

Lehninger

PRINCIPLES OF BIOCHEMISTRY

fourth edition



DAVID L. NELSON

Lehninger

PRINCIPLES OF BIOCHEMISTRY

fourth edition

DAVID L. NELSON

Professor of Biochemistry
University of Wisconsin–Madison

MICHAEL M. COX

Professor of Biochemistry
University of Wisconsin–Madison



W. H. Freeman and Company
New York

DOCKET
A L A R M

Find authenticated court documents without watermarks at docketalarm.com.

Publisher: Sara Tenney
Acquisitions Editor: Katherine Ahr
Development Editor: Morgan Ryan
Marketing Manager: Sarah Martin
Marketing Director: John Britch
Project Editor: Jane O'Neill
Design Manager: Blake Logan
Text Designer: Rae Grant
Cover Designer: Yuichiro Nishizawa
Page Makeup: Paul Lacy
Illustration Coordinator: Shawn Churchman
Illustrations: Fine Line Illustrations
Molecular Graphics/Cover Illustration: Jean-Yves Sgro
Photo Editor: Vikii Wong
Production Coordinator: Paul Rohloff
Media & Supplements Editors: Jeffrey Ciprioni, Melanie Mays, Nick Tymoczko
Media Developers: Sumanas, Inc.
Composition: TechBooks
Manufacturing: RR Donnelley & Sons Company

On the cover: The F_1 ATPase, part of a complex responsible for ATP synthesis in eukaryotic mitochondria. See Chapter 19.

Library of Congress Control Number: 2004101716

ISBN: 0-7167-4339-6

EAN: 97807167743392

© 2005, 2000, 1993, 1982 by W. H. Freeman and Company
All rights reserved.

Printed in the United States of America

Fourth printing

W. H. Freeman and Company
41 Madison Avenue
New York, NY 10010
Houndmills, Basingstoke RG21 6XS, England

www.whfreeman.com

Contents in Brief

Preface v

1 The Foundations of Biochemistry 1

I STRUCTURE AND CATALYSIS 45

- 2 Water 47
- 3 Amino Acids, Peptides, and Proteins 75
- 4 The Three-Dimensional Structure of Proteins 116
- 5 Protein Function 157
- 6 Enzymes 190
- 7 Carbohydrates and Glycobiology 238
- 8 Nucleotides and Nucleic Acids 273
- 9 DNA-Based Information Technologies 306
- 10 Lipids 343
- 11 Biological Membranes and Transport 369
- 12 Biosignaling 421

II BIOENERGETICS AND METABOLISM 481

- 13 Principles of Bioenergetics 489
- 14 Glycolysis, Gluconeogenesis, and the Pentose Phosphate Pathway 521
- 15 Principles of Metabolic Regulation: Glucose and Glycogen 560
- 16 The Citric Acid Cycle 601
- 17 Fatty Acid Catabolism 631
- 18 Amino Acid Oxidation and the Production of Urea 656
- 19 Oxidative Phosphorylation and Photophosphorylation 690
- 20 Carbohydrate Biosynthesis in Plants and Bacteria 751
- 21 Lipid Biosynthesis 787
- 22 Biosynthesis of Amino Acids, Nucleotides, and Related Molecules 833
- 23 Hormonal Regulation and Integration of Mammalian Metabolism 881

III INFORMATION PATHWAYS 921

- 24 Genes and Chromosomes 923
- 24 DNA Metabolism 948
- 26 RNA Metabolism 995
- 27 Protein Metabolism 1034
- 28 Regulation of Gene Expression 1081

Appendix A Common Abbreviations in the Biochemical Research Literature A-1

Appendix B Abbreviated Solutions to Problems AS-1

Glossary G-1

Credits C-1

Index I-1

CONTENTS

1 The Foundations of Biochemistry 1

1.1 Cellular Foundations 3

- Cells Are the Structural and Functional Units of All Living Organisms 3
- Cellular Dimensions Are Limited by Oxygen Diffusion 4
- There Are Three Distinct Domains of Life 4
- Escherichia coli* Is the Most-Studied Prokaryotic Cell 5
- Eukaryotic Cells Have a Variety of Membranous Organelles, Which Can Be Isolated for Study 6
- The Cytoplasm Is Organized by the Cytoskeleton and Is Highly Dynamic 9
- Cells Build Supramolecular Structures 10
- In Vitro Studies May Overlook Important Interactions among Molecules 11

1.2 Chemical Foundations 12

- Biomolecules Are Compounds of Carbon with a Variety of Functional Groups 13
- Cells Contain a Universal Set of Small Molecules 14
- Macromolecules Are the Major Constituents of Cells 15
- Box 1-1 Molecular Weight, Molecular Mass, and Their Correct Units 15**
- Three-Dimensional Structure Is Described by Configuration and Conformation 16
- Box 1-2 Louis Pasteur and Optical Activity: *In Vino, Veritas* 19**
- Interactions between Biomolecules Are Stereospecific 20

1.3 Physical Foundations 21

- Living Organisms Exist in a Dynamic Steady State, Never at Equilibrium with Their Surroundings 21
- Organisms Transform Energy and Matter from Their Surroundings 22
- The Flow of Electrons Provides Energy for Organisms 22
- Creating and Maintaining Order Requires Work and Energy 23
- Energy Coupling Links Reactions in Biology 23
- Box 1-3 Entropy: The Advantages of Being Disorganized 24**
- K_{eq} and ΔG Are Measures of a Reaction's Tendency to Proceed Spontaneously 26
- Enzymes Promote Sequences of Chemical Reactions 26
- Metabolism Is Regulated to Achieve Balance and Economy 27

1.4 Genetic Foundations 28

- Genetic Continuity Is Vested in Single DNA Molecules 29
- The Structure of DNA Allows for Its Replication and Repair with Near-Perfect Fidelity 29
- The Linear Sequence in DNA Encodes Proteins with Three-Dimensional Structures 29

1.5 Evolutionary Foundations 31

- Changes in the Hereditary Instructions Allow Evolution 31
- Biomolecules First Arose by Chemical Evolution 32
- Chemical Evolution Can Be Simulated in the Laboratory 32
- RNA or Related Precursors May Have Been the First Genes and Catalysts 32
- Biological Evolution Began More Than Three and a Half Billion Years Ago 34
- The First Cell Was Probably a Chemoheterotroph 34
- Eukaryotic Cells Evolved from Prokaryotes in Several

Functional Genomics Shows the Allocations of Genes to Specific Cellular Processes 38
 Genomic Comparisons Will Have Increasing Importance in Human Biology and Medicine 38

I STRUCTURE AND CATALYSIS 45

2 Water 47

2.1 Weak Interactions in Aqueous Systems 47

Hydrogen Bonding Gives Water Its Unusual Properties 47
 Water Forms Hydrogen Bonds with Polar Solutes 49
 Water Interacts Electrostatically with Charged Solutes 50
 Entropy Increases as Crystalline Substances Dissolve 51
 Nonpolar Gases Are Poorly Soluble in Water 52
 Nonpolar Compounds Force Energetically Unfavorable Changes in the Structure of Water 52
 van der Waals Interactions Are Weak Interatomic Attractions 54
 Weak Interactions Are Crucial to Macromolecular Structure and Function 54
 Solutes Affect the Colligative Properties of Aqueous Solutions 56

Box 2-1 Touch Response in Plants: An Osmotic Event 59

2.2 Ionization of Water, Weak Acids, and Weak Bases 60

Pure Water Is Slightly Ionized 60
 The Ionization of Water Is Expressed by an Equilibrium Constant 61
 The pH Scale Designates the H^+ and OH^- Concentrations 61

Box 2-2 The Ion Product of Water: Two Illustrative Problems 62

Weak Acids and Bases Have Characteristic Dissociation Constants 63
 Titration Curves Reveal the pK_a of Weak Acids 64

2.3 Buffering against pH Changes in Biological Systems 65

Buffers Are Mixtures of Weak Acids and Their Conjugate Bases 66
 A Simple Expression Relates pH, pK_a , and Buffer Concentration 66
 Weak Acids or Bases Buffer Cells and Tissues against pH Changes 67

Box 2-3 Solving Problems Using the Henderson-Hasselbalch Equation 67

Box 2-4 Blood, Lungs, and Buffer: The Bicarbonate Buffer System 69

2.4 Water as a Reactant 69

2.5 The Fitness of the Aqueous Environment for Living Organisms 70

3 Amino Acids, Peptides, and Proteins 75

3.1 Amino Acids 75

Amino Acids Share Common Structural Features 76
 The Amino Acid Residues in Proteins Are L Stereoisomers 77
 Amino Acids Can Be Classified by R Group 78
 Uncommon Amino Acids Also Have Important Functions 80

Box 3-1 Absorption of Light by Molecules: The Lambert-Beer Law 82

Amino Acids Have Characteristic Titration Curves 82
 Titration Curves Predict the Electric Charge of Amino Acids 84
 Amino Acids Differ in Their Acid-Base Properties 84

3.2 Peptides and Proteins 85

Peptides Are Chains of Amino Acids 85
 Peptides Can Be Distinguished by Their Ionization Behavior 86
 Biologically Active Peptides and Polypeptides Occur in a Vast Range of Sizes 86
 Polypeptides Have Characteristic Amino Acid Compositions 87
 Some Proteins Contain Chemical Groups Other Than Amino Acids 88
 There Are Several Levels of Protein Structure 88

3.3 Working with Proteins 89

Proteins Can Be Separated and Purified 89
 Proteins Can Be Separated and Characterized by Electrophoresis 92
 Unseparated Proteins Can Be Quantified 94

3.4 The Covalent Structure of Proteins 96

The Function of a Protein Depends on Its Amino Acid Sequence 96
 The Amino Acid Sequences of Millions of Proteins Have Been Determined 96
 Short Polypeptides Are Sequenced Using Automated Procedures 97
 Large Proteins Must Be Sequenced in Smaller Segments 99
 Amino Acid Sequences Can Also Be Deduced by Other Methods 100

Box 3-2 Investigating Proteins with Mass Spectrometry 102

Small Peptides and Proteins Can Be Chemically Synthesized 104
 Amino Acid Sequences Provide Important Biochemical Information 106

3.5 Protein Sequences and Evolution 106

Protein Sequences Can Elucidate the History of Life on Earth 107

4 The Three-Dimensional Structure of Proteins 116

4.1 Overview of Protein Structure 116

A Protein's Conformation Is Stabilized Largely by Weak Interactions 117
 The Peptide Bond Is Rigid and Planar 118

4.2 Protein Secondary Structure 120

The α Helix Is a Common Protein Secondary Structure 120
 Amino Acid Sequence Affects α Helix Stability 121

Box 4-1 Knowing the Right Hand from the Left 122

The β Conformation Organizes Polypeptide Chains into Sheets 123
 β Turns Are Common in Proteins 123
 Common Secondary Structures Have Characteristic Bond Angles and Amino Acid Content 124

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.