### I

#### NEUROSCIENCE

- 1. Fundamentals of Neuroscience 3
- 2. The Architecture of Nervous Systems 1

### II

### CELLULAR AND MOLECULAR NEUROSCIENCE

- 3. Cellular Components of Nervous Tissue 49
- Subcellular Organization of the Nervous System: Organelles and Their Functions 79
- Electrotonic Properties of Axons and Dendrites 115
- 6. Membrane Potential and Action Potential 139
- 7. Neurotransmitters 163
- 8. Release of Neurotransmitters 197
- 9. Neurotransmitter Receptors 225
- 10. Intracellular Signaling 259
- Postsynaptic Potentials and Synaptic Integration 299
- Information Processing in Complex Dendrites 319
- 13. Brain Energy Metabolism 339

### Ш

#### NERVOUS SYSTEM DEVELOPMENT

- 14. Neural Induction and Pattern Formation 363
- 15. Neurogenesis and Migration 391
- 16. Cellular Determination 417
- 17. Growth Cones and Axon Pathfinding 449

### Contents

18.	Target Selec	ction,	Topographic Mar	s, and Sy	napse
	Formation	469			-

- Programmed Cell Death and Neurotrophic Factors 499
- 20. Synapse Elimination 53321. Early Experience and Critical Periods 555

## $\frac{1 \text{ V}}{\text{SENSORY SYSTEMS}}$

- 22. Fundamentals of Sensory Systems 577
- 23. Sensory Transduction 591
- 24. Chemical Senses: Taste and Olfaction 631
- 25. The Somatosensory System 66726. Audition 699
- 27. Vision 727

### WOTOR SYSTEMS

### 28. Fundamentals of Motor Systems 753

- 29. The Spinal Cord, Muscle, and
- Locomotion 767

  30. Descending Control of Movement 7
- 31. The Basal Ganglia 815
- 32. Cerebellum 84133. Eye Movements 873

### VI REGULATORY SYSTEMS

#### The Hypothalamus: An Overview of Regulatory Systems 897

35.	Central Control of Autonomic Functions: Organization of the Autonomic Nervous		
	System 911		
36.	Neural Regulation of the Cardiovascular		

3 935 System

37. Neural Control of Breathing 38. Food Intake and Metabolism 991

39. Water Intake and Body Fluids 1011 40. Neuroendocrine Systems

41. Circadian Timing 1067 42. Sleep, Dreaming, and Wakefulness 1085 43. Motivation and Reward 1109

44. Drug Reward and Addiction

### VII

### BEHAVIORAL AND COGNITIVE NEUROSCIENCE

- 45. Human Brain Evolution 1147
- 46. Cognitive Development and Aging 1167
- 47. Visual Perception of Objects 1201
- 48. Spatial Cognition 1229
- 49. Attention 1249
- 50. Learning and Memory: Basic Mechanisms 1275
- 51. Learning and Memory: Brain Systems 1299
- 52. Language and Communication 1329
- 53. The Prefrontal Cortex and Executive Brain Functions 1353
- 54. Executive Control and Thought 1377

Preface to the First Edition xv Preface to the Second Edition xvii Acknowledgments xix

### I

#### **NEUROSCIENCE**

### 1. Fundamentals of Neuroscience

A Brief History of Neuroscience 3 The Terminology of Nervous Systems Is Hierarchical,

Distributed, Descriptive, and Historically Based

Neurons and Glia Are Cellular Building Blocks of the Nervous System 4

The Operative Processes of Nervous Systems Are Also

Hierarchical 5

Cellular Organization of the Brain 6 Organization of This Text 7

This Book Is Intended for a Broad Range of Scholars of the Neurosciences 8

Clinical Issues in the Neurosciences 8

The Spirit of Exploration Continues 8 The Genomic Inventory Is a Giant Step Forward

Neuroscience Today: A Communal Endeavor 9

The Creation of Knowledge 10 Responsible Conduct 11

Summary 13

References 13

### 2. The Architecture of Nervous Systems LARRY W. SWANSON

General Principles from an Evolutionary Perspective 15

#### Contents

Development of the Vertebrate Nervous System 23
Identity and Organization of Functional Systems 29
Some Basic Structural Features of the Nervous
System 32
References 44

### II CELLULAR AND MOLECULAR NEUROSCIENCE

3. Cellular Components of Nervous Tissue PATRICK R. HOF, BRUCE D. TRAPP, JEAN DE VELLIS, LUZ CLAUDIO, AND DAVID R. COLMAN

The Neuron 49 Neuroglia 61 Cerebral Vasculature 69 References 75

4. Subcellular Organization of the Nervous System: Organelles and Their Functions SCOTT BRADY, DAVID R. COLMAN, AND PETER BROPHY

Axons and Dendrites: Unique Structural Components of Neurons 79 Protein Synthesis in Nervous Tissue 84 Cytoskeletons of Neurons and Glial Cells 95 Molecular Motors in the Nervous System 103 Building and Maintaining Nervous System Cells 106

References 113

163

# 5. Electrotonic Properties of Axons and Dendrites GORDON M. SHEPHERD

Toward a Theory of Neuronal Information
Processing 115
Basic Tools: Cable Theory and Compartmental
Models 116
Spread of Steady-State Signals 117
Spread of Transient Signals 122
Electrotonic Properties Underlying Propagation in
Axons 124
Electrotonic Spread in Dendrites 126
Dynamic Properties of Passive Electrotonic

Relating Passive to Active Potentials

# 6. Membrane Potential and Action Potential

Membrane Potential 140 Action Potential 145 References 160

References

References

196

224

Structure 129

References 136

### 7. Neurotransmitters

ARIEL Y. DEUTCH AND ROBERT H. ROTH

Chemical Transmission 164
Classical Neurotransmitters 166
Nonclassical Neurotransmitters 186
Peptide Transmitters 188
Unconventional Transmitters 191
Synaptic Transmission in Perspective 195

Several Modes of Neuronal Communication Exist

# 8. Release of Neurotransmitters THOMAS L. SCHWARZ

Transmitter Release Is Quantal 197
Excitation—Secretion Coupling 202
Molecular Mechanisms of the Nerve Terminal
Quantal Analysis: Probing Synaptic Physiology
Short-Term Synaptic Plasticity 220

### 9. Neurotransmitter Receptors M. NEAL WAXHAM

Ionotropic Receptors 225 G-Protein Coupled Receptors 245 References 257

## 10. Intracellular Signaling HOWARD SCHULMAN AND JAMES L. ROBERTS

Signaling through G-Protein-Linked Receptors 259
Modulation of Neuronal Function by Protein Kinases and
Phosphatases 274
Intracellular Signaling Affects Nuclear Gene
Expression 288
References 297

# 11. Postsynaptic Potentials and Synaptic Integration JOHN H. BYRNE

Ionotropic Receptors: Mediators of Fast Excitatory and Inhibitory Synaptic Potentials 299 Metabotropic Receptors: Mediators of Slow Synaptic Potentials 311 Integration of Synaptic Potentials 314 References 317

# 12. Information Processing in Complex Dendrites

GORDON M. SHEPHERD

Strategies for Studying Complex Dendrites 319
An Axon Places Constraints on Dendritic
Processing 320
Dendrodendritic Interactions between Axonal Cells 321
Passive Dendritic Trees Can Perform Complex

Computations 322
Distal Dendrites Can Be Closely Linked to Axonal
Output 323

Depolarizing and Hyperpolarizing Dendritic Conductances Interact Dynamically 324

The Axon Hillock-Initial Segment Encodes Global Output 325

Retrograde Impulse Spread into Dendrites Can Have Several Functions 326

Examples of How Voltage-Gated Channels Take Part in Dendritic Integration 329

Multiple Imp	oulse Ii	nitiation S	Sites Are	under	Dynami
Control					•

Dendritic Spines Are Multifunctional Microintegrative 334

Summary: The Dendritic Tree as a Complex Information Processing System 336 References 336

### 13. Brain Energy Metabolism PIERRE J. MAGISTRETTI

Energy Metabolism of the Brain as a Whole Organ Coupling of Neuronal Activity, Blood Flow, and Energy

Metabolism Energy-Producing and Energy-Consuming Processes in the

Brain Energy Metabolism at the Cellular

Level 349

Glutamate and Nitrogen Metabolism: A Coordinated Shuttle between Astrocytes and Neurons The Astrocyte–Neuron Metabolic Unit References 360

### III

### NERVOUS SYSTEM **DEVELOPMENT**

#### 14. Neural Induction and Pattern Formation ANDREW LUMSDEN AND CHRIS KINTNER

Early Neural Patterning 371 Regionalization of the Central Nervous System Regionalization of the Prechordal Central Nervous System 385 Conclusions 388

363

389 References

Neural Induction

#### 15. Neurogenesis and Migration MARIANNE BRONNER-FRASER AND MARY BETH HATTEN

Development of the Peripheral Nervous System 391 Development of the Central Nervous System 403 References 415

ix

### 16. Cellular Determination WILLIAM A. HARRIS AND VOLKER HARTENSTEIN

Neuronal Phenotypes and Determinants 417
Determination of Neural Progenitors 419
Specification of Neural Lineages by Intrinsic
Mechanisms 426
Specification of Neural Fates by Extrinsic
Mechanisms 432
Summary 447
References 447

### 17. Growth Cones and Axon Pathfinding MARC T. TESSIER-LAVIGNE

Growth Cones Are Actively Guided 449
Guidance Cues for Developing Axons 451
Guidance Cues and the Control of Actin
Polymerization 456
Guidance in Vivo: Reusing Cues for Different Purposes and
Changing Responses to Cues 459
Future Directions 466
References 466

# 18. Target Selection, Topographic Maps, and Synapse Formation

STEVEN J. BURDEN, DARWIN BERG, AND DENNIS D. M. O'LEARY

Target Selection and Map Formation 469
Development of the Neuromuscular Synapse 483
Synapse Formation in the Central Nervous System 492
References 497

#### Programmed Cell Death and Neurotrophic Factors

RONALD W. OPPENHEIM AND JAMES E. JOHNSON

Cell Death and the Neurotrophic Hypothesis 501
Nerve Growth Factor: The Prototype Target-Derived
Neuronal Survival Factor 502
The Neurotrophin Family 506
Neurotrophin Receptors 507
Cytokines and Growth Factors in the Nervous
System 510
Neurotrophic Factors Have Multiple Activities 511
TRK Receptors Are Similar to Other Growth Factor
Receptors 514

X

Programmed Cell Death of Neurons Is Widespread in
Invertebrate and Vertebrate Species 517
Modes of Cell Death in Developing Neurons 518
The Mode of Neuronal Cell Death Reflects the
Activation of Distinct Biochemical and Molecular
Mechanisms 522
Programmed Cell Death Is Regulated by Interactions with
Targets, Afferents, and Nonneuronal Cells 525
Functions of Neuronal Programmed Cell Death 529
D 1011D 1 D 1 15 1

Targets, Afferents, and Nonneuronal Cells 525
Functions of Neuronal Programmed Cell Death 529
Programmed Cell Death, Developmental Disorders, and
Neurodegenerations 530
References 532

### 20. Synapse Elimination RACHEL O. L. WONG AND JEFFREY W. LICHTMAN

An Overview of Synapse Elimination 533 The Purpose of Synapse Elimination A Role for Interaxonal Competition Spatial Patterning of Connectivity by Synapse Elimination 541 Activity Is Required for Synapse Elimination How Widespread Is Activity-Driven Synapse Elimination? 549 How Are Synaptic Connections Altered? Is Synapse Elimination Strictly a Developmental Phenomenon? 553 References 553

# 21. Early Experience and Critical Periods ERIC I. KNUDSEN

Sound Localization: Calibrated by Early Experience in the Owl 556
Birdsong: Learned by Experience 559
Filial Imprinting: Babies Learn to Recognize Their Parents 562
Binocular Vision 564
Principles of Developmental Learning 569
References 572

### IV SENSORY SYSTEMS

22. Fundamentals of Sensory Systems STEWART H. HENDRY, STEVEN S. HSIAO, AND M. CHRISTIAN BROWN

Sensation and Perception 577

### Receptors 57

CONTENTS

Receptors 578
Peripheral Organization and Processing 580
Central Pathways and Processing 584
Sensory Cortex 585
Summary 588
References 588

### 23. Sensory Transduction

PETER R. MacLEISH, GORDON M. SHEPHERD, SUE C. KINNAMON, AND JOSEPH SANTOS-SACCHI

Phototransduction 591 Olfactory Transduction 601 Taste 613 Mechanoreception 620 References 629

# 24. Chemical Senses: Taste and Olfaction DAVID V. SMITH AND GORDON M. SHEPHERD

Taste 631 Olfaction 649 References 666

## 25. The Somatosensory System STEWART H. HENDRY AND STEVEN S. HSIAO

Peripheral Mechanisms of Somatic Sensation 668
Spinal and Brain Stem Components of the Somatosensory
System 679
The Thalamic Ventrobasal Complex 688
Somatosensory Areas of the Cerebral Cortex 689
References 696

### 26. Audition

M. CHRISTIAN BROWN

Amplitude and Frequency Ranges of Hearing 699
External and Middle Ear 700
The Cochlea 701
The Auditory Nerve 705
Descending Systems to the Periphery 710
Central Nervous System 711
References 725

### 27. Vision

Overview 727
The Eye and the Retina 729
The Retinogeniculocortical Pathway 739
References 750

#### V MOTOR SYSTEN

### 28. Fundamentals of Motor Systems STEN GRILLNER

Basic Components of the Motor System 755
Motor Programs Coordinate Basic Motor Patterns 756
Roles of Different Parts of the Nervous System in the
Control of Movement 758
Conclusion 765
References 765

### 29. The Spinal Cord, Muscle, and Locomotion

Muscles and Their Control 767 Spinal Networks and the Segmental Motor System 775 Sensory Modulation 784 References 789

## 30. Descending Control of Movement MARCH. SCHIEBER AND JAMES F. BAKER

The Medial Postural System 792
The Lateral Voluntary System 802
Summary 813
References 814

# 31. The Basal Ganglia JONATHAN W. MINK

Anatomy of Basal Ganglia 816
Signaling in Basal Ganglia 823
The Effect of Basal Ganglia Damage on Behavior 826
Fundamental Principles of Basal Ganglia Operation for Motor Control 832
Basal Ganglia Participation in Nonmotor Functions 834
References 839

ONTENTS χi

#### 32. Cerebellum

IAMES C. HOUK AND ENRICO MUGNAIN!

Overview 841 Organization of Signal Processing Modules Neurons and Their Signals Activation and Inactivation Studies Phylogenetic and Ontogenetic Development Overall Summary 870 References

### 33. Eye Movements

PAUL W. GLIMCHER

There Are Five Types of Eye Movements 873 Oculomotor Nuclei and Extraocular Muscles 874 The Vestibulo-Ocular Reflex The Optokinetic System The Saccadic System Smooth Pursuit 887 Vergence 888 Conclusions 890 References 892

#### VI REGULATORY SYSTEMS

#### 34. The Hypothalamus: An Overview of Regulatory Systems

J. PATRICK CARD, LARRY W. SWANSON, AND ROBERT Y. MOORE

Historical Perspective 897 General Organizational Principles of the Adult Hypothalamus 900 Functional Organization of the Hypothalamus 901 Effector Systems of the Hypothalamus Are Both Humoral and Synaptic 904 References 908

### 35. Central Control of Autonomic Functions: Organization of the Autonomic Nervous System

TERRY L POWLEY

Sympathetic Division: Organized to Mobilize the Body for Activity 913 Parasympathetic Division: Organized for Energy Conservation 918

XII FULL

The Enteric Division of the ANS: The Nerve Net Found in the Walls of Visceral Organs 921

ANS Pharmacology: Transmitter and Receptor Coding 921

Autonomic Controls of Homeostasis 924

Hierarchically Organized CNS Circuits 928

Perspective: Future of the Autonomic Nervous System 931

Summary and General Conclusions 932

References 932

# 36. Neural Regulation of the Cardiovascular System JOHN C. LONGHURST

Description of the System: An Anatomical 935 Framework Anatomy and Chemical Properties of Efferent Autonomic Pathways 943 A System of Generators 944 Short-Term Control Mechanisms Reflex Control of the Cardiovascular System 947 Arterial Baroreceptors 948 Peripheral Arterial Chemoreceptors 956 Cardiac Receptors Visceral Abdominal Reflexes References 965

# 37. Neural Control of Breathing JACK L. FELDMAN AND DONALD R. McCRIMMON

Early Neuroscience and the Brain Stem 967
Central Nervous System and Breathing Respiratory
Rhythm Generation 969
Where Are the Neurons That Generate the Breathin

Where Are the Neurons That Generate the Breathing Rhythm? 969

Which Neurons in the Prebötzinger Complex Are Required for Respiratory Rhythm Generation? 971 Where Are the Respiratory Neurons? 974

Discharge Patterns of Respiratory Neurons 974
Sensory Inputs and Altered Breathing 980
Mechanoreceptors in the Lungs Adjust Breathing Pattern and Initiate Protective Reflexes 982
Modulation and Plasticity of Respiratory Motor

Output 984
Suprapontine Structures and Breathing 989

References 990

# 38. Food Intake and Metabolism STEPHEN C. WOODS AND EDWARD M. STRICKER

Caloric Homeostasis 991
Role of Caloric Homeostasis in Control of Food
Intake 994
Central Control of Food Intake 1000
Neuropeptide and the Control of Food Intake 1004
References 1008

# 39. Water Intake and Body Fluids EDWARD M. STRICKER AND JOSEPH G. VERBALIS

Body Fluid Physiology 1011 Osmotic Homeostasis 1012 Volume Homeostasis 1020 References 1028

# 40. Neuroendocrine Systems ANDREA C. GORE AND JAMES L. ROBERTS

The Hypothalamus Is a Neuroendocrine Organ 1031
Hypothalamic Releasing/Inhibiting Hormones and Their
Targets 1033
Characteristics of Fact Neurolands (Fact Neurolands)

Characteristics of Each Neuroendocrine System 1036 Hypothalamic Control of Sexual Behavior 1057 References 1065

## 41. Circadian Timing ROBERT Y. MOORE

Circadian Rhythms Are a Fundamental Adaptation of Living Organisms 1067

Circadian Timing Is Inherited 1068

Circadian Timing in Animals Is a Function of the Nervous System 1070

The Suprachiasmatic Nucleus Is the Dominant Circadian Pacemaker 1072

Light Is the Dominant Entraining Stimulus 1074

Pacemaker Output Is Limited 1077

The Avian Circadian Timing System Is More Complex Than That of Mammals 1078

Circadian Timing Is Critical for Reproduction in Some Mammals 1079

The Primate Circadian Timing System Functions
Principally to Promote Behavioral

Adaptation 1081 References 1084

# 42. Sleep, Dreaming, and Wakefulness J. ALLAN HOBSON AND EDWARD F. PACE-SCHOTT

The Two States of Sleep: Slow Wave and Rapid Eye
Movement 1087
Sleep in the Modern Era of Neuroscience 1089
Anatomy and Physiology of Brain Stem Regulatory
Systems 1091
Sensimotor and Modulatory Reticular Neurons Differ
Functionally 1092
Other Brain Stem and Diencephalic Neurotransmitter

Other Brain Stem and Diencephalic Neurotransmitter Systems 1098 Modeling the Control of Behavioral State 1101

**43.** Motivation and Reward TREVOR W. ROBBINS AND BARRY J. EVERITT

Neural Mechanisms of Motivation 1110
Dopamine and the Lateral Hypothalamic
Syndrome 1112
Reinforcement Systems 1116
Brain Aversion Systems 1123
References 1125

1107

References

### 44. Drug Reward and Addiction GEORGE F. KOOB

Assessing the Reinforcing Actions of Drugs 1128
Neurobiological Substrates of Drug Reward 1131
Neurobiological Substrates for Motivation Effects of Drug
Dependence 1136
Neurochemical Adaptation in Reward
Neurotransmitters 1137
Neuroadaptation, Prolonged Abstinence, and
Relapse 1139

References 1142

# VII BEHAVIORAL AND COGNITIVE NEUROSCIENCE

**45.** Human Brain Evolution JON H. KAAS AND TODD M. PREUSS

Evolutionary and Comparative Principles 1147 Early Stages of Brain Evolution 1153 Evolution of Primate Brains 1156 Why Brain Size Is Important 1163 Conclusions 1164 References 1165

# 46. Cognitive Development and Aging PETER R. RAPP AND JOCELYNE BACHEVALIER

Brain Development 1167
Cognitive Development and Aging: A Life Span
Perspective 1172
Pathological Processes in Cognitive Development and
Aging 1186
References 1199

#### 47. Visual Perception of Objects HILLARY R. RODMAN, LUIZ PESSOA, AND LESLIE G. UNGERLIEDER

The Problem of Object Recognition 1201
Substrates of Object Perception and Recognition: Early
Evidence from Brain Damage 1202

Visual Pathways for Object Processing in Nonhuman Primates 1205

Neuronal Properties within the Object Recognition
Pathway 1208

Functional Imaging and Electrophysiology of Object Recognition in Humans 1215

Perception and Recognition of Specific Classes of Objects 1218

Object Knowledge Is Stored in a Distributed Network of Cortical Areas 1224 References 1227

### 48. Spatial Cognition CAROL L. COLBY AND CARL R. OLSON

Neuroanatomy of Spatial Cognition 1229
Parietal Cortex 1230
Frontal Cortex 1240
Hippocampus and Adjacent Cortex 1245
Spatial Cognition and Spatial Action 1246
References 1246

#### 49. Attention

JOHN H. REYNOLDS, JACQUELINE P. GOTTLIEB, AND SABINE KASTNER

Introduction 1249 Varieties of Attention 1249

xiv	FUI
Covert Spatial Attention Has Been Studied	
Intensively with the Cuing Paradigm 1250	
Neglect Syndrome: A Deficit of Spatial	
Attention 1252	
The Network Mediating Spatial Attention in Human	ns
Centers Around Frontal and Parietal Cortical	

Areas 1253 Human Frontal and Parietal Cortical Areas Provide Top-down Signals Controlling Spatial

Attention 1254 Visual Salience Maps in Monkey Parietal and Frontal Cortices Guide the Deployment of Spatial Attention 1254

Attention Increases Sensitivity and Boosts the Clarity of Signals Generated by Neurons in Parts of the Visual System Devoted to Processing Information about 1261

Attention Affects Neural Activity in the Human Visual Cortex in the Presence and Absence of Visual Stimulation 1261 The Visual Search Paradigm Has Been Used to Study the

Role of Attention in Selecting Relevant Stimuli from within a Cluttered Visual Environment 1264 Where Is the Computational Bottleneck as Revealed by Search Tasks? 1264 Neuronal Receptive Fields Are a Possible Neural Correlate of Limited Capacity

Competition Can Be Biased by Nonspatial Feedback 1267 Filtering of Unwanted Information in Humans Closely Related Mechanisms Govern Covert Orienting and Target Selection for Eye Movements Attentional State 1270 Monoamines Act as Neuromodulators

Conclusions 1272

References

1272

50. Learning and Memory: Basic Mechanisms JOHN H. BYRNE

Paradigms Have Been Developed to Study Associative and Nonassociative Learning 1276

Invertebrate Studies: Key Insights from Aplysia into Basic Mechanisms of Learning 1277

Vertebrate Studies: Long-Term Potentiation 1286 Long-Term Depression 1294 How Does a Change in Synaptic Strength Store a Complex Memory? 1295 References 1297

# 51. Learning and Memory: Brain Systems HOWARD B. EICHENBAUM

Early Proposals about Different Forms of Memory
Emergence of the Modern Conception of Memory
Systems 1300
Declarative Memory 1304
Procedural Memory 1311
Emotional Memory 1315

Cerebral Cortex and Memory Conclusions 1326 References 1326

# 52. Language and Communication DAVID N. CAPLAN AND JAMES L. GOULD

Animal Communication 1329 Human Language 1335 Conclusions 1351 References 1352

1376

## 53. The Prefrontal Cortex and Executive Brain Functions

EARL K. MILLER AND JONATHAN D. WALLIS

Controlled versus Automatic Processing 1353
Anatomy and Organization of the Prefrontal Cortex 1358
Behavioral Effects of Damage to the Prefrontal
Cortex 1359
Neurophysiology of the Prefrontal Cortex 1368
Theories of Prefrontal Cortex Function 1373

54. Executive Control and Thought EDWARD E. SMITH AND JOHN JONIDES

Introduction 1377
Working Memory: Storage and Updating 1379
Selective Attention 1383
Switching Attention 1388
What Are the Components in Complex Tasks? 1391
References 1393

Permissions 1395 Contributors 1397 Index 1401

References