



# CELL BIOLOGY

SECOND EDITION

A SHORT COURSE

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

---

# CELL BIOLOGY

## A Short Course

---

SECOND EDITION

---

**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

Copyright © 2004 by John Wiley & Sons, Inc. All rights reserved.

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

Published simultaneously in Canada.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, scanning, or otherwise, except as permitted under Section 107 or 108 of the 1976 United States Copyright Act, without either the prior written permission of the Publisher, or authorization through payment of the appropriate per-copy fee to the Copyright Clearance Center, Inc., 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400, fax 978-646-8600, or on the web at [www.copyright.com](http://www.copyright.com). Requests to the Publisher for permission should be addressed to the Permissions Department, John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, (201) 748-6011, fax (201) 748-6008.

**Limit of Liability/Disclaimer of Warranty:** While the publisher and author have used their best efforts in preparing this book, they make no representations or warranties with respect to the accuracy or completeness of the contents of this book and specifically disclaim any implied warranties of merchantability or fitness for a particular purpose. No warranty may be created or extended by sales representatives or written sales materials. The advice and strategies contained herein may not be suitable for your situation. You should consult with a professional where appropriate. Neither the publisher nor author shall be liable for any loss of profit or any other commercial damages, including but not limited to special, incidental, consequential, or other damages.

For general information on our other products and services please contact our Customer Care Department within the U.S. at 877-762-2974, outside the U.S. at 317-572-3993 or fax 317-572-4002.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print, however, may not be available in electronic format.

***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.

---

# 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 typographical 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

---

<b>1</b>	<b>CELLS AND TISSUES</b>	<b>1</b>
<b>2</b>	<b>FROM WATER TO DNA: THE CHEMISTRY OF LIFE</b>	<b>19</b>
<b>3</b>	<b>MEMBRANES AND ORGANELLES</b>	<b>51</b>
<b>4</b>	<b>DNA STRUCTURE AND THE GENETIC CODE</b>	<b>65</b>
<b>5</b>	<b>DNA AS A DATA STORAGE MEDIUM</b>	<b>87</b>
<b>6</b>	<b>TRANSCRIPTION AND THE CONTROL OF GENE EXPRESSION</b>	<b>105</b>
<b>7</b>	<b>RECOMBINANT DNA AND GENETIC ENGINEERING</b>	<b>129</b>
<b>8</b>	<b>MANUFACTURING PROTEIN</b>	<b>163</b>
<b>9</b>	<b>PROTEIN STRUCTURE</b>	<b>183</b>
<b>10</b>	<b>INTRACELLULAR PROTEIN TRAFFICKING</b>	<b>213</b>
<b>11</b>	<b>HOW PROTEINS WORK</b>	<b>237</b>
<b>12</b>	<b>ENERGY TRADING WITHIN THE CELL</b>	<b>257</b>
<b>13</b>	<b>METABOLISM</b>	<b>281</b>
<b>14</b>	<b>IONS AND VOLTAGES</b>	<b>309</b>
<b>15</b>	<b>THE ACTION POTENTIAL</b>	<b>325</b>
<b>16</b>	<b>INTRACELLULAR SIGNALING</b>	<b>341</b>
<b>17</b>	<b>INTERCELLULAR COMMUNICATION</b>	<b>363</b>
<b>18</b>	<b>MECHANICAL MOLECULES</b>	<b>381</b>
<b>19</b>	<b>CELL CYCLE AND CONTROL OF CELL NUMBER</b>	<b>401</b>
<b>20</b>	<b>CASE STUDY: CYSTIC FIBROSIS</b>	<b>423</b>



---

# CONTENTS

---

PREFACE, xv

ACKNOWLEDGMENTS, xvii

INSTRUCTOR NOTES, xix

## 1 CELLS AND TISSUES, 1

- Principles of Microscopy, 2
  - The Light Microscope, 3
  - The Electron Microscope, 8
  - The Scanning Electron Microscope, 9
- Only Two Types of Cell, 9
  - Special Properties of Plant Cells, 11
- Viruses, 11
- Origin of Eukaryotic Cells, 12
- Cell Specialization, 12
  - Epithelia, 12
  - Connective Tissue, 13
  - Nervous Tissue, 13
  - Muscle, 14
  - Plants, 15
- Summary, 16
- Review Questions, 16
- Answers to Review Questions, 17

## 2 FROM WATER TO DNA: THE CHEMISTRY OF LIFE, 19

- The Chemical Bond: Sharing  
Electrons, 19
- Interactions with Water: Solutions, 21
  - Ionic Compounds Will Dissolve Only in  
Polar Solvents, 21
  - Acids Are Molecules That Give  $H^+$  to  
Water, 21

Bases Are Molecules That Take  $H^+$  from  
Water, 25

Isoelectric Point, 25

A Hydrogen Bond Forms When a  
Hydrogen Atom Is Shared, 25

Biological Macromolecules, 27

Carbohydrates: Candy and Canes, 27

An Assortment of Sweets, 27

Disaccharides, 28

Out of the Sweet Comes Forth  
Strength, 30

Modified Sugars, 31

Nucleosides, Phosphate, and  
Nucleotides, 35

Amino Acids, Polypeptides, and Proteins, 37

Lipids, 39

Hydrolysis, 44

Summary, 46

Further Reading, 47

Review Questions, 47

Answers to Review Questions, 48

## 3 MEMBRANES AND ORGANELLES, 51

Basic Properties of Cell Membranes, 51

Straight Through the Membrane:  
Diffusion Through the Bilayer, 53

Beyond the Cell Membrane:  
The Extracellular Matrix, 53

Cell Junctions, 54

Organelles Bounded by Double-Membrane  
Envelopes, 56

The Nucleus, 56

Mitochondria and Chloroplasts, 58

- Organelles Bounded by Single-Membrane Envelopes, 58
- Peroxisomes, 59
- Endoplasmic Reticulum, 60
- Golgi Apparatus, 60
- Lysosomes, 61
- Summary, 61
- Review Questions, 62
- Answers to Review Questions, 63

## **4 DNA STRUCTURE AND THE GENETIC CODE, 65**

- Introduction, 65
- The Structure of DNA, 65
  - The DNA Molecule Is a Double Helix, 68
  - The Two DNA Chains Are Complementary, 69
  - Different Forms of DNA, 71
- DNA as the Genetic Material, 71
- Packaging of DNA Molecules into Chromosomes, 71
  - Eukaryotic Chromosomes and Chromatin Structure, 71
  - Prokaryotic Chromosomes, 73
  - Plasmids, 74
  - Viruses, 74
- The Genetic Code, 75
  - Amino Acid Names Are Abbreviated, 79
  - The Code Is Degenerate But Unambiguous, 79
  - Start and Stop Codons and the Reading Frame, 79
  - The Code Is Nearly Universal, 80
  - Missense Mutations, 80
- Summary, 81
- Further Reading, 84
- Review Questions, 84
- Answers to Review Questions, 85

## **5 DNA AS A DATA STORAGE MEDIUM, 87**

- Introduction, 87

- DNA Replication, 87
  - The DNA Replication Fork, 88
- Proteins Open up the DNA Double Helix During Replication, 88
  - DnaA Protein, 88
  - DnaB and DnaC Proteins, 90
  - Single-Strand Binding Proteins, 90
- Biochemistry of DNA Replication, 90
  - DNA Synthesis Requires an RNA Primer, 90
  - RNA Primers Are Removed, 92
  - The Self-Correcting DNA Polymerase, 92
- DNA Repair, 94
  - Spontaneous and Chemically Induced Base Changes, 94
  - Repair Processes, 94
- Gene Structure and Organization in Eukaryotes, 98
  - Introns and Exons—Additional Complexity in Eukaryotic Genes, 98
  - The Major Classes of Eukaryotic DNA, 99
- Gene Nomenclature, 101
- Summary, 101
- Further Reading, 102
- Review Questions, 102
- Answers to Review Questions, 103

## **6 TRANSCRIPTION AND THE CONTROL OF GENE EXPRESSION, 105**

- Structure of RNA, 105
- RNA Polymerase, 106
- Gene Notation, 106
- Bacterial RNA Synthesis, 106
- Control of Bacterial Gene Expression, 109
  - lac*, an Inducible Operon, 111
  - trp*, a Repressible Operon, 116
  - Eukaryotic RNA Synthesis, 118
  - Messenger RNA Processing, 118
- Control of Eukaryotic Gene Expression, 119

Glucocorticoids Cross the Cell Membrane  
to Activate Transcription, 121

Summary, 125

Further Reading, 125

Review Questions, 126

Answers to Review Questions, 127

## **7 RECOMBINANT DNA AND GENETIC ENGINEERING, 129**

DNA Cloning, 129

Creating the Clone, 130

Introduction of Foreign DNA Molecules  
into Bacteria, 130

Selection of cDNA Clones, 134

Genomic DNA Clones, 139

Uses of DNA Clones, 143

DNA Sequencing, 143

Southern Blotting, 146

In situ Hybridization, 147

Northern Blotting, 148

Production of Mammalian Proteins in  
Bacteria, 149

Protein Engineering, 149

Polymerase Chain Reaction, 150

Identifying the Gene Responsible for a  
Disease, 152

Reverse Genetics, 152

Transgenic Animals, 157

Ethics of DNA Testing for Inherited  
Disease, 157

Summary, 158

Further Reading, 159

Review Questions, 159

Answers to Review Questions, 160

## **8 MANUFACTURING PROTEIN, 163**

Attachment of an Amino Acid to Its  
tRNA, 163

Transfer RNA, the Anticodon, and the  
Wobble, 164

The Ribosome, 165

Bacterial Protein Synthesis, 168

Ribosome-Binding Site, 168

Chain Initiation, 169

The 70S Initiation Complex, 171

Elongation of the Protein Chain, 171

The Polyribosome, 173

Termination of Protein Synthesis, 174

The Ribosome Is Recycled, 175

Eukaryotic Protein Synthesis Is a Little  
More Complex, 175

Antibiotics and Protein Synthesis, 176

Summary, 178

Further Reading, 179

Review Questions, 179

Answers to Review Questions, 180

## **9 PROTEIN STRUCTURE, 183**

Naming Proteins, 184

Polymers of Amino Acids, 184

The Amino Acid Building Blocks, 184

The Unique Properties of Each Amino  
Acid, 188

Other Amino Acids Are Found in  
Nature, 191

The Three-Dimensional Structures of  
Proteins, 192

Hydrogen Bonds, 195

Electrostatic Interactions, 199

van der Waals Forces, 199

Hydrophobic Interactions, 199

Disulfide Bonds, 199

Tertiary Structure: Domains and  
Motifs, 200

Quaternary Structure: Assemblies of Protein  
Subunits, 204

Prosthetic Groups, 205

The Primary Structure Contains all the  
Information Necessary to Specify  
Higher-Level Structures, 206

Summary, 209

Further Reading, 209

Review Questions, 210

Answers to Review Questions, 211

## ❁ 10 INTRACELLULAR PROTEIN TRAFFICKING, 213

- Three Modes of Intracellular Protein Transport, 213
  - Targeting Sequences, 215
  - Retention, 215
- Transport to and from the Nucleus, 215
  - The Nuclear Pore Complex, 216
  - Gated Transport Through the Nuclear Pore, 216
  - GTPases and the GDP/GTP Cycle, 218
  - GTPases in Nuclear Transport, 218
- Transport Across Membranes, 221
  - Transport to Mitochondria, 221
  - Chaperones and Protein Folding, 221
  - Transport to Peroxisomes, 221
  - Synthesis on the Rough Endoplasmic Reticulum, 223
  - Glycosylation: The Endoplasmic Reticulum and Golgi System, 225
- Vesicular Trafficking Between Intracellular Compartments, 226
  - The Principle of Fission and Fusion, 226
  - Vesicle Formation, 228
  - Coatmer-Coated Vesicles, 228
  - Clathrin-Coated Vesicles, 229
  - The Trans-Golgi Network and Protein Secretion, 229
  - Targeting Proteins to the Lysosome, 230
  - Fusion, 231
- Summary, 232
- Further Reading, 233
- Review Questions, 233
- Answers to Review Questions, 234

- ## ❁ 11 HOW PROTEINS WORK, 237
- How Proteins Bind Other Molecules, 237
  - Dynamic Protein Structures, 238
  - Allosteric Effects, 238
  - Chemical Changes That Shift the Preferred Shape of a Protein, 240
  - Enzymes Are Protein Catalysts, 241

- The Initial Velocity of an Enzyme Reaction, 242
- Effect of Substrate Concentration on Initial Velocity, 244
- The Effect of Enzyme Concentration, 245
- The Specificity Constant, 247
- Enzyme Catalysis, 247
- Cofactors and Prosthetic Groups, 249
- Enzymes Can Be Regulated, 251
- Summary, 254
- Further Reading, 254
- Review Questions, 255
- Answers to Review Questions, 256

## ❁ 12 ENERGY TRADING WITHIN THE CELL, 257

- Cellular Energy Currencies, 258
  - Reduced Nicotinamide Adenine Dinucleotide (NADH), 259
  - Nucleoside Triphosphates (ATP plus GTP, CTP, TTP, and UTP), 259
  - The Hydrogen Ion Gradient Across the Mitochondrial Membrane, 261
  - The Sodium Gradient Across the Plasma Membrane, 262
- Energy Currencies Are Interconvertible, 263
  - Exchange Mechanisms Convert Between the Four Energy Currencies, 263
  - Electron Transport Chain, 265
  - ATP Synthase, 269
  - Sodium/Potassium ATPase, 270
  - ADP/ATP Exchanger, 271
  - Photosynthesis, 271
  - All Carriers Can Change Direction, 275
- Summary, 278
- Further Reading, 278
- Review Questions, 278
- Answers to Review Questions, 279

## ❁ 13 METABOLISM, 281

- The Krebs Cycle: The Central Switching Yard of Metabolism, 283

From Glucose to Pyruvate: Glycolysis, 284

Glycolysis Without Oxygen, 286

Glycogen Can Provide Glucose for Glycolysis, 288

Glucose May Be Oxidized to Produce Pentose Sugars, 289

From Fats to Acetyl-CoA:  $\beta$  Oxidation, 290

Amino Acids as Another Source of Metabolic Energy, 292

Making Glucose: Gluconeogenesis, 295

Making Glycogen: Glycogenesis, 298

Making Fatty Acids and Glycerides, 300

Synthesis of Amino Acids, 300

Carbon Fixation in Plants, 302

Control of Energy Production, 303

Feedback and Feedforward, 303

Negative Feedback Control of Glycolysis, 304

Feedforward Control in Muscle Cells, 304

Summary, 306

Further Reading, 306

Review Questions, 307

Answers to Review Questions, 308

## ❁ 14 IONS AND VOLTAGES, 309

The Potassium Gradient and the Resting Voltage, 309

Potassium Channels Make the Plasma Membrane Permeable to Potassium Ions, 310

Concentration Gradients and Electrical Voltage Can Balance, 311

The Chloride Gradient, 314

General Properties of Channels, 314

General Properties of Carriers, 316

The Glucose Carrier, 316

The Sodium–Calcium Exchanger, 317

Carriers with an Enzymatic Action: The Calcium ATPase, 318

Summary, 322

Further Reading, 322

Review Questions, 322

Answers to Review Questions, 324

## ❁ 15 THE ACTION POTENTIAL, 325

The Calcium Action Potential in Sea Urchin Eggs, 325

Effect of Egg Transmembrane Voltage on Sperm Fusion, 325

The Voltage-Gated Calcium Channel, 327

The Calcium Action Potential, 328

The Voltage-Gated Sodium Channel in Nerve Cells, 330

The Voltage-Gated Sodium Channel, 330

Electrical Transmission down a Nerve Cell Axon, 332

Myelination and Rapid Action Potential Transmission, 334

Summary, 337

Further Reading, 338

Review Questions, 338

Answers to Review Questions, 339

## ❁ 16 INTRACELLULAR SIGNALING, 341

Calcium, 341

Calcium Can Enter from the Extracellular Medium, 341

Calcium Can Be Released from the Endoplasmic Reticulum, 344

Processes Activated by Cytosolic Calcium Are Extremely Diverse, 348

Return of Calcium to Resting Levels, 350

Cyclic Adenosine Monophosphate, 350

Cyclic Guanosine Monophosphate, 353

Multiple Messengers, 353

Biochemical Signaling, 353

Receptor Tyrosine Kinases and the MAP Kinase Cascade, 353

Growth Factors Can Trigger a Calcium Signal, 356

Protein Kinase B and the Glucose Transporter: How Insulin Works, 356

- Crosstalk—Signaling Pathways or Signaling Webs?, 357
- Summary, 359
- Further Reading, 360
- Review Questions, 360
- Answers to Review Questions, 361

## ❁ 17 INTERCELLULAR COMMUNICATION, 363

- Classifying Transmitters and Receptors, 363
  - Ionotropic Cell Surface Receptors, 364
  - Metabotropic Cell Surface Receptors, 365
  - Intracellular Receptors, 365
- Intercellular Communication in Action: The Gastrocnemius Muscle, 365
- Telling the Muscle to Contract: The Action of Motoneurons, 367
- Controlling the Blood Supply: Paracrine Transmitters, 368
- New Blood Vessels in Growing Muscle, 371
- Synapses Between Neurons, 372
- Summary, 376
- Further Reading, 377
- Review Questions, 377
- Answers to Review Questions, 378

## ❁ 18 MECHANICAL MOLECULES, 381

- The Cytoskeleton is Both Strong and Motile, 381
- Microtubules, 381
- Microtubule-Based Motility, 386
  - Cilia and Flagella, 386
  - Intracellular Transport, 389
- Microfilaments, 390
  - Muscle Contraction, 393
  - Cell Locomotion, 395
  - Cytoplasmic Streaming, 395
- Intermediate Filaments, 396
  - Anchoring Cell Junctions, 396
- Summary, 398

- Further Reading, 398
- Review Questions, 398
- Answers to Review Questions, 400

## ❁ 19 CELL CYCLE AND CONTROL OF CELL NUMBER, 401

- Stages of Mitosis, 402
- Meiosis and Fertilization, 404
  - Meiosis, 405
  - Fertilization and Inheritance, 406
  - Dominant Genetic Disease, 408
  - Crossing Over and Linkage, 408
- Control of the Cell Division Cycle, 408
  - Molecular Regulation of the G2/M (Interphase/Mitosis) Cell Cycle Control Point, 410
  - What About the G1/S Control Point?, 412
- Apoptosis, 415
  - Instructed Death: Death Domain Receptors, 416
  - Default Death: Absence of Growth Factors, 416
  - The Sick Are Left to Die: Stress-Activated Apoptosis, 417
- Summary, 419
- Further Reading, 420
- Review Questions, 420
- Answers to Review Questions, 421

## ❁ 20 CASE STUDY: CYSTIC FIBROSIS, 423

- Introduction, 423
- Cystic Fibrosis is a Severe Genetic Disease, 423
- The Fundamental Lesion in Cystic Fibrosis Lies in Chloride Transport, 424
- Homing in on the *CF* Gene, 425
- Cloning the Gene for CF, 426
- The *CFTR* Gene Codes for a Chloride Ion Channel, 426
- Gene Therapy for CF, 427
- Diagnostic Tests for CF, 431

The Future, 432

Summary, 433

Further Reading, 433

Review Questions, 434

Answers to Review Questions, 435

APPENDIX: CHANNELS AND  
CARRIERS, 437

GLOSSARY, 441

INDEX, 501

---

# 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 ( $1 \text{ trillion} = 10^{12}$ ) which are mostly organized into collectives called **tissues**. Cells are, with a few notable exceptions, small (Fig. 1.1) with lengths measured in micrometers ( $\mu\text{m}$ , where  $1000 \mu\text{m} = 1 \text{ mm}$ ) 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



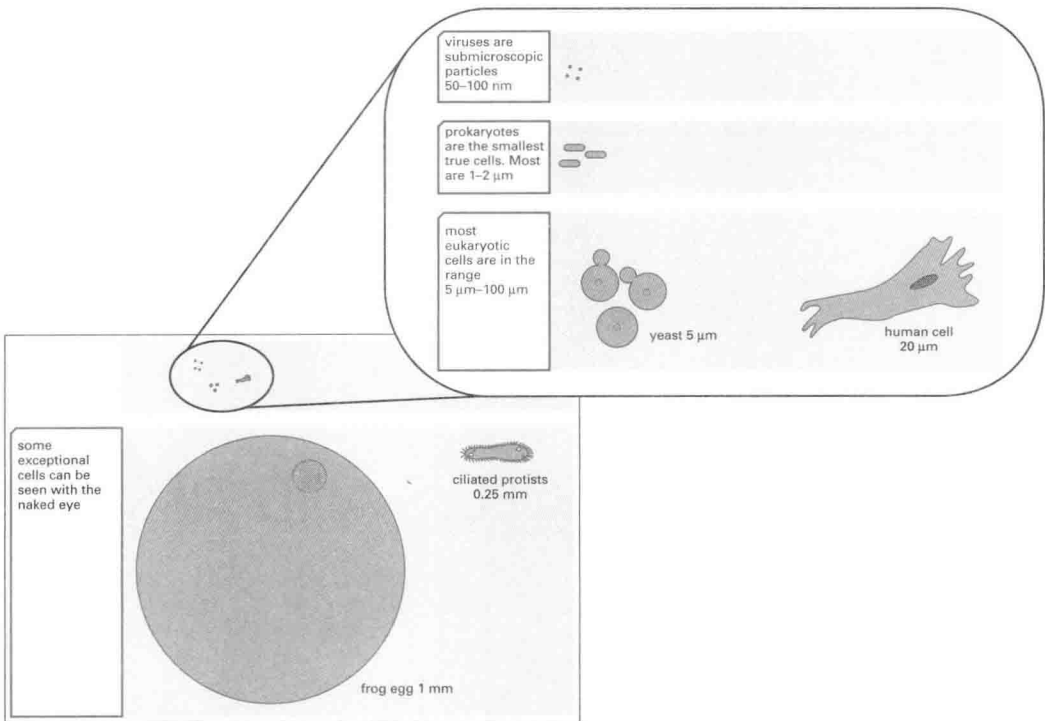


Figure 1.1. Dimensions of some example cells. 1 mm =  $10^{-3}$  m; 1  $\mu\text{m}$  =  $10^{-6}$  m; 1 nm =  $10^{-9}$  m.

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  $\mu\text{m}$ ), 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