Molecular Dynamics Simulations of the *E.coli* Cell Envelope: capturing the complexity

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Gram-negative bacteria such as *E.coli* are typically regarded as "simple" model organisms, yet their cell envelopes are surprisingly complex. Recent experimental and theoretical studies have revealed that contrary to the traditional view of the cell membrane as a passive bystander in membrane protein function, it plays a key role in protein folding, assembly, and function. To study the dynamics of native membrane proteins and antimicrobials within the cell envelope we are constructing a virtual *E.coli* cell envelope. Our atomistic-level model incorporates the heterogeneity of the inner leaflet lipids, the biochemical complexity of the lipopolysaccharide outer leaflet and also includes the peptidoglycan matrix within the periplasmic space. We have performed a series of simulations exploring how these various membrane components influence the structure and dynamics, and therefore function of the proteins that reside within them.

Coarse-grain models that enable simulation of larger systems on longer timescale are also being used to explore the lateral mobility and aggregation of membrane proteins within the *E.coli* inner and outer membranes

Our approach of running extended simulations of complex systems i.e. incorporating the molecular complexities at both atomistic and coarse-grained levels of details, and performing simulations at of hundreds of nanoseconds to microseconds, is enabling us to gain new insights into specific protein-protein and protein-drug interactions and also the interactions of these species with the surrounding environment.

References

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