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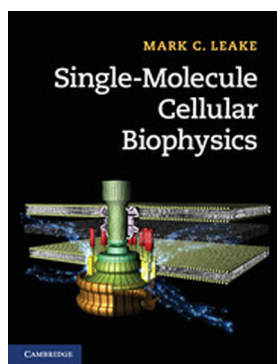
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BOOK REVIEWS

Single-Molecule Cellular Biophysics

Mark C. Leake, 175 pages + ix, ISBN: 978-1-107-00583-9, Cambridge University Press, New York (2013), \$80.00, hardcover.

Reviewed by Barry R. Masters, Fellow of AAAS, OSA, and SPIE



Research on single-molecule cellular biophysics is an emerging field that is rapidly advancing based on the development of new instrumentation and experimental designs. To understand complex biological systems, researchers require instrumentation and techniques that span many orders of scale. The measured units include length, force, energy, time, and concentration and the validation of measurements

for both *in vivo* and *in vitro* studies, as well as the limitations of the techniques and an understanding of the perturbations that the techniques induce in the experimental systems.

Single-molecule cellular biophysics is an interdisciplinary field populated by both life scientists and physical scientists. Mark Leake wrote this textbook with the aim of ensuring that his book could be easily understood by students and researchers from both fields. This concise book is based on lecture notes from a course on single-molecule methods that the author and his colleagues taught at Oxford University.

This book has several unique features that work to fulfill the author's aim. In a short book that covers the entire field of single-molecule cellular biophysics, an innovative approach is required. Each chapter begins with a quotation that introduces a unique viewpoint about the material contained in the chapter. Then the content of the chapter is presented in a paragraph labeled "General Idea." The text is supplemented with small but high-resolution black and white figures. These figures are clearly labeled, and the figure legends are sufficiently detailed to be independent of the text. There are boxes in each chapter that are labeled "Physics-Extra" or "Bio-Extra" that contain details aimed at readers with backgrounds in either physics or the life sciences. Throughout the text, "Key Point" boxes appear to highlight the salient facts for the reader. Each chapter ends with several useful features. First there is a part called "The Gist," which consists of bulleted points of major importance, and a "Take-Home Message" to concisely summarize the chapter. The references are separated into two sections, General and Advanced, which is helpful for the reader. Second, there are two sets of questions, one for the life scientists and one for the physical scientists. And for those readers who are uncertain to which group they belong, there are additional questions in the section

"for those who have not made up their mind." I found these features and all of the end-of-chapter questions to be provocative and useful to amplify my understanding of the chapters' contents. An index is provided.

There are a few typographical errors in the book. In the index under the term FRET, Förster's name is misspelled. In the text, Planck's name is repeatedly misspelled. The length labeling in Figure 1.5 is incorrect.

A textbook that is directed towards students should do more than transfer knowledge. It should also convey the author's enthusiasm for the subject and a sense of the author's ethics and caution in pursuing a career in science and education. Perusal of Leake's textbook demonstrates the care, caution, and skepticism of the author. There are numerous illustrative examples, and I present a few. While fluorescent protein technology has had many successes, the author reminds the reader that often artificial over-expression conditions are employed; the result is possible nonphysiological behaviors of the cell. In the section on Förster resonance energy transfer the author discussed the technical problems of performing FRET measurements and correctly interpreting the measurements. In the author's "Key Point" on super-resolution fluorescence imaging studies, we read the following: "Caution needs to be applied." This refers to studies described as "live-cell," or "*in vivo*." The assumption that these studies (PALM, STORM, STED) are performed under physiological conditions is often not demonstrated. The degree of photodamage in these techniques is often not investigated. In fact, there is a paucity of careful studies on the effects of light (single-photon and two-photon techniques) on the structure and the physiological functions of cells and tissues. In the absence of careful validation experiments one should be skeptical when reading the literature.

Another example of the pedagogical value of this book is the section on "What makes a 'seminal' single-molecule biophysics study? In the same chapter the author presents his highly personal and potentially biased list of the 'top ten' single-molecule biophysics papers of all time. The book ends with a speculative chapter, pointing to the challenging questions about cellular processes that provide research opportunities for the next generation of investigators. Their success will continue to be driven on the enthusiasm of the scientists, those with the courage to explore the unknown and to collaborate with colleagues from disparate fields of knowledge.

Single-Molecule Cellular Biophysics is recommended as a good textbook to guide the researcher into this emerging field of research. While there is no substitute for reading the fascinating papers that are referenced, I found that the textbook is a good guide to understand what is known, what are the key instruments and techniques that led researchers to this knowledge, and what are their limitations and artifacts.