



# Advanced Nutrition and Human Metabolism

EIGHTH EDITION

**Sareen S. Gropper**

**Jack L. Smith | Timothy P. Carr**

# Dietary Reference Intakes (DRI)

The Dietary Reference Intakes (DRI) include two sets of values that serve as goals for nutrient intake—Recommended Dietary Allowances (RDA) and Adequate Intakes (AI). The RDA reflect the average daily amount of a nutrient considered adequate to meet the needs of most healthy people. If there is insufficient evidence to determine an RDA, an AI is set. AI are more tentative than RDA, but both may be used as goals for nutrient intakes. (Chapter 9 provides more details.)

In addition to the values that serve as goals for nutrient intakes (presented in the tables on these two pages), the DRI include a set of values called Tolerable Upper Intake Levels (UL). The UL represent the maximum amount of a nutrient that appears safe for most healthy people to consume on a regular basis. Turn the page for a listing of the UL for selected vitamins and minerals.

## Estimated Energy Requirements (EER), Recommended Dietary Allowances (RDA), and Adequate Intakes (AI) for Water, Energy, and the Energy Nutrients

Age (yr)	Reference BMI (kg/m <sup>2</sup> )	Reference Height cm (in)	Reference Weight kg (lb)	Water <sup>a</sup> AI (L/day)	Energy EER <sup>b</sup> (kcal/day)	Carbohydrate RDA (g/day)	Total Fiber AI (g/day)	Total Fat AI (g/day)	Linoleic Acid AI (g/day)	Linolenic Acid <sup>c</sup> AI (g/day)	Protein RDA (g/day) <sup>d</sup>	Protein RDA (g/kg/day)
<b>Males</b>												
0–0.5	—	62 (24)	6 (13)	0.7 <sup>e</sup>	570	60	—	31	4.4	0.5	9.1	1.52
0.5–1	—	71 (28)	9 (20)	0.8 <sup>f</sup>	743	95	—	30	4.6	0.5	11	1.20
1–3 <sup>g</sup>	—	86 (34)	12 (27)	1.3	1046	130	19	—	7	0.7	13	1.05
4–8 <sup>g</sup>	15.3	115 (45)	20 (44)	1.7	1742	130	25	—	10	0.9	19	0.95
9–13	17.2	144 (57)	36 (79)	2.4	2279	130	31	—	12	1.2	34	0.95
14–18	20.5	174 (68)	61 (134)	3.3	3152	130	38	—	16	1.6	52	0.85
19–30	22.5	177 (70)	70 (154)	3.7	3067 <sup>h</sup>	130	38	—	17	1.6	56	0.80
31–50	22.5 <sup>i</sup>	177 (70) <sup>i</sup>	70 (154) <sup>i</sup>	3.7	3067 <sup>h</sup>	130	38	—	17	1.6	56	0.80
>50	22.5 <sup>i</sup>	177 (70) <sup>i</sup>	70 (154) <sup>i</sup>	3.7	3067 <sup>h</sup>	130	30	—	14	1.6	56	0.80
<b>Females</b>												
0–0.5	—	62 (24)	6 (13)	0.7 <sup>e</sup>	520	60	—	31	4.4	0.5	9.1	1.52
0.5–1	—	71 (28)	9 (20)	0.8 <sup>f</sup>	676	95	—	30	4.6	0.5	11	1.20
1–3 <sup>g</sup>	—	86 (34)	12 (27)	1.3	992	130	19	—	7	0.7	13	1.05
4–8 <sup>g</sup>	15.3	115 (45)	20 (44)	1.7	1642	130	25	—	10	0.9	19	0.95
9–13	17.4	144 (57)	37 (81)	2.1	2071	130	26	—	10	1.0	34	0.95
14–18	20.4	163 (64)	54 (119)	2.3	2368	130	26	—	11	1.1	46	0.85
19–30	21.5	163 (64)	57 (126)	2.7	2403 <sup>j</sup>	130	25	—	12	1.1	46	0.80
31–50	21.5 <sup>i</sup>	163 (64) <sup>i</sup>	57 (126) <sup>i</sup>	2.7	2403 <sup>j</sup>	130	25	—	12	1.1	46	0.80
>50	21.5 <sup>i</sup>	163 (64) <sup>i</sup>	57 (126) <sup>i</sup>	2.7	2403 <sup>j</sup>	130	21	—	11	1.1	46	0.80
<b>Pregnancy</b>												
<i>1st trimester</i>				3.0	+0	175	28	—	13	1.4	46	0.80
<i>2nd trimester</i>				3.0	+340	175	28	—	13	1.4	71	1.10
<i>3rd trimester</i>				3.0	+452	175	28	—	13	1.4	71	1.10
<b>Lactation</b>												
<i>1st 6 months</i>				3.8	+330	210	29	—	13	1.3	71	1.30
<i>2nd 6 months</i>				3.8	+400	210	29	—	13	1.3	71	1.30

NOTE: For all nutrients, values for infants are AI. Dashes indicate that values have not been determined.  
<sup>a</sup>The water AI includes drinking water, water in beverages, and water in foods; in general, drinking water and other beverages contribute about 70 to 80 percent, and foods, the remainder. Conversion factors: 1 L = 33.8 fluid oz; 1 L = 1.06 qt; 1 cup = 8 fluid oz.  
<sup>b</sup>The Estimated Energy Requirement (EER) represents the average dietary energy intake that will maintain energy balance in a healthy person of a given gender, age, weight, height, and physical activity level. The values listed are based on an “active” person at the reference height and weight and at the midpoint ages for each group

until age 19. Chapter 8 provides equations and tables to determine estimated energy requirements.  
<sup>c</sup>The linolenic acid referred to in this table and text is the omega-3 fatty acid known as alpha-linolenic acid.  
<sup>d</sup>The values listed are based on reference body weights.  
<sup>e</sup>Assumed to be from human milk.  
<sup>f</sup>Assumed to be from human milk and complementary foods and beverages. This includes approximately 0.6 L (~2½ cups) as total fluid including formula, juices, and drinking water.  
<sup>g</sup>For energy, the age groups for young children are 1–2 years and 3–8 years.

<sup>h</sup>For males, subtract 10 kcalories per day for each year of age above 19.  
<sup>i</sup>Because weight need not change as adults age if activity is maintained, reference weights for adults 19 through 30 years are applied to all adult age groups.  
<sup>j</sup>For females, subtract 7 kcalories per day for each year of age above 19.  
 SOURCE: Adapted from the *Dietary Reference Intakes* series, National Academies Press. Copyright 1997, 1998, 2000, 2001, 2002, 2004, 2005, 2011 by the National Academies of Sciences.

## Recommended Dietary Allowances (RDA) and Adequate Intakes (AI) for Vitamins

Age (yr)	Thiamin RDA (mg/day)	Riboflavin RDA (mg/day)	Niacin RDA (mg/day) <sup>a</sup>	Biotin AI (µg/day)	Pantothenic acid AI (mg/day)	Vitamin B <sub>6</sub> RDA (mg/day)	Folate RDA (µg/day) <sup>b</sup>	Vitamin B <sub>12</sub> RDA (µg/day)	Choline AI (mg/day)	Vitamin C RDA (mg/day)	Vitamin A RDA (µg/day) <sup>c</sup>	Vitamin D RDA (IU/day) <sup>d</sup>	Vitamin E RDA (mg/day) <sup>e</sup>	Vitamin K AI (µg/day)
<b>Infants</b>														
0–0.5	0.2	0.3	2	5	1.7	0.1	65	0.4	125	40	400	400 (10 µg)	4	2.0
0.5–1	0.3	0.4	4	6	1.8	0.3	80	0.5	150	50	500	400 (10 µg)	5	2.5
<b>Children</b>														
1–3	0.5	0.5	6	8	2	0.5	150	0.9	200	15	300	600 (15 µg)	6	30
4–8	0.6	0.6	8	12	3	0.6	200	1.2	250	25	400	600 (15 µg)	7	55
<b>Males</b>														
9–13	0.9	0.9	12	20	4	1.0	300	1.8	375	45	600	600 (15 µg)	11	60
14–18	1.2	1.3	16	25	5	1.3	400	2.4	550	75	900	600 (15 µg)	15	75
19–30	1.2	1.3	16	30	5	1.3	400	2.4	550	90	900	600 (15 µg)	15	120
31–50	1.2	1.3	16	30	5	1.3	400	2.4	550	90	900	600 (15 µg)	15	120
51–70	1.2	1.3	16	30	5	1.7	400	2.4	550	90	900	600 (15 µg)	15	120
>70	1.2	1.3	16	30	5	1.7	400	2.4	550	90	900	800 (20 µg)	15	120
<b>Females</b>														
9–13	0.9	0.9	12	20	4	1.0	300	1.8	375	45	600	600 (15 µg)	11	60
14–18	1.0	1.0	14	25	5	1.2	400	2.4	400	65	700	600 (15 µg)	15	75
19–30	1.1	1.1	14	30	5	1.3	400	2.4	425	75	700	600 (15 µg)	15	90
31–50	1.1	1.1	14	30	5	1.3	400	2.4	425	75	700	600 (15 µg)	15	90
51–70	1.1	1.1	14	30	5	1.5	400	2.4	425	75	700	600 (15 µg)	15	90
>70	1.1	1.1	14	30	5	1.5	400	2.4	425	75	700	800 (20 µg)	15	90
<b>Pregnancy</b>														
≤18	1.4	1.4	18	30	6	1.9	600	2.6	450	80	750	600 (15 µg)	15	75
19–30	1.4	1.4	18	30	6	1.9	600	2.6	450	85	770	600 (15 µg)	15	90
31–50	1.4	1.4	18	30	6	1.9	600	2.6	450	85	770	600 (15 µg)	15	90
<b>Lactation</b>														
≤18	1.4	1.6	17	35	7	2.0	500	2.8	550	115	1200	600 (15 µg)	19	75
19–30	1.4	1.6	17	35	7	2.0	500	2.8	550	120	1300	600 (15 µg)	19	90
31–50	1.4	1.6	17	35	7	2.0	500	2.8	550	120	1300	600 (15 µg)	19	90

NOTE: For all nutrients, values for infants are AI.

<sup>a</sup>Niacin recommendations are expressed as niacin equivalents (NE), except for recommendations for infants younger than 6 months, which are expressed as preformed niacin.

<sup>b</sup>Folate recommendations are expressed as dietary folate equivalents (DFE).

<sup>c</sup>Vitamin A recommendations are expressed as retinol activity equivalents (RAE).

<sup>d</sup>Vitamin D recommendations are expressed as cholecalciferol and assume an absence of adequate exposure to sunlight.

<sup>e</sup>Vitamin E recommendations are expressed as α-tocopherol.

## Recommended Dietary Allowances (RDA) and Adequate Intakes (AI) for Minerals

Age (yr)	Sodium AI (mg/day)	Chloride AI (mg/day)	Potassium AI (mg/day)	Calcium RDA (mg/day)	Phosphorus RDA (mg/day)	Magnesium RDA (mg/day)	Iron RDA (mg/day)	Zinc RDA (mg/day)	Iodine RDA (µg/day)	Selenium RDA (µg/day)	Copper RDA (µg/day)	Manganese AI (mg/day)	Fluoride AI (mg/day)	Chromium AI (µg/day)	Molybdenum RDA (µg/day)
<b>Infants</b>															
0–0.5	120	180	400	200	100	30	0.27	2	110	15	200	0.003	0.01	0.2	2
0.5–1	370	570	700	260	275	75	11	3	130	20	220	0.6	0.5	5.5	3
<b>Children</b>															
1–3	1000	1500	3000	700	460	80	7	3	90	20	340	1.2	0.7	11	17
4–8	1200	1900	3800	1000	500	130	10	5	90	30	440	1.5	1.0	15	22
<b>Males</b>															
9–13	1500	2300	4500	1300	1250	240	8	8	120	40	700	1.9	2	25	34
14–18	1500	2300	4700	1300	1250	360	15	9	150	55	890	1.6	3	24	43
19–30	1500	2300	4700	1000	700	310	18	8	150	55	900	1.8	3	25	45
31–50	1500	2300	4700	1000	700	320	18	8	150	55	900	1.8	3	25	45
51–70	1300	2000	4700	1000	700	320	8	8	150	55	900	1.8	3	20	45
>70	1200	1800	4700	1200	700	420	8	8	150	55	900	2.3	4	30	45
<b>Females</b>															
9–13	1500	2300	4500	1300	1250	240	8	8	120	40	700	1.6	2	21	34
14–18	1500	2300	4700	1300	1250	360	15	9	150	55	890	1.6	3	24	43
19–30	1500	2300	4700	1000	700	310	18	8	150	55	900	1.8	3	25	45
31–50	1500	2300	4700	1000	700	320	18	8	150	55	900	1.8	3	25	45
51–70	1300	2000	4700	1200	700	320	8	8	150	55	900	1.8	3	20	45
>70	1200	1800	4700	1200	700	320	8	8	150	55	900	1.8	3	20	45
<b>Pregnancy</b>															
≤18	1500	2300	4700	1300	1250	400	27	12	220	60	1000	2.0	3	29	50
19–30	1500	2300	4700	1000	700	350	27	11	220	60	1000	2.0	3	30	50
31–50	1500	2300	4700	1000	700	360	27	11	220	60	1000	2.0	3	30	50
<b>Lactation</b>															
≤18	1500	2300	5100	1300	1250	360	10	13	290	70	1300	2.6	3	44	50
19–30	1500	2300	5100	1000	700	310	9	12	290	70	1300	2.6	3	45	50
31–50	1500	2300	5100	1000	700	320	9	12	290	70	1300	2.6	3	45	50

NOTE: For all nutrients, values for infants are AI.

## Tolerable Upper Intake Levels (UL) for Vitamins

Age (yr)	Niacin (mg/day) <sup>a</sup>	Vitamin B <sub>6</sub> (mg/day)	Folate (µg/day) <sup>a</sup>	Choline (mg/day)	Vitamin C (mg/day)	Vitamin A (µg/day) <sup>b</sup>	Vitamin D (IU/day)	Vitamin E (mg/day) <sup>c</sup>
<b>Infants</b>								
0–0.5	—	—	—	—	—	600	1000 (25 µg)	—
0.5–1	—	—	—	—	—	600	1500 (38 µg)	—
<b>Children</b>								
1–3	10	30	300	1000	400	600	2500 (63 µg)	200
4–8	15	40	400	1000	650	900	3000 (75 µg)	300
9–13	20	60	600	2000	1200	1700	4000 (100 µg)	600
<b>Adolescents</b>								
14–18	30	80	800	3000	1800	2800	4000 (100 µg)	800
<b>Adults</b>								
19–70	35	100	1000	3500	2000	3000	4000 (100 µg)	1000
>70	35	100	1000	3500	2000	3000	4000 (100 µg)	1000
<b>Pregnancy</b>								
≤18	30	80	800	3000	1800	2800	4000 (100 µg)	800
19–50	35	100	1000	3500	2000	3000	4000 (100 µg)	1000
<b>Lactation</b>								
≤18	30	80	800	3000	1800	2800	4000 (100 µg)	800
19–50	35	100	1000	3500	2000	3000	4000 (100 µg)	1000

<sup>a</sup>The UL for niacin and folate apply to synthetic forms obtained from supplements, fortified foods, or a combination of the two.

<sup>c</sup>The UL for vitamin E applies to any form of supplemental α-tocopherol, fortified foods, or a combination of the two.

<sup>b</sup>The UL for vitamin A applies to the preformed vitamin only.

## Tolerable Upper Intake Levels (UL) for Minerals

Age (yr)	Sodium (mg/day)	Chloride (mg/day)	Calcium (mg/day)	Phosphorus (mg/day)	Magnesium (mg/day) <sup>d</sup>	Iron (mg/day)	Zinc (mg/day)	Iodine (µg/day)	Selenium (µg/day)	Copper (µg/day)	Manganese (mg/day)	Fluoride (mg/day)	Molybdenum (µg/day)	Boron (mg/day)	Nickel (mg/day)	Vanadium (mg/day)
<b>Infants</b>																
0–0.5	—	—	1000	—	—	40	4	—	45	—	—	0.7	—	—	—	—
0.5–1	—	—	1500	—	—	40	5	—	60	—	—	0.9	—	—	—	—
<b>Children</b>																
1–3	1500	2300	2500	3000	65	40	7	200	90	1000	2	1.3	300	3	0.2	—
4–8	1900	2900	2500	3000	110	40	12	300	150	3000	3	2.2	600	6	0.3	—
9–13	2200	3400	3000	4000	350	40	23	600	280	5000	6	10	1100	11	0.6	—
<b>Adolescents</b>																
14–18	2300	3600	3000	4000	350	45	34	900	400	8000	9	10	1700	17	1.0	—
<b>Adults</b>																
19–50	2300	3600	2500	4000	350	45	40	1100	400	10,000	11	10	2000	20	1.0	1.8
51–70	2300	3600	2000	4000	350	45	40	1100	400	10,000	11	10	2000	20	1.0	1.8
>70	2300	3600	2000	3000	350	45	40	1100	400	10,000	11	10	2000	20	1.0	1.8
<b>Pregnancy</b>																
≤18	2300	3600	3000	3500	350	45	34	900	400	8000	9	10	1700	17	1.0	—
19–50	2300	3600	2500	3500	350	45	40	1100	400	10,000	11	10	2000	20	1.0	—
<b>Lactation</b>																
≤18	2300	3600	3000	4000	350	45	34	900	400	8000	9	10	1700	17	1.0	—
19–50	2300	3600	2500	4000	350	45	40	1100	400	10,000	11	10	2000	20	1.0	—

<sup>d</sup>The UL for magnesium applies to synthetic forms obtained from supplements or drugs only.

NOTE: An Upper Limit was not established for vitamins and minerals not listed and for those age groups listed with a dash (—) because of a lack of data, not because these nutrients are safe to consume at any level of intake. All nutrients can have adverse effects when intakes are excessive.

SOURCE: Adapted with permission from the *Dietary Reference Intakes* series, National Academies Press. Copyright 1997, 1998, 2000, 2001, 2002, 2005, 2011 by the National Academies of Sciences.



## Fit your coursework into your hectic life.

Make the most of your time by learning your way. Access the resources you need to succeed wherever, whenever.



Study with digital flashcards, listen to audio textbooks and take quizzes.



Review your current course grade and compare your progress with your peers.



Get the free Cengage Mobile App and learn wherever you are.

Break Limitations. Create your own potential, and be unstoppable with *MindTap*.

**MindTap.** Powered by You.



[cengage.com/mindtap](https://cengage.com/mindtap)

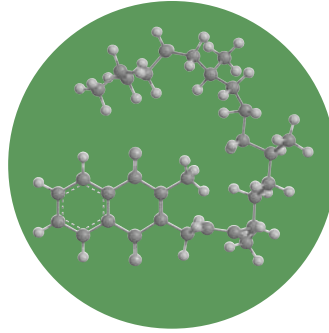
Copyright 2022 Cengage Learning. All Rights Reserved. May not be copied, scanned, or duplicated, in whole or in part. WCN 02-200-203

Copyright 2022 Cengage Learning. All Rights Reserved. May not be copied, scanned, or duplicated, in whole or in part. Due to electronic rights, some third party content may be suppressed from the eBook and/or eChapter(s). Editorial review has deemed that any suppressed content does not materially affect the overall learning experience. Cengage Learning reserves the right to remove additional content at any time if subsequent rights restrictions require it.

# ADVANCED NUTRITION AND HUMAN METABOLISM

**EIGHTH EDITION**





# ADVANCED NUTRITION AND HUMAN METABOLISM

**EIGHTH EDITION**

**Sareen S. Gropper**

**FLORIDA ATLANTIC UNIVERSITY**

**AUBURN UNIVERSITY (PROFESSOR EMERITUS)**

**Jack L. Smith**

**UNIVERSITY OF DELAWARE**

**Timothy P. Carr**

**UNIVERSITY OF NEBRASKA-LINCOLN**



Australia • Brazil • Canada • Mexico • Singapore • United Kingdom • United States

Copyright 2022 Cengage Learning. All Rights Reserved. May not be copied, scanned, or duplicated, in whole or in part. WCN 02-200-203

Copyright 2022 Cengage Learning. All Rights Reserved. May not be copied, scanned, or duplicated, in whole or in part. Due to electronic rights, some third party content may be suppressed from the eBook and/or eChapter(s). Editorial review has deemed that any suppressed content does not materially affect the overall learning experience. Cengage Learning reserves the right to remove additional content at any time if subsequent rights restrictions require it.



This is an electronic version of the print textbook. Due to electronic rights restrictions, some third party content may be suppressed. Editorial review has deemed that any suppressed content does not materially affect the overall learning experience. The publisher reserves the right to remove content from this title at any time if subsequent rights restrictions require it. For valuable information on pricing, previous editions, changes to current editions, and alternate formats, please visit [www.cengage.com/highered](http://www.cengage.com/highered) to search by ISBN#, author, title, or keyword for materials in your areas of interest.

Important Notice: Media content referenced within the product description or the product text may not be available in the eBook version.

***Advanced Nutrition and Human Metabolism,***  
**Eighth Edition**  
**Sareen S. Gropper, Jack L. Smith, and**  
**Timothy P. Carr**

SVP, Higher Education & Skills Product: Erin Joyner

VP, Higher Education & Skills Product:  
Thais Alencar

Product Team Manager: Maureen McLaughlin

Product Manager: Courtney Heilman

Product Assistant: Hannah Shin

Marketing Manager: Shannon Hawkins

Content Manager: Samantha Rundle

Learning Designer: Paula Dohnal

IP Analyst: Ann Hoffman

IP Project Manager: Betsy Hathaway

Text and Photo Researcher:  
Lumina Datamatics, Ltd.

Production Service and Compositor: SPI Global

Art Director: Lizz Anderson

Text Designer: Nadine Ballard

Cover Designer: Lizz Anderson

Cover Illustration: bestber/Shutterstock.com;  
iStockPhoto.com/BlackJack3D

© 2022, 2018, 2013 Cengage Learning, Inc.

ALL RIGHTS RESERVED. No part of this work covered by the copyright herein may be reproduced or distributed in any form or by any means, except as permitted by U.S. copyright law, without the prior written permission of the copyright owner.

For product information and technology assistance, contact us at  
**Cengage Customer & Sales Support, 1-800-354-9706**  
or **support.cengage.com**.

For permission to use material from this text or product, submit all  
requests online at **www.cengage.com/permissions**.

Library of Congress Control Number: 2020922497

Student Edition:  
ISBN: 978-0-357-44981-3

Loose-leaf Edition:  
ISBN: 978-0-357-45006-2

**Cengage**  
200 Pier 4 Boulevard  
Boston, MA 02210  
USA

Cengage is a leading provider of customized learning solutions with employees residing in nearly 40 different countries and sales in more than 125 countries around the world. Find your local representative at:  
**www.cengage.com**.

To learn more about Cengage platforms and services, register or access your online learning solution, or purchase materials for your course, visit **www.cengage.com**.

*To my children Michelle and Michael and their spouses, and to my husband, Daniel, for their ongoing encouragement, support, faith, and love and to the students who continue to impress and inspire me.*

**Sareen Gropper**

*To my wife, Carol, for her continued support, constant inspiration, and assistance in the preparation of this book.*

**Jack Smith**

*To my wife, Marion, and my children, Erin and Rebecca, for their love, humor, and support. And to the many students who have made my career so worthwhile.*

**Tim Carr**





# BRIEF CONTENTS

*Preface xvii*

## **SECTION I** Cells and Their Nourishment

- 1** The Cell: A Microcosm of Life 1
- 2** The Digestive System: Mechanism for Nourishing The Body 29

## **SECTION II** Macronutrients and Their Metabolism

- 3** Carbohydrates 63
- 4** Fiber 113
- 5** Lipids 131
- 6** Protein 187
- 7** Integration and Regulation of Metabolism and the Impact of Exercise 261
- 8** Energy Expenditure, Body Composition, and Healthy Weight 293

## **SECTION III** The Regulatory Nutrients

- 9** Water-Soluble Vitamins 321
- 10** Fat-Soluble Vitamins 401
- 11** Major Minerals 463
- 12** Water and Electrolytes 499
- 13** Essential Trace and Ultratrace Minerals 525
- 14** Nonessential Trace and Ultratrace Minerals 595

*Glossary 609*

*Index 615*



# CONTENTS

Preface xvii

## SECTION I CELLS AND THEIR NOURISHMENT

---

### CHAPTER 1 The Cell: A Microcosm of Life 1

- 1.1 Components of Cells 1
  - Plasma Membrane 1
  - Cytosol and Cytoskeleton 4
  - Mitochondrion 5
  - Nucleus 6
  - Endoplasmic Reticulum and Golgi Apparatus 10
  - Lysosomes and Peroxisomes 11
- 1.2 Selected Cellular Proteins 11
  - Receptors 11
  - Catalytic Proteins (Enzymes) 13
- 1.3 Apoptosis 17
- 1.4 Biological Energy 18
  - Energy Release and Consumption in Chemical Reactions 18
  - Units and Expressions of Energy 19
  - The Role of High-Energy Phosphate in Energy Storage 22
  - Coupled Reactions in the Transfer of Energy 23
  - Reduction Potentials 24
- Summary 25
- PERSPECTIVE Nutritional Genomics 26

### CHAPTER 2 The Digestive System: Mechanism for Nourishing The Body 29

- 2.1 The Structures of the Digestive Tract and the Digestive and Absorptive Processes 29
  - The Oral Cavity 33
  - The Esophagus 34
  - The Stomach 36
  - The Small Intestine 41
  - The Accessory Organs 45
  - The Absorptive Process 50
  - The Colon (Large Intestine) 52
- 2.2 Coordination and Regulation of the Digestive Process 56
  - Neural Regulation 56

Regulatory Peptides 57

Summary 59

PERSPECTIVE The Nutritional Impact of Roux-En-Y Gastric Bypass, A Surgical Approach for the Treatment of Obesity 60

## SECTION II MACRONUTRIENTS AND THEIR METABOLISM

---

### CHAPTER 3 Carbohydrates 63

- 3.1 Simple Carbohydrates 63
  - Monosaccharides 63
  - Disaccharides 66
- SYRUPS - LIQUID SUGAR 67
- 3.2 Complex Carbohydrates 68
  - Oligosaccharides 68
  - Polysaccharides 69
- 3.3 Digestion 69
  - Digestion of Polysaccharides 70
  - Digestion of Disaccharides 70
- 3.4 Absorption and Transport 72
  - Membrane Transport 72
  - Intestinal Absorption of Glucose and Galactose 75
  - Intestinal Absorption of Fructose 75
  - Hepatic Metabolism of Dietary Monosaccharides 76
- 3.5 Maintenance of Blood Glucose Concentration 76
  - Role of Insulin 76
  - Blood-Tissue Barriers 78
  - Glycemic Response to Carbohydrates 78
- 3.6 Integrated Metabolism in Tissues 80
  - Glycogenesis 80
  - Glycogenolysis 83
  - Glycolysis 85
  - The Tricarboxylic Acid Cycle 88
  - Formation of ATP 92
  - The Pentose Phosphate Pathway (Hexose Monophosphate Shunt) 98
- UNCOUPLING ELECTRON TRANSPORT AND ATP SYNTHESIS 98
  - Gluconeogenesis 100
- 3.7 Regulation of Metabolism 103
  - Allosteric Enzyme Modulation 103
  - Covalent Regulation 104
  - Directional Shifts in Reversible Reactions 104

Enzyme Translocation 104  
 Genetic Regulation 105  
 Metabolic Control of Glycolysis and  
 Gluconeogenesis 105  
**Summary 106**  
**PERSPECTIVE What Carbohydrates Do Americans Eat? 109**

## CHAPTER 4 Fiber 113

**4.1 Definitions 113**  
**4.2 Fiber and Plants 114**  
**4.3 Chemistry and Characteristics of Fiber 114**  
 Cellulose 114  
 Hemicellulose 117  
 Pectins 117  
 Lignin 117  
 Gums 117  
 β-Glucans 118  
 Fructans 118  
 Galactans 118  
 Resistant Starch 118  
 Mucilages (Psyllium) 119  
 Polydextrose and Polyols 119  
 Chitin and Chitosan 119  
**4.4 Selected Properties of Fiber and Their  
 Physiological Impact 120**  
 Solubility in Water 120  
 Viscosity and Gel Formation 121  
 Fermentability 121  
**4.5 Health Benefits of Fiber 122**  
 Cardiovascular Disease 122  
 Diabetes Mellitus 123  
 Appetite and/or Satiety and Weight Control 123  
 Gastrointestinal Disorders 123  
**4.6 Food Labels and Health Claims 124**  
**4.7 Recommended Fiber Intake 125**  
**Summary 126**  
**PERSPECTIVE The Flavonoids: Roles in Health and Disease  
 Prevention 127**

## CHAPTER 5 Lipids 131

**5.1 Structure and Biological Importance 132**  
 Fatty Acids 132  
 Triacylglycerols (Triglycerides) 135  
 Phospholipids 137  
 Sphingolipids 139  
 Sterols 140  
**5.2 Dietary Sources 142**  
 Recommended Intakes 145  
**5.3 Digestion 145**  
 Triacylglycerol Digestion 145  
**THE GALLBLADDER 146**

Phospholipid Digestion 148  
 Cholesterol Ester Digestion 148  
**5.4 Absorption 148**  
 Fatty Acid, Monoacylglycerol, and Lysophospholipid  
 Absorption 148  
 Cholesterol Absorption 149  
 Lipid Release into Circulation 150  
**5.5 Transport and Storage 151**  
 Lipoprotein Structure 151  
 Lipoprotein Metabolism 153  
**5.6 Lipids, Lipoproteins, and Cardiovascular  
 Disease Risk 159**  
 The Lipid Hypothesis 160  
 Lipoprotein(a) 160  
 Apolipoprotein E 160  
 Dietary Cholesterol 161  
 Saturated and Unsaturated Fatty Acids 161  
**COCONUT OIL: HERO OR VILLAIN? 162**  
*Trans* Fatty Acids 162  
**5.7 Integrated Metabolism in Tissues 163**  
 Catabolism of Triacylglycerols and Fatty Acids 163  
 Formation of Ketone Bodies 167  
 Synthesis of Fatty Acids 169  
 Synthesis of Triacylglycerols and Phospholipids 174  
 Synthesis, Catabolism, and Whole-Body Balance  
 of Cholesterol 174  
**5.8 Regulation of Lipid Metabolism 176**  
 Fatty Acids 176  
 Cholesterol 176  
**5.9 Brown Fat Thermogenesis 177**  
**5.10 Ethyl Alcohol: Metabolism and  
 Biochemical Impact 178**  
 The Alcohol Dehydrogenase Pathway 179  
 The Microsomal Ethanol Oxidizing System 179  
 The Catalase System 179  
 Alcoholism: Biochemical and Metabolic  
 Alterations 180  
 Alcohol in Moderation: The Brighter Side 181  
**Summary 181**  
**PERSPECTIVE The Role of Lipoproteins and Inflammation in  
 Atherosclerosis 184**

## CHAPTER 6 Protein 187

**6.1 Amino Acid Classification 187**  
 Structure 188  
 Net Electrical Charge 188  
 Polarity 188  
 Essentiality 190  
**6.2 Sources of Amino Acids 191**  
**6.3 Digestion 191**  
 Stomach 191  
 Small Intestine 193



**6.4 Absorption 193**

Intestinal Cell Absorption 194  
 Extraintestinal Cell Absorption 197

**6.5 Amino Acid Catabolism 197**

Transamination of Amino Acids 198  
 Deamination of Amino Acids 199  
 Disposal of Ammonia 200  
 Carbon Skeleton/ $\alpha$ -Keto Acid Uses 201  
 Hepatic Catabolism and Uses of Aromatic  
 Amino Acids 202  
 Hepatic Catabolism and Uses of Sulfur-Containing  
 Amino Acids 205  
 Hepatic Catabolism and Uses of Branched-Chain  
 Amino Acids 209  
 Hepatic Catabolism and Uses of Basic  
 Amino Acids 209

**SOME ROLES OF NITRIC OXIDE 211**

Hepatic Catabolism and Uses of Other Selected  
 Amino Acids 212

**6.6 Protein Synthesis 214**

Slow versus Fast Proteins 214  
 Plant versus Animal Proteins 214  
 Hormonal Effects 214  
 mTOR, Intracellular Signaling, and Amino Acids 215  
 Protein Intake, Distribution, and Quantity at Meals 216

**6.7 Protein Structure and Organization 216****6.8 Functional Roles of Proteins 219**

Catalysts 219  
 Messengers 219  
 Structural Elements 219  
 Buffers 220  
 Fluid Balancers 220  
 Immunoprotectors 220  
 Transporters 221  
 Acute-Phase Responders 222  
 Other Roles 222

**6.9 Functional Roles of Nitrogen-Containing Nonprotein Compounds 223**

Glutathione 223  
 Carnitine 223  
 Creatine 225  
 Carnosine 226  
 Choline 226  
 Purine and Pyrimidine Bases 227

**6.10 Interorgan “Flow” of Amino Acids and Organ-Specific Metabolism 232**

Intestinal Cell Amino Acid Metabolism 232  
 Amino Acids in the Plasma 233  
 Glutamine and the Muscle, Intestine, Liver,  
 and Kidneys 234  
 Alanine and the Liver and Muscle 235  
 Skeletal Muscle Use of Amino Acids 235  
 Amino Acid Metabolism in the Kidneys 239  
 Brain and Accessory Tissues and Amino Acids 241

**6.11 Catabolism of Tissue/Cell Proteins and Protein Turnover 243**

Autophagy-Lysosome Systems 243  
 Ubiquitin Proteasomal Pathway 244  
 Calpains 245

**6.12 Changes in Body Mass with Age 246**

Loss of Muscle Mass and Disease 246

**6.13 Protein Quality and Protein and Amino Acid Needs 248**

Evaluation of Protein Quality 248  
 Protein Information on Food Labels 251  
 Assessing Protein and Amino Acid Needs 251  
 Recommended Protein and Amino Acid Intakes 252  
 Protein Deficiency/Malnutrition 254  
**Summary 255**

**PERSPECTIVE Stress and Inflammation: Impact on Protein 257**

**CHAPTER 7 Integration and Regulation of Metabolism and the Impact of Exercise 261****7.1 Energy Homeostasis in the Cell 262**

Regulatory Enzymes 262

**7.2 Integration of Carbohydrate, Lipid, and Protein Metabolism 266**

Interconversion of Fuel Molecules 266  
 Energy Distribution among Tissues 267

**7.3 The Fed-Fast Cycle 271**

The Fed State 271  
 The Postabsorptive State 273  
 The Fasting State 274  
 The Starvation State 274

**7.4 Hormonal Regulation of Metabolism 278**

Insulin 278

**HOW IS TYPE 1 DIABETES SIMILAR TO STARVATION? 279**

Glucagon 280  
 Epinephrine 280  
 Cortisol 280  
 Growth Hormone 280  
 Adiponectin 281

**7.5 Exercise and Nutrition 281**

Muscle Function 281  
 Energy Sources in Resting Muscle 282  
 Muscle ATP Production during Exercise 282  
 Fuel Sources during Exercise 284

**Summary 287**

**PERSPECTIVE The Role of Dietary Supplements in Sports Nutrition  
 by Karsten Koehler, PhD 289**

**CHAPTER 8 Energy Expenditure, Body Composition, and Healthy Weight 293****8.1 Measuring Energy Expenditure 293**

Direct Calorimetry 294

Indirect Calorimetry 294  
 Doubly Labeled Water 296  
**HOW TO MEASURE WHAT PEOPLE EAT 297**  
**8.2 Components of Energy Expenditure 298**  
 Basal and Resting Metabolic Rate 298  
 Energy Expenditure of Physical Activity 299  
 Thermic Effect of Food 300  
 Thermoregulation 301  
**8.3 Body Weight: What Should We Weigh? 301**  
 Ideal Body Weight Formulas 301  
 Body Mass Index 302  
**8.4 Measuring Body Composition 303**  
 Field Methods 304  
 Laboratory Methods 306  
**8.5 Regulation of Energy Balance and Body Weight 307**  
 Hormonal Influences 308  
 Intestinal Microbiota 310  
 Environmental Chemicals 310  
 Lifestyle Influences 311  
**8.6 Health Implications of Altered Body Weight 311**  
 Metabolic Syndrome 311  
 Insulin Resistance 312  
 Weight-Loss Methods 313  
**Summary 313**  
**PERSPECTIVE Eating Disorders 315**

**SECTION III**  
**THE REGULATORY NUTRIENTS**

**CHAPTER 9 Water-Soluble Vitamins 321**

**DIETARY REFERENCE INTAKES (DRIS) 325**  
**DAILY VALUES AND PERCENTAGE DAILY VALUES 326**  
**9.1 Vitamin C (Ascorbic Acid) 326**  
 Sources 327  
 Digestion and Absorption 328  
 Transport, Tissue Uptake, and Storage 329  
 Functions and Mechanisms of Action 329  
 Interactions with Other Nutrients 335  
 Metabolism and Excretion 335  
 Recommended Dietary Allowance 335  
 Deficiency: Scurvy 336  
 Toxicity 337  
 Assessment of Nutriture 337  
**9.2 Thiamin (Vitamin B<sub>1</sub>) 338**  
 Sources 338  
 Digestion and Absorption 339  
 Transport, Tissue Uptake, and Storage 339  
 Functions and Mechanisms of Action 340  
 Metabolism and Excretion 344  
 Recommended Dietary Allowance 344

Deficiency: Beriberi 344  
 Toxicity 346  
 Assessment of Nutriture 346  
**9.3 Riboflavin (Vitamin B<sub>2</sub>) 346**  
 Sources 346  
 Digestion and Absorption 348  
 Transport, Tissue Uptake, and Storage 348  
 Functions and Mechanisms of Action 349  
 Metabolism and Excretion 351  
 Recommended Dietary Allowance 351  
 Deficiency: Ariboflavinosis 351  
 Toxicity 352  
 Assessment of Nutriture 352  
**9.4 Niacin (Vitamin B<sub>3</sub>) 352**  
 Sources 353  
 Digestion and Absorption 354  
 Transport, Tissue Uptake, and Storage 354  
 Functions and Mechanisms of Action 355  
 Metabolism and Excretion 356  
 Recommended Dietary Allowance 357  
 Deficiency: Pellagra 357  
 Toxicity 358  
 Assessment of Nutriture 358  
**9.5 Pantothenic Acid 358**  
 Sources 358  
 Digestion and Absorption 360  
 Transport, Tissue Uptake, and Storage 360  
 Functions and Mechanisms of Action 360  
 Metabolism and Excretion 363  
 Adequate Intake 363  
 Deficiency: Burning Foot Syndrome 363  
 Toxicity 363  
 Assessment of Nutriture 363  
**9.6 Biotin (Vitamin B<sub>7</sub>) 364**  
 Sources 364  
 Digestion, Absorption, Transport, Tissue Uptake, and Storage 364  
 Functions and Mechanisms of Action 365  
 Metabolism and Excretion 368  
 Adequate Intake 369  
 Deficiency 369  
 Toxicity 369  
 Assessment of Nutriture 370  
**9.7 Folate (Vitamin B<sub>9</sub>) 370**  
 Sources 370  
 Digestion and Absorption 372  
 Transport, Tissue Uptake, and Storage 372  
 Functions and Mechanisms of Action 373  
 Interactions with Other Nutrients 379  
 Association with Diseases 379  
 Metabolism and Excretion 380  
 Recommended Dietary Allowance 381  
 Deficiency: Megaloblastic Macrocytic Anemia 381

Toxicity	382
Assessment of Nutriture	382
<b>9.8 Vitamin B<sub>12</sub> (Cobalamin)</b>	<b>383</b>
Sources	384
Digestion and Absorption	384
Transport, Tissue Uptake, and Storage	386
Functions and Mechanisms of Action	386
Metabolism and Excretion	387
Recommended Dietary Allowance	387
Deficiency: Megaloblastic Macrocytic Anemia and Neuropathy	388
Toxicity	389
Assessment of Nutriture	389
<b>9.9 Vitamin B<sub>6</sub></b>	<b>390</b>
Sources	391
Digestion and Absorption	391
Transport, Tissue Uptake, and Storage	391
Functions and Mechanisms of Action	392
Metabolism and Excretion	395
Recommended Dietary Allowance	395
Deficiency	395
Toxicity	396
Assessment of Nutriture	396
<b>Summary</b>	<b>397</b>
<b>PERSPECTIVE Types of Human Research Studies and Their Limitations</b>	<b>398</b>

## CHAPTER 10 Fat-Soluble Vitamins 401

<b>10.1 Vitamin A and Carotenoids</b>	<b>402</b>
Sources	403
Digestion and Absorption	405
Transport, Tissue Uptake, and Storage	408
Functions and Mechanisms of Action	411
Interactions with Other Nutrients	419
Metabolism and Excretion	419
Recommended Dietary Allowance	420
<b>INTERNATIONAL UNITS – VITAMIN A</b>	<b>420</b>
Deficiency	420
Toxicity	421
Assessment of Nutriture	422
<b>10.2 Vitamin D</b>	<b>423</b>
Sources	423
Absorption	425
Transport, Tissue Uptake, and Storage	425
Functions and Mechanisms of Action	427
Interactions with Other Nutrients	432
Metabolism and Excretion	432
Recommended Dietary Allowance	432
Deficiency	432
Toxicity	434
Assessment of Nutriture	434

<b>10.3 Vitamin E</b>	<b>435</b>
Sources	435
Digestion and Absorption	437
Transport, Tissue Uptake, and Storage	437
Functions and Mechanisms of Action	438
Interactions with Other Nutrients	441
Metabolism and Excretion	441
Recommended Dietary Allowance	442
<b>INTERNATIONAL UNITS – VITAMIN E</b>	<b>442</b>
Deficiency	442
Toxicity	443
Assessment of Nutriture	443
<b>10.4 Vitamin K</b>	<b>443</b>
Sources	443
Absorption	444
Transport, Tissue Uptake, and Storage	445
Functions and Mechanisms of Action	445
Interactions with Other Nutrients	449
Metabolism and Excretion	449
Adequate Intake	449
Deficiency	449
Toxicity	450
Assessment of Nutriture	450
<b>Summary</b>	<b>451</b>
<b>PERSPECTIVE Antioxidant Nutrients, Reactive Species, and Disease</b>	<b>452</b>

## CHAPTER 11 Major Minerals 463

<b>11.1 Calcium</b>	<b>464</b>
Sources	464
Digestion, Absorption, and Transport	465
Regulation and Homeostasis	468
Functions and Mechanisms of Action	470
<b>AN OVERVIEW OF BONE</b>	<b>471</b>
Interactions with Other Nutrients	474
Excretion	475
Recommended Dietary Allowance	476
Deficiency	476
Toxicity	477
Assessment of Nutriture	477
<b>11.2 Phosphorus</b>	<b>478</b>
Sources	478
Digestion, Absorption, and Transport	479
Regulation and Homeostasis	480
Functions and Mechanisms of Action	481
Excretion	483
Recommended Dietary Allowance	483
Deficiency	484
Toxicity	484
Assessment of Nutriture	485

**11.3 Magnesium 485**

- Sources 485
- Digestion, Absorption, and Transport 486
- Regulation and Homeostasis 487
- Functions and Mechanisms of Action 488
- Interactions with Other Nutrients 489
- Excretion 489
- Recommended Dietary Allowance 489
- Deficiency 489
- Toxicity 491
- Assessment of Nutriture 491

**Summary 492**

**PERSPECTIVE Osteoporosis and Diet 493**

**CHAPTER 12 Water and Electrolytes 499**

**12.1 Water Functions 499**

**12.3 Body Water Content and Distribution 500**

**12.3 Water Losses, Sources, and Absorption 501**

**12.4 Recommended Water Intake 501**

**12.5 Water (Fluid) and Sodium Balance 502**

- Osmotic Pressure 502
- Hydrostatic (Fluid/Capillary) Pressure 503
- Colloidal Osmotic Pressure 504
- Extracellular Fluid Volume and Osmolarity and Hormonal Controls 504

**THE KIDNEYS: A BRIEF REVIEW 505**

**12.6 Sodium 508**

- Sources 508
- ELECTROLYTES: CALCULATING MILLIEQUIVALENTS (MEQ) 509**
- Absorption and Transport 510
- Functions and Interactions with Other Nutrients 511
- Excretion 511
- Recommendations, Deficiency, Toxicity, and Assessment of Nutriture 511

**12.7 Potassium 512**

- Sources 512
- Absorption, Secretion, and Transport 512
- Functions and Interactions with Other Nutrients 513
- Excretion 513
- Recommendations, Deficiency, Toxicity, and Assessment of Nutriture 513

**12.8 Chloride 514**

- Sources 514
- Absorption, Secretion, and Transport 514
- Functions 515
- Excretion 515
- Recommendations, Deficiency, Toxicity, and Assessment of Nutriture 516

**12.9 Acid–Base Balance: Control of Hydrogen Ion Concentration 516**

- Chemical Buffer Systems 517

**PRINCIPLES OF BUFFERS 517**

- Respiratory Regulation 519

- Renal Regulation 520

**Summary 521**

**PERSPECTIVE Macrominerals and Hypertension 522**

**CHAPTER 13 Essential Trace and Ultratrace Minerals 525**

**13.1 Iron 525**

- Sources 526
- Digestion, Absorption, Transport, and Storage 528
- Functions and Mechanisms of Action 536
- Turnover 540
- Interactions with Other Nutrients 541
- Excretion 542
- Recommended Dietary Allowance 542
- Deficiency 542
- Toxicity 544
- Assessment of Nutriture 544

**13.2 Zinc 546**

- Sources 546
- Digestion, Absorption, Transport, and Storage 547
- Functions and Mechanisms of Action 551
- Interactions with Other Nutrients 554
- Excretion 555
- Recommended Dietary Allowance 555
- Deficiency 555
- Toxicity 556
- Assessment of Nutriture 556

**13.3 Copper 557**

- Sources 557
- Digestion, Absorption, Transport, and Storage 557
- Functions and Mechanisms of Action 560
- Interactions with Other Nutrients 562
- Excretion 563
- Recommended Dietary Allowance 564
- Deficiency 564
- Toxicity 565
- Assessment of Nutriture 565

**13.4 Selenium 566**

- Sources 566
- THE SHIFTING SANDS OF SELENIUM 567**
- Digestion, Absorption, Transport, and Storage 568
- Metabolism 568
- Functions and Mechanisms of Action 570
- Interactions with Other Nutrients 572
- Excretion 573
- Recommended Dietary Allowance 573
- Deficiency 573
- Toxicity 574
- Assessment of Nutriture 574

**13.5 Chromium 575**

- Sources 575
- Digestion, Absorption, Transport,  
and Storage 575
- Functions and Mechanisms of Action 576
- Excretion 577
- Adequate Intake 577
- Deficiency 577
- Toxicity 577
- Assessment of Nutriture 577

**13.6 Iodine 578**

- Sources 578
- Digestion, Absorption, Transport, and Storage 579
- Functions and Mechanisms of Action 579
- Interactions with Other Nutrients 581
- Excretion 582
- Recommended Dietary Allowance 582
- Deficiency 582
- Toxicity 583
- Assessment of Nutriture 583

**13.7 Manganese 584**

- Sources 584
- Digestion, Absorption, Transport,  
and Storage 584
- Functions and Mechanisms of Action 585
- Interactions with Other Nutrients 586
- Excretion 586
- Adequate Intake 586
- Deficiency 586
- Toxicity 586
- Assessment of Nutriture 586

**13.8 Molybdenum 587**

- Sources 587
- Digestion, Absorption, Transport,  
and Storage 587
- Functions and Mechanisms of Action 587
- Interactions with Other Nutrients 589
- Excretion 590
- Recommended Dietary Allowance 590
- Deficiency 590
- Toxicity 590

Assessment of Nutriture 590

**PERSPECTIVE Nutrient–Drug Interactions 591****CHAPTER 14 Nonessential Trace and Ultratrace Minerals 595****14.1 Fluoride 595**

- Sources 595
- Absorption, Transport, Tissue Uptake, Storage,  
and Excretion 597
- Functions and Deficiency 597
- Recommended Intake, Toxicity, and Assessment  
of Nutriture 598

**14.2 Boron 598**

- Sources 598
- Absorption, Transport, Tissue Uptake, Storage,  
and Excretion 599
- Functions and Deficiency 599
- Recommended Intake, Toxicity, and Assessment  
of Nutriture 600

**14.3 Silicon 600**

- Sources 600
- Absorption, Transport, Storage, and Excretion 601
- Functions and Deficiency 601
- Recommended Intake, Toxicity, and Assessment  
of Nutriture 601

**14.4 Vanadium 602**

- Sources 602
- Absorption, Transport, Storage, and Excretion 602
- Functions and Deficiency 602
- Recommended Intake, Toxicity, and Assessment  
of Nutriture 603

**14.5 Cobalt 603****Summary 604**

**PERSPECTIVE No, Silver Is Not Another Essential Ultratrace Mineral: Tips to Identifying Bogus Claims and Selecting Dietary Supplements 605**

*Glossary 609**Index 615*



# PREFACE

Since the first edition was published in 1990, much has changed in the science of nutrition. But the purpose of the text—to provide thorough coverage of normal metabolism for upper-division undergraduate and graduate students majoring in nutrition or other health-related fields—remains the same. We continue to strive for a level of detail and scope of material that satisfy the needs of both instructors and students. With each succeeding edition, we have responded to suggestions from instructors, content reviewers, and students that have improved the text by enhancing the clarity of the material and by ensuring accuracy. In addition, we have included the latest and most pertinent nutrition science available to provide future nutrition professionals with the fundamental information vital to their careers and to provide the basis for assimilating new scientific discoveries.

Just as the body of information on nutrition science has increased, so has the team of authors working on this text. Dr. James Groff and Dr. Sara Hunt coauthored the first edition. In subsequent editions, Dr. Sareen Gropper became a coauthor as Dr. Hunt entered retirement. In the fourth edition, Dr. Jack L. Smith joined the author team now led by Dr. Gropper. In the seventh and eighth editions, Dr. Tim Carr has provided additional expertise and coauthorship on several chapters following Dr. Smith's retirement.

## NEW TO THIS EDITION

All chapters of the eighth edition have been updated and feature new or enhanced tables and illustrations. The organization of the content among the chapters has remained similar to the previous editions.

### Chapter 1 The Cell: A Microcosm of Life

- Expanded content in several sections including, for example, the nucleus where additional information is presented on genes and chromosomes
- Added additional information on mechanism of apoptosis
- Created new Perspective on Nutritional Genomics

### Chapter 2 The Digestive System: Mechanism for Nourishing the Body

- Expanded information on the structural features of the small intestine
- Added new information on probiotics and intestinal conditions

### Chapter 3 Carbohydrates

- Reorganized the chapter sections to improve flow and readability
- Revised sections on stereoisomers, ring structures, and derivatives of monosaccharides
- Added new information related to dextrans and dextrose equivalents
- Added new information on SGLTs and GLUTs
- Expanded sections on blood–tissue barriers and the electron transport chain
- Reorganized sections related to carbohydrate absorption and transport; added new discussion on membrane transport
- Revised section on metabolic regulation; added new information on enzyme translocation
- Updated and modified several figures and figure legends
- Added new Box feature on syrups
- Added new Box feature on uncoupling oxidative phosphorylation
- Updated the end-of-chapter Perspective

### Chapter 4 Fiber

- Added new information on another form of resistant starch
- Provided new information on the properties of fiber important for laxation
- Added information on a new mechanism by which phytochemicals may regulate mRNA translation

## Chapter 5 Lipids

- Added new section on odd-chain and branched-chain fatty acids
- Expanded discussion related to conjugated linoleic acid
- Revised information related to trans fatty acids, mono- and diacylglycerols, and the biological roles of phospholipids
- Updated information on fatty acid transport into enterocytes
- Added new section on the lipid hypothesis
- Expanded discussion on  $\beta$ -oxidation, including new sections related to oxidation of odd-chain and branched-chain fatty acids
- Updated and modified several figures and figure legends
- Added new Box feature on the gallbladder
- Added new Box feature on coconut oil

## Chapter 6 Protein

- Added a new figure showing intestinal amino acid transport
- Expanded the discussion addressing the mechanisms of protein degradation
- Expanded the discussion on the need for protein with aging
- Expanded the section addressing plant proteins

## Chapter 7 Integration and Regulation of Metabolism and the Impact of Exercise

- Revised Table 7.1
- Added new section on adiponectin; updated Table 7.3 to include adiponectin
- Revised figures and figure legends
- Added new Box feature on the metabolic similarity between type 1 diabetes and starvation

## Chapter 8 Energy Expenditure, Body Composition, and Healthy Weight

- Added new information on the origin of body mass index
- Revised section related to adiponectin regulation
- Added new and updated information in the end-of-chapter Perspective on eating disorders
- Revised figures and figure legends

- Added new Box feature of how to measure what people eat

## Chapter 9 Water-Soluble Vitamins

- Updated daily values
- Added photos showing the physical manifestations of several vitamin deficiencies
- Added information on another coenzyme role of thiamin tied to fatty acid oxidation
- Expanded the figures showing pantothenic acid metabolism
- Added new information on the functions of pantothenic acid linking it to folate metabolism
- Expanded the information on the non-coenzyme roles of biotin
- Added a new figure showing folate metabolism within the cytosol, nucleus, and mitochondria
- Expanded the discussion of intracellular chaperones involved in vitamin B<sub>12</sub> transport
- Added information on the Dietary Reference Intakes, including chronic disease risk reduction
- Developed a new Perspective addressing types of research study designs

## Chapter 10 Fat-Soluble Vitamins

- Updated daily values
- Provided more details on the mechanisms of absorption of vitamins A, E, and K
- Added a new figure and information on the functions and metabolism of vitamin E
- Added new figures showing some manifestations of deficiencies of vitamins A and D
- Added a new figure showing phyloquinone metabolism
- Created a new table providing the phyloquinone and menaquinone contents of foods
- Expanded information on the carotenoid content of foods

## Chapter 11 Major Minerals

- Expanded discussion of calcium functions
- Expanded the discussion providing an overview of bone
- Expanded discussions of calcium, phosphate, and magnesium homeostasis
- Added a new table showing factors regulating serum phosphate
- Improved figure depicting phosphate absorption



- Added information on the use of topical magnesium oils
- Updated daily values

## Chapter 12 Water and Electrolytes

- Expand list of dietary sources for sodium and potassium
- Added a table with food sources of potassium
- Updated recommendations and daily values
- Added information on the chronic disease risk reduction recommendation for sodium
- Updated the Perspective on macrominerals and hypertension to reflect the latest dietary recommendations

## Chapter 13 Essential Trace and Ultratrace Minerals

- Revised tables showing food sources of trace minerals
- Expanded section on iron as a pro-oxidant
- Added new information describing zinc/cancer association
- Added new information on mercury/selenium interaction
- Updated the Daily Value for each mineral
- Added photos showing deficiency symptoms of zinc, copper, selenium, and iodine
- Revised figures and figure legends
- Added new Box feature on selenium in the environment

## Chapter 14 Nonessential Trace and Ultratrace Minerals

- Expanded the sections on the sources of fluoride and supplemental forms of boron
- Expanded the discussions addressing fluoride's and boron's mechanisms of action
- Updated information on recommendations for intake of boron
- Updated information on toxicity-related concerns with vanadium
- Expanded the Perspective to include information to consider when buying supplements

## PRESENTATION

The presentation of the text is designed to make the book easy for the reader to use. The added color(s) draws attention to important elements in the text, tables, and figures

and helps generate reader interest. The Perspectives provide applications or expansion of the information in the chapter text.

Because this book focuses on normal human nutrition and physiological function, it is an effective resource for students majoring in either nutrition sciences or dietetics and for other health care professionals enrolled in a graduate nutrition course. Intended for a course in advanced nutrition, the text presumes a sound background in the biological sciences. At the same time, however, it provides a review of the basic sciences, particularly biochemistry and physiology, which are important to understanding the material. This text applies biochemistry to nutrient use from consumption through digestion, absorption, distribution, and cellular metabolism. Health practitioners may find that the book is a useful resource to refresh their memories with regard to metabolic and physiological interrelationships and to obtain a concise update on current concepts related to human nutrition.

We continue to present nutrition as the science that integrates life processes from the molecular to the cellular level and on through the multisystem operation of the whole organism. Our primary goal is to give a comprehensive picture of cell reactions at the tissue, organ, and system levels. Subject matter has been selected for its relevance to meeting this goal.

## ORGANIZATION

Each of the 14 chapters begins with a topic outline, followed by a brief introduction to the chapter's subject matter. These features are followed in order by the chapter text, a brief summary that ties together the ideas presented in the chapter, a reference list, and a Perspective with its own reference list.

The text is divided into three sections. Section I (Chapters 1 and 2) focuses on cell structure, gastrointestinal tract anatomy, and function with respect to digestion and absorption.

Section II (Chapters 3–8) discusses metabolism of the macronutrients. This section reviews primary metabolic pathways for carbohydrates, lipids, and proteins, emphasizing those reactions particularly relevant to issues of health. Since most of the body's energy production is associated with glycolysis or the tricarboxylic acid cycle by way of the electron transport chain and oxidative phosphorylation, the carbohydrates chapter (Chapter 3) covers these aspects of energy transformation. We include a separate chapter (Chapter 4) on fiber. The metabolism of alcohol, which contributes to the caloric intake of many people, is discussed within the lipids chapter (Chapter 5). Alcohol's chemical structure more closely resembles that of carbohydrates, but its metabolism is more similar to that of lipids. Chapter 7 discusses the interrelationships among the metabolic pathways that are common to the

macronutrients. This chapter also includes a discussion of the regulation of the metabolic pathways and a description of the metabolic dynamics of the fed-fast cycle, along with a presentation of the effects of physical exertion on the body's metabolic pathways. Chapter 8 focuses on energy expenditure, energy balance, and healthy weight and also includes a brief discussion of measuring body composition and the health implications of altered body weight.

Section III (Chapters 9–14) concerns those nutrients considered regulatory in nature: the water- and fat-soluble vitamins and the minerals, including the major minerals, trace minerals, and ultratrace minerals. These chapters cover nutrient features such as digestion, absorption, transport, function, metabolism, excretion, deficiency, toxicity, and assessment of nutriture, as well as the latest Recommended Dietary Allowances or Adequate Intakes for each nutrient. Information about the major minerals has been split into two chapters: Chapter 11 addresses calcium, phosphorus, and magnesium, and Chapter 12 discusses sodium, potassium, and chloride. Chapter 12 integrates coverage of the maintenance of the body's homeostatic environment—including discussions of body fluids, electrolyte balance, and pH maintenance—with the presentation of the electrolytes.

## SUPPLEMENTARY MATERIAL

MindTap for Gropper's *Advanced Nutrition and Human Metabolism*, 8th Edition, is a digital learning solution that empowers learners to go beyond memorization—enabling a deeper understanding of concepts and topics. MindTap provides engaging content and activities that help build student confidence. Accelerate progress with MindTap. Visit [cengage.com/login](http://cengage.com/login) to learn more. Additional instructor resources for this product are available online. Instructor assets include an Instructor's Manual, Educator's Guide, PowerPoint® slides, and a test bank powered by Cognero®. Sign up or sign in at [www.cengage.com](http://www.cengage.com) to search for and access this product and its online resources.

## ACKNOWLEDGMENTS

Although this textbook represents countless hours of work by the authors, it is also the work of many other hardworking individuals. We cannot possibly list everyone who has helped, but we would like to call attention to a few individuals who have played particularly important roles. We thank our undergraduate and graduate nutrition students for their ongoing feedback. We thank

the product manager, Courtney Heilman; our art director, Lizz Anderson; our marketing manager, Shannon Hawkins; our content manager, Samantha Rundle; and our permissions analysts, Ann Hoffman. We extend special thanks to our production team and our copy editor, Laura Specht Patchkofsky.

We appreciate the writing contribution of Karsten Koehler, PhD, for the Perspective “The Role of Dietary Supplements in Sports Nutrition.”

We owe special thanks to the reviewers whose thoughtful comments, criticisms, and suggestions were indispensable in shaping this text.

### Eighth Edition Reviewers

Michael Crosier, Framingham State University  
Janet Colson, Middle Tennessee State University  
La-Tonya J. Dixon, Alabama A&M University  
Erika Ireland, California State University, Fresno  
Jennifer Farrell, Florida State University  
Long Wang, California State University, Long Beach  
Norma L. Dawkins, Tuskegee University

### Seventh Edition Reviewers

Michael E. Bizeau, Metropolitan State University  
of Denver  
Janet Colson, Middle Tennessee State University  
Michael Crosier, Framingham State University  
J. Andrew Doyle, Georgia State University  
Elizabeth A. Kirk, Bastyr University  
Kevin L. Schalinske, Iowa State University  
Long Wang, California State University, Long Beach

### Sixth Edition Reviewers

Jodee L. Dorsey, Florida State University  
Jennifer Hemphill, Florida State University  
Elizabeth A. Kirk, Bastyr University and University  
of Washington  
Steven E. Nizielski, Grand Valley State University  
Scott K. Reaves, California Polytechnic State University,  
San Luis Obispo  
Karla P. Shelnett, University of Florida

### Fifth Edition Reviewers

Richard C. Baybutt, Kansas State University  
Patricia B. Brevard, James Madison University  
Marie A. Caudill, California Polytechnic State University,  
Pomona  
Prithiva Chanmugam, Louisiana State University

Michele M. Doucette, Georgia State University  
Michael A. Dunn, University of Hawaii at Mānoa  
Steve Hertzler, Ohio State University  
Steven Nizielski, Grand Valley State University  
Kimberli Pike, Ball State University

William R. Proulx, State University of New York, Oneonta  
Scott K. Reaves, California Polytechnic State University,  
San Luis Obispo  
Donato F. Romagnolo, University of Arizona, Tucson  
James H. Swain, Case Western Reserve University



# THE CELL: A MICROCOSM OF LIFE

## LEARNING OBJECTIVES

- 1.1 Identify cellular components and their functions.
- 1.2 Describe the roles of cell receptors and enzymes.
- 1.3 Explain the mechanisms by which enzymatic reactions are regulated.
- 1.4 Discuss the need for and pathways involved in apoptosis.
- 1.5 Describe how energy is released and utilized in chemical reactions.

**C**ELLS ARE THE VERY ESSENCE OF LIFE. Cells may be defined as the basic living, structural, and functional units of the human body. They vary greatly in size, chemical composition, and function, but each one is a remarkable miniaturization of human life. Cells move, grow, ingest “food,” excrete wastes, react to their environment, and reproduce. This chapter provides a brief review of the basics of a cell, including cellular components, biological energy, and an overview of a cell’s natural life span.

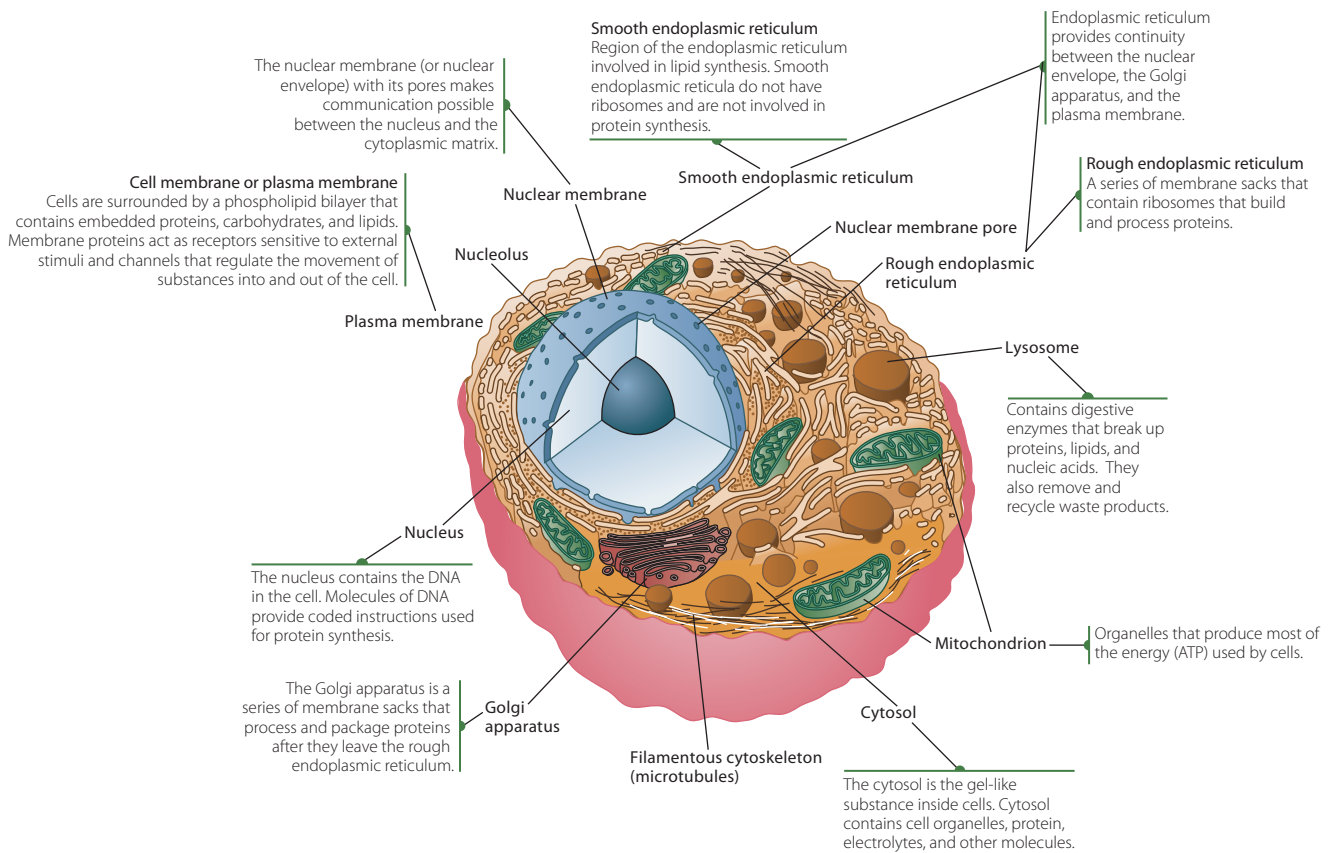
Cells of multicellular organisms are called **eukaryotic cells** (from the Greek *eu* meaning “true” and *karyon* meaning “nucleus”). Eukaryotic cells evolved from simpler, more primitive cells called **prokaryotic cells** (from the Greek meaning “before nucleus”). One distinguishing feature between the two cell types is that eukaryotic cells possess a defined nucleus, whereas prokaryotic cells do not. Also, eukaryotic cells are larger and much more complex structurally and functionally than their ancestors. Because this text addresses human metabolism and nutrition, all descriptions of cellular structure and function in this and subsequent chapters pertain to eukaryotic cells.

While specialization among cells is necessary for life, cells, in general, have certain basic similarities. All human cells have a **plasma membrane** and a nucleus (or have had a nucleus), and most contain an endoplasmic reticulum, Golgi apparatus, and mitochondria. For convenience of discussion, a “typical cell” is presented (Figure 1.1) to enable the identification of the various organelles and their functions, which characterize cellular life. Our discussion begins with the plasma membrane, which forms the outer boundary of the cell, and then moves inward to examine the organelles found within the cell.

## 1.1 COMPONENTS OF CELLS

### Plasma Membrane

The plasma membrane is a sheetlike structure that encapsulates and surrounds the cell, allowing it to exist as a distinct unit. The plasma membrane, like other membranes within the cell, has distinct structural characteristics and functions.



**Figure 1.1** Three-dimensional depiction of a typical mammalian liver cell.

Source: Cengage Learning Inc. Reproduced by permission. [www.cengage.com/permissions](http://www.cengage.com/permissions)

- Plasma membranes are asymmetrical, with different inside and outside “faces.”
- Plasma membranes are not static but are fluid structures.

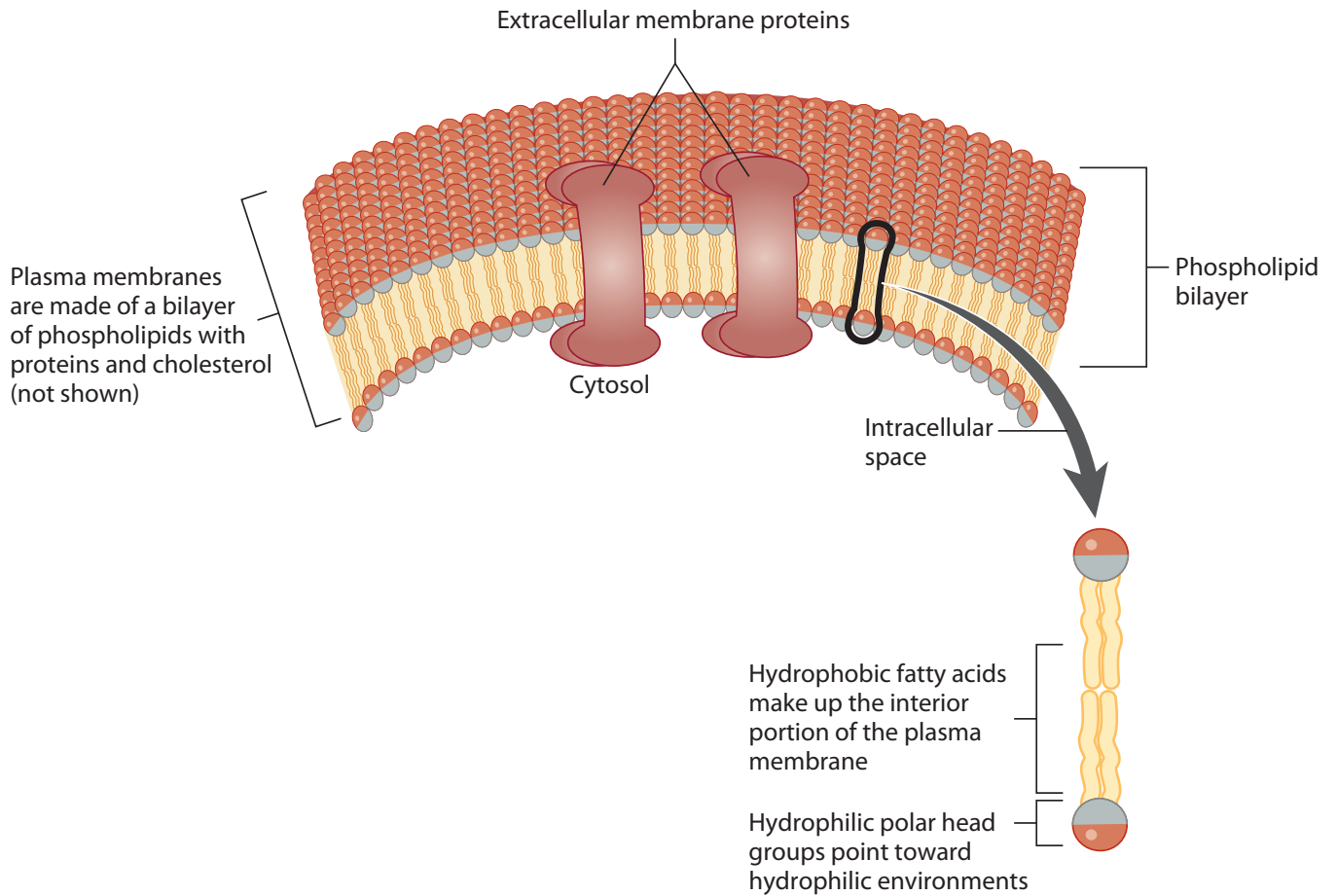
Plasma membranes are composed primarily of proteins, cholesterol, and phospholipids. Phospholipids, shown in Figure 1.2, provide both a **hydrophobic** and a hydrophilic moiety that allows them to spontaneously form bimolecular sheets, called lipid bilayers, in aqueous environments like the human body. It is this lipid bilayer that determines the structure of the plasma membrane. The fatty acid portion (hydrocarbon chain) of the phospholipids forms the hydrophobic (water-fearing) core of the membrane bilayer; it also inhibits many water-soluble compounds from passing into the cell and helps to retain water-soluble substances within the cell. The glycerol and phosphate-containing portions (polar head) of the phospholipid are hydrophilic (i.e., polar, water loving) and thus are oriented toward the cell’s aqueous environments found both outside the cell and in the cell cytosol.

Another important membrane lipid is cholesterol (Figure 1.3). Cholesterol influences the fluidity and thus permeability of membranes, affecting what may pass into and out of the cell; membranes with higher levels of cholesterol are less fluid. Within the membrane, cholesterol’s

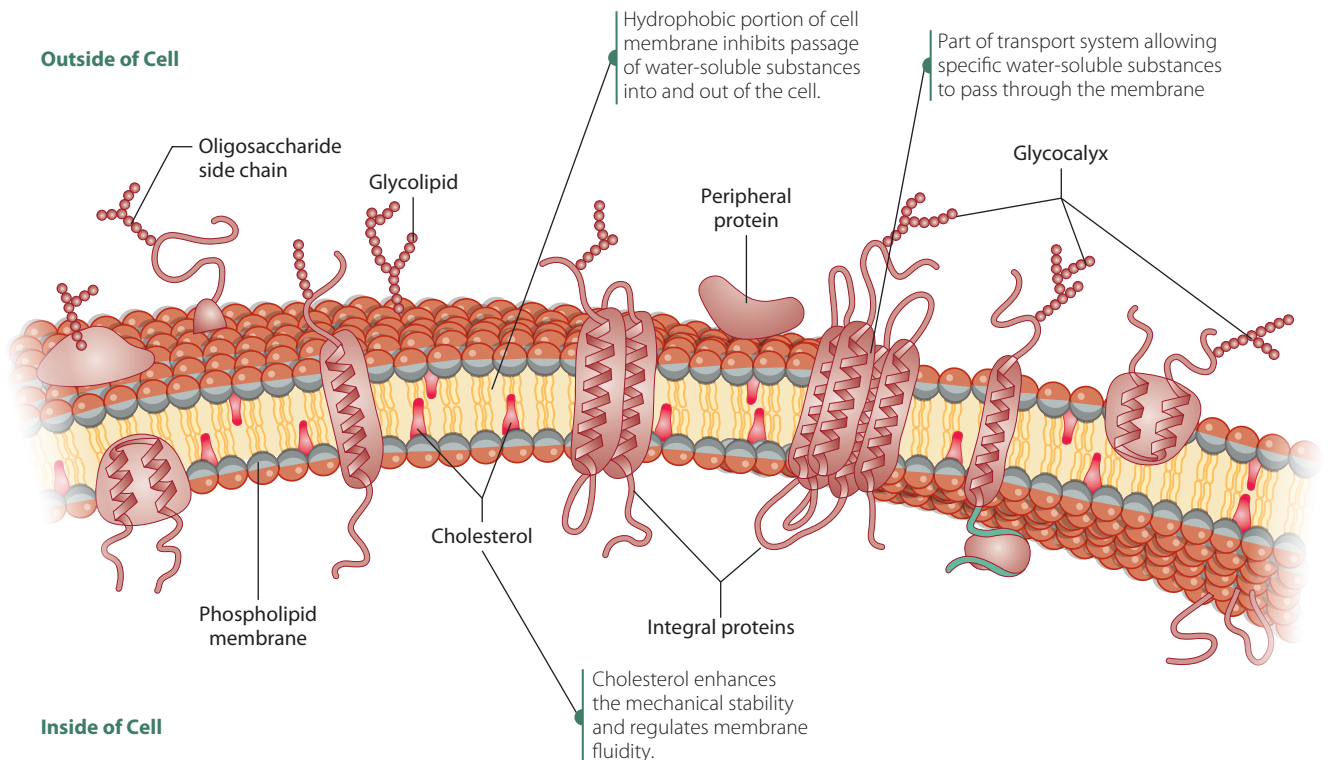
hydrocarbon side chain associates with that of phospholipids, and cholesterol’s hydroxyl groups are positioned close to the phospholipid’s polar head groups. Cholesterol’s rigid planar steroid rings are positioned so as to interact with and stabilize the regions of the hydrocarbon chains closest to the polar head groups of the phospholipids. The rest of the hydrocarbon chain remains flexible and fluid.

Both integral and peripheral proteins are found interspersed with the plasma membrane’s lipid bilayer (Figure 1.3). These proteins are responsible for several membrane functions including mediating information transfer (as **receptors**), transporting ions and molecules (as channels, carriers, gates, and pumps), acting as cell adhesion molecules, and speeding up metabolic activities (as **enzymes**). Integral proteins are attached and embedded in the membrane through hydrophobic interactions; they are often transmembrane, spanning the entire structure. Peripheral proteins, in contrast, are associated with membranes through ionic interactions and are located on or near the membrane surface. Peripheral proteins may be attached to integral membrane proteins either directly or through intermediate proteins. Many of these membrane proteins have either lipid or carbohydrate attachments.

Carbohydrates are present in plasma membranes as glycolipids and glycoproteins. While some carbohydrate



**Figure 1.2** Lipid bilayer structure of biological membranes.



**Figure 1.3** Fluid model of cell membrane. Lipids and proteins are mobile and can move laterally in the membrane.

is found in all membranes, most of the glycolipids and glycoproteins of the cell are associated with the plasma membrane. The carbohydrate moiety of the membrane glycoproteins and glycolipids provides asymmetry to the membrane because the oligosaccharide side chains are located exclusively on the membrane layer facing the cell's outer surface (and not toward the cytosol). In plasma membranes, these outer sugar residues form what is called the glycocalyx, the layer of carbohydrate on the cell's outer surface. On the membranes of the organelles within the cell, however, the oligosaccharides are directed inward. The plasma membrane glycoproteins may serve as the receptors for hormones, certain nutrients, and other substances that influence cellular function. Glycoproteins also may help regulate the intracellular communication necessary for cell growth and functions. Intracellular communication occurs through pathways that convert information from one part of a cell to another in response to external stimuli. Generally, it involves the passage of chemical messengers from organelle to organelle or within the lipid bilayers of membranes. Intracellular communication is examined more closely in the “Receptors and Intracellular Signaling” section of this chapter.

Membranes are not structurally distinct from the aqueous compartments of the cell they surround. For example, the **cytosol**—which is the aqueous, gel-like, transparent substance—fills the cell and, together with a system of filaments, connects the various membranes of the cell. This interconnection creates a structure that makes it possible for a signal generated at one part of the cell to be transmitted quickly and efficiently to other regions of the cell.

## Cytosol and Cytoskeleton

The **cytoplasm**, found inside the cell's plasma membrane but outside of the nucleus, includes the cytosol (a gel-like liquid), a cytoskeletal/cytomatrix, and organelles. The cytoskeleton consists of a system of filaments or fibers (Figures 1.1 and 1.4). The cytoskeleton provides cells with:

- structural support, which defines the cell's shape and helps to maintain its function
- a framework for positioning the various organelles (such as microvilli, which are extensions of intestinal cells)
- a network to direct the movement of materials and organelles within the cells
- a means of independent locomotion for specialized cells (such as sperm, white blood cells, and fibroblasts)
- a pathway for intercellular communication among cellular components (vital for cell activation and survival)
- possible transfer of RNA and DNA.

The cytoskeleton is made up of three groups of fibers: **microtubules**, **intermediate filaments**, and **microfilaments**.

## Microtubules, Intermediate Filaments, and Microfilaments

Microtubules are hollow (with about a 24 nm outer diameter), relatively rigid tubular structures (Figure 1.4). They consist of primarily two proteins— $\alpha$ -tubulin and  $\beta$ -tubulin—which form heterodimers that polymerize end-to-end. Microtubules, once formed, can be further lengthened at one end by the addition of more dimers; the other end, however, may undergo disassembly. Microtubules interact with a number of intracellular components, including proteins. They provide mechanical support, like a platform or scaffold, to influence cell shape. They also provide a structure for the intracellular movement of organelles and the assembly of cellular components (such as spindle fibers for mitosis). Flagella and cilia also rely on microtubules for movement.

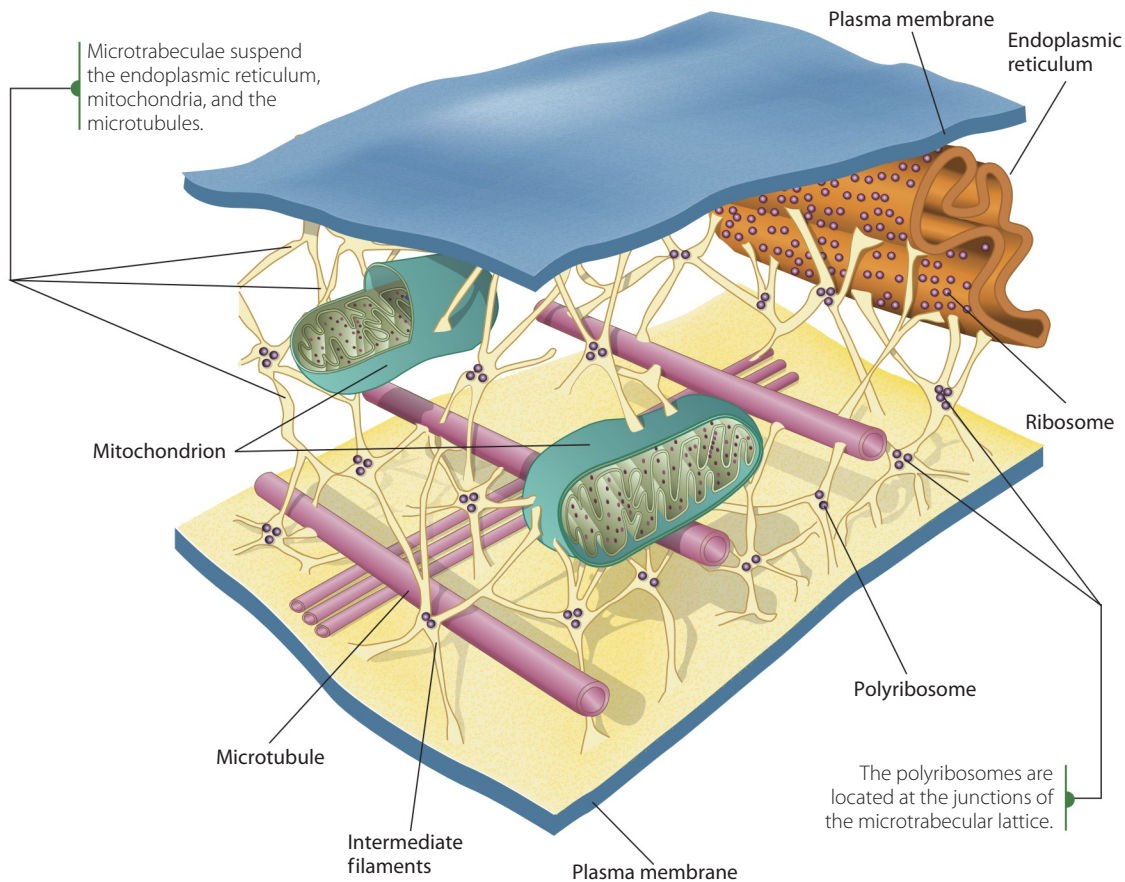
Intermediate filaments, about 10 nm in diameter, are a heterogeneous group of fibers that are dynamic, undergoing constant assembly and disassembly, controlled in part by phosphorylation and dephosphorylation. Intermediate filaments (Figure 1.4) provide mechanical strength to cells that are subjected to physical stress, such as neurons, muscle cells, and epithelial cells lining body cavities.

Microfilaments, the thinnest (about 4–6 nm in diameter) of the fibers making up the cytoskeleton, are long, linear, solid fibers made up of actin. Microfilaments, like the other fibers, polymerize and unpolymerize according to the needs of the cells. Microfilaments provide scaffolding or tracks for various cell functions. Microfilaments interact with microtubules to facilitate the movement of cellular organelles and vesicles, and their interactions with intermediate filaments are thought to enable communication from extracellular stimuli to organelles within the cytosol.

## Structural Arrangement

The structural arrangement within the cell influences metabolic pathways. The fluid portion of the matrix contains small molecules such as glucose, amino acids, oxygen, and carbon dioxide. This aqueous part of the cell is in contact with the cytoskeleton over a very broad surface area and enables enzymes that are associated with the polymeric lattice to be in close proximity to their substrate molecules in the aqueous portion. Furthermore, the enzymes that catalyze the reactions of many metabolic pathways are oriented sequentially so that the product of one reaction is released in close proximity to the next enzyme for which it is a substrate; this enhances the velocity of the overall metabolic pathway. Such an arrangement exists among the enzymes that participate in glycolysis. Some other metabolic pathways that occur in the cytoplasmic matrix and that might be similarly affected include the **hexose monophosphate shunt** (pentose phosphate pathway), glycogenesis, glycogenolysis, and fatty acid synthesis. The cytoplasmic matrix of eukaryotic cells contains a number of organelles,





**Figure 1.4** The cytoskeleton (microtrabecular lattice) provides a structure for cell organelles, microvilli (as found in intestinal mucosa cells), and large molecules. The cytosol is shown at about 300,000 times its actual size and was derived from hundreds of images of cultured cells viewed in a high-voltage electron microscope.

Source: Adapted from Porter and Tucker, "The Ground Substance of the Cell," 1981, *Scientific American*.

enclosed in bilayer membranes and described briefly in the following sections.

## Mitochondrion

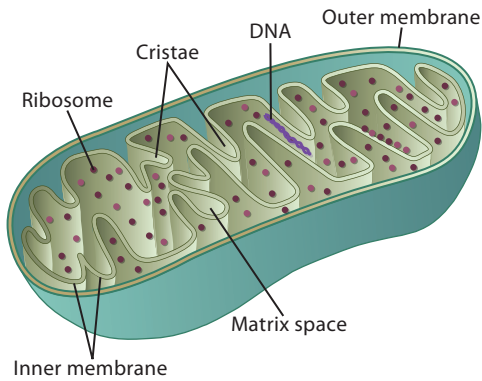
The **mitochondria** are the primary sites of oxygen use in cells and are responsible for most of the metabolic energy (ATP) produced in cells. All cells in the body, with the exception of the erythrocyte, possess mitochondria. The erythrocyte disposes of its mitochondria and nucleus during the maturation process and then must depend solely on energy produced through anaerobic mechanisms, primarily glycolysis. The mitochondria in different tissues vary according to the function of the tissue. In muscle, for example, the mitochondria are held tightly among the fibers of the contractile system. In the liver, however, the mitochondria have fewer restraints and move freely through the cytoplasmic matrix. Mitochondria are surrounded by two bilayer membranes.

### Mitochondrial Membrane

The mitochondrion consists of a matrix or interior space surrounded by a double membrane (Figures 1.5 and 1.6). The mitochondrial outer membrane is relatively porous

(allowing for free diffusion of molecules up to about 5 kDa), whereas the inner membrane is selectively permeable (preventing free diffusion except for oxygen and carbon dioxide), serving as a barrier between the cytoplasmic matrix and the mitochondrial matrix. The inner membrane has many invaginations, called the cristae, which increase its surface area and has all the components of the electron transport chain embedded within it.

The electron transport (respiratory) chain is central to the process of **oxidative phosphorylation**, the mechanism by which most cellular ATP is produced. The components of the electron transport chain carry electrons and hydrogens during the catalytic oxidation of nutrients by enzymes in the mitochondrial matrix. The details of this process are described more fully in Chapter 3. Briefly, the mitochondria carry out the flow of electrons through the electron transport chain. This electron flow is strongly exothermic, and the energy released is used in part for ATP synthesis, an endothermic process. Molecular oxygen is ultimately, but indirectly, the oxidizing agent in these reactions. The function of the **electron transport chain** is to couple the energy released by nutrient oxidation to the formation of ATP. The chain components are precisely positioned within the inner mitochondrial membrane, an important



**Figure 1.5** The mitochondrion.

feature of the mitochondria because it brings the products released in the matrix into close proximity with molecular oxygen. Figure 1.6 shows the flow of major reactants into and out of the mitochondrion.

### Mitochondrial Matrix

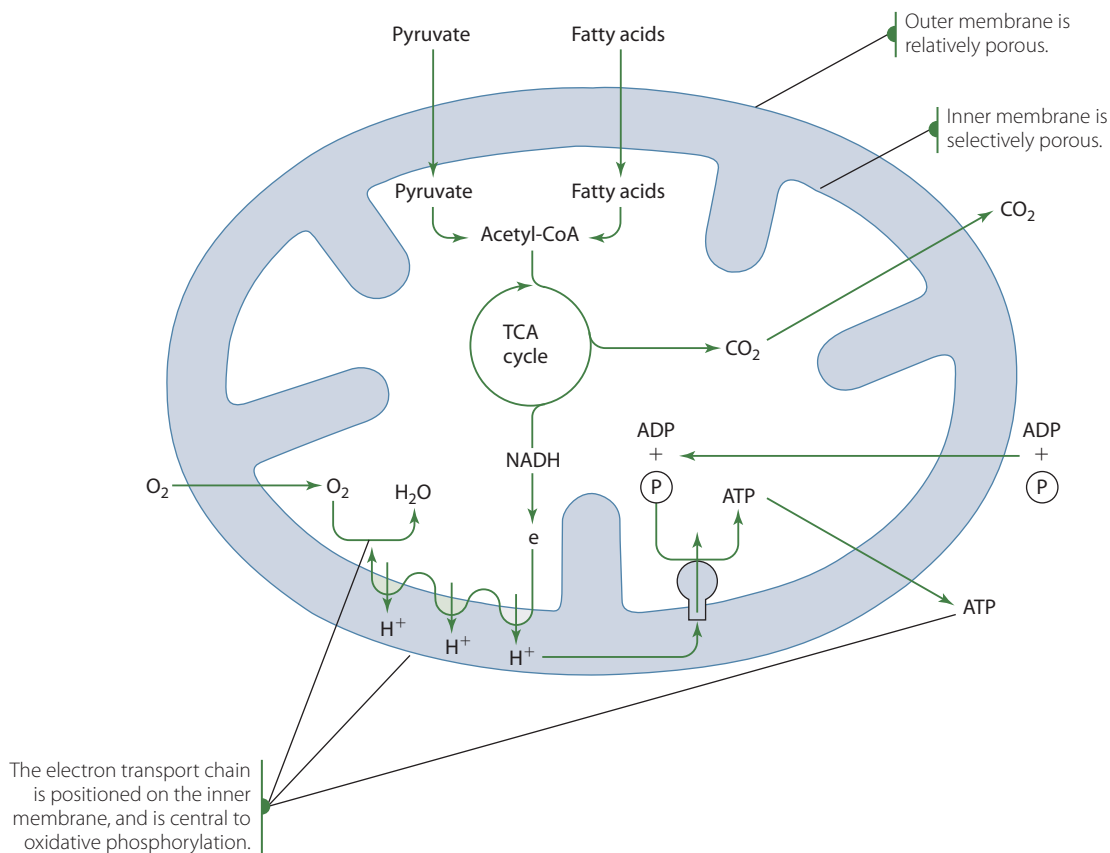
Among the metabolic enzyme systems functioning in the mitochondrial matrix are those that catalyze the reactions of the tricarboxylic cycle (TCA cycle; Chapter 3) and fatty acid oxidation (Chapter 5). Other enzymes are involved in the oxidative decarboxylation and carboxylation of

pyruvate (Chapter 3) and in certain reactions of amino acid metabolism (Chapter 6).

Mitochondria are capable of both fission and fusion, depending on the needs of the cell. They reproduce by dividing in two. Although the nucleus contains most of the cell's deoxyribonucleic acid (DNA), the mitochondrial matrix contains a small amount of DNA and a few ribosomes, enabling limited synthesis of protein within the mitochondrion. Most mitochondrial enzymes are coded by nuclear DNA, synthesized on the rough endoplasmic reticulum (RER) in the cytosol, and then incorporated into existing mitochondria. The genes contained in mitochondrial DNA, unlike those in the nucleus, are inherited only from the mother and code primarily for proteins needed for normal mitochondrial function and for ATP production. Several diseases—such as cytochrome c oxidase deficiency (also called complex IV deficiency), Leigh syndrome, and Kearns-Sayre syndrome—result from mutations in mitochondrial genes.

### Nucleus

The nucleus (see Figure 1.1) is the largest of the organelles within the cell. Because of its DNA content, the nucleus initiates and regulates most cellular activities. Surrounding



**Figure 1.6** Overview of a cross section of the mitochondria.

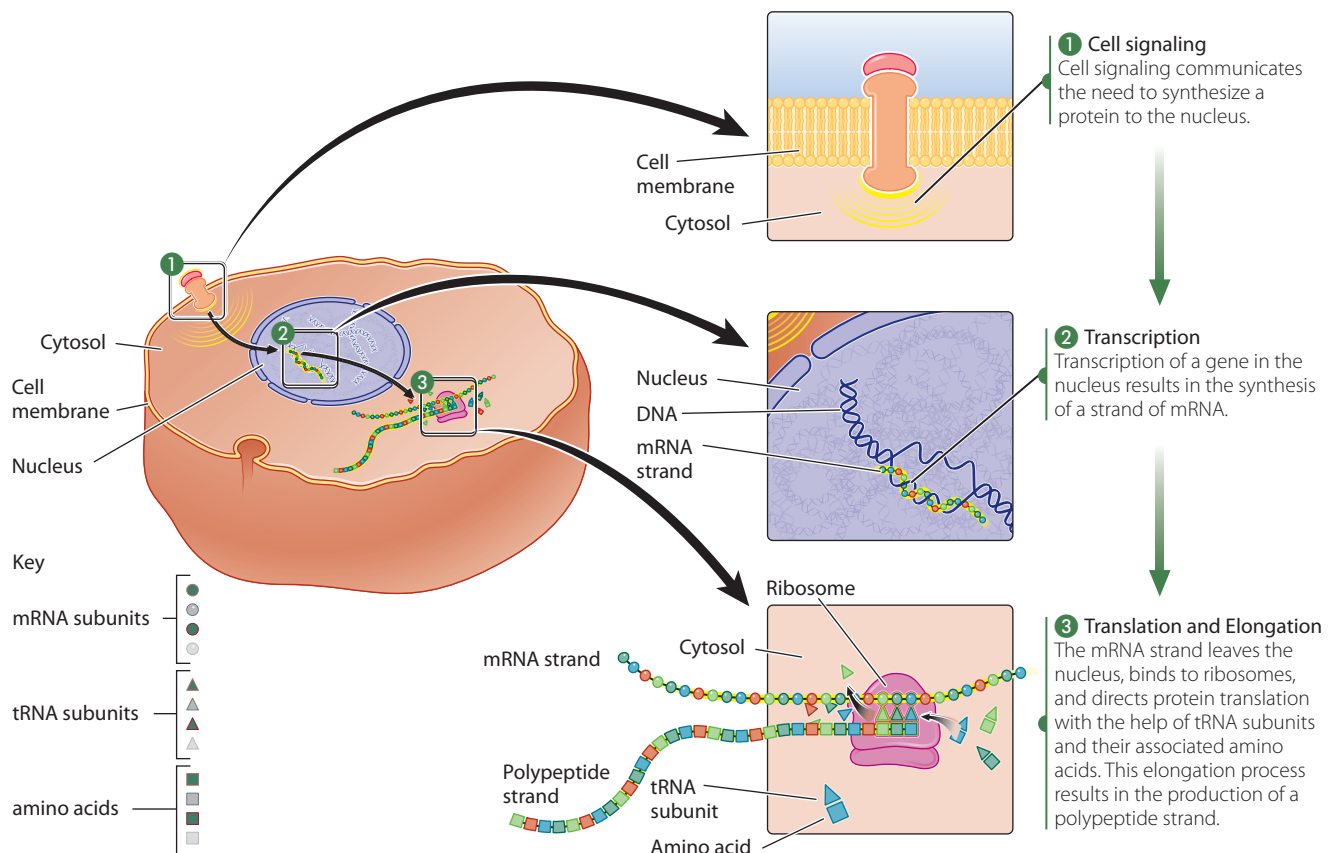
the nucleus is the **nuclear envelope**, a dynamic structure composed of an inner and an outer membrane. The dynamic nature of these membranes makes communication possible between the nucleus and the cytoplasmic matrix and allows a continuous channel between the nucleus and the endoplasmic reticulum. At various intervals the two membranes of the nuclear envelope fuse, creating pores in the envelope. Clusters of proteins on the outer nuclear membrane serve as microtubule organization centers (MTOCs); these centers function to begin polymerizing and organizing the microtubules during mitosis. Within the nucleus, a matrix exists to facilitate nuclear functions.

The nucleus (or nuclear matrix) contains substances such as minerals needed for nuclear function and molecules of DNA. DNA encodes the cell's genetic information plus all the enzymes needed for its duplication. DNA is found wrapped around proteins called histones and organized into structures called chromatin. Long strands of DNA and histones are known as chromosomes. Also, within the nucleus is the **nucleolus**, a non-membrane-bound structure, containing ribosomal RNA (rRNA), proteins, and DNA; it is the site of rRNA transcription and processing and of ribosome assembly/synthesis.

Encoded within the nuclear DNA are thousands of **genes** that direct the synthesis of proteins. Each gene can be thought of as a nucleotide sequence that codes for an amino acid sequence representing a single specific protein. Genes are found on chromosomes. Human cells contain 23 pairs of chromosomes, which makes up the genome.

The cell **genome** is the entire set of genetic information, that is, all of the DNA within the cell. During cell division, the 23 pairs of chromosomes are duplicated to create daughter cells. Barring mutations that may arise in the DNA, daughter cells, produced from a parent cell by mitosis, possess the identical genomic makeup of the parent cell. During meiosis (cell reproduction), one from each of the original pairs of chromosomes is found in the sperm or ovum cell. Individuals receive a copy of each gene (allele) from each parent.

The process of DNA replication within cells enables the DNA to be precisely copied at the time of mitosis. After the cell receives a signal that protein synthesis is needed, protein biosynthesis occurs in phases referred to as transcription, translation, and elongation (Figure 1.7). Each phase requires DNA activity, RNA activity, or both. These phases, together with replication, are reviewed briefly in this chapter, but the scope of this subject is large; interested



**Figure 1.7** Steps of protein synthesis. (1) Signals that protein synthesis needs to occur. (2) Transcription: The DNA molecule (gene) synthesizes the corresponding mRNA. (3) Translation: The corresponding mRNA molecule binds to a ribosome and directs protein synthesis based on the codon for each amino acid and the appropriate tRNA.

Source: Cengage Learning Inc. Reproduced by permission. [www.cengage.com/permissions](http://www.cengage.com/permissions)

readers should consult a current cell biology text or comprehensive biochemistry text for a more thorough description of protein biosynthesis.

### Nucleic Acids

Nucleic acids (DNA and RNA) are macromolecules formed from repeating units called **nucleotides**, sometimes referred to as nucleotide bases or just bases. Structurally, they consist of a nitrogenous core (either purine or pyrimidine), a pentose sugar (ribose in RNA, deoxyribose in DNA), and phosphate. Five different nucleotides are contained in the structures of nucleic acids: adenylic acid and guanylic acid are purines and cytidylic acid, uridylic acid, and thymidylic acid are pyrimidines. The nucleotides are more commonly referred to by their nitrogenous base core only—namely, adenine, guanine, cytosine, uracil, and thymine, respectively. For convenience, particularly in describing the sequence of the polymeric nucleotides in a nucleic acid, the single-letter abbreviations are most often used. Adenine (A), guanine (G), and cytosine (C) are common to both DNA and RNA, whereas uracil (U) is unique to RNA and thymine (T) is found only in DNA. When two strands of nucleic acids interact with each other—as occurs in replication, transcription, and translation—bases in one strand pair specifically with bases in the second strand: A always pairs with T or U and G pairs with C, in what is called **complementary base pairing**.

The nucleotides are connected by phosphates esterified to hydroxyl groups on the pentose—that is, deoxyribose or ribose—component of the nucleotide. The carbon atoms of the pentoses are assigned prime (') numbers for identification. The phosphate group connects the 3' carbon of one nucleotide with the 5' carbon of the next nucleotide in the sequence. The 3' carbon of the latter nucleotide in turn is connected to the 5' carbon of the next nucleotide in the sequence, and so on. Therefore, nucleotides are attached to each other by 3', 5' diester bonds. The ends of a nucleic acid chain are called either the free 3' end or the free 5' end, meaning that the hydroxyl groups at those positions are not attached by phosphate to another nucleotide.

### Cell Replication

Cell replication involves the synthesis of daughter DNA molecules that are identical to the parental DNA. At cell division, the cell must copy its genome with a high degree of fidelity. Each strand of the DNA molecule acts as a template for synthesizing a new strand (Figure 1.8). The DNA molecule consists of two large strands of nucleic acid that are intertwined to form a double helix. During cell division the two unravel, with each forming a template for synthesizing a new strand through complementary base pairing. Incoming nucleotide bases first pair with their complementary bases in the template and then are connected through phosphate diester bonds by the enzyme DNA polymerase. The end result of the **replication** process is

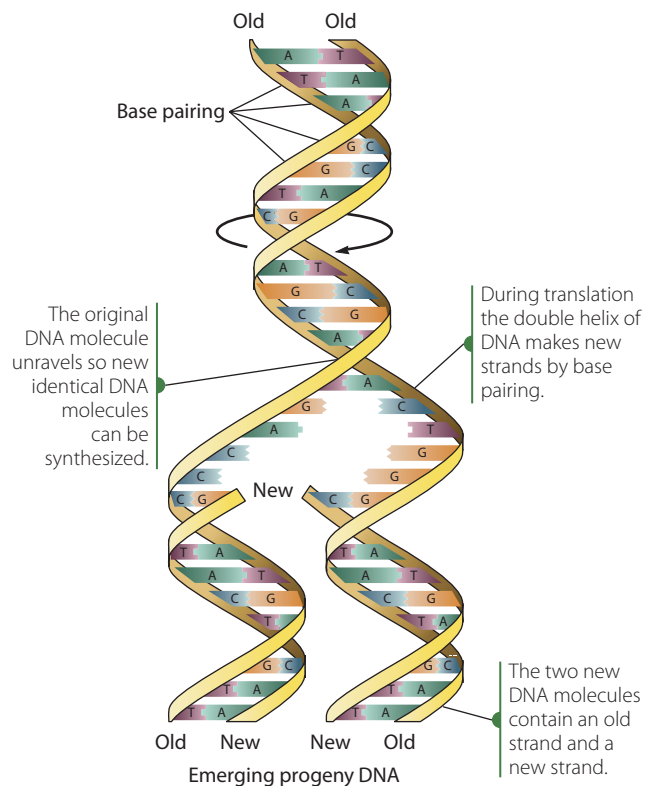


Figure 1.8 DNA replication.

two new DNA chains that join with the two chains from the parent molecule to produce two new DNA molecules. Each new DNA molecule is therefore identical in base sequence to the parent, and each new cell of a tissue consequently carries within its nucleus identical information to direct its functioning. The two strands in the DNA double helix are antiparallel, which means that the free 5' end of one strand is connected to the free 3' end of the other. With this process, a cell is able to copy or replicate its genes before it passes them on to the daughter cell. Although errors sometimes occur during replication, mechanisms exist that correct or repair mismatched or damaged DNA.

### Transcription

**Transcription** is the process by which the genetic information (through the sequence of base pairs) in a single strand of DNA makes a specific sequence of bases in a messenger RNA (mRNA) chain (see Figure 1.7). A single strand of DNA can make many copies of the corresponding mRNA, which become multiple templates for the assembly of a specific protein. This process multiplies the information contained in the DNA to produce many corresponding protein molecules. Transcription may require **transcription factors**, discussed under the subsection “Control of Gene Expression.”

Transcription proceeds continuously throughout the entire life cycle of the cell. In the process, various sections of the DNA molecule unravel, and one strand—called

the **sense strand**—serves as the template for synthesizing mRNA. Sequences of DNA known as promoters allow genes to be turned “off” or “on” and can initiate transcription; this promoter is usually found near (upstream) of the gene. The genetic code (gene) of the DNA is transcribed into mRNA through complementary base pairing, as in DNA replication, except that the purine adenine (A) pairs with the pyrimidine uracil (U) instead of with thymine (T). Genes are composed of critically sequenced base pairs along the entire length of the DNA strand that is being transcribed. A gene, on average, is just over 1,000 base pairs in length, compared with the nearly 5 million ( $5 \times 10^6$ ) base pair length of typical chromosomal DNA chains. Although these figures provide a rough estimate of the number of genes per transcribed DNA chain, not all the base pairs of a gene are transcribed into functional mRNA.

Many genes for specific proteins are located on regions of the DNA nucleotide sequences that are not adjacent to each other. Those regions that are part of the gene but do not code for a protein product are called **introns** (intervening sequences) and have to be removed from the mRNA before it is translated into protein (see the “Translation” section of this chapter). Enzymes excise the introns from the newly formed mRNA, and the ends of the functional, active mRNA segments are spliced together in a process called post-transcriptional processing. The gene segments that get both transcribed and translated into the protein product are called **exons** (expressed sequences).

### Translation

**Translation** is the process by which genetic information in an mRNA molecule is turned into the sequence of amino acids in the protein. After the mRNA is synthesized in the nucleus (see Figure 1.7), the mRNA is exported into the cytoplasmic matrix, where it is attached to ribosomal RNA (rRNA) of the ribosomes of the RER or to the free-standing polyribosomes (also called polysomes). On the ribosomes, the transcribed genetic code in the mRNA is used to bring amino acids into a specific sequence that produces the specified protein.

The genetic code for specifying the amino acid sequence of a protein resides in the mRNA in the form of three-base sequences called **codons**. Each codon codes for a single amino acid. Although a given amino acid may have several codons (e.g., the codons CUU, CUC, CUA, and CUG all code for the amino acid leucine), codons can code for only one amino acid. Each amino acid has one or more transfer RNAs (tRNAs), which deliver the amino acid to the mRNA for peptide synthesis. The three-base sequences of the tRNA attach to the codons by complementary base pairing.

Amino acids are first activated by ATP at their carboxyl end and then transferred to their specific tRNAs that bear the **anticodon** complementary to each amino acid’s codon. For example, because codons that code for leucine are

sequenced CUU, CUC, CUA, or CUG, the only tRNAs to which an activated leucine can be attached would need to have the anticodon sequence GAA, GAG, GAU, or GAC. The tRNAs then bring the amino acids to the mRNA situated at the protein synthesis site on the ribosomes. After the amino acids are positioned according to codon–anticodon association, peptide bonds are formed between the aligned amino acids in a process called **elongation** (see Figure 1.7). Elongation extends the polypeptide chain of the protein product by translation. Each incoming amino acid is connected to the end of the growing peptide chain with a free carboxyl group (C-terminal end) by formation of further peptide bonds. New amino acids are incorporated until all the codons (corresponding to one completed protein or polypeptide chain) of the mRNA have been translated. At this point, the process stops, signaled by a “nonsense” codon that does not code for any amino acid. The completed protein dissociates from the mRNA. After translation, the newly synthesized protein may require some chemical, structural, or spatial (three-dimensional) modification to attain its active form.

Post-translational modifications of proteins may involve, for example, the covalent addition of functional groups or the cleavage of a portion of the protein. Common modifications include phosphorylation as well as glycosylation, ubiquitination, methylation, and acetylation, among others. An example of protein modifications involving proteolytic cleavage is that needed to convert zymogens, such as those involved in protein digestion, to active enzymes.

### Control of Gene Expression

Each cell in the body contains a complete set of genes. Only a portion of the genes are expressed in specialized cells of a given organ. The regulation of gene expression occurs primarily at three different levels.

- Transcription-level control mechanisms determine if a particular gene can be transcribed. Transcriptional control is accomplished by large numbers of proteins (called transcriptional factors) that bind to the DNA at a site other than the one involved in serving as a template for the mRNA. These transcriptional factors can enhance, inhibit, or, in some cases, alter the frequency (number of times transcription occurs within a specified time span) of the gene’s transcription. Several hormones, such as insulin, thyroid hormone, glucagon, and glucocorticoids, as well as nutrients, such as essential fatty acids and vitamins A and D, can alter the transcription of DNA by binding along with transcription-factor proteins to DNA. Expression may be activated or silenced fully or partially to meet the ever-changing needs of the cells; these actions often occur to a greater extent in metabolically active (vs. lesser active) cells such as in the liver. Further examples of such interactions