

Book review

A Clear View of the Cell Cycle

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The Cell Cycle: Principles of Control (David O Morgan, New Science Press, 2007) pp 297. ISBN-13:978-0-19-920610-0

In 1993 Andrew Murray and Tim Hunt published a terrific textbook titled "*The Cell Cycle: An Introduction*." It was a timely book, coming right on the heels of the discovery that cyclin-dependent kinases (Cdks) drive cell-cycle transitions in diverse eukaryotes. It was a good read too, using clear writing and an emphasis on concepts to effectively convey the sense of an important field at an exciting time.

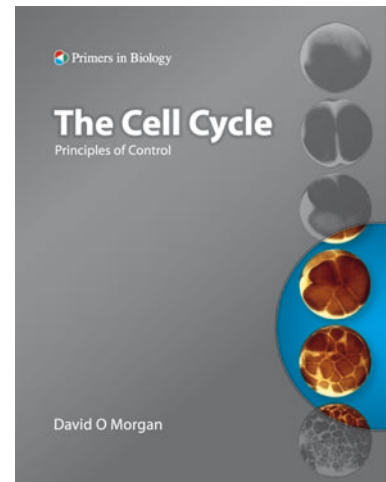
The past thirteen years have brought much in the way of new information and insights to the cell cycle field; it was clearly time for a new book. Enter "*The Cell Cycle: Principles of Control*", by David Morgan, just published by New Science Press. It is up-to-date, authoritative, balanced, and accessible — an exceptionally good book on a fascinating subject, and a more-than-worthy successor to Murray and Hunt's.

Morgan's cell cycle book is organized into twelve chapters, with each chapter sub-divided into a number of modular, two-page 'topics'. For example, Chapter 6 is titled "Assembly of the Mitotic Spindle" and it includes topics such as "Microtubule Structure and Behavior," "The Kinetochore," "Bi-Orientation of Sister Chromatids," and ten others. This organizational plan is to be shared by all of the volumes in New Science Press's "Primers in Biology" series, of which Morgan's book is the second member (the first was Petsko and Ringe's outstanding "*Protein Structure and Function*", published in 2003). Each two-page topic includes its own illustrations, references, and glossary terms; the cumulative reference list and

glossary are also included at the back of the book. The idea behind this modular structure is that it will make it easy for readers to find and extract the chunks of information they need. To my mind it works well.

Morgan begins with a short introduction to the cell cycle, followed by a short but useful survey of the model organisms and methods that have contributed the most to the field. The book picks up steam in the third chapter, titled "The Cell Cycle Control System", which introduces cyclins, Cdks, ubiquitin ligases, and so on. This chapter also introduces various features of the cell cycle regulatory circuit, such as thresholds and feedback loops, that are critical for allowing these proteins to function as a reliable system. Highlights of the chapter include the discussion of the allosteric activation of Cdk2 by cyclin A, explained through a lucid series of crystal structures and schematic diagrams. The same clarity accompanies Morgan's discussion of the additional modes of regulation layered on top of this allosteric activation: Cdks are further regulated by the addition of a substrate binding phosphoepitope (pThr 160), by regulated localization, and by the binding of the accessory adaptor protein Cks1.

The control system chapter is followed by a beautiful account of the replication of chromosomes (Chapter 4). This chapter not only includes a crystal-clear account of our current understanding of the regulation of DNA replication, replete with Orc proteins, Mcm proteins, and so on, but also delves into a number of exciting and much less well understood aspects of how the whole chromosome — DNA and protein organized in a complex, self-maintaining structure — is reproduced. Right from the start Morgan emphasizes that "it is not enough simply to duplicate the DNA molecule at the core of each chromosome. Chromatin structure must also be reproduced in each daughter chromosome." How various specialized chromatin structures are established and epigenetically maintained is an important unanswered question,



and Morgan does a fine job with the subject.

The heart of Morgan's book is its detailed, five-chapter discussion of M-phase, arguably the most beautiful, most dramatic, and best-understood part of the cell cycle. Chapter 5 focuses on mitotic entry. Chapter 6 moves on to the assembly of the mitotic spindle. Chapter 7 deals with mitotic exit, and chapter 8 with cytokinesis. Finally, chapter 9 centers on meiotic M-phase. The M-phase chapters constitute almost half of the book, and as good as the rest of the book is, the treatment of M-phase is where Morgan really shines.

The remainder of the book includes fine chapters on G1/S control (Chapter 10), and the DNA damage response (Chapter 11), and cancer (Chapter 12). The book ends on a hopeful note, the crystal structure of the anti-cancer agent Gleevec (imatinib) blocking the active site of the Abl tyrosine kinase — a fitting illustration on how an understanding of regulatory proteins and signaling networks may, with the proper insight and perseverance, lead to important therapeutic advances.

A successful textbook on the cell cycle needs to accomplish at least three things. First it must introduce the cell biological phenomenology of the cell cycle and the terminology for these events. Morgan does this well, both in the first chapters of the book and in the opening sections of each subsequent chapter.

Second, the book must introduce the proteins that mediate and regulate cell cycle progression. Just keeping the proteins straight can be extremely difficult for newcomers to the field (and not so easy for old pros either), given that homologous proteins go by different names and sometimes mediate different processes in different model systems. Morgan's solution is to include numerous comprehensive tables of protein names and functions. This may not sound too exciting, but its usefulness cannot be overstated; the set of tables alone is worth the price of the book.

Third the book should extract insights out of the facts of cell cycle regulation — to use the specifics of cell cycle regulation to gain an understanding of the principles of protein regulation and systems regulation. This task is clearly at the forefront of Morgan's thinking — hence the subtitle of the book, "*Principles of Control*". Morgan does a good job of pointing out design principles and recurring themes that arise out of our understanding of cell cycle regulation.

Throughout the book Morgan makes excellent use of crystal structures, primary data, fluorescence photomicrographs, electron micrographs, and schematic diagrams to get his points across. I have some quibbles about a few figures in the first two chapters, but in general the visual presentations are as clear and substantive as the writing.

David Morgan is to be congratulated on a superb book — lucid, scholarly, and compelling, start to finish. This should be an outstanding textbook for graduate-level classes on cell cycle regulation, as well as an indispensable reference book for those of us devoted to the field. I would enthusiastically recommend it to anyone even vaguely interested in cell growth and division.