Computer Simulation Studies of Biological Membrane Systems

Rakwoo Chang

Department of Applied Chemistry, University of Seoul, Republic of Korea

With the fast growth of the computational power, theoretical studies using computer simulations are being widely used in biological systems. However, there is still a significant gap between what experimental scientists expect and what computer simulation scientists can offer. I will discuss the general features of the capabilities and the limitations of computer simulations using several examples, especially biological membrane systems. As the first example, chlorosulfolipids (CSLs) are major components of flagellar membranes in sea algae. Unlike typical biological lipids, CSLs contain hydrophilic sulfate and chloride groups in the hydrocarbon tail; this has deterred the prediction of the CSL membrane structure since 1960. In this study, we combine coarse-grained (CG) and atomistic molecular dynamics (MD) simulations to gain significant insights into the membrane structure of Danicalipin A, which is one of the typical CSLs. It is observed from the CG MD that Danicalipin A lipids form a stable monolayer membrane structure wherein the hydrocarbon moieties are sandwiched by hydrophilic sulfate and chloride groups in both the head and tail regions. Based on the mesoscopic structure, we have built the corresponding atomistic model to investigate the integrity of the CSL monolayer membrane structure. The monolayer membrane comprising bent lipids shows high thermal stability up to 313 K. The gel−liquid crystalline phase transition is observed around 300 K. The second topic, polyhexamethylene guanidine (PHMG), has recently been the most infamous chemical in South Korea because it caused several fatalities while used as a humidifier disinfectant. In a mouse experiment on the toxic effects of inhalation, it was confirmed that inhalation of these toxic components could cause increased mortality, hyperplasia of alveoli and bronchioles, alveolar emphysema, and pulmonary fibrosis. In this study, we have performed MD simulation to study effects of PHMG on lung surfactant membranes. The lung surfactant was modeled as a monolayer of dipalmitoylphosphatidylcholine (DPPC), which is the main component of the lung surfactant membrane. In addition, a water droplet containing PHMG mimicking aerosol and a bare PHMG were used to investigate the effects of water droplets upon the PHMG permeation into the blood stream. From MD simulations of around 100 ns, we have observed that the water droplet smeared into the water phase leaving PHMG behind in the membrane region in dilute concentration. On the other hand, it was also observed that PHMG induces endocytosis in high c

oncentration. We have additionally examined structural effects of PHMG on DPPC mono layer by calculating translational and orientational pair correlation functions.