New and Notable

Combining Modeling and Experiment to Understand Bacterial Growth

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We often take for granted the elegantly simple shapes adopted by bacteria. Spheres, crescents, helices, and other shapes fill the prokaryotic world (1). Despite the relative simplicity of these shapes compared to a scraggly Purkinje cell in the cerebellar cortex or even the crowned and tailed unicellular choanoflagellate, truly fundamental questions about bacterial growth remain unanswered. Nearly all bacteria use an exoskeletal, peptidoglycan cell wall to define their shape and structural properties. Cell growth can be incredibly fast, with doubling times on the order of 10 min, and involves the biogenesis of peptidoglycan material and its insertion into and modification of the existing cell wall.

The generation of cellular-scale wall features such as micron lengths and widths are thought to be the result of spatial-temporal patterning of cell-wall insertion and modification. How molecular-scale enzymes collectively act to build a cell remains an open question in bacterial morphogenesis. This is largely due to the lack of tools that can probe scales between the molecular and the cellular regions—exactly those needed to understand cell shape and many other cellular-scale phenomena. On the smallest scales, structural and biochemical probes are able to provide atomistic details of protein form and function. Above the diffraction limit of visible light, light microscopy can provide vital information about biological processes. However, a dearth of techniques to probe biological dynamics on scales from 10 nm to 200 nm has hindered progress in understanding bacterial growth. Very recently, however, biophysical modeling has emerged as a tool to bridge these spatial scales (see, e.g., Huang et al. (2) and Gardner et al. (3)).

In a recent issue of the *Biophysical Journal*, Misra et al. (4) use just this strategy to attack the problem of cell-wall thickness and the growth of Gram-positive bacteria. The Gram-positive *Bacillus subtilis* is a rod-shaped cell surrounded by a multilayered, thick cell wall. By combining a physical model of cell-wall growth and degradation with molecular-scale electron microscopy data and cellular-scale growth rate measurements, the authors find that a coupling between cell-wall synthesis and hydrolysis, a molecular-scale phenomenon, yields a fixed wall thickness and strain even when the rate of growth is increased substantially. Because the cell wall is under considerable turgor pressure, hydrolysis can generate as much strain in the material as insertion. This work also helps to explain seemingly confusing data from the 1970s, which reported that cell-wall hydrolysis itself can increase growth rate (5).

This powerful combination of theory and experiment provides a guiding framework for dealing with scientific problems that lack direct experimental support. New techniques, such as superresolution light microscopy and high-resolution AFM imaging, may eventually serve to directly test these ideas. For now, though, a combination of new experimental designs and the development of more realistic and complex models of biological systems will continue to provide a window into the inner workings of the cell.

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