

Structural transition in Lipid A bilayers driven by physical and chemical factors.

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Abstract: Lipid A constitutes the hydrophobic region of lipopolysaccharides (LPS) molecules, which are the main component of external membrane of Gram-negative bacteria. The Lipid A is the endotoxic factor inducing bacterial toxicity. Chemical modifications of the Lipid A structure promotes changes on its aggregation form and biological properties. In order to understanding the microscopic details involving structure, biological activity and physical properties of these membranes, we have extended the GROMOS 53A6 force field to different Lipid A phenotypes of *P. aeruginosa* [1] and *E. coli* and carried out atomistic molecular dynamics simulations of bilayers at different conditions on the NpT ensemble for 200 ns. The structural dynamics and transition between distinct aggregate forms of Lipid A bilayers were investigated at different temperature conditions (278K, 300K, 328K and 343K), type of cations (Mg^{2+} and Na^+) and structural phenotypes (hexa-, penta- and tetraacilated and mono and diphosphorylated). Structural analyses of the simulated systems were performed with the program SuAVE [2] which takes into account changes in the membrane curvature during transitions between different aggregate states. Properties such as area per lipid, bilayer thickness, deuterium order parameters of acyl chains, curvature degree, coordination number and spatial chemical group density profile were calculated and compared for the simulated systems. The present simulations show that i. Lipid A bilayers undergo a lamellar to non-lamellar arrangement in the presence of monovalent cation independent of the phenotype; ii. Divalent cations stabilize the lamellar arrangement of Lipid A by means of crosslinking phosphate groups in neighbor lipids, whereas monovalent cations are not able to interact in this way as previous reported [3]; iii. Lipid A in non-lamellar structures adopt an average conical shape, while in lamellar one it adopts a conical conformation; iv. Changes in the phase organization shows to be strongly influenced by number and length of acyl chains in the Lipid A structure. Our finds reveal the intrinsic relationship between Lipid A chemical structure, conformation and aggregate arrangement.



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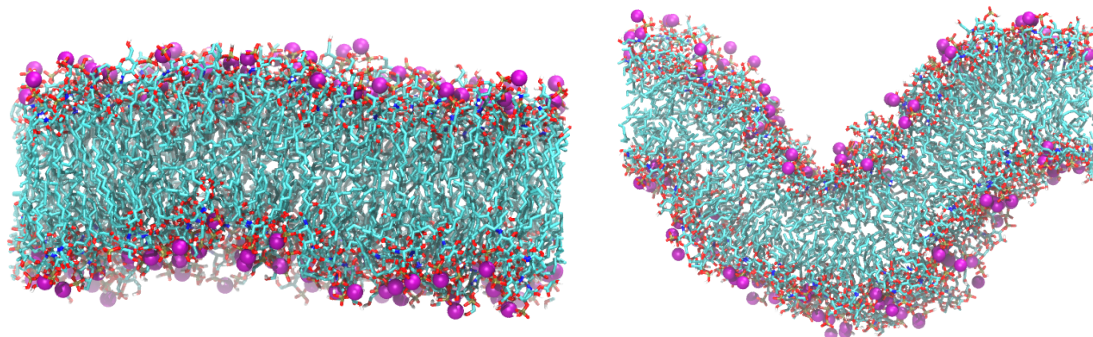


Figure 1: Lamellar (left) and Ripple (right) bilayer arrangement for Lipid A with different phenotypes (hexa- and tetraacylated, respectively). Magnesium cations are represented by purple atoms.

Key-words: Bacterial outer membrane, force field parameters, metal hydration in membrane environments, atomistic computational simulations.

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