Tips and Tools

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The Atlas of Bacterial & Archaeal Cell Structure: an Interactive Open-Access Microbiology Textbook

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INTRODUCTION

Currently, students may complete general biology courses without a full understanding of what bacterial cells look like and what structures they contain. This is because such cells are on the scale of 1 μm in size, orders of magnitude smaller than eukaryotic cells and mere specks when viewed through a light microscope. While higher-resolution electron microscopy (EM) has been in use since the 1930s, traditional sample preparation (involving fixation, dehydration, resin embedding, and staining) disrupts or destroys many cellular structures, a problem that is particularly acute for bacterial and archaeal cells, which lack the large, robust organelles of eukaryotes. Only in the past 20 years, with the advent of cryogenic EM (cryo-EM), have researchers been able to visualize the internal structure of small cells like bacteria and archaea in a native, unperturbed state. The result has been a revolution in our understanding of bacterial and archaeal cells, replacing the idea of bags of small molecules with a view of impressively complex macromolecular machinery (1).

Unfortunately, this view remains off-limits for most students. Unlike light microscopy, cryo-EM requires specialized expertise and equipment that costs millions of dollars to purchase and maintain. Cryo-EM images are published in research articles but are not yet widely included in primary textbooks for cell biology and microbiology. A similar access gap existed in the 1960s, when traditional electron microscopists had amassed considerable knowledge of the structures of eukaryotic cells and tissues but the images had not yet reached medical students. In response, authors like Don Fawcett and John Dodge published "atlases" of electron micrographs, which remain valuable resources decades later (2, 3). Following in that tradition, we have created *The Atlas of Bacterial & Archaeal Cell Structure*, an open-access digital textbook using cryo-EM images to illustrate microbial cell biology. By offering it as a free online resource, we hope it will be widely accessible to students throughout the United States and in other countries.

PROCEDURE

The Atlas of Bacterial & Archaeal Cell Structure, which is available at cellstructureatlas.org, draws from more than 40,000 imaging data sets collected by the Jensen laboratory at the California Institute of Technology (4). These data sets were acquired using cryogenic electron tomography (cryo-ET), a cryo-EM technique in which a sample such as an intact frozen-hydrated bacterial cell is imaged at different angles in order to calculate a three-dimensional reconstruction, or tomogram, of the cell and the macromolecular structures it contains (5). More than 150 tomograms are featured in the *Atlas*, representing around 70 unique species of bacteria and archaea.

The book begins with an optional chapter discussing the methods used to visualize cells and their components. This provides a helpful comparison of what microbes look like when imaged with different microscopy methods, e.g., light microscopy or transmission EM. While useful for understanding how the images in the book were acquired, it can be skipped if there is insufficient time to cover the material or if the goal is simply a high-level introduction to what cells look like, for instance, in a biology survey course for nonmajors. Everything a general reader needs to know to be able to use the book is summarized in a 2-min video in the introduction.

The main content of the book offers a narrative that walks students through a set of challenges faced by an imaginary cell and the structures that real cells have evolved to answer these challenges. After reading each short text section,

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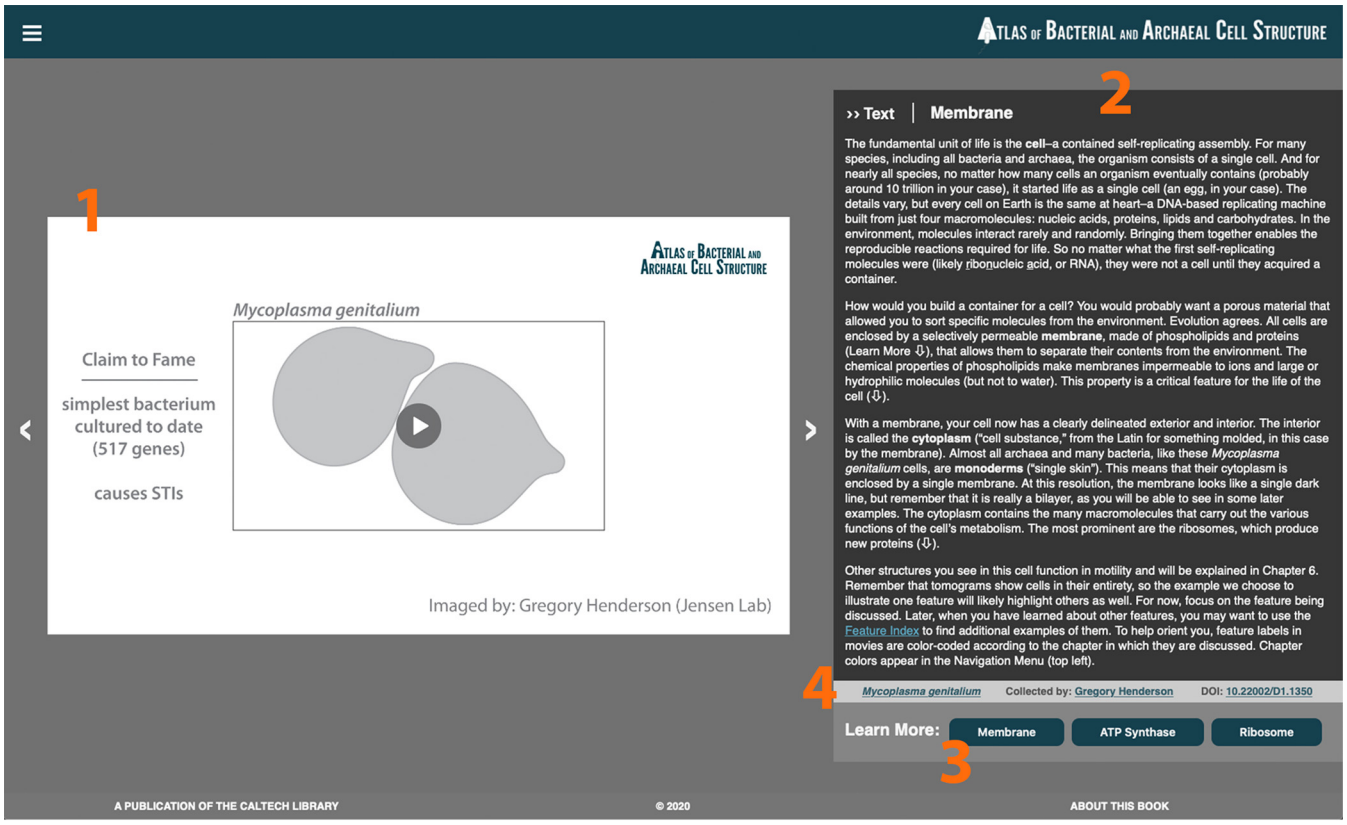

FIG 1. Resource interface. A screenshot of the user interface of *The Atlas of Bacterial & Archaeal Cell Structure* shows the elements of a content page: (1) a video highlighting a cellular structure in a three-dimensional tomogram; (2) accompanying narrative text; (3) buttons to access additional information and animations; (4) links to related appendix information (phylogenetic tree and scientist profile) and the record in the Caltech Data Repository, where the video can be downloaded (for example, to use in teaching).

the student watches a video highlighting the discussed structure in a tomogram of a cell (Fig. 1). Optional "Learn More" buttons bring up additional details such as an atomic model of the structure or an animation of how it works. The final page of each chapter offers a simple summary animation of the main concepts, along with suggestions for further reading and a set of review questions to test concept retention. Instructors may wish to use these concept check questions in homework and exams; if so, please contact us for an accompanying answer key. Appendix material offers students additional context, including biographies of the scientists who collected the data, a phylogenetic tree, and an index of cellular features so the reader can compare how they look in different species.

The only prerequisite knowledge for the textbook is a familiarity with basic concepts in biology. The main content is targeted to undergraduate students in general biology or cell biology courses, as well as students in medical, nursing, or veterinary microbiology courses. The material would also be appropriate for high school students. Optional additional material is targeted to more advanced students, such as those in graduate-level microbiology seminars. The main content can be digested in several hours, so we recommend assigning the book as a supplementary resource to accompany the first few sessions of a course, giving students an appreciation of what bacteria and archaea look like before moving on to study particular aspects of their metabolism or medical relevance.

The book is published by the Caltech Library under a Creative Commons CC BY-NC 4.0 license, making all content available for noncommercial reuse with attribution. To facilitate use in lectures, videos are archived in the Caltech Data Repository and can be downloaded through stable Digital Object Identifier (DOI) links from the pages on which they appear. The original source data for the videos can also be accessed through the repository records, from the public Caltech Electron Tomography Database (ETDB-Caltech) (6). We expect to update *The Atlas of Bacterial & Archaeal Cell Structure* frequently to expand features and to reflect new results from what is still an active field of research. Information about what has been added in each new edition will be catalogued on the "About this Book" page to keep instructors up to date, and previous editions will remain available through the Caltech Library.

Safety issues

No biological or chemical safety concerns are associated with use of this online resource.

CONCLUSION

Here, we describe an open-access resource for microbiology education, *The Atlas of Bacterial & Archaeal Cell Structure*. Released in December 2020, it has not yet been tested in a formal course setting. In development, however, it was read by students at different educational stages, e.g., having completed 1 year of high school biology or having completed multiple undergraduate biology courses and worked in a microbiology laboratory. In all cases, students reported that the content was comprehensible and the interactive format enjoyable. We look forward to improving future editions in response to feedback from educators who use the resource in their classes.

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