamics also accounts for the box-size dependence of the rotational diffusion of macromolecules. We show that the rotational diffusion tensors of proteins and nucleic acids can be determined directly from the time-dependent covariances of the quaternion describing their orientations in space. However, in molecular dynamics simulations the rotational dynamics is slowed as a result of the imposition of periodic boundary conditions. A simple hydrodynamic correction accounts quantitatively for this finite-size effect and makes it possible to estimate proper infinite-system rotational diffusion coefficients from simulations using small boxes.

Overall, the analysis of long simulation trajectories of large membrane, protein, and nucleic acid systems demonstrates that both translational and rotational diffusion coefficients suffer from significant finite-size effects. Hydrodynamics allows us to correct for the system-size dependences, giving us diffusion coefficients that can be compared to experiment.