Atomistic Simulations of OmpA and Peptidoglycan: A Step Towards the Virtual Bacterial Envelope

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Gram-negative bacteria are protected by an exceptionally complex cellular envelope containing two layers of membranes separated by a periplasmic space housing a network of peptidoglycan (PGN) cell wall. The outer membrane is adhered to the PGN scaffold via non-covalent interactions with integral outer membrane proteins, such as the ubiquitous OmpA. Here we report atomistic molecular dynamics simulations of the full-length OmpA models embedded in a realistic representation of the outer membrane, with the C-terminal domain (CTD) attached to the PGN strands [1]. Comparative analysis of OmpA CTD from different bacteria revealed a universally conserved PGN binding mode. The binding of PGN to OmpA was found to be labile, whereby unbinding and rebinding were observed during the simulations. In its monomeric form, OmpA CTD interacted with the lower leaflet of the outer membrane, while OmpA dimer retained its CTD within the periplasmic region, suggesting that dimerisation may be crucial for interactions with PGN. Crucially, our work represents a step forward towards building a computational model of the bacterial cell envelope to enhance our understanding of the structure-function relationships of its major molecular components.

References

[1] Samsudin F, Ortiz-Suarez ML, Piggot TJ, Bond PJ, Khalid S, OmpA: A Flexible Clamp for Bacterial Cell Wall Attachment, Structure **24**, 2227–2235 (2016)