

*Handbook of*  
***Neurochemistry***

---

**SECOND EDITION**

---

**Volume 1**  
**CHEMICAL AND CELLULAR  
ARCHITECTURE**

*Edited by*

***Abel Lajtha***

*Handbook of*  
***Neurochemistry***  
—  
***SECOND EDITION***

*Volume 1*  
**CHEMICAL AND CELLULAR  
ARCHITECTURE**

*Edited by*  
***Abel Lajtha***

*Center for Neurochemistry  
Ward's Island, New York*



**PLENUM PRESS · NEW YORK AND LONDON**

## *Contributors*

- A. M. Benjamin*, Division of Neurological Sciences, University of British Columbia, Vancouver, British Columbia V6T 1W5, Canada
- Kenneth A. Bonnet*, Department of Psychiatry, New York University School of Medicine, New York, New York 10016
- Alan A. Boulton*, Psychiatric Research Division, University Hospital, Saskatoon, Saskatchewan S7N OXO, Canada
- R. S. Bourke*, Division of Neurosurgery, Albany Medical College, Albany, New York 12208
- M. J. Brownstein*, Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland 20205
- Arsélio P. Carvalho*, Center for Cell Biology, Department of Zoology, University of Coimbra, 3049 Coimbra Codex, Portugal
- Bert Csillik*, Department of Anatomy, University Medical School, Szeged, Hungary
- Csaba Fajsz*, Institute of Biophysics, Biological Research Center, Hungarian Academy of Sciences, 6701 Szeged, Hungary
- H. Gainer*, Laboratory of Developmental Neurobiology, National Institute of Child Health and Human Development, Bethesda, Maryland 20205
- E. Martin Gál*, Neurochemical Research Laboratories, Department of Psychiatry, University of Iowa, Iowa City, Iowa 52242
- Robert M. Gould*, Laboratory of Membrane Biology, Institute for Basic Research in Mental Retardation, Staten Island, New York 10314
- L. Hertz*, Department of Pharmacology, University of Saskatchewan, Saskatoon, Saskatchewan S7N OWO, Canada
- Augusto V. Juorio*, Psychiatric Research Division, University Hospital, Saskatoon, Saskatchewan S7N OXO, Canada
- H. K. Kimelberg*, Division of Neurosurgery, and Department of Biochemistry and Anatomy, Albany Medical College, Albany, New York 12208

*László Latzkovits*, Institute of Experimental Surgery, Medical School of Szeged, 6701 Szeged, Hungary

*Dan Matsumoto*, Laboratory of Membrane Biology, Institute for Basic Research in Mental Retardation, Staten Island, New York 10314

*Gary Mattingly*, Laboratory of Membrane Biology, Institute for Basic Research in Mental Retardation, Staten Island, New York 10314

*Hanna M. Pappius*, Donner Laboratory of Experimental Neurochemistry, Montreal Neurological Institute, and Department of Neurology and Neurosurgery, McGill University, Montreal, Quebec H3A 2B4, Canada

*Thomas L. Perry*, Department of Pharmacology, University of British Columbia, Vancouver, British Columbia V6T 1W5, Canada

*Leonid Pevzner*, The Saul R. Korey Department of Neurology, Albert Einstein College of Medicine, Bronx, New York 10461

*N. Seiler*, Centre de Recherche Merrell International, 67100 Strasbourg, France

*James H. Wood*, Cerebral Blood Flow Laboratories, Division of Neurosurgery, Emory University Clinic, Atlanta, Georgia 30322

## *Preface*

After the completion of the first edition of this series, this editor thought that a new edition would not be warranted in less than 15, perhaps 20, years, but it seems that we live in a time in which rapid changes are the norm and findings in a field such as neurochemistry develop exponentially. The task of a future editor attempting to get a comprehensive neurochemical handbook for the year 2000 would be even less enviable, but by then information processing may be very different.

The approach, the design, and the areas covered by each volume and each chapter are necessarily arbitrary, and it is likely that other editors or authors would have approached the coverage or the organization in a different manner. It is hoped, however, that readers will find the series helpful for beginning or for continuing work. There may be some overlap among the various chapters, but insisting on single coverage of an area would at times have restricted treatment to only one point of view and might have truncated and hurt the logical flow of some of the chapters.

Chapters in this series do not cover small areas in detail, but each covers a subject that could have been expanded to a book or could have been discussed in a week-long symposium. Still, one definition of a handbook is that it can be lifted and carried by hand. This series may be on the borderline of such a definition, but perhaps it fits "that by being brief it is of more help." Although they facilitate the finding of information and directions, such short presentations always gravely restrict details or background of the information presented. For these restrictions authors are not to be blamed. Clearly, full coverage is not possible, but the emphasis is on good chapters that are of support to those who turn to the book.

Most important, the editor wishes to thank the authors whose hard work is presented here; they are busy, have deadlines and unexpected emergencies, and, no doubt, this series has added just another difficult task to the long list. For their excellent contributions and cooperation we all are indeed grateful. The Handbook reflects not only the excitement of past findings but also, through the rapidly expanding present, the exciting possibilities of the future in our field.

Abel Lajtha

# *Contents*

## *Chapter I*

### *Cation Transport*

*László Latzkovits and Csaba Fajszi*

1. Introduction .....	1
1.1. Basic Concepts of Cation Transport .....	1
1.2. Do Cation Transport Phenomena That Can be Exclusively Attributed to Any Function of the Nervous System Exist at All? .....	2
2. General Correlates of Cation Transport .....	3
2.1. Role of Cations and Significance of Cation Transport in the Control of General Cell Functions .....	3
2.2. Supramolecular and Morphological Structures Involved in Cation Movements .....	4
3. Validity and Reliability of the Formal Treatments Used for Analyzing Cation Transport Phenomena .....	5
3.1. Problems Concerning the Application of Michaelis-Menten Kinetics .....	6
3.2. Tracer Kinetic Treatment .....	7
4. Regulation of Cellular Cation Transport .....	8
4.1. Movements of $\text{Na}^+$ and $\text{K}^+$ via $\text{Na}^+, \text{K}^+$ -ATPase-Determined Ion Pump .....	8
4.2. The $\text{Ca}^{2+}, \text{Mg}^{2+}$ -ATPase-Determined $\text{Ca}^{2+}$ Pump: Transport of $\text{Ca}^{2+}$ .....	14
4.3. Cation Movements via Dissipators. Passive Fluxes of Cations, and Transport of $\text{Mg}^{2+}$ and $\text{Li}^+$ .....	16
4.4. Regulatory Interrelationships among Mechanisms Controlling Cation Transport .....	20
5. Peculiarities of Cellular Cation Transport in the Nervous System ..	20
5.1. Characteristics of the Neuronal Cation Transport .....	21
5.2. Characteristics of the Cation Transport by Glial Cells .....	23
5.3. Glial-Neuronal Interactions in Cation Transport .....	24
6. Cationic Environment of the Neuron and Glia .....	26
6.1. Cation Transport by the Blood-Brain Barrier .....	26
6.2. Role of External Cations in the Regulation of Cellular Cation Transport in the Nervous System .....	26

7. Concluding Remarks: Cation Transport and Brain Functions .....	27
References .....	27

*Chapter 2**Anion Transport in the Nervous System**H. K. Kimelberg and R. S. Bourke*

1. Introduction .....	31
2. Anion Transport in Non-Nervous-System Tissues .....	33
2.1. Muscle .....	33
2.2. Erythrocytes .....	34
2.3. Epithelia .....	35
3. Transport of Anions into and out of the Central Nervous System ..	36
3.1. The Blood-Brain Barrier .....	36
3.2. Anion Transport and the Secretion of Cerebrospinal Fluid ....	37
4. Transport of Anions in the Nervous System .....	41
4.1. Compartmentation of Anions .....	41
4.2. Anion Transport in Brain Slices .....	45
4.3. Anion Transport in Superfused Cerebral Cortex .....	47
4.4. Anion Transport and Putative Transmitters .....	47
4.5. Anion Transport in Astroglial Cultures .....	50
4.6. Model of Anion Transport in Astrocytes .....	52
4.7. Chloride Content of Neurons .....	55
4.8. Effects of Chloride on Neuronal Potentials .....	57
4.9. Anion Transport Mechanisms in Neurons .....	58
5. Conclusions .....	62
References .....	64

*Chapter 3**Calcium in the Nerve Cell**Arsélio P. Carvalho*

1. Introduction .....	69
2. Technology for Measuring Calcium .....	70
2.1. Atomic Absorption Spectrometry .....	70
2.2. Calcium Electrodes .....	70
2.3. Indicators for Measuring Ionized Calcium .....	71
2.4. Chlorotetracycline, an Indicator for Bound Calcium .....	73
2.5. Methods for Localizing Calcium in the Cell .....	74
2.6. Calcium-EGTA Buffers: A Practical Approach .....	76
3. Calcium Ionophores .....	79
4. How Nerve Cell Calcium is Regulated .....	80
4.1. Ionized Calcium in Axons .....	80
4.2. Intracellular Calcium Buffers .....	81
4.3. Calcium Influx in the Axon .....	82
4.4. Calcium Efflux in the Axon .....	83

4.5. Fluxes of Calcium in Synaptosomes and Synaptic Membranes Vesicles .....	85
5. Calcium Storage and Binding by Subcellular Fractions .....	86
5.1. Mitochondrial and Nonmitochondrial Calcium Stores in Synaptosomes .....	86
5.2. ATP-Dependent Calcium Uptake by Synaptic Plasma Membranes .....	88
5.3. ATP-Dependent Calcium Uptake by Microsomes .....	89
5.4. Passive Calcium Binding to Nerve Membranes .....	90
6. Regulation of Enzyme Activity by Calcium .....	92
6.1. Interaction of Calcium with Calmodulin .....	92
6.2. Calcium and Regulation of Cyclic Nucleotide Level .....	94
6.3. Calcium and Membrane Protein Phosphorylation .....	95
6.4. Calcium-Stimulated ATPases .....	98
6.5. Other Enzymes Regulated by Calcium .....	100
7. Some Calcium Functions: Overview .....	100
7.1. Excitation-Secretion Coupling .....	100
7.2. Calcium and the Action of Narcotics .....	103
7.3. Calcium and the Action of Ethanol and Barbiturates .....	105
7.4. Calcium and Fast Axoplasmic Transport .....	107
8. Summary and Conclusions .....	107
References .....	110

## *Chapter 4*

### *Ammonia*

*A. M. Benjamin*

1. Introduction .....	117
2. Methods of Estimation of Ammonia .....	117
3. Ammonia Concentrations <i>in Vivo</i> and <i>in Vitro</i> .....	118
3.1. Ammonia Contents of Normal Brain, Blood, and Cerebrospinal Fluid .....	118
3.2. Conditions Affecting Ammonia Levels <i>in Vivo</i> .....	119
3.3. Control of Ammonia Formation by Brain Tissue <i>in Vitro</i> .....	120
4. Ammonia Metabolism in Brain <i>in Vivo</i> and <i>in Vitro</i> .....	122
4.1. Ammonia-Forming Processes: Sources of Ammonia in Brain .....	122
4.2. Ammonia-Utilizing Processes .....	125
5. Transport of Ammonia Across Cell Membranes <i>in Vivo</i> and <i>in Vitro</i> .....	126
5.1. pH and Ammonia Transport .....	126
5.2. Apparent Nonaccumulative Uptake of Ammonia in Brain .....	128
5.3. Ammonium Ions and the Sodium Pump .....	128
5.4. Membrane Permeabilities to Ammonium Ions .....	129
6. Covert Involvement of Ammonia in Brain Function .....	129
7. Effects of Ammonia <i>in Vivo</i> and <i>in Vitro</i> .....	130
7.1. Ammonia Toxicity .....	130

7.2. Effects of Ammonium on Electrical Activities and Ion Content of Brain Cells .....	130
7.3. Effects of Ammonium on Brain Cell Energetics and Morphology .....	131
7.4. Effects of Ammonium on Neurotransmitter Synthesis and Release .....	133
References .....	134

***Chapter 5******Water Spaces****Hanna M. Pappius*

1. Introduction .....	139
2. Definition of "Spaces" .....	139
3. Methodology .....	140
3.1. Inherent Problems .....	140
3.2. Experiments <i>in Vivo</i> .....	141
3.3. Experiments <i>in Vitro</i> .....	141
4. Spaces <i>in Vivo</i> .....	142
4.1. Marker Spaces .....	142
4.2. Extracellular Space Determined by Electrical Impedance Measurements .....	145
4.3. Lability of Fluid Compartments in Cerebral Tissue .....	145
4.4. Abnormal Spaces .....	146
5. Spaces <i>in Vitro</i> .....	146
6. Morphological Correlates of Marker Distribution Spaces and Delineation of Cellular Spaces .....	147
7. Conclusion .....	147
References .....	148

***Chapter 6******Cerebral Amino Acid Pools****Thomas L. Perry*

1. Introduction .....	151
2. Methods of Separating and Quantitating Amino Compounds in Brain .....	151
2.1. Deproteinization of Brain Homogenates .....	152
2.2. Measurement of One or a Few Amino Acids .....	152
2.3. Measurement of a Large Number of Amino Acids .....	152
2.4. Newer Techniques .....	153
3. Changes in Brain Amino Compounds with Increasing Death-to-Freezing Intervals .....	156
3.1. Experimental Animals .....	156
3.2. Human Brain .....	157

4. Free Amino Compounds in Brains of Laboratory Animals .....	158
5. Free Amino Compounds in Biopsied Human Brain .....	163
6. Regional Distribution of Amino Compounds in Brain .....	165
6.1. Human Brain .....	165
6.2. Regional Distribution of Brain Amino Acids in Laboratory Animals .....	167
7. Changes in Brain Amino Acid Content with Increasing Age .....	169
7.1. Changes with Age in Laboratory Mammals .....	169
7.2. Changes with Age in Human Brain .....	170
7.3. Changes in Brain GABA Content in Older Patients .....	170
8. Effects of Drugs on Brain Amino Acids .....	172
8.1. Drug Effects on the GABA System .....	172
8.2. Drug Effects on Other Brain Amino Acids .....	172
9. Abnormalities of Brain Amino Compounds in Human Disease .....	173
9.1. Genetically Determined Enzyme Deficiencies .....	173
9.2. Brain Amino Compounds in Autosomal Dominant Disorders ..	175
9.3. Amino Acid Changes in Other Neuropsychiatric Diseases ....	176
References .....	177

### *Chapter 7*

#### *Neuropeptides: An Overview*

*M. L. Brownstein and H. Gainer*

1. Introduction .....	181
2. Anatomy of Peptidergic Neurons .....	181
3. Biosynthesis of Peptides .....	184
4. Peptide Receptors .....	185
5. Peptide Degradation .....	185
6. Concluding Remarks .....	186
References .....	186

### *Chapter 8*

#### *Brain Trace Amines*

*Alan A. Boulton and Augusto V. Juorio*

1. Introduction .....	189
2. Methods .....	190
3. $\beta$ -Phenylethylamine .....	190
3.1. Presence and Regional Distribution .....	190
3.2. Neurophysiological Studies .....	192
3.3. Synthesis and Catabolism .....	192
3.4. Storage .....	194
3.5. Release .....	194
3.6. Drug Effects .....	195
4. Tyramines .....	195

4.1. Presence and Regional Distribution .....	195
4.2. Neurophysiological Studies .....	196
4.3. Synthesis and Catabolism .....	197
4.4. Storage .....	200
4.5. Uptake and Release .....	201
4.6. Drug Effects .....	204
5. Phenylethanolamine .....	207
6. Octopamines .....	208
6.1. Presence and Regional Distribution .....	208
6.2. Neurophysiological Studies .....	209
6.3. Synthesis and Catabolism .....	210
6.4. Storage .....	210
6.5. Uptake and Release .....	210
6.6. Drug Effects .....	211
7. Synephrine .....	211
8. Tryptamine .....	211
8.1. Presence and Regional Distribution .....	211
8.2. Neurophysiological Studies .....	212
8.3. Synthesis and Catabolism .....	212
8.4. Storage .....	214
8.5. Uptake and Release .....	215
9. Clinical Relevance .....	215
10. Hypotheses and Conclusions .....	217
References .....	217

*Chapter 9**Polyamines**N. Seiler*

1. Introduction .....	223
2. Synthetic and Catabolic Processes .....	225
2.1. Enzymes of Polyamine Biosynthesis .....	227
2.2. Enzymes Involved in the Interconversion and Catabolism of Polyamines .....	230
3. Polyamine Concentration in Brain .....	232
3.1. Developmental Aspects .....	233
3.2. Regional Distribution .....	237
3.3. Subcellular Localization .....	238
3.4. Transport .....	240
4. Turnover .....	241
4.1. The Experimental Approach .....	242
4.2. The Reutilization of Putrescine and Spermidine .....	242
4.3. The Physiological Significance of Putrescine and Spermidine Reutilization .....	243
4.4. The Validity of Turnover Rate Determinations .....	243

5. Polyamines and Brain Tumors .....	244
6. Effects of Exogenous Polyamines .....	245
7. Modulation of Polyamine Metabolism .....	247
8. Functional Considerations .....	248
References .....	249

*Chapter 10**Cyclic Nucleotides in the Central Nervous System**Kenneth A. Bonnet*

1. Introduction .....	257
1.1. Scope of the Chapter .....	257
1.2. The Role of Cyclic Nucleotides as Second Messengers in the Nervous System .....	257
2. Methods for Determining Cyclic Nucleotide Levels .....	259
2.1. Problems Associated with Rapid Postmortem Changes in Brain Cyclic Nucleotide Levels .....	259
2.2. Rapid Fixation Procedures to Stabilize Postmortem Levels for Measurement .....	259
2.3. Tissue Extraction Procedures for Cyclic Nucleotide Measurement .....	262
2.4. Methods of Quantitating Cyclic Nucleotides in Samples .....	262
3. Cyclic Nucleotides in the Central Nervous System .....	263
3.1. Cyclic Nucleotide Structure, Levels, and Distribution in Nervous System Tissue .....	263
3.2. Enzymes Synthesizing Cyclic Nucleotides .....	264
3.3. The Phosphodiesterases .....	264
4. Hormonal and Neurotransmitter Regulation of Cyclic Nucleotide Metabolism .....	265
5. Cyclic Nucleotide Regulation of Protein Phosphorylation .....	268
6. Cyclic Nucleotide Regulation of Neurotransmitter Synthesis and Release .....	269
6.1. Cyclic Nucleotide Regulation of Neurotransmitter Synthesis ..	269
6.2. Cyclic Nucleotide Regulation of Neurotransmitter Release ....	269
6.3. Cyclic Nucleotide Regulation of Neurotransmitter Receptor State .....	270
7. Neuropharmacology of Cyclic Nucleotides in the Central Nervous System .....	270
8. Cyclic Nucleotide Mediation of Behavior and Psychoendocrinology	271
8.1. Regulation of Hormone Release .....	271
8.2. Cyclic Nucleotides in Behavioral Systems .....	271
9. Cyclic Nucleotides in Blood and Other Body Fluids: Contributions from the Central Nervous System .....	273

9.1. Method for Determining Cyclic Nucleotide Levels in Body Fluids .....	273
9.2. Levels of Cyclic Nucleotides in Body Fluids .....	273
9.3. Changes in Cyclic Nucleotide Levels that Reflect Acute States .....	274
9.4. Changes in Cyclic Nucleotides in Body Fluids with Pathological States of Central Nervous System Function .....	274
References .....	275

*Chapter 11**Biopterin**E. Martin Gál*

1. Introduction .....	281
2. Occurrence of Pterins in Mammalian Brain .....	281
3. Cerebral Metabolism .....	284
3.1. Synthesis of Pterins <i>in Vivo</i> .....	284
3.2. Synthesis of Pterins <i>in Vitro</i> .....	286
4. Enzymology of Cerebral Biopterin Synthesis .....	287
4.1. Conversion of GTP to FPyd-P <sub>3</sub> .....	287
4.2. D-Erythro- <i>q</i> -dihydronopterin Triphosphate Synthetase .....	288
4.3. L-Erythro- <i>q</i> -dihydrobiopterin Synthetase .....	288
4.4. Quinonoid-Dihydropteridine Reductase .....	289
5. Catabolism of Pterins in the Brain .....	291
6. Cofactorial Role of Pterins in the Brain .....	291
6.1. Monooxygenases .....	291
6.2. Oxygenases and Other Enzymes .....	293
6.3. Mitochondrial Respiration .....	294
7. Clinical Aspects of Defects in Biopterin Synthesis .....	294
References .....	296

*Chapter 12**Neurons**Bert Csillik*

1. Building Blocks of the Nervous System .....	299
2. Structural Overview .....	300
3. Neuronal Proteins .....	301
4. Dale's Principle .....	302
5. Generation and Degeneration of Neurons .....	307
6. The Intracellular Signaling System of the Neuron .....	309
7. The Neuron: A Synaptochemical Entity of Protein Metabolism .....	312
References .....	315

***Chapter 13******Astrocytes****L. Hertz*

1. Introduction .....	319
2. Energy Metabolism .....	321
2.1. Basal Conditions .....	321
2.2. Effects of Ionic Deviations .....	323
3. Uptake and Metabolism of Amino Acids Including Amino Acid Transmitters .....	326
3.1. $\gamma$ -Aminobutyric Acid .....	326
3.2. Glutamate .....	330
3.3. Other Amino Acids .....	332
4. Uptake, Receptor Binding, and Effects of Other Transmitters and Drugs .....	332
4.1. Neuronal Signaling to Astrocytes .....	332
4.2. Uptake and Metabolism .....	333
4.3. Receptor Binding .....	335
4.4. Neurochemical Consequences of Receptor Occupancy .....	338
5. Transport of Inorganic Ions .....	340
5.1. Potassium .....	340
5.2. Sodium .....	344
5.3. Lithium .....	344
5.4. Calcium .....	344
5.5. Chloride .....	345
6. Macromolecular Constituents .....	346
6.1. Proteins .....	346
6.2. Nucleic Acids .....	347
6.3. Lipids .....	347
6.4. Carbohydrates .....	348
7. Concluding Remarks .....	348
References .....	348

***Chapter 14******Oligodendrocytes****Leonid Pevzner*

1. Introduction .....	357
2. Main Morphological Features of Oligodendrocytes .....	358
3. Main Physiological Features of Oligodendrocytes .....	358
4. Methods of Isolation of Oligodendrocytes .....	362
4.1. Microdissection of Perineuronal Satellite Oligodendrocytes ...	363
4.2. Bulk Isolation .....	363
4.3. Glial Cell Lines .....	364
4.4. Histochemistry <i>in Situ</i> .....	365

<b>5. Biochemical Markers for Oligodendrocytes .....</b>	<b>366</b>
5.1. Galactocerebrosides .....	366
5.2. Myelin Proteins .....	367
5.3. 2',3'-Cyclic Nucleotide 3'-Phosphohydrolase .....	367
5.4. Carbonic Anhydrase .....	368
5.5. Glycerol-3-Phosphate Dehydrogenase .....	368
<b>6. Biochemistry of Oligodendrocytes .....</b>	<b>368</b>
6.1. Oxidative Metabolism .....	368
6.2. Carbohydrate and Phosphorus Metabolism .....	370
6.3. Mineral and Amino Acid Composition .....	371
6.4. Lipid Metabolism .....	371
6.5. DNA Metabolism .....	374
6.6. RNA Metabolism .....	376
6.7. Protein Metabolism .....	378
<b>7. Functional Changes in the Oligodendrocyte Metabolism .....</b>	<b>380</b>
<b>8. Conclusion .....</b>	<b>387</b>
<b>References .....</b>	<b>388</b>

*Chapter 15**The Schwann Cell**Robert M. Gould, Dan Matsumoto, and Gary Mattingly*

<b>1. Introduction .....</b>	<b>397</b>
<b>2. Morphology .....</b>	<b>397</b>
2.1. Mature Nerve .....	397
2.2. Development of Peripheral Nerve .....	401
2.3. Response of the Schwann Cell to Injury .....	401
<b>3. Biochemistry of the Schwann Cell .....</b>	<b>402</b>
3.1. Mature Nerve .....	402
3.2. Development of Peripheral Nerve .....	406
3.3. Response to Injury .....	409
<b>4. Conclusion .....</b>	<b>411</b>
<b>References .....</b>	<b>412</b>

*Chapter 16**Physiological Neurochemistry of Cerebrospinal Fluid**James H. Wood*

<b>1. Introduction .....</b>	<b>415</b>
<b>2. Solute Composition .....</b>	<b>415</b>
2.1. Ions .....	416
2.2. Glucose .....	419
2.3. Lactic and Pyruvic Acids .....	420
2.4. Amino Acids .....	420
2.5. Protein .....	421

2.6. Ammonia and Glutamine .....	426
2.7. Urea, Creatinine, and Uric Acid .....	426
2.8. Polyamines .....	427
2.9. Lipids .....	427
2.10. Prostaglandins .....	427
2.11. Adenosine .....	428
3. Neurotransmitters, Their Precursors and Metabolites, and Cyclic Nucleotides .....	429
3.1. Biochemical Physiology .....	429
4. Peptides, Steroids, and Other Hormones .....	450
4.1. Entry into Cerebrospinal Fluid .....	451
4.2. Endogenous and Exogenous Hormones and Neuropeptides in Cerebrospinal Fluid .....	452
5. Enzymes .....	465
5.1. Glycolytic and Mitochondrial Enzymes .....	465
5.2. Neurotransmitter Metabolism .....	466
5.3. Lysosomal Enzymes .....	467
5.4. Amino Acid and Protein Metabolism .....	467
5.5. Miscellaneous Enzymes .....	468
5.6. Investigational Considerations .....	468
6. Conclusions .....	468
References .....	469
<i>Index</i> .....	489

# Cation Transport

*László Latzkovits and Csaba Fajszi*

## 1. INTRODUCTION

### 1.1. Basic Concepts of Cation Transport

According to the traditional concept<sup>1-3</sup> of cation transport, there are "active" and "passive" fluxes: the former drives cations uphill (against an electrochemical gradient) at the expense of ATP consumption, whereas the latter moves cations downhill (in the direction of the electrochemical gradient) by simple diffusion across membrane "imperfections" or "pores." This traditional concept of active and passive cation fluxes has proved to be inadequate for two main reasons.<sup>4-11</sup> (1) It has been demonstrated that the "active" pump transporting both  $\text{Na}^+$  and  $\text{K}^+$ , usually uphill, by direct consumption of ATP can also drive cation movements "on the level" (i.e., in the absence of any concentration gradient) or even downhill.<sup>4,5</sup> (2) Evidence has been collected that demonstrates that "passive" fluxes of cations are highly organized and are closely associated with important physiological functions<sup>6</sup>: many of them take place as part of counter- or cotransport mechanisms.<sup>5-9</sup> Thus, the energy of the electrochemical gradient of the cation actually moving downhill is not dissipated but is mostly consumed in promotion of the transport of different compounds (e.g., sugars, amino acids, other cations), in some cases even against a concentration gradient. In this way, "passive" fluxes of cations moving downhill can build up a concentration gradient for other cations without any waste of ATP.<sup>5-9</sup> Selectivity of the membrane for some "passive" cation fluxes enables it to convert the energy of primary ionic gradients into the energy needed for the maintenance of resting membrane potential as well as for cell excitation.<sup>6,10,11</sup>

The above facts gave the impetus for the construction of more appropriate new concepts and models of cation transport, but the various attempts have introduced quite divergent operational definitions of rather fictitious entities

---

*László Latzkovits* • Institute of Experimental Surgery, Medical School of Szeged, 6701 Szeged, Hungary. *Csaba Fajszi* • Institute of Biophysics, Biological Research Center, Hungarian Academy of Sciences, 6701 Szeged, Hungary.