

140d Modeling of Transport of Nanoparticles across a Lipid Bilayer

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Understanding transport of nanoparticles across cell membranes plays an important role in developing novel drug delivery vehicles. Moreover, investigations of the nanoparticle transport and interactions between nanoparticles and the lipid bilayers are necessary to assess possible health hazards of manufactured nanomaterials due to damage caused by nanomaterials to the living cells. In this talk, we present results of a molecular modeling of the transport of nanoparticles through a cell membrane. The cell membrane is modeled by a bilayer composed of dipalmitoylphosphatidylcholine (DPPC) lipids.

The studies are performed using a coarse-grained molecular dynamics model, which represents groups of several atoms as united atoms (beads). This allows one to significantly speed up simulations while retaining the key system dynamics. The intermolecular interactions are modeled by the Lennard-Jones and Coulombic potentials. The computational model for a bilayer is prepared by simulations of self-assembly of the lipids starting from a random initial distribution. Two types of coarse-grained models for nanoparticles are considered: spherical nanoparticles (represented by hydrophobic Lennard-Jones spheres of varying effective diameters) and linear nanoparticles (represented by chains of Lennard-Jones spheres connected by a harmonic spring). We investigate effects of hydrophobicity of the nanoparticles on their transport properties. This is accomplished by varying the potentials of interaction between the nanoparticles and the coarse-grained polar beads which represent water molecules and lipid headgroups.

One of the main challenges in the investigation of the nanoparticle transport across the lipid bilayer is the long timescale of events of interest, which is not accessible by direct molecular dynamics simulations. In order to overcome this limitation, we obtain an effective stochastic Langevin equation for the nanoparticle diffusion across the lipid bilayer. The components of this equation (the mean potential force and the magnitude of the random force) are obtained using the constrained simulations method, as well as a novel kinetic method based on a statistical analysis of a series of short-scale molecular dynamics simulations with judiciously chosen initial conditions. The obtained Langevin equation is solved to obtain the nanoparticle transport rates.

In order to gain detailed understanding of the mechanism of the nanoparticle transport, we further analyze the internal microstructure of the lipid bilayer and correlations between dynamics of the nanoparticle and dynamics of the lipids. The effects of the nanoparticle transport on the structure of the lipid bilayer are reported along with an assessment of long-term membrane degradation.