THE BACTERIAL CYTOSKELETON ALTERS THE CELL MEMBRANE IN MOLECULAR DYNAMICS SIMULATIONS

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Abstract
Antimicrobial resistance is predicted to cause 10 million deaths annually by 2050. New antibiotics are needed, and a better understanding of essential bacterial processes will facilitate structure-based design in this field. MreB is a bacterial actin homologue which defines the shape of rod-shaped bacteria by coordinating peptidoglycan synthesis in the elongasome. MreB forms filaments that interact with the cytosolic leaflet of the cell membrane as well as membrane proteins and other cytosolic proteins. The details of protein-protein and protein-lipid interactions in the elongasome are currently unknown. In this study, interactions of MreB with the membrane are investigated by molecular dynamics simulations. The simulations reveal cardiolipin recruitment and membrane bending towards the peptidoglycan caused by MreB filaments. Cardiolipin has a concentration-dependent effect on bending, suggesting an importance of cardiolipin in this system. Bending is observed across different species despite lack of conservation of cardiolipin-binding residues, and MreB mutants reveal select residues which collectively impact membrane bending. This study uncovers a novel mechanism by which MreB modifies the cellular membrane and has implications for how other proteins are recruited to the filament in the elongasome.