

Preface

ARTHUR KORNBERG ADMONISHED US TO "never do clean experiments on dirty enzymes." There is a formidable history of the bacterial cell as an exquisite system to analyze the inner workings of the smallest and simplest cell. Biochemists broke open the bacterial cell, collected the soup, and carried out chemical analyses of its constituent parts and biosynthetic pathways. The biochemical clarity provided by this approach provided much of our knowledge about the reaction mechanisms that form the basis of molecular biology. The combination of *in vitro* biochemistry and the elegant logic of genetic manipulation led to the general perception that we understood the operation of the bacterial cell. But this was a misleading perception because it did not take into account something crucial: the inner and dynamic organization of the bacterial cell.

Little more than two decades ago, the leading microbiology textbooks of the day depicted the bacterial cell as a relatively amorphous vessel in which proteins and DNA were distributed in a relatively haphazard fashion. The bacterial cell was sometimes considered to be a "bag of enzymes" and its content a "cell sap." Electron microscopy revealed a layered cell envelope and various appendages, such as flagella and pili, that protruded from the cells. Ribosomes were seen as broadly distributed puncta across the cytoplasm, with the nuclear material occupying a broad central zone. It was not until the 1990s with the application of immunoelectron and immunofluorescence microscopy and the introduction of the Green Fluorescent Protein that a new era of bacterial cell biology commenced. As we now know, and despite its small size, the bacterial cell has an intricate and dynamic three-dimensional organization that is inseparable from its biology. It is this revolution in our understanding of the bacterial cell that is the subject of this volume.

The early chapters by Toro and Shapiro and Thanbichler in this book reveal the extraordinary three-dimensional organization of the bacterial chromosome, the nucleoid, its dynamic behavior during the cell cycle, and the coupling mechanisms that coordinate chromosome dynamics with cell division. A further, major advance in the cytology of bacteria was the discovery that like eukaryotic cells, these most primitive of cells have a dynamic cytoskeleton that guides cytokinesis, growth of the cell envelope, and the movement of chromosomes. The chapter by Shaevitz and Gitai tells us about the working of tubulin-like and actin-like cytoskeletal proteins in the bacterial cell. The next two chapters, by Rudner and Losick and by Kirkpatrick and Viollier, focus on the localization of specific proteins within the cell, the underlying mechanisms that govern protein positioning, and how this positioning gives rise to polar structures.

We don't usually think of bacteria as having organelles, but classic experiments by Leon Heppel revealed that Gram-negative bacteria have an outer compartment, the periplasm, that is a focus of great interest, as presented by Silhavy, Kahne, and Walker. Other bacteria also have specialized membrane-bounded compartments, such as the magnetosome, whose function and assembly are described in the chapter by Murat, Byrne, and Komeili. In addition, bacteria have macromolecular machines embedded in their membranes that carry out specialized functions. Erhardt, Namba, and Hughes describe the exquisite ultrastructure of the flagellum and type III injectisome and how these motors pump proteins out of cells. Another category of macromolecular machine mediates the transport of highly charged DNA molecules across membranes. Burton and Dubnau tell us how these DNA translocases carry out this feat.

The next series of chapters focus on multicellularity. Bacteria were traditionally viewed as solitary creatures that go about their business individually. Now we know that many, indeed likely most,

bacteria form complex assemblies of cells. Two classic examples are fruiting body formation in myxobacteria, as presented by Kaiser, Robinson, and Kroos, and heterocyst formation, as presented by Kumar, Mella-Herrera, and Golden. In both cases, multicellular arrays—three-dimensional in the case of the former and one-dimensional in the case of the latter—of cells communicate with each other to govern the differentiation of specialized cell types. Another more prevalent example of multicellularity is the formation of architecturally complex communities of cells on surfaces. These biofilms, which are important in medicine, agriculture, and industry, are the subject of the review by López, Vlamakis, and Kolter.

This volume would not be complete without a peek into the future. A second revolution is now unfolding, driven by electron cryotomography, as explained by Tocheva, Li, and Jensen, single-molecule and super-resolution imaging as presented by Biteen and Moerner, and automated quantitative live-cell fluorescence microscopy, as summarized by Fero and Pogliano. These explosive advances in combination with the availability of full genome sequences of hundreds of bacterial species and innovative bioinformatics are providing a new and deeper understanding of biochemical processes in the living cell. Indeed, we now know that the dynamic, three-dimensional organization of the bacterial cell plays an inextricable role in the regulatory mechanisms that control life.

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