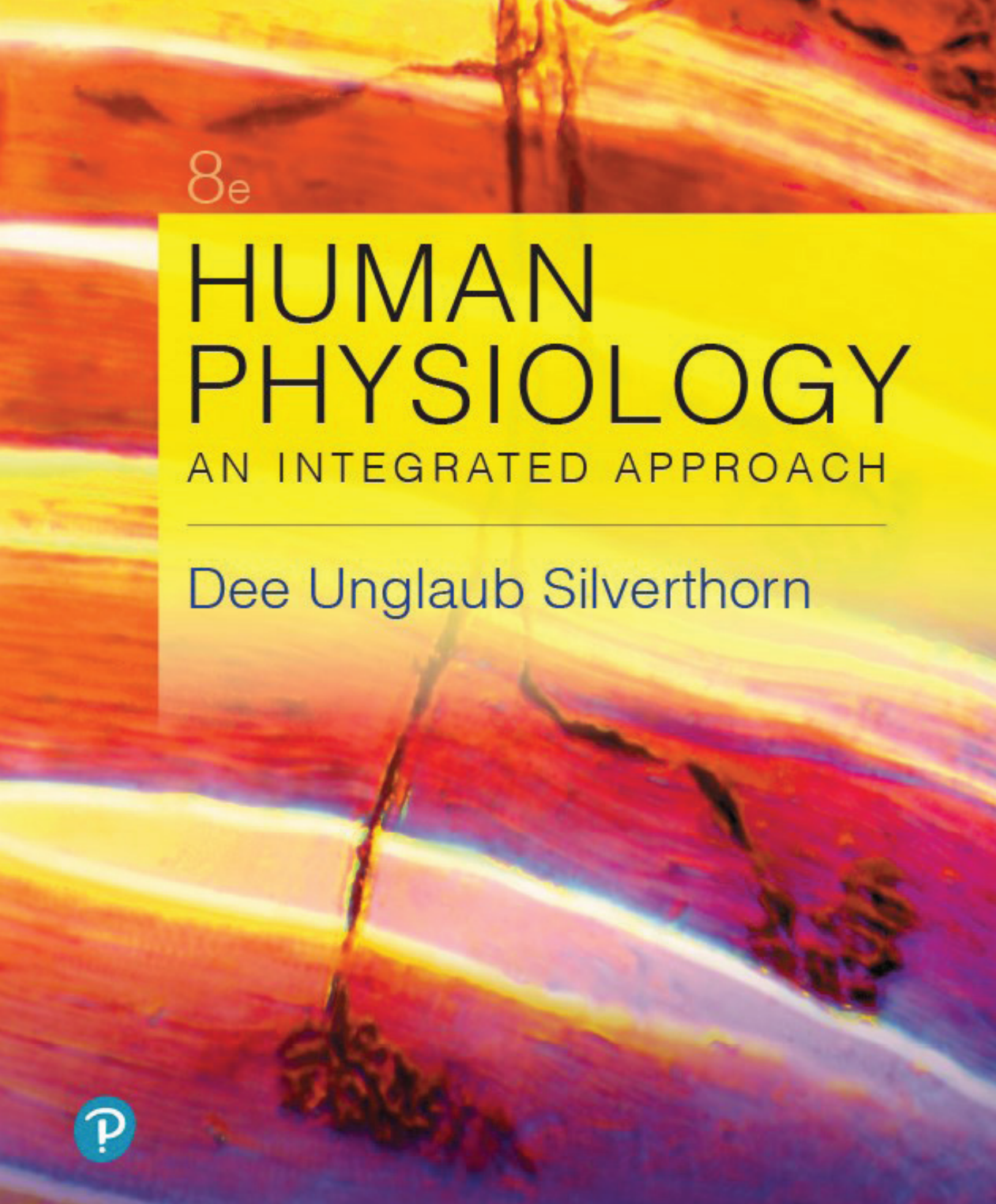

8e
HUMAN
PHYSIOLOGY
AN INTEGRATED APPROACH
Dee Unglaub Silverthorn

Contents in Brief

Strategies for Success

Top Ten Ways to Succeed in Classes that Use Active Learning

By Marilla Svinicki, Ph.D., former Director of the University of Texas Center for Teaching Effectiveness

1. Make the switch from an authority-based conception of learning to a self-regulated conception of learning. Recognize and accept your own responsibility for learning.
2. Be willing to take risks and go beyond what is presented in class or the text.
3. Be able to tolerate ambiguity and frustration in the interest of understanding.
4. See errors as opportunities to learn rather than failures. Be willing to make mistakes in class or in study groups so that you can learn from them.
5. Engage in active listening to what's happening in class.
6. Trust the instructor's experience in designing class activities and participate willingly if not enthusiastically.
7. Be willing to express an opinion or hazard a guess.
8. Accept feedback in the spirit of learning rather than as a reflection of you as a person.
9. Prepare for class physically, mentally, and materially (do the reading, work the problems, etc.).
10. Provide support for your classmate's attempts to learn. The best way to learn something well is to teach it to someone who doesn't understand.

Dr. Dee's Eleventh Rule:
DON'T PANIC! Pushing yourself beyond the comfort zone is scary, but you have to do it in order to improve.

Word Roots for Physiology

Simplify physiology and medicine by learning Latin and Greek word roots. The list below has some of the most common ones.

Using the list, can you figure out what *hyperkalemia* means?*

a- or **an-** without, absence
anti- against
-ase signifies an enzyme
auto self
bi- two
brady- slow
cardio- heart
cephalo- head
cerebro- brain
contra- against
-crine a secretion
crypt- hidden
cutan- skin
-cyte or **cyto-** cell
de- without, lacking
di- two
dys- difficult, faulty
-elle small
-emia in the blood
endo- inside or within
epi- over
erythro- red
exo- outside
extra- outside
gastro- stomach
-gen, -genie produce
gluco-, glyco- sugar or sweet
hemi- half
hemo- blood
hepato- liver
homo- same
hydro- water
hyper- above or excess
hypo- beneath or deficient
inter- between
intra- within
-itis inflammation of
kali- potassium
leuko- white
lipo- fat
lumen inside of a hollow tube
-lysis split apart or rupture
macro- large
micro- small
mono- one
multi- many
myo- muscle
oligo- little, few
para- near, close
patho-, -pathy related to disease
peri- around
poly- many
post- after
pre- before
pro- before
pseudo- false
re- again
retro- backward or behind
semi- half
sub- below
super- above, beyond
supra- above, on top of
tachy- rapid
trans- across, through

* Hyper = excess, kali = potassium, -emia = in the blood, or elevated blood potassium

Owner's Manual

Welcome to Human Physiology! As you begin your study of the human body, one of your main tasks will be to construct for yourself a global view of the body, its systems, and the many processes that keep the systems working. This "big picture" is what physiologists call the integration of systems, and it is a key theme in this book. To integrate information, however, you must do more than simply memorize it. You need to truly understand it and be able to use it to solve problems that you have never encountered before. If you are headed for a career in the health professions, you will do this in the clinics. If you plan a career in biology, you will solve problems in the laboratory, field, or classroom. Analyzing, synthesizing, and evaluating information are skills you need to develop while you are in school, and I hope that the features of this book will help you with this goal.

One of my aims is to provide you not only with information about how the human body functions but also with tips for studying and problem solving. Many of these study aids have been developed with the input of my students, so I think you may find them particularly helpful.

On the following pages, I have put together a brief tour of the special features of the book, especially those that you may not have encountered previously in textbooks. Please take a few minutes to read about them so that you can make optimum use of the book as you study.

Each chapter begins with a list of Learning Outcomes to guide you as you read the chapter. Within the chapters look for the **Running Problem**, **Phys in Action**, and **Try It!** activities. **Phys in Action** are online video clips that I created with the assistance of some of my students. Look for the references to Mastering A&P in the figures with associated Phys in Action clips, and watch Kevin and Michael as they demonstrate physiology in action.

Play Phys in Action
@Mastering Anatomy & Physiology

Pattern recognition is important for all healthcare professionals, so you can begin to develop this skill by learning the key concepts of physiology that repeat over and over as you study different organ systems. Chapter 1 includes two special Focus On features: one on concept mapping, a study strategy that is also used for decision-making in the clinics, and one on constructing and interpreting graphs. The Running Problem in Chapter 1 introduces you to effective ways to find information on the Internet.

Be sure to look for the Essentials and Review figures throughout the book. These figures distill the basics about a topic onto one or two pages, much as the Anatomy Summaries do. My students tell me they find them particularly useful for review when there isn't time to go back and read all the text.

We have also retained the four approaches to learning physiology that proved so popular since this book was first published in 1998.

1. Cellular and Molecular Physiology

Most physiological research today is being done at the cellular and molecular level, and there have been many exciting developments in molecular medicine and physiology in the 10 years since the first edition. For example, now scientists are paying more attention to primary cilia, the single cilium that occurs on most cells of the body. Primary cilia are thought to play a role in some kidney and other diseases. Look for similar links between molecular and cellular biology, physiology, and medicine throughout the book.

FIG. 3.5 Cilia and flagella

(a) Cilia on surface of respiratory epithelium

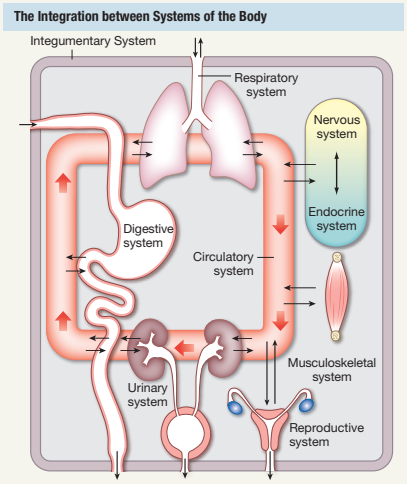
2. Physiology as a Dynamic Field

Physiology is a dynamic discipline, with numerous unanswered questions that merit further investigation and research. Many of the "facts" presented in this text are really only our current theories, so you should be prepared to change your mental models as new information emerges from scientific research.

EMERGING CONCEPTS

How to Use this Book

3. An Emphasis on Integration



The organ systems of the body do not work in isolation, although we study them one at a time. To emphasize the integrative nature of physiology, three chapters (Chapters 13, 20, and 25) focus on how the physiological processes of multiple organ systems coordinate with each other, especially when homeostasis is challenged.

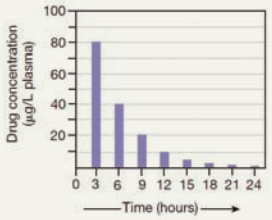
4. A Focus on Problem Solving

One of the most valuable life skills students should acquire is the ability to think critically and use information to solve problems. As you study physiology, you should be prepared to practice these skills. You will find a number of features in this book, such as the Concept Check questions and Figure and Graph Questions. These "test yourself" questions are designed to challenge your critical thinking and analysis skills. In each chapter, read the Running Problem as you work through the text and see if you can apply what you're reading to the clinical scenario described in the problem.

Also, be sure to look at the back of the text, where we have combined the index and glossary to save time when you are looking up unfamiliar words. The appendices have the answers to the Concept Check questions, Figure and Graph Questions, and end-of-chapter questions, as well as reviews of physics, logarithms, and basic genetics. The back end papers include a periodic table of the elements, diagrams of anatomical positions of the body, and tables with conversions and normal values of blood components. Take a few minutes to look at all these features so that you can make optimum use of them.

Level Four Quantitative Problems

30. The following graph represents the disappearance of a drug from the blood as the drug is metabolized and excreted. Based on the graph, what is the half-life of the drug?



It is my hope that by reading this book, you will develop an integrated view of physiology that allows you to enter your chosen profession with respect for the complexity of the human body and a clear vision of the potential of physiological and biomedical research. May you find physiology as fun and exciting I do. Good luck with your studies!

Warmest regards,
Dr. Dee (as my students call me)
silverthorn@utexas.edu

Phys in Action Video Topics:

pp. 130–131 Fig. 5.4 Osmolarity & Tonicity
pp. 154–155 Fig. 5.23 Membrane Potential
pp. 458–459 Fig.14.15 Electrocardiogram
p. 494 Fig. 15.14 Cardiovascular Control
p. 545 Fig. 17.7 The Spirometer
p. 549 Fig. 17.10 Respiratory Pressure
p. 557 Fig. 17.13 Alveolar Gases
p. 573 Fig. 18.7 Hemoglobin-Oxygen Transport
p. 610 Fig. 19.13 Renal Clearance
p. 793 Fig. 25.8 Blood Pressure & Exercise

Try It Activities:

p. 21 Graphing
p. 135 Membrane Models (Lipid bylayer)
p. 251 Action Potentials
p. 325 Salty-Sweet Taste Experiment
p. 468 Frank-Starling Law of the Heart
p. 605 Insulin
p. 682 Oral Rehydration Therapy

EIGHTH EDITION

HUMAN PHYSIOLOGY

Dee Unglaub Silverthorn, Ph.D.
UNIVERSITY OF TEXAS, AUSTIN

with contributions by

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ABOUT THE AUTHOR

DEE UNGLAUB SILVERTHORN studied biology as an undergraduate at Newcomb College of Tulane University, where she did research on cockroaches. For graduate school, she switched to studying crabs and received a Ph.D. in marine science from the Belle W. Baruch Institute for Marine and Coastal Sciences at the University of South Carolina. Her research interest is epithelial transport, and most recently work in her laboratory has focused on transport properties of the chick allantoic membrane. Her teaching career started in the Physiology Department at the Medical University of South Carolina but over the years she has taught a wide range of students, from medical and college students to those still preparing for higher education. At the University of Texas–Austin, she teaches physiology in both lecture and laboratory settings, and instructs graduate students on developing teaching skills in the life sciences. In 2015 she joined the faculty of the new UT-Austin Dell Medical School. She has received numerous teaching awards and honors, including a 2011 UT System Regents' Outstanding Teaching Award, the 2009 Outstanding Undergraduate Science Teacher Award from the Society for College Science Teachers, the American Physiological Society's Claude Bernard Distinguished Lecturer and Arthur C. Guyton Physiology Educator of the Year, and multiple awards from UT–Austin, including the Burnt Orange Apple Award. The first edition of her textbook won the 1998 Robert W. Hamilton Author Award for best textbook published in 1997–1998 by a University of Texas faculty member. Dee was the president of the Human Anatomy and Physiology Society in 2012–2013, has served as editor-in-chief of Advances in Physiology Education, and is currently chair of the American Physiological Society Book Committee. She works with members of the International Union of Physiological Sciences to improve physiology education in developing countries, and this book has been translated into seven languages. Her free time is spent creating multimedia fiber art and enjoying the Texas hill country with her husband, Andy, and their dogs.

Michael Chirillo, Dee Silverthorn, and Kevin Christmas

About the Illustrators

William C. Ober, M.D. (*art coordinator and illustrator*) received his undergraduate degree from Washington and Lee University and his M.D. from the University of Virginia. He also studied in the Department of Art as Applied to Medicine at Johns Hopkins University. After graduation, Dr. Ober completed a residency in Family Practice and later was on the faculty at the University of Virginia in the Department of Family Medicine and in the Department of Sports Medicine. He also served as Chief of Medicine of Martha Jefferson Hospital in Charlottesville, VA. He is currently a visiting Professor of Biology at Washington & Lee University, where he has taught several courses and led student trips to the Galapagos Islands. He was part of the Core Faculty at Shoals Marine Laboratory, where he taught Biological Illustration for 22 years. The textbooks illustrated by Medical & Scientific Illustration have won numerous design and illustration awards.

Claire E. Ober, R.N. (*illustrator*) practiced pediatric and obstetric nursing before turning to medical illustration as a full-time career. She returned to school at Mary Baldwin College where she received her degree with distinction in studio art. Following a five-year apprenticeship, she has worked as Dr. Ober's partner in Medical and Scientific Illustration since 1986. She was also on the Core Faculty at Shoals Marine Laboratory and co-taught Biological Illustration at both Shoals Marine Lab and at Washington and Lee University.

About the Clinical Consultant

Andrew C. Silverthorn, M.D. is a graduate of the United States Military Academy (West Point). He served in the infantry in Vietnam, and upon his return entered medical school at the Medical University of South Carolina in Charleston. He was chief resident in family medicine at the University of Texas Medical Branch, Galveston, and is currently a family physician in solo practice in Austin, Texas. When Andrew is not busy seeing patients, he may be found on the golf course or playing with his two rescue dogs, Molly and Callie.

About the Contributor

Bruce Johnson, Ph.D. is a Senior Research Associate in the Department of Neurobiology and Behavior at Cornell University. He earned biology degrees at Florida State University (B.A.), Florida Atlantic University (M.S.), and at the Marine Biological Laboratory in Woods Hole (Ph.D.) through the Boston University Marine Program. For three decades, he has led Cornell's highly-praised Principles of Neurophysiology course, in which students receive hands-on instruction in principles and methods in neurophysiology. He is a coauthor of *Crawdad: a CD-ROM Lab Manual for Neurophysiology* and the *Laboratory Manual for Physiology*. Bruce has directed and taught in neuroscience faculty workshops sponsored by NSF (Crawdad), ADInstruments (Crawdad and CrawFly), the Grass Foundation and the Faculty for Undergraduate Neuroscience (FUN). He has also lead workshops and neuroscience courses at the Universities of Copenhagen (Denmark), Cologne (Germany), Ibadan (Nigeria), and the Marine Biological Laboratory. Bruce has been named a Most Influential Faculty Member by the graduating senior class at Cornell and awarded the John M. and Emily B. Clark Award for Distinguished Teaching at Cornell. His other teaching awards include the FUN Educator of the Year Award, FUN Career Service Award, and co-recipient of the 2016 Award for Education in Neuroscience, sponsored by the Society for Neuroscience. He is currently the Editor-in-Chief of the *Journal of Undergraduate Neuroscience Education*. Bruce's research addresses the cellular and synaptic mechanisms of motor network plasticity.

DEDICATION

The 8th edition is dedicated to my colleagues who read every word of the first edition manuscript and provided valuable feedback that helped shape the book.

Park City, Utah, June 1995
(Standing, L to R): Judy Sullivan, Patricia Munn, Dee Silverthorn, Mary Ann Rokitka, Richard Walker, Pat Berger, Norman Scott
(Seated) Shana Ederer, Prentice Hall development editor

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NEW TO THIS EDITION

The Eighth Edition of *Human Physiology: An Integrated Approach* builds upon the thorough coverage of integrative and molecular physiology topics that have always been the foundation of this book. The biggest change is a completely revised Chapter 24 on immunology. This field has expanded dramatically since the First Edition published in 1997, and it was time to step back and re-think the presentation of this complicated and complex subject. Neurophysiology is also changing rapidly, requiring multiple updates in Chapters 8 through 11. In nearly every chapter the latest developments in research and medicine meant changes to the presentation of information.

Continuing the revision of the art introduced in the Seventh Edition, we created additional Review and Essentials figures that students can use for quick review as well as new Anatomy Summaries and concept maps. Figures from previous editions that were significantly modified or eliminated are still available to instructors on the Instructor's DVD and in the Instructor Resources area of Mastering A&P.

In addition to the online Phys in Action videos that are referenced in related figures, we have new Try It! activities throughout the book. These activities present data, usually from classic experiments, and ask the students to interpret the results. Topics include Benjamin Franklin's little-known experiment that helped development of the phospholipid bilayer model of the membrane, and the experiments that resulted in oral rehydration therapy for treating cholera.

HIGHLIGHTS OF CONTENT UPDATES

Chapter 1 Introduction to Physiology

- New Focus on Graphing with a new Try It! activity
- Added information on the connectome and microbiome
- Updated information on literature searches and citations

Chapter 2 Molecular Interactions

- Four new element names in the periodic table, inside the back cover of the text
- Added ribbon diagram/Richardson diagram of proteins

Chapter 3 Compartmentation: Cells and Tissues

- Explanations of light and electron microscopy
- New Emerging Concepts box on induced pluripotent stem cells (iPSs)

Chapter 5 Membrane Dynamics

- New Try It! activity on lipid bilayers
- Three Phys in Action video references in Figures 5.4, 5.6, and 5.23

Chapter 6 Communication, Integration, and Homeostasis

- Juxtacrine signaling
- Updated information on NIH Common Fund's *Building Blocks, Biological Pathways, and Networks* Program
- Updated the discussion on cytokine families
- Re-classified receptor-enzymes as catalytic receptors
- GPCR for eicosanoids

Chapter 7 Introduction to the Endocrine System

- Updated information on calcitonin gene-related peptide
- Updated information on melatonin and melatonin-related drugs

Chapter 8 Neurons: Cellular and Network Properties

- Update on mechanisms of axonal transport and associated diseases: dynein, kinesin, fragile X, Alzheimer's, microcephaly
- Try It! activity on action potentials
- New link to online calculator for Nernst and GHK equations
- Added discussion of resistance of extracellular fluid to discussion of resistance to current flow
- Added space constant discussion

Chapter 9 The Central Nervous System

- Added lateral sulcus, insula, cerebral aqueduct
- Re-classification of stages of sleep
- Pericytes in blood-brain barrier formation
- Dopaminergic pathways and addiction

Chapter 10 Sensory Physiology

- New Try It! activity on sweet and salty taste
- Additional information on non-neural sensors and Merkel cells

Chapter 11 Efferent Division: Autonomic and Somatic Motor Control

- Expanded table on properties of autonomic neurotransmitter receptors
- Added N_N and N_M nicotinic subtypes
- Added discussion of sarin nerve gas
- Updated anti-nicotine vaccine
- Etiology of diabetic neuropathy

Chapter 12 Muscles

- Expanded discussion of myosin light chains in striated muscle
- New table with autonomic effects on smooth muscles

Chapter 13 Integrative Physiology I: Control of Body Movement

- Addition information on reflexes and muscle tone
- Updated Parkinson's treatments
- Expanded tetanus Running Problem

Chapter 14 Cardiovascular Physiology

- New Running problem on atypical presentation of myocardial infarction in a woman
- New section and new figure on coronary circulation
- New Try It! activity on Starling's law of the heart
- Added discussion of echocardiography
- Expanded ejection fraction discussion
- New discussion of ion channel subtypes

Chapter 15 Blood Flow and the Control of Blood Pressure

- Updated information on pericytes and their functions
- New discussion of blood-retinal barrier
- Updated discussion of angiogenesis including angiopoietin and angiopoietin/Tie signaling pathway.
- New Review quantitative question on Bernoulli's principle of fluid flow
- New sections on coronary blood flow and cerebral blood flow
- Updated statistics on CV diseases
- Added neurogenic shock

Chapter 16 Blood

- Revised art, includes Figures 16.2, 16.4, 16.6, and 16.7
- Updated information on treatment for sickle cell disease

Chapter 17 Mechanics of Breathing

- Forced vital capacity test
- FEV_1/FVC ratio
- New figure and Figure Question for forced vital capacity test
- Antenatal corticosteroids to prevent NRDS

Chapter 18 Gas Exchange and Transport

- Updated information on action of carbonic anhydrase
- Updated information on hemoglobin-based blood substitutes
- Carotid body plasticity in disease states

Chapter 19 The Kidneys

- New map for factors influencing GFR
- Updated model of organic anion transport, including OAT family transporters
- New figure and table on renal handling of some common substances
- New Try It! activity on glucosuria and the discovery of insulin
- PAH clearance and calculation of renal plasma flow discussion
- New term: renal handling
- New Figure Question
- Updated glomerular filtration barrier to include glomerular capillary glycocalyx, slit diaphragm

Chapter 20 Integrative Physiology II: Fluid and Electrolyte Balance

- New section on role of kidney in hypertension
- New Concept Check question
- Expanded discussion of K^+ handling
- Added zona gomerulosa, paraventricular and supraoptic nuclei
- New section on endocrine pathologies in fluid balance
- New Level 3 Review question on Liddle's syndrome

Chapter 21 The Digestive System

- New Try It! activity on role of the SGLT in treating diarrhea
- New information on cholera vaccine
- Updated discussion on microfold cells
- Added guanylate cyclase-C (GC-C), uroguanylin and guanylin, plecanatide

Chapter 22 Metabolism and Energy Balance

- Updated model for appetite
- Updated pharmacological trials for anorexia
- Latent autoimmune diabetes; also called type 1.5; gestational diabetes (GDM); MODY, maturity-onset diabetes of the young.
- Added mechanism of action of metformin
- Added cardiovascular risk calculator link

Chapter 23 Endocrine Control of Growth and Metabolism

- Expanded discussion of melanocortins and their receptors in the control of food intake.
- Agouti-related protein (AGRP), MC4R receptors
- Added explanation of the role of ghrelin in growth hormone release
- New figure for feedback control of growth hormone release
- Updated discussion on off-label use of growth hormone in adults
- Primary cilia in chrondrocytes and osteocytes act as mechnotransducers
- Role of calcium-sensing receptor and NALCN channel in neuronal excitability
- New figure and discussion of intestinal and renal Ca^{2+} transport
- Skeletal deformaties in ciliopathies
- New figure and discussion of bone remodeling, including RANK, RANKL, osteoprotegerin, osteoid
- New Review question on osteopetrosis

Chapter 24 The Immune System

- 6 NEW figures. Most art significantly revised.
- Added concepts include long-lived plasma cells, mucosa-associated lymphoid tissue (MALT), self-antigens, negative selection, hygiene hypothesis, Zika virus, DAMPS – danger-associated molecular patterns, B cell receptors, regulatory T cells (Tregs)
- Updated information on IgD, contact-dependent signaling

Chapter 26 Reproduction and Development

- Kisspeptin control of GNRH and role in puberty
- Origin of the acrosome
- *Flibanserin* for low libido in women

ACKNOWLEDGMENTS

Writing, editing, and publishing a textbook is a group project that requires the talent and expertise of many people. No one scientist has the detailed background needed in all areas to write a book of this scope, and I am indebted to all my colleagues who so generously share their expertise in each edition. I particularly want to acknowledge Bruce Johnson, Cornell University, Department of Neurobiology and Behavior, a superb neurobiologist and educator, who once again ensured that the chapters on neurobiology are accurate and reflect the latest developments in that rapidly changing field. I would also like to thank Michael Chirillo, a former graduate teaching assistant of mine, for his work developing the Try It! features in between interviewing for and starting a medical residency program. Peter English, a colleague and former student, has also joined the team helping with this revision.

A huge thank you goes to immunologists Natalie Steinel, from UT-Austin Dell Medical School, and Tynan A. Becker, from University of Alaska, for their assistance and critical review of the Chapter 24 revision. Brian Sumner, a 3rd year medical student at the George Washington University School of Medicine, graciously volunteered time out of his busy clinical rotations to read the revised chapter and ensure that it was student-friendly.

The art team of Bill Ober, M.D. and Claire Ober, R.N. has worked with me since the first edition, and I am always grateful for their scientifically astute suggestions and revisions. They were joined in the last edition by Anita Impagliazzo, who brought a fresh eye and new figure ideas.

Instructors and students often contact me directly about the book, and for this edition I would particularly like to thank Allison Brekke, James Mayer, and Dean A. Wiseman for comments and suggestions. Thanks also to my students who keep me informed of the typos that creep in no matter how many people look at the manuscript and pages.

Many other people devoted their time and energy to making this book a reality, and I would like to thank them all, collectively and individually. I apologize in advance to anyone whose name I have omitted.

Reviewers

I am particularly grateful to the instructors who reviewed one or more chapters of the last edition. There were many suggestions in their thoughtful reviews that I was unable to include in the text, but I appreciate the time and thought that went into their comments. The reviewers for this edition include:

Jake Brashears, San Diego City College
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Many other instructors and students took time to write or e-mail queries or suggestions for clarification, for which I thank them. I am always delighted to have input, and I apologize that I do not have room to acknowledge them all individually.

Specialty Reviews

No one can be an expert in every area of physiology, and I am deeply thankful for my friends and colleagues who reviewed entire chapters or answered specific questions. Even with their help, there may be errors, for which I take full responsibility. The specialty reviewers for this edition were:

Natalie Steinel, UT-Austin Dell Medical School
Tynan A. Becker, University of Alaska

Photographs

I would like to thank Kristen Harris, University of Texas who generously provided micrographs from her research.

Supplements

Damian Hill once again worked with me to revise and improve the Instructor Resource Manual that accompanies the book. I believe that supplements should reflect the style and approach of the text, so I am grateful that Damian has continued to be my alter-ego for so many editions. Peter English is helping with Mastering activities this revision.

I would also like to thank my colleagues who helped with the test bank and media supplements for this edition:

Heidi Bustamante, University of Colorado, Boulder
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Cheryl Neudauer, Minneapolis Community & Technical College

The Development and Production Team

Writing a manuscript is only a first step in the long and complicated process that results in a bound book with all its ancillaries. The team that works with me on book development deserves a lot of credit for the finished product. Gary Hespenheide designed a bright and cheerful cover that continues our tradition of images that show science as art. Anne A. Reid, my long-time developmental

editor, is always wonderful to work with, and provides thoughtful suggestions that improve what I wrote.

The team at Pearson Education worked tirelessly to see this edition move from manuscript to bound book. My acquisitions editor, Kelsey Volker Churchman, was joined by Lauren Harp, Senior Acquisitions Editor for the second part of this revision. Ashley Williams and Kate Abderholden, assistant editors, kept track of everyone and everything for us. Chriscelle Palaganas, Program Manager, provided excellent guidance and support throughout the whole production process.

The task of coordinating production fell to Pearson Content Producer Deepti Agarwal. Nathaniel Jones handled composition and project management, and Project Manager Stephanie Marquez at the art house, Imagineering, managed the team that prepared the art for production. Katrina Mohn was the photo researcher who found the wonderful new photos that appear in this edition. Nicole Constantine was the assistant media producer who kept my supplements authors on task and on schedule. Wendy Mears is the product marketing manager who works with the excellent sales teams at Pearson Education and Pearson International, and Derek Perrigo is the Field Marketing Manager for the anatomy and physiology list.

Special Thanks

As always, I would like to thank my students and colleagues who looked for errors and areas that needed improvement. I've learned that awarding one point of extra credit for being the first student to report a typo works really well. My graduate teaching assistants over the years have all played a huge role in my teaching, and their input has helped shape how I teach. Many of them are now faculty members themselves. They include:

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Kurt Venator, Ph.D.
Kira Wenstrom, Ph.D.

Finally, special thanks to my colleagues in the American Physiological Society, the Human Anatomy & Physiology Society, and the International Union of Physiological Sciences whose experiences in the classroom have enriched my own understanding of how to teach physiology. I would also like to recognize a special group of friends for their continuing support: Penelope Hansen (Memorial University, St. John's), Mary Anne Rokitka (SUNY Buffalo), Rob Carroll (East Carolina University School of Medicine), Cindy Gill (Hampshire College), and Joel Michael (Rush Medical College), as well as Ruth Buskirk, Jeanne Lagowski, Jan M. Machart and Marilla Svinicki (University of Texas).

As always, I thank my family and friends for their patience, understanding, and support during the chaos that seems inevitable with book revisions. The biggest thank you goes to my husband Andy, whose love, support, and willingness to forgo home-cooked meals on occasion help me meet my deadlines.

A Work in Progress

One of the most rewarding aspects of writing a textbook is the opportunity it has given me to meet or communicate with other instructors and students. In the 20 years since the first edition was published, I have heard from people around the world and have had the pleasure of hearing how the book has been incorporated into their teaching and learning.

Because science textbooks are revised every 3 or 4 years, they are always works in progress. I invite you to contact me or my publisher with any suggestions, corrections, or comments about this edition. I am most reachable through e-mail at silverthorn@utexas.edu. You can reach my editor at the following address:

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CONTENTS

UNIT 2 Homeostasis and Control

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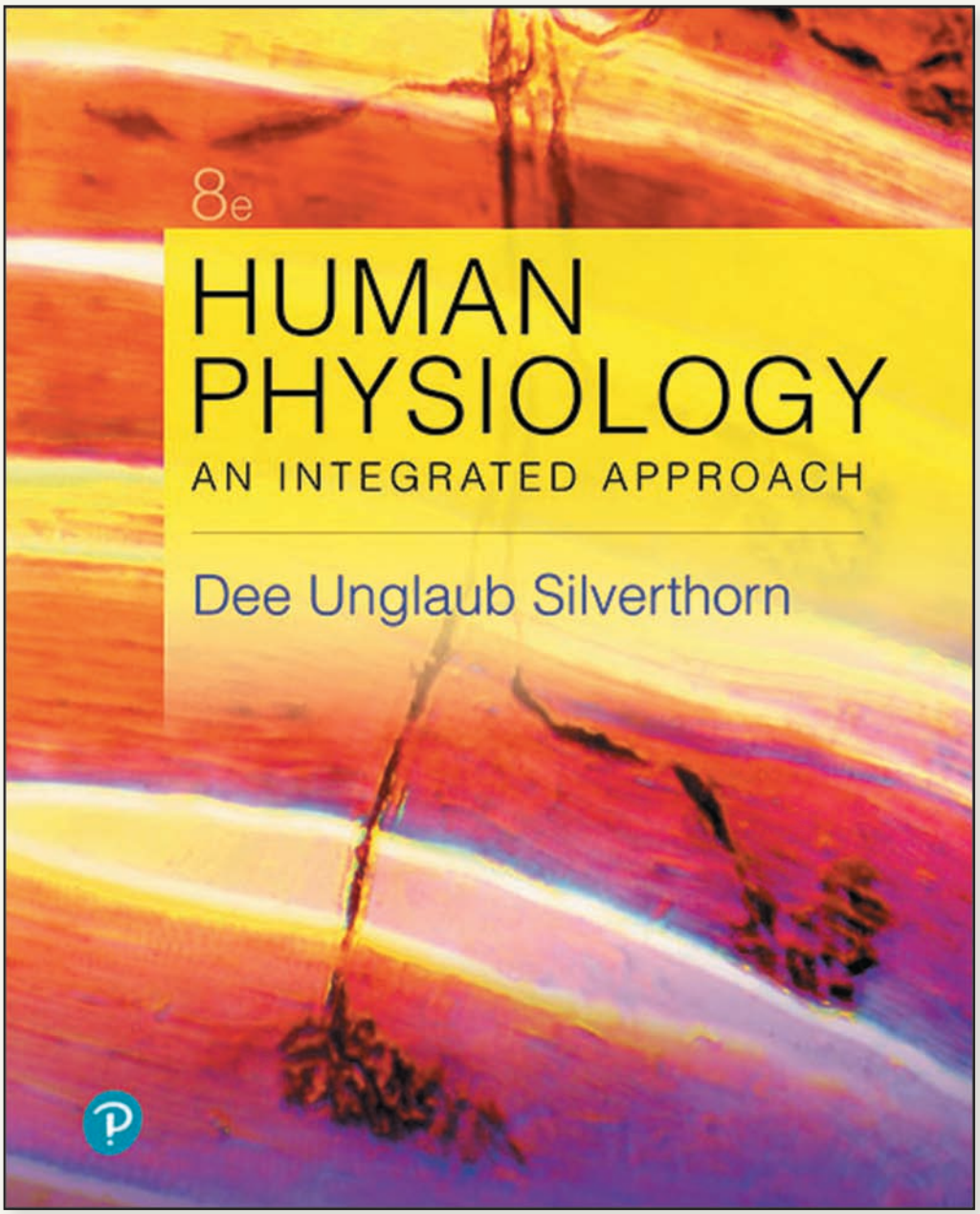
Move Beyond Memorization:
Prepare for Tomorrow's Challenges

The goals for the **Eighth Edition** of ***Human Physiology: An Integrated Approach*** are to provide an integrated and up-to-date introduction to core concepts in physiology and to equip you with skills for solving real-world problems.



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Challenge Yourself:
Apply What You Learn

Learning physiology requires that you use information rather than simply memorizing what you think will be on the test. The Eighth Edition text and Mastering™ A&P program provide multiple opportunities for you to practice answering the more challenging types of questions that you are likely to see on a test or exam.

Running Problems explore a real-world disease or disorder that unfolds in short segments throughout the chapter. You can check your understanding by comparing your answers with those in Problem Conclusion at the end of each chapter. Related Coaching Activities can be assigned in Mastering A&P.

RUNNING PROBLEM

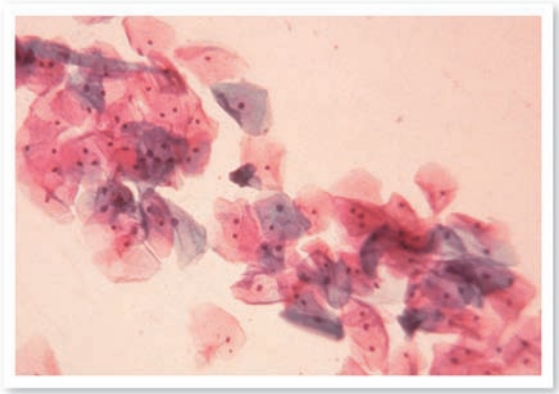
The day after Jan's visit, the computerized cytology analysis system rapidly scans the cells on the slide of Jan's cervical tissue, looking for abnormal cell size or shape. The computer is programmed to find multiple views for the cytologist to evaluate. The results of Jan's two Pap tests are shown in FIGURE 3.14.

Q6: *Has Jan's dysplasia improved or worsened? What evidence do you have to support your answer?*

Q7: *Use your answer to question 6 to predict whether Jan's HPV infection has persisted or been cleared by her immune system.*

59 61 65 79 **84** 87

see pp. 84–85



Additional Practice Questions include **Concept Check Questions,** which are placed at intervals throughout the chapter, and Review Questions, which are provided at the end of the chapter and organized into four levels of difficulty. An answer key is in Appendix A.

FIG. 7.15 Hypocortisolism

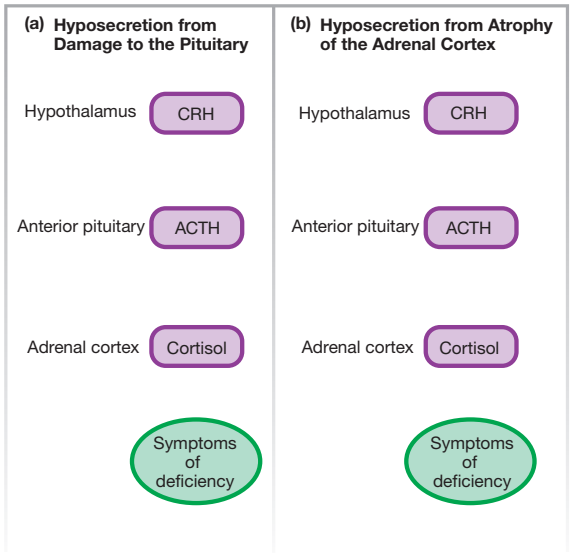


FIGURE QUESTION

For each condition, use arrows to indicate whether levels of the three hormones in the pathway will be increased, decreased, or unchanged. Draw in negative feedback loops where functional.

Figure Questions challenge you to apply visual literacy skills as you read an illustration or photo. Answers to these questions appear at the end of the text, in Appendix A.

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Practice Solving Real-World Problems

NEW! "Try it" boxes present a real-world research problem or classic experiment and guide you through the process of analyzing the data and thinking like a scientist.

NEW! Additional questions for each "Try it" activity are available in **Mastering A&P**. Topics include Graphing (Chapter 1), Cell Membranes (Chapter 5), Action Potentials (Chapter 8), Salty-Sweet Taste Experiment (Chapter 10), Frank-Starling Law of the Heart (Chapter 14), Insulin (Chapter 19) and Oral Rehydration Therapy (Chapter 21).

Instructors: A version of this Try it! Activity can be assigned in Mastering Anatomy & Physiology

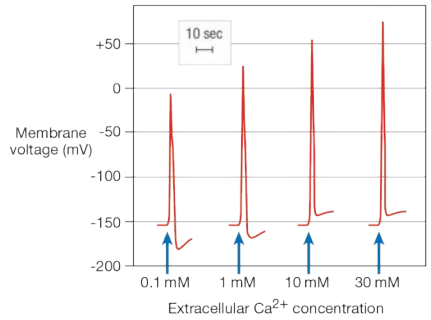
TRY IT! Action Potential

What do carnivorous plants and your neurons have in common? Most students learn that action potentials (APs) transmit information rapidly along neurons in an animal's nervous system. While this is true, APs were actually first described in algae! Another plant that uses APs is the Venus flytrap (*Dionaea muscipula*). Because these plants grow in nutrient-poor soil, they are carnivorous. The tips of their two leaves have evolved into *capture organs*, which snap shut when prey, such as a fly, moves over them. Charles Darwin himself, captivated by this phenomenon, encouraged other scientists to describe its mechanism.

In 1873, the English physiologist Sir John Scott Burdon-Sanderson was able to show that electric current flows through the Venus flytrap when a fly touches *trigger hairs* on the inner surface of the capture organs. The hairs act as mechanoreceptors that generate an action potential when bent. The AP closes the leaf tips, trapping the fly inside so the plant can digest it. In a series of experiments, researchers recorded APs in flytrap cells while varying the extracellular concentration of Ca^{2+}.

(a) The capture organ of a Venus flytrap with trigger hairs.

(b) Data from Hodick and Sievers, 1986.[1] Arrows indicate when trigger hairs were bent.



GRAPH QUESTIONS

1. Using the results shown in the graph, explain what increasing the concentration of Ca^{2+} does to the flytrap APs.
2. These results suggest that the rising phase of a flytrap AP is primarily due to which ion? Is this ion entering or leaving the cell? How does this compare to APs in your neurons?
3. What experiments could you design to determine which ion is responsible for the repolarization phase of the flytrap's AP?

[1] Hodick, D. & Sievers, A. (1986). The influence of Ca^{2+} on the action potential in mesophyll cells of *Dionaea muscipula* Ellis. *Protoplasma* 133, 83–84.

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Graph Questions encourage you to interpret real data presented in graphs. Answers to these questions appear at the end of the text, in Appendix A.

Study More Efficiently Using the Figures

Eye-tracking research has shown that learning and comprehension levels are higher for students who study both the figures and the text together than for students who only read the text. This book offers dozens of illustrations designed to help you learn physiology more efficiently, and make the best use of your study time.

Essentials Figures distill the basics of a topic into one or two pages, helping you to see the big picture of human physiology. Instructors can assign **related Mastering A&P coaching activities** that explore these topics in greater depth.

Selected figures from the text are explored in accompanying **Phys in Action video tutors** and in **coaching activities** in **Mastering A&P**.

FIG. 5.23 ESSENTIALS Membrane Potential

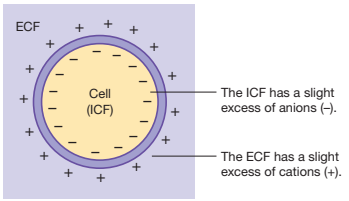
Play Phys in Action
@Mastering Anatomy & Physiology

The electrical disequilibrium that exists between the extracellular fluid (ECF) and intracellular fluid (ICF) of living cells is called the **membrane potential difference** (V_m), or membrane potential for short. The membrane potential results from the uneven distribution of electrical charge (i.e., ions) between the ECF and ICF.

What creates the membrane potential?

1. Ion concentration gradients between the ECF and ICF
2. The selectively permeable cell membrane

(a) In illustrations, this uneven distribution of charge is often shown by the charge symbols clustered on each side of the cell membrane.

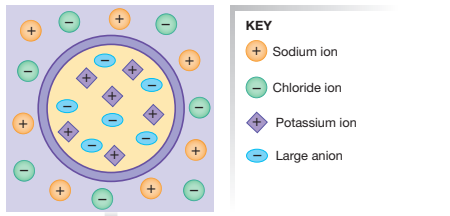


Creation of a Membrane Potential in an Artificial System

To show how a membrane potential difference can arise from ion concentration gradients and a selectively permeable membrane, we will use an artificial cell system where we can control the membrane's permeability to ions and the composition of the ECF and ICF.

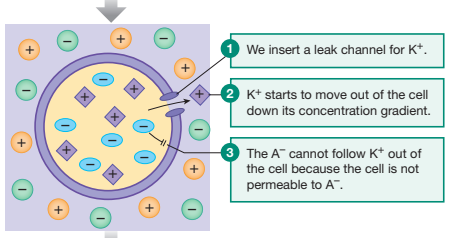
(b) When we begin, the cell has no membrane potential: The ECF (composed of Na^+ and Cl^- ions) and the ICF (K^+ and large anions, A^-) are electrically neutral.

The system is in chemical disequilibrium, with concentration gradients for all four ions. The cell membrane acts as an insulator to prevent free movement of ions between the ICF and ECF.



(c) Now we insert a leak channel for K^+ into the membrane, making the cell freely permeable to K^+.

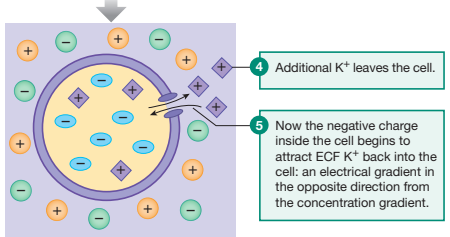
The transfer of just one K^+ from the cell to the ECF creates an electrical disequilibrium: the ECF has a net positive charge (+1) while the ICF has a net negative charge (–1). The cell now has a membrane potential difference, with the inside of the cell negative relative to the outside.



(d) As additional K^+ ions leave the cell, going down their concentration gradient, the inside of the cell becomes more negative and the outside becomes more positive.

How much K^+ will leave the cell?

If K^+ was uncharged, like glucose, it would diffuse out of the cell until the concentration outside $[K]_{out}$ equaled the concentration inside $[K]_{in}$. But K^+ is an ion, so we must consider its electrical gradient. Remember the rule for movement along electrical gradients: Opposite charges attract, like charges repel.



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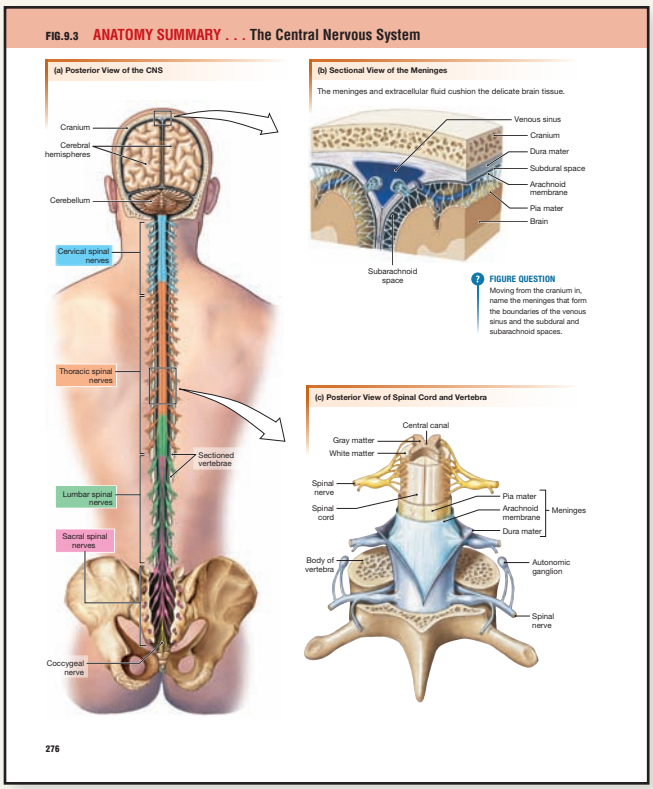
Anatomy Summary Figures provide succinct visual overviews of a physiological system from a macro to micro perspective. Whether you are learning the anatomy for the first time or refreshing your memory, these summaries show you the essential features of each system in a single figure.

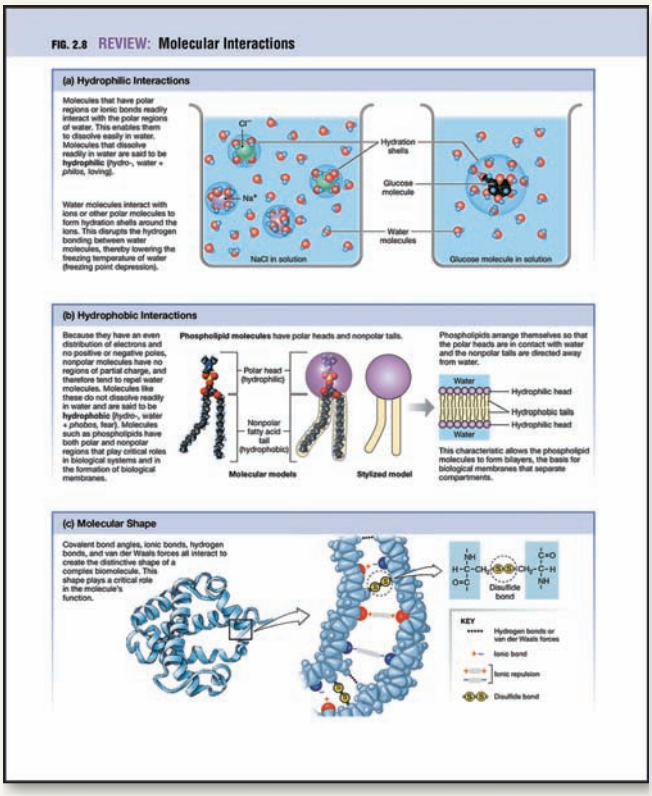
See p. 276



Review Figures visually present foundational concepts that you may already be familiar with. You may find it helpful to check out these figures before learning new physiology concepts.

Selected figures from the text can be assigned as **Art-Labeling Activities in Mastering A&P.**

See p. 44

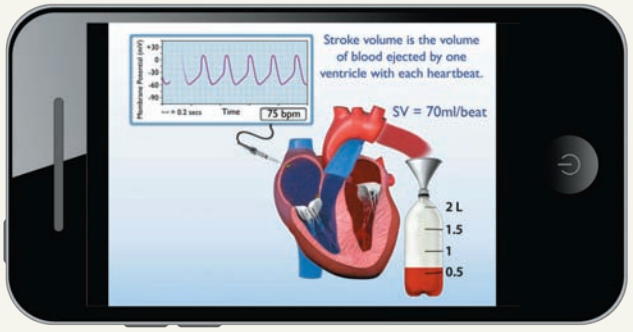


Get Online Coaching Through Mastering A&P

Mastering A&P provides tutorials and review questions that you can access before, during, and after class.

Phys in Action! Video Tutors and Coaching Activities help you visualize and master challenging physiological concepts by demonstrating laboratory procedures and real-world applications. Demonstrations include pulmonary function test, tilt table, exercise testing, and more.

EXPANDED! Interactive Physiology 2.0 Coaching Activities teach complex physiological processes using exceptionally clear animations, interactive tutorials, games, and quizzes. IP2 features new graphics, quicker navigation, and a mobile-friendly design. New topics include Generation of an Action Potential and Cardiac Cycle. IP2 and IP animations can be assigned from the Mastering A&P Item Library or accessed through the Mastering A&P Study Area.



Mastering A&P offers thousands of tutorials, activities, and questions that can be used to test yourself, or assigned for homework and practice. Additional highlights include:

- **Nurses Need Physiology Case Studies** guide you through the steps of diagnosing and treating patients in real-world clinical scenarios.
- **A&P Flix Animations** use 3-D, movie-quality graphics to help you visualize complex physiology processes.
- **Dynamic Study Modules** are manageable, mobile-friendly sets of questions with extensive feedback for you to test, learn, and retest yourself on basic concepts.
- **PhysioEx Laboratory Simulations** offer a supplement or substitute for wet labs due to cost, time, or safety concerns.

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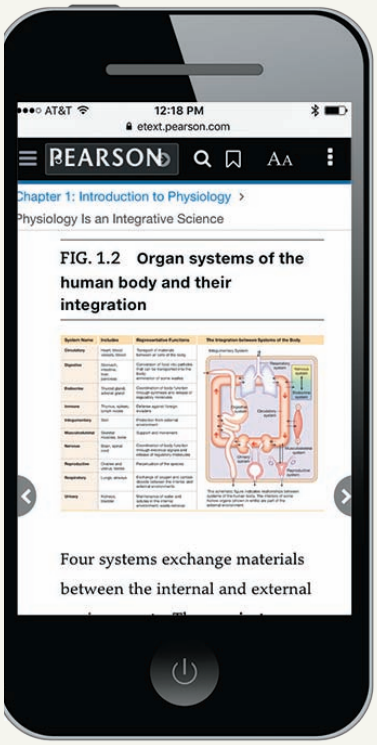
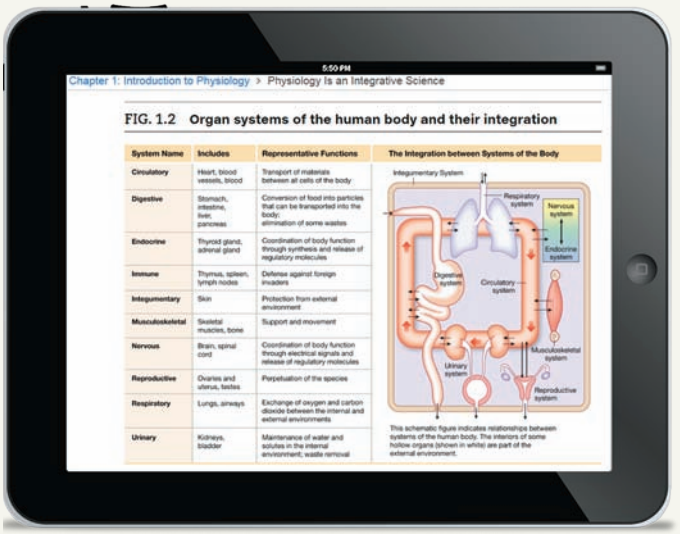
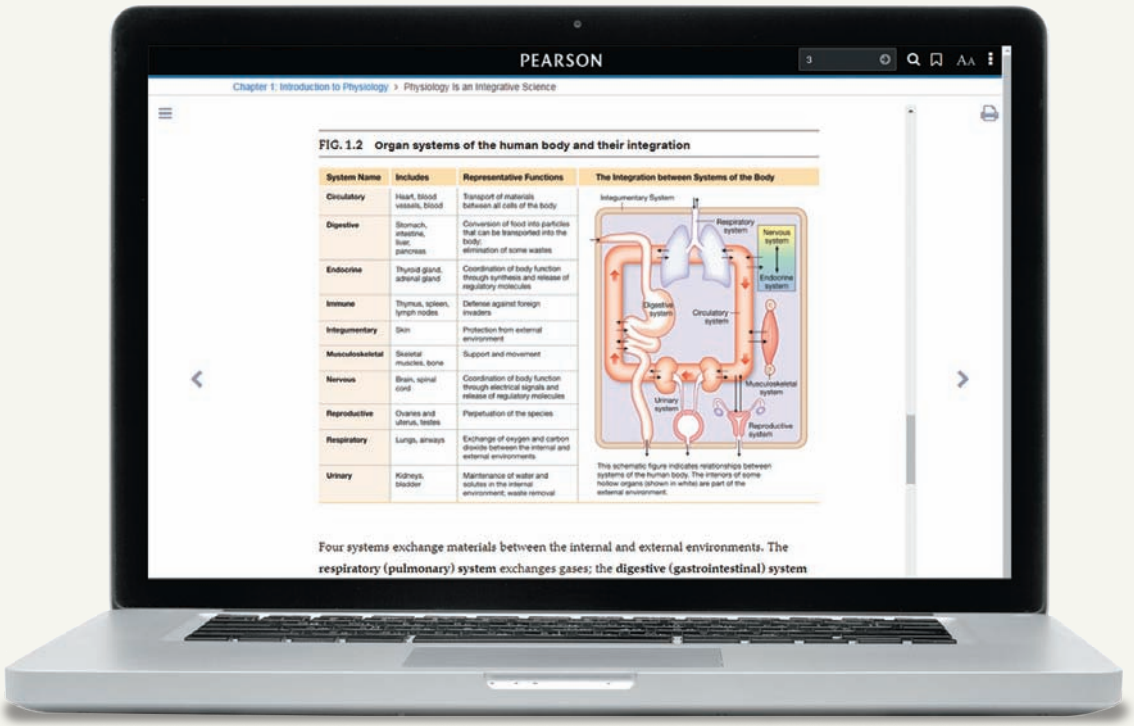




Powerful interactive and customization functions in the eText platform include instructor and student note-taking, highlighting, bookmarking, search, and links to glossary terms.



Additional Support for Students & Instructors

NEW! Ready-to-Go Teaching Modules help instructors efficiently make use of the best teaching tools before, during, and after class. Accessed through the Instructor Resources area of Mastering A&P, and curated by author Dee Silverthorn, modules include skill development applications for Human Physiology including Concept Mapping and Graphing.

Learning Catalytics allows students to use their smartphone, tablet, or laptop to respond to questions in class. Visit learningcatalytics.com to learn more.

The Mastering A&P Instructor Resources Area includes the following downloadable tools for instructors who adopt the Eighth Edition for their classes:

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- **All of the figures, photos, and tables from the text** are available in JPEG and PowerPoint® formats, in labelled and unlabelled versions, and with customizable labels and leader lines.
- **Test bank** provides thousands of customizable questions across Bloom's taxonomy levels. Each question is tagged to chapter learning outcomes that can also be tracked within Mastering Anatomy & Physiology assessments. Available in Microsoft® Word and TestGen® formats.
- **Animations and videos** bring human physiology concepts to life.
- **A comprehensive Instructor Resource Manual**, co-authored by Dee Silverthorn and Damian Hill, includes a detailed teaching outline for each chapter, along with a wealth of activities, examples, and analogies that have been thoroughly class-tested with thousands of students.
- **Customizable Study Questions**, co-authored by Dee Silverthorn and Damian Hill, help students focus their reading on the most important points in each chapters and are organized by chapter section headers for easy editing to reflect the material covered in class.

Welcome to the fascinating study of the human body! For most of recorded history, humans have been interested in how their bodies work. Early Egyptian, Indian, and Chinese writings describe attempts by physicians to treat various diseases and to restore health. Although some ancient remedies, such as camel dung and powdered sheep horn, may seem bizarre, we are still using others, such as blood-sucking leeches and chemicals derived from medicinal plants. The way we use these treatments has changed through the centuries as we have learned more about the human body.

There has never been a more exciting time in human physiology. **Physiology** is the study of the normal functioning of a living organism and its component parts, including all its chemical and physical processes. The term *physiology* literally means "knowledge of nature." Aristotle (384–322 BCE) used the word in this broad sense to describe the functioning of all living organisms, not just of the human body. However, Hippocrates (ca. 460–377 BCE), considered the father of medicine, used the word *physiology* to mean "the healing power of nature," and thereafter the field became closely associated with medicine. By the sixteenth century in Europe, physiology had been formalized as the study of the vital functions of the human body. Currently the term is again used to refer to the study of animals and plants.

Today, we benefit from centuries of work by physiologists who constructed a foundation of knowledge about how the human body functions. Since the 1970s, rapid advances in the fields of cellular and molecular biology have supplemented this work. A few decades ago, we thought that we would find the key to the secret of life by sequencing the human *genome*, which is the collective term for all the genetic information contained in the DNA of a species. However, this deconstructionist view of biology has proved to have its limitations, because living organisms are much more than the simple sum of their parts.

1.1 Physiology Is an Integrative Science

Many complex systems—including those of the human body—possess **emergent properties,** which are properties that cannot be predicted to exist based only on knowledge of the system's individual components. An emergent property is not a property of any single component of the system, and it is greater than the simple sum of the system's individual parts. Emergent properties result from complex, nonlinear interactions of the different components.

For example, suppose someone broke down a car into its nuts and bolts and pieces and laid them out on a floor. Could you predict that, properly assembled, these bits of metal and plastic would become a vehicle capable of converting the energy in gasoline into movement? Who could predict that the right combination of elements into molecules and assemblages of molecules would result in a living organism? Among the most complex emergent properties in humans are emotion, intelligence, and other aspects of brain function. None of these properties can be predicted from knowing the individual properties of nerve cells.

RUNNING PROBLEM **What to Believe?**

Jimmy had just left his first physiology class when he got the text from his mother: *Please call. Need to ask you something.* His mother seldom texted, so Jimmy figured it must be important. "Hi, Mom! What's going on?"

"Oh, Jimmy, I don't know what to do. I saw the doctor this morning and he's telling me that I need to take insulin. But I don't want to! My type of diabetes doesn't need insulin. I think he's just trying to make me see him more by putting me on insulin. Don't you think I'm right?"

Jimmy paused for a moment. "I'm not sure, Mom. He's probably just trying to do what's best for you. Didn't you talk to him about it?"

"Well, I tried but he didn't have time to talk. You're studying these things. Can't you look it up and see if I really need insulin?"

"I guess so. Let me see what I can find out." Jimmy hung up and thought. "Now what?"

2 5 9 12 16 19 24

When the Human Genome Project (*www.genome.gov*) began in 1990, scientists thought that by identifying and sequencing all the genes in human DNA, they would understand how the body worked. However, as research advanced, scientists had to revise their original idea that a given segment of DNA contained one gene that coded for one protein. It became clear that one gene may code for many proteins. The Human Genome Project ended in 2003, but before then researchers had moved beyond genomics to *proteomics*, the study of proteins in living organisms.

Now scientists have realized that knowing that a protein is made by a particular cell does not always tell us the significance of that protein to the cell, the tissue, or the functioning organism. The exciting new areas in biological research are called functional genomics, systems biology, and integrative biology, but fundamentally these are all fields of physiology. The **integration of function** across many **levels of organization** is a special focus of physiology. (To *integrate* means to bring varied elements together to create a unified whole.)

FIGURE 1.1 illustrates levels of organization ranging from the molecular level all the way up to populations of different species living together in *ecosystems* and in the *biosphere*. The levels of organization are shown along with the various subdisciplines of chemistry and biology related to the study of each organizational level. There is considerable overlap between the different fields of study, and these artificial divisions vary according to who is defining them. Notice, however, that physiology includes multiple levels, from molecular and cellular biology to the ecological physiology of populations.

At all levels, physiology is closely tied to anatomy. The structure of a cell, tissue, or organ must provide an efficient physical base for its function. For this reason, it is nearly impossible to study the physiology of the body without understanding the underlying anatomy. Because of the interrelationship of anatomy and physiology, you will find Anatomy Summaries throughout the book.

EMERGING CONCEPTS

The Changing World of Omics

If you read the scientific literature, it appears that contemporary research has exploded into an era of "omes" and "omics." What is an "ome"? The term apparently derives from the Latin word for a mass or tumor, and it is now used to refer to a collection of items that make up a whole, such as a genome. One of the earliest uses of the "ome" suffix in biology is the term *biome*, meaning all organisms living in a major ecological region, such as the marine biome or the desert biome. A genome, for example, is a collection of all the genetic material of an organism. Its physiome describes the organism's coordinated molecular, cellular, and physiological functioning.

The related adjective "omics" describes the research related to studying an "ome." Adding "omics" to a root word has become the cutting-edge way to describe a research field. For example, *pharmacogenomics* (the influence of genetics on the body's response to drugs) is now as important as *genomics*, the sequencing of DNA (the genome). There is even a journal named *OMICS!*

New "omes" emerge every year. The human connectome project (www.neuroscienceblueprint.nih.gov/connectome/) sponsored by the American National Institutes of Health is a collaborative effort by multiple institutions to map all the neural connections of the human brain. NIH also sponsors the human microbiome project (https://commonfund.nih.gov/hmp/overview), whose goal is to study the effects of microbes that normally live on or in the human body. Ignored as unimportant for many years, these microbes are now being shown to have an influence on both health and disease.

These special review features illustrate the anatomy of the physiological systems at different levels of organization.

At the most basic level of organization shown in Figure 1.1, atoms of elements link together to form molecules. Collections of molecules in living organisms form **cells,** the smallest unit of structure capable of carrying out all life processes. A lipid and protein barrier called the **cell membrane** (also called the *plasma membrane*) separates cells from their external environment. Simple organisms are composed of only one cell, but complex organisms have many cells with different structural and functional specializations.

Collections of cells that carry out related functions are called **tissues** {*texere*, to weave}. Tissues form structural and functional units known as **organs** {*organon*, tool}, and groups of organs integrate their functions to create **organ systems.** Chapter 3 reviews the anatomy of cells, tissues, and organs.

The 10 physiological organ systems in the human body are illustrated in FIGURE 1.2. Several of the systems have alternate names, given in parentheses, that are based on the organs of the system rather than the function of the system. The **integumentary system** {*integumentum*, covering}, composed of the skin, forms a protective boundary that separates the body's internal environment from the external environment (the outside world). The **musculoskeletal system** provides support and body movement.

Four systems exchange materials between the internal and external environments. The **respiratory (pulmonary) system** exchanges gases; the **digestive (gastrointestinal) system** takes up nutrients and water and eliminates wastes; the **urinary (renal) system** removes excess water and waste material; and the **reproductive system** produces eggs or sperm.

The remaining four systems extend throughout the body. The **circulatory (cardiovascular) system** distributes materials by pumping blood through vessels. The **nervous** and **endocrine systems** coordinate body functions. Note that the figure shows them as a continuum rather than as two distinct systems. Why? Because the lines between these two systems have blurred as we have learned more about the integrative nature of physiological function.

The one system not illustrated in Figure 1.2 is the diffuse **immune system,** which includes but is not limited to the anatomical structures known as the *lymphatic system*. The specialized cells of the immune system are scattered throughout the body. They protect the internal environment from foreign substances by intercepting material that enters through the intestines and lungs

FIG. 1.1 Levels of organization and the related fields of study

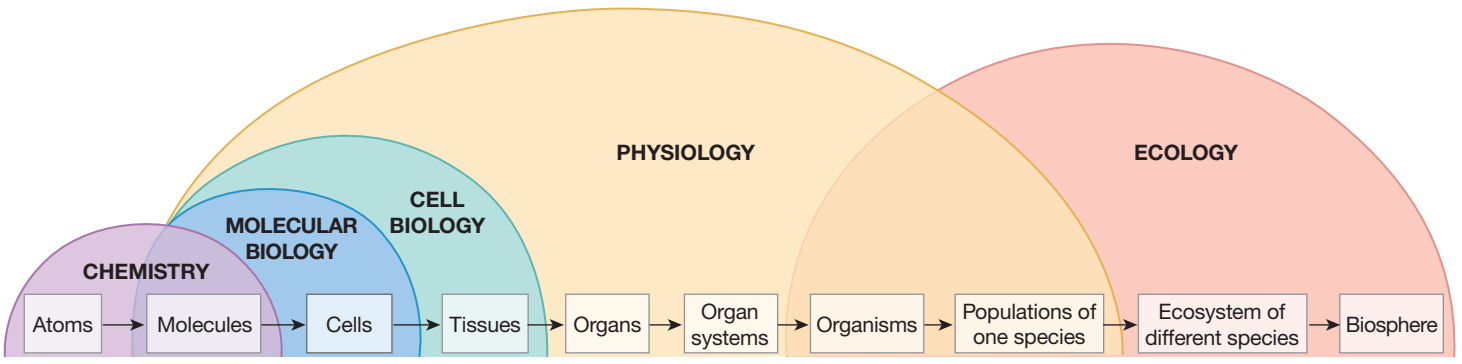
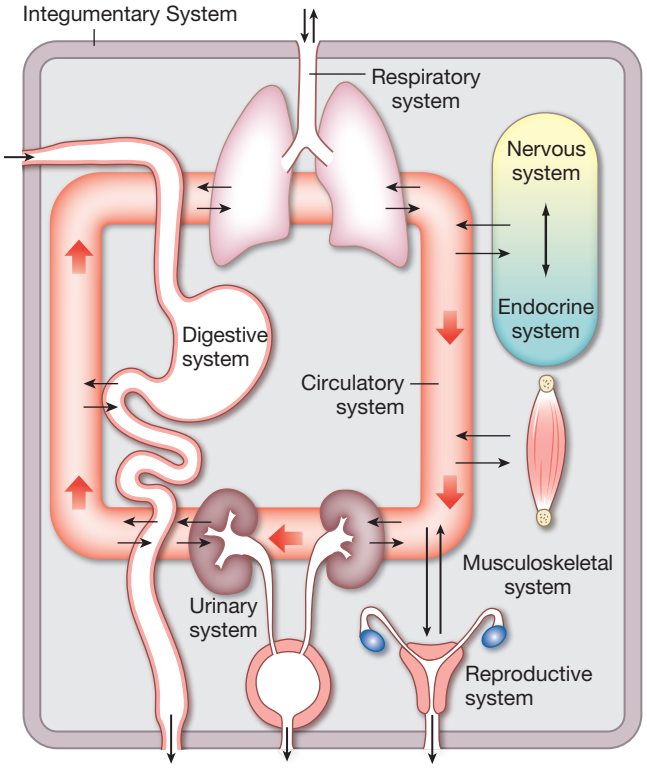


FIG. 1.2 Organ systems of the human body and their integration

FIG. 1.2 Organ Systems of the Human Body and their Integration

System Name	Includes	Representative Functions
Circulatory	Heart, blood vessels, blood	Transport of materials between all cells of the body
Digestive	Stomach, intestine, liver, pancreas	Conversion of food into particles that can be transported into the body; elimination of some wastes
Endocrine	Thyroid gland, adrenal gland	Coordination of body function through synthesis and release of regulatory molecules
Immune	Thymus, spleen, lymph nodes	Defense against foreign invaders
Integumentary	Skin	Protection from external environment
Musculoskeletal	Skeletal muscles, bone	Support and movement
Nervous	Brain, spinal cord	Coordination of body function through electrical signals and release of regulatory molecules
Reproductive	Ovaries and uterus, testes	Perpetuation of the species
Respiratory	Lungs, airways	Exchange of oxygen and carbon dioxide between the internal and external environments
Urinary	Kidneys, bladder	Maintenance of water and solutes in the internal environment; waste removal

The Integration between Systems of the Body



This schematic figure indicates relationships between systems of the human body. The interiors of some hollow organs (shown in white) are part of the external environment.

or through a break in the skin. In addition, immune tissues are closely associated with the circulatory system.

Traditionally, physiology courses and books are organized by organ system. Students study cardiovascular physiology and regulation of blood pressure in one chapter, and then study the kidneys and control of body fluid volume in a different chapter. In the functioning human, however, the cardiovascular and renal systems communicate with each other, so that a change in one is likely to cause a reaction in the other. For example, body fluid volume influences blood pressure, while changes in blood pressure alter kidney function because the kidneys regulate fluid volume. In this book, you will find several integrative physiology chapters that highlight the coordination of function across multiple organ systems.

Understanding how different organ systems work together is just as important as memorizing facts, but the complexity of interactions can be challenging. One way physiologists simplify and integrate information is by using visual representations of physiological processes called maps. The Focus on Mapping feature in this chapter will help you learn how to make maps. The first type of map, shown in **FIGURE 1.3a**, is a schematic representation of structure or function. The second type of map, shown in Figure 1.3b, diagrams a physiological process as it proceeds through time. These process maps are also called *flow charts, and they are frequently used in health care*. You will be able to practice mapping with special end-of-chapter questions throughout the book.

1.2 Function and Mechanism

We define physiology as the normal functioning of the body, but physiologists are careful to distinguish between *function* and *mechanism*. The **function** of a physiological system or event is the "why" of the system or event: Why does a certain response help an animal survive in a particular situation? In other words, what is the *adaptive significance* of this event for this animal?

For example, humans are large, mobile, terrestrial animals, and our bodies maintain relatively constant water content despite living in a dry, highly variable external environment. Dehydration is a constant threat to our well-being. What processes have evolved in our anatomy and physiology that allow us to survive in this hostile environment? One is the production of highly concentrated urine by the kidney, which allows the body to conserve water. This statement tells us *why* we produce concentrated urine but does not tell us *how* the kidney accomplishes that task.

Thinking about a physiological event in terms of its adaptive significance is the **teleological approach** to science. For example, the teleological answer to the question of why red blood cells transport oxygen is "because cells need oxygen and red blood cells bring it to them." This answer explains *why* red blood cells transport oxygen—their function—but says nothing about *how* the cells transport oxygen.

In contrast, most physiologists study physiological processes, or **mechanisms**—the "how" of a system. The **mechanistic approach** to physiology examines process. The mechanistic answer to the question "How do red blood cells transport oxygen?" is "Oxygen binds to hemoglobin molecules in the red blood cells." This very concrete answer explains exactly how oxygen transport occurs but says nothing about the significance of oxygen transport to the animal.

Students often confuse these two approaches to thinking about physiology. Studies have shown that even medical students tend to answer questions with teleological explanations when the more appropriate response would be a mechanistic explanation.[1] Often they do so because instructors ask why a physiological event occurs when they really want to know how it occurs. Staying aware of the two approaches will help prevent confusion.

Although function and mechanism seem to be two sides of the same coin, it is possible to study mechanisms, particularly at the cellular and subcellular level, without understanding their function in the life of the organism. As biological knowledge becomes more complex, scientists sometimes become so involved in studying complex processes that they fail to step back and look at the significance of those processes to cells, organ systems, or the animal. Conversely, it is possible to use teleological thinking incorrectly by saying, "Oh, in this situation the body needs to do this." *This* may be a good solution, but if a mechanism for doing *this* doesn't exist, the situation cannot be corrected.

Applying the concept of integrated functions and mechanisms is the underlying principle in **translational research,** an approach sometimes described as "bench to bedside." Translational research uses the insights and results gained from basic biomedical research on mechanisms to develop treatments and strategies for preventing human diseases. For example, researchers working on rats found that a chemical from the pancreas named *amylin* reduced the rats' food intake. These findings led directly to a translational research study in which human volunteers injected a synthetic form of amylin and recorded their subsequent food intake, but without intentionally modifying their lifestyle.[2] The drug suppressed food intake in humans, and was later approved by the Food and Drug Administration for treatment of diabetes mellitus.

[1] D. R. Richardson. A survey of students' notions of body function as teleologic or mechanistic. *Advan Physiol Educ* 258: 8–10, Jun 1990. Access free at *http://advan.physiology.org*.

[2] S. R. Smith *et al.* Pramlintide treatment reduces 24-h caloric intake and meal sizes and improves control of eating in obese subjects: a 6-wk translational research study. *Am J Physiol Endocrinol Metab* 293: E620–E627, 2007.

RUNNING PROBLEM

When Jimmy got back to his room, he sat down at his computer and went to the Internet. He typed *diabetes* in his search box—and came up with 267 million results. "That's not going to work. What about *insulin*?" Nearly 48 million results. "How in the world am I going to get any answers?" He clicked on the first sponsored ad that advertised "Information for type 2 diabetes." That might be good. His mother had type 2 diabetes. But it was for a pharmaceutical company trying to sell him a drug. "Maybe my physiology prof can help me with this search. I'll ask tomorrow."

Q1: *What search terms could Jimmy have used to get fewer results?*

2 5 9 12 16 19 24

At the systems level, we know about most of the mechanics of body function from centuries of research. The unanswered questions today mostly involve integration and control of these mechanisms, particularly at the cellular and molecular levels. Nevertheless, explaining what happens in test tubes or isolated cells can only partially answer questions about function. For this reason, animal and human trials are essential steps in the process of applying basic research to treating or curing diseases.

1.3 Themes in Physiology

"Physiology is not a science or a profession but a point of view."[3] Physiologists pride themselves on relating the mechanisms they study to the functioning of the organism as a whole. For students, being able to think about how multiple body systems integrate their function is one of the more difficult aspects of learning physiology. To develop expertise in physiology, you must do more than simply memorize facts and learn new terminology. Researchers have found that the ability to solve problems requires a conceptual framework, or "big picture," of the field.

This book will help you build a conceptual framework for physiology by explicitly emphasizing the basic biological concepts, or themes, that are common to all living organisms. These concepts form patterns that repeat over and over, and you will begin to recognize them when you encounter them in specific contexts. Pattern recognition is an important skill in healthcare professions, and it will also simplify learning physiology.

In the past few years, three different organizations issued reports to encourage the teaching of biology using these fundamental concepts. Although the descriptions vary in the three reports, five major themes emerge:

1. structure and function across all levels of organization
2. energy transfer, storage, and use
3. information flow, storage, and use within single organisms and within a species of organism

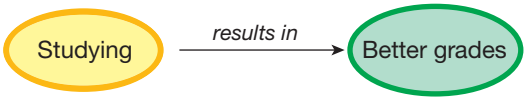
[3] R. W. Gerard. *Mirror to Physiology: A Self-Survey of Physiological Science.* Washington, DC: American Physiology Society, 1958.

FIG. 1.3 Focus on . . . Mapping

Why use maps to study physiology? The answer is simple: maps will help you organize information you are learning in a way that makes sense to you and they will make that information easier to recall on a test. Creating a map requires higher-level thinking about the relationships among items on the map.

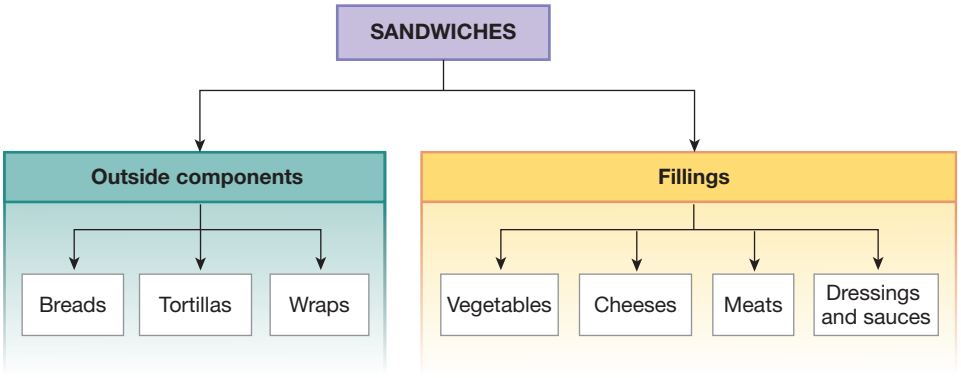
Mapping is not just a study technique. Scientists map out the steps in their experiments. Healthcare professionals create maps to guide them while diagnosing and treating patients. You can use mapping for almost every subject you study.

What is a map? Mapping is a nonlinear way of organizing material. A map can take a variety of forms but usually consists of terms (words or short phrases) linked by arrows to indicate associations. You can label the connecting arrows to describe the type of linkage between the terms (structure/function, cause/effect) or with explanatory phrases.

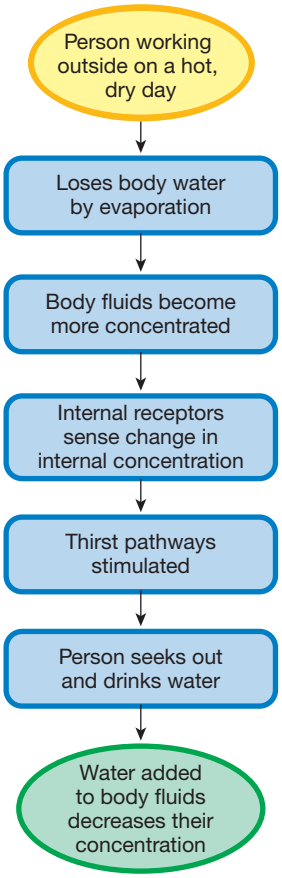


Here are two typical maps used in physiology.

Structure/function maps focus on the relationships between anatomical structures and their functions.



Process maps or **flow charts** follow normal homeostatic control pathways or the body's responses to abnormal (pathophysiological) events as they unfold over time.



Practice making maps. Many maps appear in this textbook, and they can serve as the starting point for your own maps. However, the real benefit of mapping comes from preparing maps yourself rather than memorizing someone else's maps. Your instructor can help you get started.

The next page walks you through the process of creating a structure-function map.

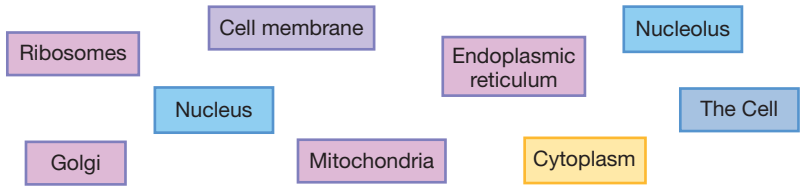
HINTS

- To help you get started, the end-of-chapter questions in this book include at least one list of terms to map for each chapter.
- Write your terms on individual slips of paper or small sticky notes so that you can rearrange the map more easily.
- Some terms may seem to belong to more than one group. Do not duplicate the item but make a note of it, as this term will probably have several arrows pointing to it or leading away from it.
- If arrows crisscross, try rearranging the terms on the map.
- Use color to indicate similar items.
- Add pictures and graphs that are associated with specific terms in your map.

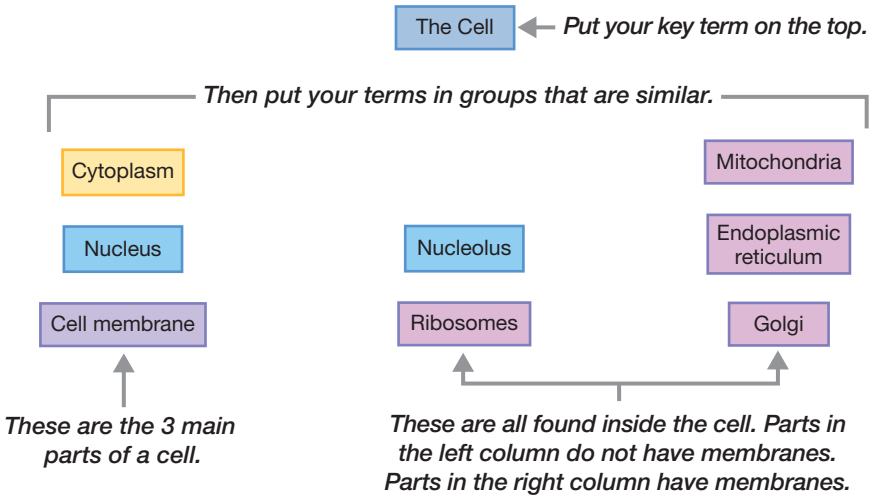
Electronic mapping. Some people do not like the messiness of hand-drawn maps. There are several electronic ways of making maps, including PowerPoint or free and commercial software programs. Free concept mapping software is available from IHMC CmapTools at http://cmap.ihmc.us. Or search for the term free concept map to find other resources on the Web. A popular commercial program for mapping is Inspiration (www.inspiration.com).

STEP 1: Write out the terms to map.

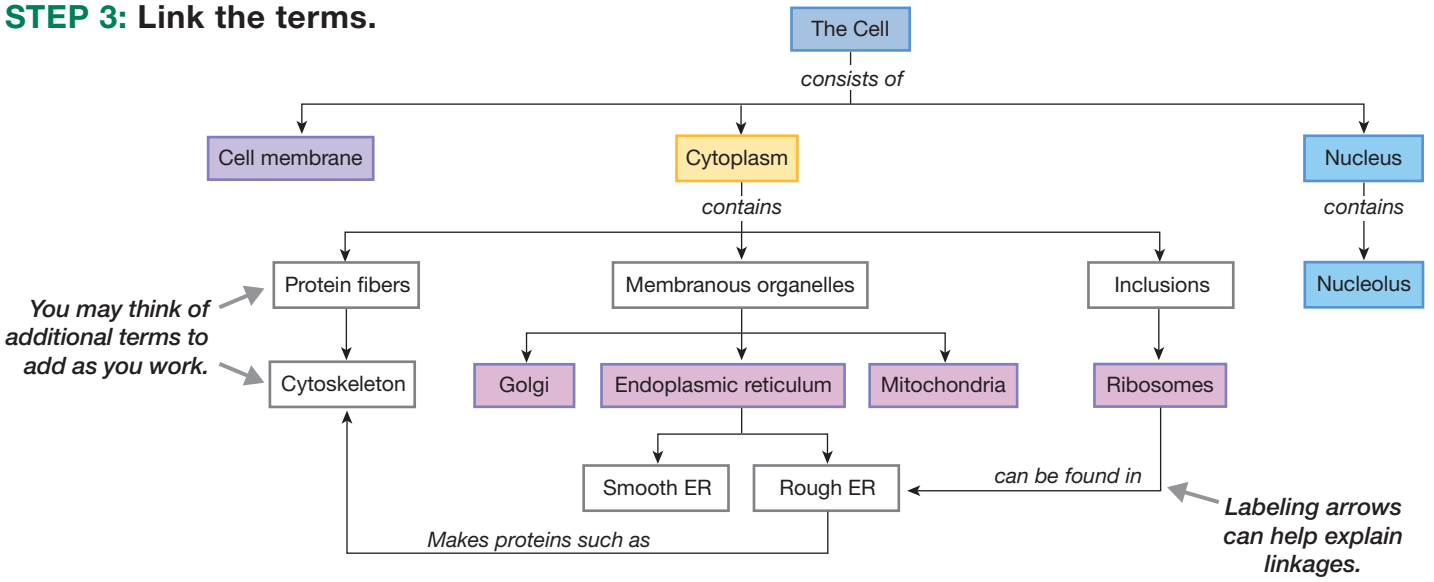
If you need help generating ideas for topics to map, the end-of-chapter mapping questions in each chapter have lists of terms to help you get started.



STEP 2: Organize the terms.



STEP 3: Link the terms.



Once you have created your map, sit back and think about it. Are all the items in the right place? You may want to move them around once you see the big picture. Add new concepts or correct wrong links. Review by recalling the main concept and then moving to the more specific details. Ask yourself questions like, What is the cause and what is the effect? What parts are involved? What are the main characteristics?

Science is a collaborative field. A useful way to study with a map is to **trade maps with a classmate** and try to understand each other's maps. Your maps will almost certainly not look the same! It's OK if they are different. Remember that your map reflects the way you think about the subject, which may be different from the way someone else thinks about it. Did one of you put in something the other forgot? Did one of you have an incorrect link between two items?

4. homeostasis and the control systems that maintain it
5. evolution

In addition, all three reports emphasize the importance of understanding how science is done and of the quantitative nature of biology. **TABLE 1.1** lists the core concepts in biology from the three reports.

In this book, we focus on the four themes most related to physiology: structure-function relationships, biological energy use, information flow within an organism, and homeostasis and the control systems that maintain it. The first six chapters introduce the fundamentals of these themes, which you may already be familiar with from earlier biology or chemistry classes. The themes and their associated concepts, with variations, then re-appear over and over in subsequent chapters of this book. Look for them in the summary material at the end of the chapters and in the end-of-chapter questions as well.

Theme 1: Structure and Function Are Closely Related

The integration of structure and function extends across all levels of organization, from the molecular level to the intact body. This theme subdivides into two major ideas: molecular interactions and compartmentation.

Molecular Interactions The ability of individual molecules to bind to or react with other molecules is essential for biological function. A molecule's function depends on its structure and shape, and even a small change to the structure or shape may have significant effects on the function. The classic example of this phenomenon is the change in one amino acid of the hemoglobin protein. (Hemoglobin is the oxygen-carrying pigment of the blood.) This one small change in the protein converts normal hemoglobin to the form associated with sickle cell disease.

Many physiologically significant molecular interactions that you will learn about in this book involve the class of biological molecules called *proteins*. Functional groups of proteins include *enzymes* that speed up chemical reactions, *signal molecules* and the *receptor proteins* that bind signal molecules, and specialized proteins that function as biological pumps, filters, motors, or transporters. Chapter 2 describes molecular interactions involving proteins in more detail.

Interactions between proteins, water, and other molecules influence cell structure and the mechanical properties of cells and tissues. Mechanical properties you will encounter in your study of physiology include *compliance* (ability to stretch), *elastance* (stiffness or the ability to return to the unstretched state), strength, flexibility, and fluidity (*viscosity*).

Compartmentation **Compartmentation** is the division of space into separate compartments. Compartments allow a cell, a tissue, or an organ to specialize and isolate functions. Each level of organization is associated with different types of compartments. At the macroscopic level, the tissues and organs of the body form discrete functional compartments, such as body cavities or the insides of hollow organs. At the microscopic level, cell membranes separate cells from the fluid surrounding them and also create tiny compartments within the cell called organelles. Compartmentation is the theme of Chapter 3.

Theme 2: Living Organisms Need Energy

Growth, reproduction, movement, homeostasis—these and all other processes that take place in an organism require the continuous input of energy. Where does this energy come from, and how is it stored? We will answer those questions and describe some of

TABLE 1.1 Biology Concepts

Scientific Foundations for Future Physicians (HHMI and AAMC)[1]	Vision and Change (NSF and AAAS)[2]	The 2010 Advanced Placement Biology Curriculum (College Board)[3]
Structure/function from molecules to organisms	Structure and function (anatomy and physiology)	Relationship of structure to function
Physical principles applied to living systems Chemical principles applied to living systems	Pathways and transformations of energy and matter	Energy transfer
Biomolecules and their functions	Information flow, exchange, and storage	Continuity and change
Organisms sense and control their internal environment and respond to external change	Systems	Regulation ("a state of dynamic balance")
Evolution as an organizing principle	Evolution	Evolution

[1] *Scientific Foundations for Future Physicians*. Howard Hughes Medical Institute (HHMI) and the Association of American Medical Colleges (AAMC), 2009. *www.aamc.org/scientificfoundations*
[2] *Vision and Change: A Call to Action*. National Science Foundation (NSF) and American Association for the Advancement of Science (AAAS). 2011. *http://visionandchange.org/finalreport*. The report mentioned the integration of science and society as well.
[3] *College Board AP Biology Course Description*, The College Board, 2010. *http://apcentral.collegeboard.com/apc/public/repository/ap-biology-course-description.pdf*. The AP report also included "Interdependence in Nature" and "Science, Technology and Society" as two of their eight themes.