ABSTRACT

Biological membranes play a vital role in the structure of living cells by allowing the compartmentalization of specific functions within the cell and protecting them from their environments. Membranes also play an active role in the regulation of protein function and signaling through chemical and mechanical interactions. To understand how membrane mechanics affects protein function we use atomic molecular dynamics simulations of model bacterial membranes. Through the calculation of the stress tensor within the simulation volume, we can obtain 2-dimensional stress profiles along the bilayer normal, which are directly connected to elastic properties such as bending and compressibility moduli. These stress profiles are highly dependent on the membrane composition and provide a detailed view of the forces acting on integral proteins within the lipid membrane. An important component of bacterial membranes is the hopanoid tetrahydroxybacteriohopane, which may modulate membrane mechanical properties in a similar way to sterols in eukaryotic membranes.

INTRODUCTION

While the composition of the plasma membrane in bacteria can vary significantly between species, one of the main components is 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoethanolamine (POPE, Fig. 1A). In recent years, the sterol-like membrane components known as hopanoids have gained significant interest due to the structural and mechanical changes they may induce on membranes similarly to the effects that sterols have on eukaryotic membranes. One of the most common bacterial hopanoids is tetrahydroxybacteriohopane (THB, Fig. 1A), which in many cases is a precursor for other more complex hopanoids. We aim to systematically study the effects of THB on POPE membranes using highly detailed atomic molecular dynamics simulations (MD) of small membrane patches (200+ lipids, Fig. 2). From these simulations, we can obtain the pressure tensor within the simulation volume, which allows us to calculate stress profiles and observe changes in the mechanical behavior due to THB in a similar manner to what we have observed in previous work with ergosterol containing membranes (Fig. 1B).

SIMULATIONS

Atomistic molecular dynamics simulations are performed using the Gromacs 4.5 simulation package and the recently developed 43A1-S34 force-field which provides a unified set of parameters for lipids, sterol-like molecules with fused rings, and proteins.

Stress profiles are obtained from the diagonal elements of the pressure tensor averaged over the membrane plane. The local pressure tensor can be expressed in terms of an "energy density" with a kinetic and configurational component, and is obtained from the positions and velocities of the atoms:

\[ P(r) = \sum_i m_i v_i \otimes v_i + \frac{1}{V} \sum_{i<j} F_{ij} \otimes r_{ij} \]

Diagonal elements averaged over the membrane (xy) plane

\[ \pi(z) = \left( P_{xx} + P_{yy} \right)/2 + P_{zz} \]

Stress profiles can then be used to calculate important mechanical properties of the membrane such as the bending moduli, area compressibility modulus, and membrane tension.

REFERENCES