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The Physics of Bacterial Growth and Form

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Cells typically maintain characteristic shapes, but the mechanisms of self-organization for robust morphological maintenance remain unclear in most systems. In this talk, I will describe how we have interrogated this complex question at multiple length scales using a combination of molecular and cellular mechanochemical simulations and novel imaging techniques. Precise regulation of rod-like shape in Escherichia coli cells requires the MreB actin-like cytoskeleton, but the mechanism by which MreB maintains rod-like shape is unknown. We have used time-lapse and 3D imaging coupled with computational analysis to map the growth, geometry, and cytoskeletal organization of single bacterial cells at subcellular resolution. Our results demonstrate that feedback between cell geometry and MreB localization maintains rod-like cell shape by targeting cell wall growth to regions of negative cell wall curvature. Pulse-chase labeling indicates that growth is heterogeneous and correlates spatially and temporally with MreB localization, whereas MreB inhibition results in more homogeneous growth, including growth in polar regions previously thought to be inert. Biophysical simulations establish that curvature feedback on the localization of cell wall growth is an effective mechanism for cell straightening and suggest that surface deformations caused by cell wall insertion could direct circumferential motion of MreB. Molecular dynamics simulations show that MreB filaments have tunable curvature and twisting that can explain the cell wall patterning observed in experiments. We also demonstrate that the bitopic protein RodZ regulates the biophysical properties of MreB and alters the spatial organization of new cell wall growth in Escherichia coli. We find that the relative expression of MreB and RodZ change in a manner commensurate with variations in growth rate and cell width. We present molecular dynamics simulations and quantitative microscopy demonstrating that RodZ alters the curvature sensitivity of MreB, and cell shape as a consequence. Finally, we identify MreB mutants that mimic the molecular properties of RodZ binding, and that rescue cell shape in the absence of RodZ . Together, our results describe how E. coli alters its cell width by differentially regulating RodZ and MreB to alter the patterning of cell wall insertion. Our findings indicate the potential for rich regulatory landscape of MreB molecular biophysics that can drive changes in cell shape across bacteria.