Every living organism—including Earth’s simplest life form, the bacterium—is loaded with molecular devices that are breathtaking in their design, complexity, and efficiency. Eukaryotes have long been known to possess sophisticated subcellular architecture in which DNA, RNA, and proteins are localized to the right place at the right time. Bacteria, in contrast, have until recently been thought to be unorganized bags of goop. Consequently, cell biology was generally restricted to eukaryotes. However, remarkable recent advances in imaging technologies, including fluorescent reporter proteins in an array of colors; confocal and two-photon microscopy; super-resolution imaging methods such as photoactivated localization microscopy (PALM)/stochastic optical reconstruction microscopy (STORM) and stimulated emission depletion (STED); and methods for measuring protein dynamics and interactions such as fluorescence recovery after photobleaching (FRAP), fluorescence loss in photobleaching (FLIP), and fluorescence resonance energy transfer (FRET) have made it so that we can now peer into bacterial cells as we traditionally peered into bigger eukaryotic cells (reviewed in Gitai, 2009). These technologies have revealed that bacteria are decidedly organized (reviewed in Shapiro et al., 2009). As a microbiologist, I offer a few examples from the bacteria to suggest that there exists an especially bright future in cell biological studies of microbes.

Although bacteria are considered primitive, they build molecular gadgets of mind-boggling complexity. Bacteria have miniature motors that operate like boat engines complete with propellers (flagella). The motors use a proton gradient as fuel, and this contraption allows cells to swim at a pace that, given their size, would make Olympian Michael Phelps envious. Bacteria possess similarly stunning equipment to control information flow—marvelous multipart machines constructed from component proteins. One such apparatus (the replisome) rapidly copies and proofreads the millions of nucleotide bases that compose the genome. In terms of accuracy, if a human being typed, say, 40 words per minute, and that human being typed 8 h a day, 5 d a week, it would be as if he or she made one mistake every 40 years!

How do bacteria accomplish such feats? Bacteria do it like eukaryotes do it. Actually, to put things in proper perspective, eukaryotes do it like bacteria do it. Bacteria were here first. Bacteria invented the rules for cellular organization. But, because of technological limitations, scientists initially learned cell biology from eukaryotes and, only now, are they beginning to learn about cell biology in bacteria.

In eukaryotes, cellular organization is largely established through a cytoskeletal network made up of actin, tubulin, and intermediate filament proteins. It turns out that bacteria have their own versions of
actin (MreB), tubulin (FtsZ), and intermediate filament proteins (CreS) that polymerize and disassemble to organize the cell. Other filament systems coordinate metabolic processes, an aspect that seems conserved from bacteria to humans (Ingerson-Mahar et al., 2010). Bacteria also possess remarkably accurate oscillators to keep track of time and curvature-finding proteins that self-organize to generate cellular landmarks.

We now need to identify more of the relevant players that establish and propagate bacterial cellular architecture. New studies demonstrate that many more proteins, mostly of unknown function, also exist in specific locations in bacteria (Werner et al., 2009). This tantalizing finding begs the question of how and why all these proteins get to and stay at their proper destinations.

We are also now on the verge of being able to exploit the techniques that we have in hand for studying single bacterial cells to investigate cell biological features of populations: colonies, single- and multispecies biofilms, and host–pathogen and host–commensal interactions. The ease of manipulation of bacteria, coupled with our ability to quickly and simultaneously interrogate large numbers of cells, makes such studies feasible. Furthermore, the potential for making rapid gains in our understanding of basic cell biology is tremendous because, for the most part, analogous explorations are not yet possible in the relevant eukaryotic counterparts: tissues, organs, whole animals, and populations of animals.

One long-standing question in cell biology is whether there is a cell biological “central dogma.” Researchers have characterized organisms that seem to use different solutions to solve analogous cell biological problems. Is this because every cell type has evolved its own optimized strategy, or is this because we have too few characterized systems to appreciate the recurring universal themes? Again, bacteria to the rescue! Because bacterial diversity far surpasses that of eukaryotes, and because bacteria are easy to manipulate, microbial cell biologists can deconstruct the cellular architecture of a sufficient number of species to establish if, in fact, there are unifying principles. Comparative bacterial cell biology could reveal the rules underpinning why particular cell biological tasks require proteins harboring specific properties. For example, why do some filaments exhibit treadmilling kinetics, whereas others function through dynamic instability? In addition to being diverse, bacteria are ancient. Bacterial cell biological experiments therefore promise to provide fundamental insight into the origins and evolution of intracellular architecture. Beyond protein machines that assemble and become localized, DNA, RNA, lipids, and small molecules are also subject to specific temporal and spatial localization regimes in bacteria. Generally, we have no idea how these gadgets work so superbly, nor how these molecules get to where they are going or why they need to be there. This treasure trove of molecules promises to be the cell biologist’s playground for decades to come.

We know that millions of bacterial species exist. Scientists have studied only a handful of them. That means that there are millions of biological devices and structures awaiting discovery and analysis by cell biologists. If we can understand these gadgets and structures deeply, they could conceivably be used as prototypes for real machines or real construction projects. Thus, bacteria provide the next generation of cell biologists an essentially limitless resource for investigating the vast diversity and majestic architecture of the awe-inspiring natural world.

REFERENCES


FIGURES AND TABLES

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