CELL BIOLOGY

SECOND EDITION

A SHORT COURSE

STEPHEN R. BOLSOVER
JEREMY S. HYAMS
ELIZABETH A. SHEPHARD
HUGH A. WHITE
CLAUDIA G. WIEDEMANN

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Stephen R. Bolsover
Department of Physiology
University College London

Jeremy S. Hyams
Department of Biology
University College London

Elizabeth A. Shephard
Department of Biochemistry and Molecular Biology
University College London

Hugh A. White
Department of Biochemistry and Molecular Biology
University College London

Claudia G. Wiedemann
Department of Physiology
University College London

WILEY-LISS
A JOHN WILEY & SONS, INC., PUBLICATION

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Published by John Wiley & Sons, Inc., Hoboken, New Jersey.

Published simultaneously in Canada.

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Library of Congress Cataloging-in-Publication Data:

Cell biology : a short course / Stephen R. Bolsover . . . [et al.].—2nd ed.
p. cm.
Includes bibliographical references and index.
ISBN 0-471-26393-1 (Paper)
1. Cytology. I. Bolsover, Stephen R., 1954–
QH581.2.C425 2003
571.6—dc21 2003000577

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

PREFACE

Cell Biology, A Short Course aims to cover a wide area of cell biology in a form especially suitable for first year undergraduates. We have deliberately kept the book to a manageable size so that neither the cost, the content, nor the weight is too daunting for the student.

The overall theme for the book is the cell as the unit of life. We begin (Chapters 1–3) by describing the components of the cell as seen under the microscope. We then (Chapters 4–8) turn to the central dogma of molecular biology and describe how DNA is used to make RNA which in turn is used to make protein. The next section (Chapters 9–11) describes how proteins are delivered to the appropriate location inside or outside the cell, and how proteins perform their many functions. We then (Chapters 12–14) turn to cell energetics and metabolism. Signaling within and between cells is covered in Chapters 15 through 17. To conclude the book, Chapter 18 describes the composition and function of the cytoskeleton, Chapter 19 covers cell birth and cell death, while Chapter 20 uses the example of the common and severe genetic disease cystic fibrosis to illustrate many of the themes discussed earlier in the book.

Boxed material throughout the book is divided into ***examples*** to illustrate the topics covered in the main text, explanations of the ***medical relevance*** of the material, and ***in depth*** sections that extend the coverage beyond the content of the main text. ***Questions*** are provided at the end of each chapter to help the reader assess how well they have assimilated and understood the material.

As well as giving references to printed material, we reference ***material available on the internet*** in many places in the book. Rather than give detailed addresses, we provide links to all these sites and many others from the book's homepage at http://www.physiol.ucl.ac.uk/sbolsover/teaching/cbasc/cbasc.html.

ACKNOWLEDGMENTS

We thank all the students, colleagues and family members who read the initial versions of the book and whose suggestions and constructive criticism helped enormously.

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INSTRUCTOR NOTES

Molecular cell biology courses now form a foundation for many subsequent specializations in areas outside cell biology. We therefore cover molecular genetics, metabolic pathways and electrophysiology in sufficient detail to make ***Cell Biology*** a suitable course book for first year students who will later specialize in genetics, biochemistry, pharmacology or physiology.

Each chapter comprises:

- The ***main text,*** with figures and tables.
- A numbered ***summary***.
- ***Review questions*** with ***answers*** for student self-assessment. These questions concern the main text only; no knowledge of the boxed material is required.
- ***Example*** boxes that illustrate the points made in the main text.
- ***Medical relevance*** boxes to show how basic cell biological knowledge illuminates medical problems or has provided solutions.
- ***In Depth*** boxes that extend the content.

Self-assessment questions can form the basics for tutorials, with students asked to defend the correct answer. They are also easily modified to generate new questions for student assessment. Instructors are encouraged to submit new questions for inclusion on the CBASC website.

Instructors may wish to specify parts of ***Cell Biology*** as core material for courses targeted to particular specialties. The parts chosen can be customized to the particular specialty in two ways:

1. By selecting from the complete set of twenty chapters. The following sections could be used to support particular teaching modules:

Chapters 4 through 7	DNA, RNA and genetic engineering.
Chapters 8 through 10	Protein synthesis, structure and trafficking.
Chapters 11 through 13	Metabolism and cellular energetics.
Chapters 14 through 17	Electrophysiology and cell signaling.
Chapter 18	The cytoskeleton and cell motility.
Chapter 19	Cell division and apoptosis.

Chapters 16, 17 and 19 might in contrast be selected in a module concentrating on the control of development, since these describe how growth factors and other extracellular chemicals regulate cell division and cell death.

2. By including In Depth boxes. The following boxes are especially to be noted:

In Depth 1.2:	Fluorescence Microscopy
In Depth 8.1:	How We Study Proteins in One Dimension *describes SDS-PAGE*
In Depth 9.1:	Chirality and Amino Acids
In Depth 9.2:	Hydropathy Plotting—The PDGF Receptor
In Depth 9.3:	Curing Mad Mice with Smelly Fish *introduces the concept of osmolarity and osmosis and extends the coverage of chaotropic and structure stabilizing agents*
In Depth 11.1:	What to Measure in an Enzyme Assay
In Depth 11.2:	Determination of V_m and K_M *the Lineweaver-Burk plot*
In Depth 12.2:	ATP Synthase, Rotary Motor, and Synthetic Machine
In Depth 12.3:	Can It Happen? The Concept of Free Energy
In Depth 13.1:	The Urea Cycle—The First Metabolic Cycle Discovered
In Depth 13.2:	The Glyoxylate Shunt
In Depth 14.1:	The Nernst Equation
In Depth 14.2:	Measuring the Transmembrane Voltage
In Depth 15.1:	Frequency Coding in the Nervous System
In Depth 16.1:	Ryanodine Receptors
In Depth 19.1:	A Worm's Eye View of Cell Death
In Depth 20.1:	Lipid Bilayer Voltage Clamp

For example, a course emphasizing protein structure would include In Depth 8.1, 9.1, 9.2 and 9.3, while a course concentrating on metabolic pathways would include In Depth 13.1 and 13.2.

The CBASC website is maintained by the authors. As well as providing over one hundred links to sites with information that extends or illustrates the material in the book, we will use the site to post typological or other errors, comments and test questions sent to us by readers. The full address is http://www.physiol.ucl.ac.uk/sbolsover/teaching/cbasc/cbasc.html or simply type 'CBASC' into a search engine.

CONTENTS IN BRIEF

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CELLS AND TISSUES

The **cell** is the basic unit of life. Microorganisms such as bacteria, yeast, and amoebae exist as single cells. By contrast, the adult human is made up of about 30 trillion cells (1 trillion = 10^{12}) which are mostly organized into collectives called **tissues.** Cells are, with a few notable exceptions, small (Fig. 1.1) with lengths measured in micrometers (μm, where 1000 μm = 1 mm) and their discovery stemmed from the conviction of a small group of seventeenth-century microscope makers that a new and undiscovered world lay beyond the limits of the human eye. These pioneers set in motion a science and an industry that continues to the present day.

The first person to observe and record cells was Robert Hooke (1635–1703) who described the *cella* (open spaces) of plant tissues. But the colossus of this era of discovery was a Dutchman, Anton van Leeuwenhoek (1632–1723), a man with no university education but with unrivaled talents as both a microscope maker and as an observer and recorder of the microscopic living world. van Leeuwenhoek was a contemporary and friend of the Delft artist Johannes Vermeer (1632–1675) who pioneered the use of light and shade in art at the same time that van Leeuwenhoek was exploring the use of light to discover the microscopic world. Sadly, none of van Leeuwenhoek's microscopes have survived to the present day. Despite van Leeuwenhoek's Herculean efforts, it was to be another 150 years before, in 1838, the botanist Matthias Schleiden and the zoologist Theodor Schwann formally proposed that all living organisms are composed of cells. Their "cell theory," which nowadays seems so obvious, was a milestone in the development of modern biology. Nevertheless general acceptance took many years, in large part because the **plasma membrane,** the membrane

Cell Biology: A Short Course, Second Edition, by Stephen R. Bolsover, Jeremy S. Hyams, Elizabeth A. Shephard, Hugh A. White, Claudia G. Wiedemann
ISBN 0-471-26393-1 Copyright © 2004 by John Wiley & Sons, Inc.

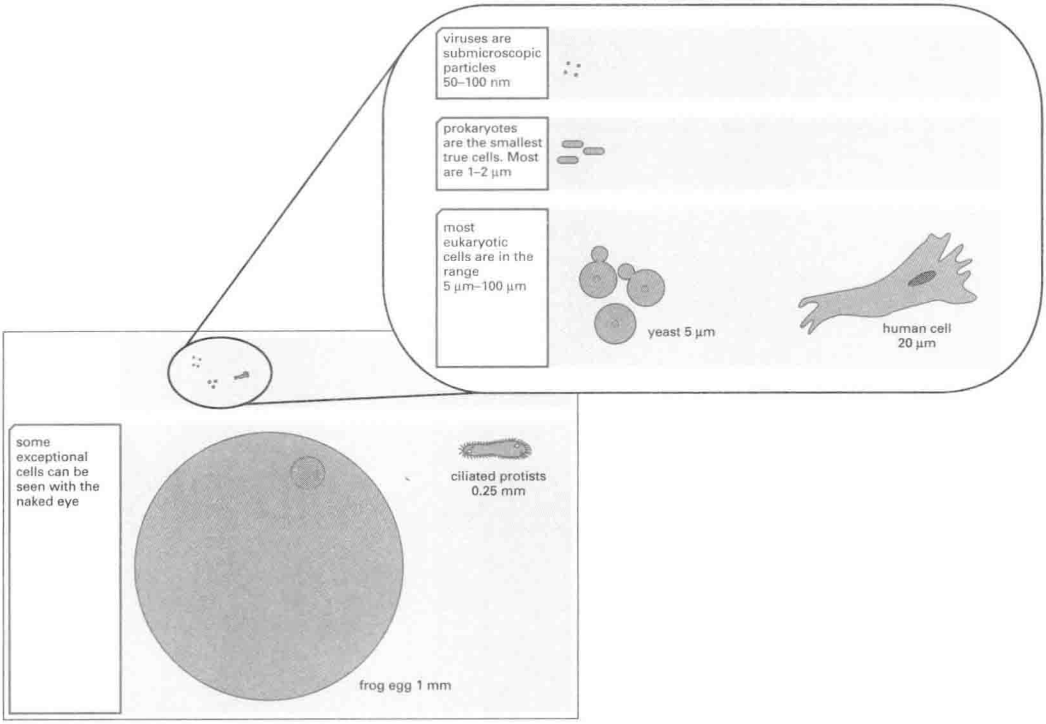

Figure 1.1. Dimensions of some example cells. 1 mm = 10^{-3} m; 1 μm = 10^{-6} m; 1 nm = 10^{-9} m.

surrounding the cell that divides the living inside from the nonliving **extracellular medium** (Fig. 1.2) is too thin to be seen using a light microscope.

PRINCIPLES OF MICROSCOPY

Microscopes make small objects appear bigger. A light microscope will magnify an image up to 1500 times its original size. Electron microscopes can achieve magnifications up to 1 million times. However, bigger is only better when more details are revealed. The fineness of detail that a microscope can reveal is its resolving power. This is defined as the smallest distance that two objects can approach one another yet still be recognized as being separate. The resolution that a microscope achieves is mainly a function of the wavelength of the illumination source it employs. The smaller the wavelength, the smaller the object that will cause diffraction, and the better the resolving power. The light microscope, because it uses visible light of wavelength around 500 nanometers (nm, where 1000 nm = 1 μm), can distinguish objects as small as about half this: 250 nm. It can therefore be used to visualize the smallest cells and the major intracellular structures or organelles. The microscopic study of cell structure organization is known as **cytology.** An electron microscope is required to reveal the **ultrastructure** (the fine detail) of the organelles and other cytoplasmic structures (Fig. 1.2).

The wavelength of an electron beam is about 100,000 times less than that of white light. In theory, this should lead to a corresponding increase in resolution. In practice, the

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