COMPUTATIONAL MULTISCALE MODELING AND ANALYSIS OF LIPID MEMBRANES: A CASE STUDY ON GRAM-NEGATIVE BACTERIA

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Gram-negative bacteria have attained the “superbug” status since they have become resistant to a broad range of antibiotics. The multi-drug resistance developed by them are a major concern worldwide causing chronic and biofilm associated infections making it to critical both for biomedical and microbial research They are also important in material science research since the adhesion of bacteria onto the solid surfaces of industrial applications lead to economic losses by formation of biofilm. In order to design drugs and develop microbial coatings against these bacteria information about the interactions of bacterial cell envelope to its surroundings is crucial. Earlier theoretical and experimental studies have discovered and analyzed the structure of Gram-negative bacteria. From those works it is understood that the shape and structure of outer membrane of Gram-negative play a significant role in design drugs that can penetrate the impermeable membrane. Lipids play an important role in cell signaling and physiological processes. Lipopolysaccharides (LPS) are very much part of the outer leaflet outer membrane of the bacteria functioning as a barrier and shield protecting the bacteria from external or environmental threats.[2]. Abnormalities in membranes cause variety of diseases. And these membranes are proved to be very good targets for drug therapy [1]. The structural and dynamical descriptions of membrane can be derived using Molecular Dynamics (MD) simulations approach instead of conducting experiments. Still it is important to validate the molecular dynamics results with the experimental data.[3]

Our work involves using computational methods to study and analyze Gram-negative bacterial membranes. We use a combination of web-based platforms, online and in-house tools for analysis and visualization and molecular dynamics simulations software packages available for high-performance computing and facilities for our research. Using these methods, we generated membrane models, performed simulations and analyzed the models and results. Based on the results we can proceed further to develop new membrane models to understand their interactions with nanoparticles and drugs. In future we plan to insert small molecules into the heterogenous lipid membrane models and perform simulations.

Lipid type	System	Upper Leaflet	Lower Leaflet	Total number of Lipids
POPE:POPG	1:1	21:21	21:21	42:42
POPE:POPG	3:1	33:11	33:11	44:44
POPE:POPG	5:1	40:08	40:08	48:48
POPE:POPG		41:123	41:123	164:164

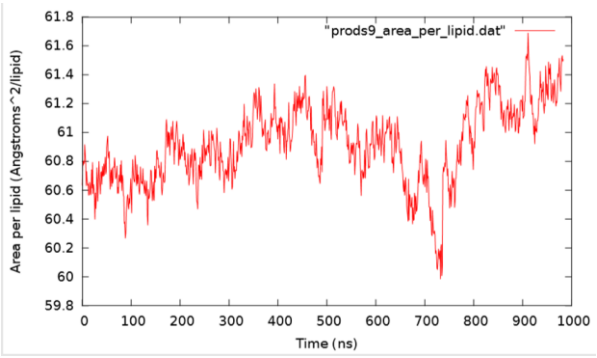

Figure 1: Summary of different membrane systems built and analyzed using heterogenous lipids and large-scale membrane system (POPE: POPG – 1:3-41:123 = 164 lipids) analysis - area per lipid.

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