Computational Simulations of Outer Membrane Proteins of Pseudomonas aeruginosa embedded in Lipopolysaccharide Membranes.

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In recent years, significant progress has been made in applying simulation methodologies to the study of biological membranes. These applications have focused exclusively on lipid bilayer membranes and on membrane proteins in lipid bilayers. Bacterial outer membrane is strictly asymmetric and consists of a phospholipid inner leaflet and a lipopolysaccharide (LPS) outer leaflet. Despite differences in physical-chemical properties of LPS membrane and phospholipid bilayer, a number of simulation studies of bacterial outer membrane proteins (OMPs) have been reported using lipid bilayers. Yet, because the structure and conformation of LPS molecules determine the physical and chemical properties of the outer membrane such as fluidity and charge density with implications for its biological function, a realistic computational simulation of OMPs should account for an accurate description of the LPS layer. An atomistic model of the LPS membrane of P. aeruginosa has been previously developed (Lins and Straatsma, 2000), validated against experimental measurements (Soares and Straatsma, 2008) and applied to simulations of the outer membrane protein OprF (Straatsma and Soares, 2009). In the present study, molecular dynamics simulations of OMPs (OprF and OprM) of P. aeruginosa embedded in LPS membranes are discussed and compared to simulations in lipid bilayers. It is found that the conformational ensembles of OMPs from different lipid matrices exhibit significant differences, particularly in the extra-cellular structural motifs. Because of the strong interactions between the loop regions of OMPs and functional groups in the saccharide core of the LPS, the entrance to the channel from the extracellular space is widened compared to the lipid bilayer simulations in which the loops are extruding in the solvent with implications to gating mechanisms in these systems.

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