

Atomistic Simulations of Bacterial Outer Membrane Models

Thereza A. Soares

Departamento de Química Fundamental, Universidade Federal de Pernambuco, Brazil

Department of Chemistry and Umeå Centre for Microbial Research, Umeå University, Sweden

Lipopolysaccharides (LPS) are the major constituent of bacterial outer membranes, acting as an effective permeability barrier against xenobiotic agents and the host cell defence system. LPS is also a potent activator of the mammalian immune system in amounts as little as fmol. Variable external conditions prompt structural and chemical modifications of the bacterial outer membrane, enhancing the organism ability to evade the host immune defence and colonize specific tissues. Changes in temperature and/or specific ion concentration have been shown to trigger lamellar to non-lamellar transitions in LPS membranes. We have previously developed and validated an atomistic model of the LPS membrane of *Pseudomonas aeruginosa*, which has been used to investigate its structural dynamics, hydration and electrostatic properties.^{1,2} We have further expanded our atomistic model to include novel LPS chemotypes expressed by *P. aeruginosa* during outer membrane remodeling.^{3,4} We have found that decrease in the LPS polysaccharide chain length occurs with increase in the diffusion coefficients for the Ca^{2+} counter-ions, increase in acyl chain packing (decrease in membrane fluidity), and decrease of the negative potential across the LPS surface. We have also investigated the effect of mono- and divalent cations on the stability of LPS and Lipid-A membranes.⁵ Our findings indicate that the stability of LPS membranes reflects a balance between effective membrane hydration, ionic valence and aptness to cross-link neighbouring molecules. These findings reproduce experimental trends while providing atom-level structural information on the rough LPS chemotypes that can help to rationalize antibiotic resistance and bacterial adhesion processes.

References

1. K.N. Kirschner, R.D. Lins, A. Mass, T.A. Soares. 2012. *J. Chem. Theor. Comp.* 8, 4719-4731.
2. F.J.S. Pontes, V.H. Rusu, T.A. Soares, R.D. Lins. 2012. *J. Chem. Theory Comp.* 2012, 8, 3830-3838.
3. R.D. Dias, G.C.A. da Hora, M. Ramstedt, T.A. Soares. 2014. *J. Chem. Theor. Comp.* 2014, 10, 2488-2497.
4. R.D. Dias, L. Li, T.A. Soares, E. Alexov. 2014. *J. Comp. Chem.* 35, 1418-1429.
5. A. Nascimento, F.J.S. Pontes, R.D. Lins; T.A. Soares. 2013. *Chem. Comm.* 50, 231-233.