

## CONTENTS

<b>PREFACE</b>	v
<b>I NEUROANATOMY AND PHYSIOLOGY</b>	<b>1</b>
<b>1.1 PASSIVE MODELS OF EXCITABLE CELLS</b>	
Johannes Jan Struijk	
1. Introduction .....	3
2. Properties of Various Excitable Cells .....	6
2.1. Excitable cells .....	6
2.2. Membrane .....	6
2.3. Ion channels.....	7
2.4. Ion transporters.....	8
3. Action Potential.....	8
4. Resting Potential .....	9
4.1. Diffusion .....	10
4.2. Migration .....	10
4.3. Nernst-Planck equation.....	11
4.4. Nernst equation.....	12
4.5. Donnan equilibrium.....	13
4.6. Sodium-potassium pump .....	13
4.7. Goldman's equation.....	14
5. Subthreshold Phenomena .....	15
5.1. I-t curve (based on passive model of membrane patch).....	15
5.2. Passive axon model (unmyelinated axon).....	18
5.3. Myelinated axon .....	22
5.4. Extracellular stimulation.....	22
5.5. Spherical cells .....	23
5.6. Nerve fibers.....	24
5.7. Rheobase and chronaxy for the case of external stimulation .....	27
References.....	28
<b>1.2 PERIPHERAL NERVOUS SYSTEM</b>	
K. W. Horch and P. R. Burgess	
1. Introduction .....	30
2. Proximal Component.....	30
3. Distal Component.....	31
3.1. Somatosensory system.....	32
3.2. Proprioceptive system .....	36
3.3. Skeletal motor system.....	41

4. Peripheral Nerves .....	41
5. Summary .....	44
References .....	45

### 1.3 ANATOMY AND PHYSIOLOGY OF THE CENTRAL NERVOUS SYSTEM

Vivian K. Mushahwar, Taleen Hanania, James Ingram, Kelvin E. Jones,  
Susan K. Patrick, and Kenneth W. Horch

1. Introduction .....	48
2. Spinal Cord .....	52
2.1. Overview .....	52
2.2. Structure .....	52
2.3. Function .....	59
2.4. Neuroprosthetics .....	64
3. Brainstem .....	69
3.1. Overview .....	69
3.2. Structure .....	70
3.3. Function .....	77
3.4. Neuroprosthetics .....	82
4. Cerebellum .....	84
4.1. Overview .....	84
4.2. Structure .....	85
4.3. Function .....	88
4.4. Neuroprosthetics .....	94
5. Thalamus .....	94
5.1. Overview .....	94
5.2. Structure .....	95
5.3. Function .....	99
5.4. Neuroprosthetics .....	103
6. The Basal Ganglia .....	104
6.1. Overview .....	104
6.2. Structure .....	105
6.3. Connectivity and function .....	108
6.4. Neuroprosthetics .....	114
7. Primary Somatosensory and Motor Cortex .....	114
7.1. Overview .....	114
7.2. Structure .....	115
7.3. Function .....	121
7.4. Neuroprosthetics .....	124
8. Summary .....	124
Acknowledgement .....	125
References .....	125

### 1.4 AUTONOMIC NERVOUS SYSTEM

Gurpreet Singh Dhillon and K. W. Horch

1. Introduction .....	137
2. Overview .....	137

3. Neuroanatomy of the Sympathetic Nervous System.....	139
4. Neuroanatomy of the ParaSympathetic Nervous System.....	141
5. Nerve Recordings and Efferent Fiber Activity .....	143
6. Cardiovascular Effects.....	144
7. Afferent Pathways .....	147
8. Vagal Nerve Stimulation .....	148
9. Enteric Nervous System .....	149
10. Central Control.....	150
11. Health and the Autonomic Nervous System .....	150
12. Challenges for Developing ANS Neuroprostheses .....	150
References.....	151

## 1.5 SKELETAL MUSCLE

Stanley Salmons

1. What Are Muscle Cells?.....	158
2. The Structure of Skeletal Muscle .....	159
3. Innervation of Skeletal Muscle.....	160
4. Motor Units and Motor Control.....	161
4.1. Motor units and their recruitment .....	161
4.2. The fibre types of adult skeletal muscle.....	162
4.3. Fatigue and the functional significance of motor unit organization .....	166
4.4. Fibre type transformation and the adaptive capacity of skeletal muscle .....	167
4.5. The difference between voluntary activation and electrical stimulation .....	169
5. Growth and Regulation of Skeletal Muscle Size .....	170
5.1. Growth and regulation of fibre diameter.....	170
5.2. Growth and regulation of fibre length.....	171
5.3. Denervation and disuse atrophy.....	172
6. Form and Function in Skeletal Muscles.....	172
6.1. Naming of muscles .....	172
6.2. Fibre architecture.....	173
6.3. Functional implications .....	173
6.4. Muscles and movement .....	176
References.....	179

## 1.6 VOLUNTARY MOTOR CONTROL

Ronald R. Riso

1. Introduction.....	184
2. Functional Anatomy and Physiology.....	187
2.1. Functions of the motor-cortex in the production of movement .....	187
2.2. Feedback loops involving the motor cortex .....	192
2.3. Anatomical structure of neo-cortex .....	192
2.4. The pyramidal track — an exclusive feature of higher primates.....	198
2.5. What is the unit of elemental control enacted by a pyramidal track fiber?.....	198
2.6. Descending inhibition from the cortex — a necessary function of the normal brain .....	200
2.7. Other brain structures involved in motor control — basal ganglia and cerebellum.....	201
2.8. EMG as a source of volitional commands in neuroprostheses .....	207
3. Motor Performance.....	210
3.1. Variability of reaction times .....	210

3.2. Size of the motor output buffer.....	210
3.3. Control of reaching movements.....	212
3.4. Assembly of complex movements from elemental parts.....	215
3.5. Sensory feedback for neuroprosthesis systems that restore movement in disabled individuals.....	219
4. Summary.....	224
References.....	226

## 1.7 THE VISUAL SYSTEM AS A NEUROPROSTHESIS SUBSTRATE: ANATOMY, PHYSIOLOGY, FUNCTION

Gislin Dagnelie and Eyal Margalit

1. Introduction.....	235
2. Anatomy and Physiology.....	237
2.1. Anatomy and physiology: The eye.....	237
2.2. Anatomy and physiology: Retina.....	238
2.3. Anatomy and physiology: Retino-cortical pathway.....	242
2.4. Anatomy and physiology: Visual cortex.....	244
2.5. Anatomy and physiology: Subcortical pathways.....	245
3. Function.....	247
3.1. Function: Roles of central (foveal) vision.....	247
3.2. Function: Roles of peripheral vision.....	248
3.3. Function: Roles of eye movements.....	249
3.4. Function: Other visual functions.....	250
3.5. Function: Effects of principal blinding diseases of the visual system.....	252
3.6. Function: A few remarks regarding visual development.....	254
4. Prospects for Prosthetic Vision Restoration.....	254
References.....	255

## 1.8 THE AUDITORY SYSTEM

R. K. Shepherd

1. Introduction.....	260
2. External and Middle Ears.....	260
3. The Cochlea.....	261
3.1. Cochlear anatomy.....	262
3.2. Cochlear neuroanatomy.....	264
3.3. Cochlear mechanics.....	265
3.4. The endocochlear potential.....	269
3.5. Hair cell transduction.....	269
3.6. The response of the auditory nerve.....	270
3.7. Conclusion.....	273
4. The Central Auditory System.....	273
4.1. Cochlear nucleus.....	274
4.2. Superior olivary complex.....	275
4.3. Inferior colliculus.....	275
4.4. Medial geniculate nucleus.....	276
4.5. Auditory cortex.....	276
5. Conclusion.....	277

Acknowledgments .....	277
References .....	277

## 1.9 NEUROPLASTICITY

Pablo A. Celnik, Michael J. Makley, Esteban Fridman, and Leonardo G. Cohen

1. Introduction .....	281
2. Technical Considerations for the Study of Plasticity in Humans .....	282
3. Studies of Cortical Reorganization in Intact Humans Using TMS .....	284
3.1. Transient deafferentation .....	284
3.2. Use-dependent plasticity .....	285
3.3. Disuse and plasticity .....	286
3.4. Procedural learning and plasticity .....	286
4. Studies of Cortical Reorganization in Patient Populations Using TMS .....	287
4.1. Amputees .....	287
4.2. Swallowing disorders .....	288
4.3. Spinal cord injury .....	289
4.4. Bell's palsy .....	289
4.5. Blindness .....	289
5. Modulation of Plasticity .....	291
6. Mechanisms Involved in Human Plasticity .....	292
7. Conclusions .....	292
References .....	293

## 1.10 SPINAL PLASTICITY

Victor Pikov

1. Introduction .....	302
2. Anatomy of Spinal Cord Reflexes and Their Supraspinal Control .....	303
3. Activity-dependent Plasticity of Somatic Spinal Cord Reflexes Following SCI .....	304
4. Plasticity in the Spinal Cord Reflexes Mediating Lower Urinary Tract Function Following SCI .....	305
5. Functional Electrical Stimulation to Promote Activity-Dependent Plasticity in the Spinal Cord .....	308
References .....	309

## II: EXTRACELLULAR STIMULATION AND RECORDING

317

### 2.1 ELECTRICAL STIMULATION OF THE PERIPHERAL NERVOUS SYSTEM: BIOPHYSICS AND EXCITATION PROPERTIES

Warren M. Grill

1. Introduction .....	319
2. The Peripheral Axon .....	321
3. Models of the Axon Membrane .....	322
3.1. Passive model of a membrane patch .....	322
3.2. Active model of a membrane patch .....	324
4. Reconstruction of the Action Potential .....	326
5. Models of the Axon .....	329

6. Excitation Properties of Myelinated Axons .....	331
6.1. Strength-duration relationship .....	333
6.2. Charge-duration relationship .....	333
6.3. Current-distance relationship .....	335
6.4. Current-diameter relationship .....	335
6.5. Conduction velocity .....	336
6.6. Stimulus polarity .....	336
6.7. Refractory period .....	338
7. Conclusions .....	338
Acknowledgement .....	339
References .....	339

## 2.2 THE THEORY OF PERIPHERAL NERVE RECORDING

Ken Yoshida and Johannes Struijk

1. Introduction — Components of the Recording System .....	342
1.1. Overview .....	342
1.2. The peripheral nervous system .....	343
1.3. The interface subsystem .....	345
1.4. The interpretation subsystem .....	346
2. Theory and Models for the Analysis of Nerve Signals .....	348
2.1. Some useful properties of the potential field .....	348
2.2. Volume conductor models .....	352
2.3. A model to analyse extracellular recordings from myelinated nerve fibers .....	356
3. Measuring Bio-Electrochemical Potentials .....	369
3.1. The electrochemical cell .....	370
3.2. Thermodynamics .....	375
3.3. Impedance and conductance .....	385
3.4. Electrode types .....	392
3.5. Recording .....	404
4. Signal and Noise .....	411
4.1. The signal .....	411
4.2. The noise .....	412
4.3. Evaluating signal quality .....	414
4.4. Voltage signal to noise ratio .....	416
4.5. Power signal to noise ratio .....	418
4.6. Spectral characteristics of the signal .....	419
4.7. Effect of filters .....	423
5. Concluding Remarks .....	426
References .....	426

## 2.3 CENTRAL NERVOUS SYSTEM STIMULATION

F. Rattay

1. Introduction .....	429
2. Calculation of the Electric Field .....	430
3. Compartment Model of a Target Neuron .....	432
4. Cochlear Neurons in Man and Cat .....	434
4.1. Influence of ion channel current fluctuations .....	436

4.2. Recording of neural activities .....	436
4.3. Finite element cochlea model .....	439
5. Electrically Stimulated Retinal Cells .....	440
6. Deep Brain and Spinal Cord Stimulation .....	443
References .....	445

## 2.4 THE THEORY OF CENTRAL NERVOUS SYSTEM RECORDING

Shy Shoham and Srikantan Nagarajan

1. Introduction .....	448
2. Extracellular Recording of Action Potentials .....	449
3. Multi-Unit Detection and Classification .....	454
4. Local-Field Potential and Far-Field Recordings .....	459
5. Representation of Time-Varying Information in Spike Trains .....	461
6. Stimulus Encoding in CNS Spike Trains .....	462
7. Conclusions .....	464
References .....	465

## III: MATERIALS FOR STIMULATION AND RECORDING

473

### 3.1 ELECTRODE MATERIALS FOR RECORDING AND STIMULATION

Thomas Stieglitz

1. Introduction .....	475
2. Requirements for Recording and Stimulation Electrodes .....	476
3. Basic Mechanisms at the Electrode-Electrolyte Phase Boundary .....	477
3.1. Capacitive mechanisms .....	478
3.2. Irreversible Faradic reactions .....	479
3.3. Reversible Faradic reactions .....	480
3.4. Valence change oxides .....	480
3.5. Estimation of the reversible potential limits for charge injection .....	481
4. Classification of Recording Electrodes .....	482
4.1. Polarization of electrodes .....	485
5. Electrical Modeling of the Phase Boundary .....	486
5.1. Noise of microelectrodes .....	489
6. Characterization of Electrodes .....	490
6.1. Measurement of the electrode impedance .....	490
6.2. Measurement of electrode surface reactions and detection of potential limits .....	493
6.3. Current pulse test .....	494
7. Material Properties .....	496
7.1. The maximum charge delivery capacity .....	496
7.2. Effects of stimulus waveforms on the reversible charge injection .....	497
7.3. An overview of electrode materials .....	499
7.4. Non-noble metal electrodes .....	499
7.5. Noble metal electrodes: Platinum .....	501
7.6. Valence change oxides: Iridium oxide .....	502
7.7. Capacitive electrodes .....	503
7.8. Glass microelectrodes .....	504
7.9. Carbon microelectrodes .....	505

7.10. Silicon based electrodes.....	505
7.11. Recording electrodes based on a field effect transistor.....	506
8. Technologies for Electrode Optimization.....	506
9. Concluding Remarks.....	510
References.....	511
Text Books.....	516

### 3.2 INSULATING BIOMATERIALS

David J. Edell

1. Introduction.....	517
1.1. History of insulating biomaterials.....	518
1.2. Insulating biomaterials for neuroprostheses.....	519
1.3. Historical failures of insulating biomaterials.....	521
1.4. Goals of current insulating biomaterials research.....	521
2. Approach — <i>in-vitro</i> and <i>in-vivo</i> .....	522
2.1. Accelerated testing.....	523
3. Methods.....	528
3.1. Designs.....	528
3.2. Measurement systems.....	529
3.3. Assembly of PassChip for implantation.....	541
3.4. PassChip Implant Results.....	542
4. Materials and Evaluations.....	547
4.1. Use of silicones as an implantable material.....	548
4.2. Use of fluorocarbons as an implantable material.....	563
4.3. <i>In-vivo</i> evaluations.....	565
4.4. Other materials and tests.....	567
4.5. Commercial materials — summary of results.....	573
5. Conclusions.....	574
Acknowledgements.....	575
References.....	575

### 3.3 VAPOR DEPOSITION OF BIOPASSIVATION COATINGS FOR NEUROPROSTHESES

Shashi K. Murthy, David J. Edell, and Karen K. Gleason

1. Introduction.....	580
1.1. Plasma enhanced chemical vapor deposition.....	581
1.2. Hot-filament chemical vapor deposition.....	582
2. Fluorocarbon Thin Films.....	582
3. Organosilicon Thin Films.....	586
4. Fluorocarbon-Organosilicon Copolymers.....	589
References.....	590

### 3.4 TISSUE REACTION TO ELECTRODES: THE PROBLEM OF SAFE AND EFFECTIVE STIMULATION OF NEURAL TISSUE

Douglas McCreery

1. Introduction.....	592
----------------------	-----



2. Electrochemistry of Charge Injection Into Physiologic Fluids .....	593
3. Stimulation-Induced Axonal Injury in the Ventral Cochlear Nucleus .....	598
4. Stimulation-Induced Injury and Safe Stimulation of Peripheral Nerves .....	600
5. Stimulation-Induced Depression of Neuronal Excitability .....	602
6. Summary and Conclusion .....	606
References .....	607

## IV: PERIPHERAL STIMULATION AND RECORDING

613

### 4.1 FUNCTIONAL ADAPTATION OF SKELETAL MUSCLE AND ITS APPLICATION TO CARDIAC ASSISTANCE

Eric Monnet and Stanley Salmons

1. Introduction .....	615
2. Muscle Transformation .....	616
2.1. Biochemical transformation .....	616
2.2. Physiological transformation .....	618
3. Differences Between Species .....	619
4. Dynamic Cardiomyoplasty: An Example of the Clinical Application of Muscle Transformation .....	620
4.1. Surgical technique for cardiomyoplasty .....	621
4.2. Mechanism of action of cardiomyoplasty .....	622
4.3. Skeletal muscle deterioration after dynamic cardiomyoplasty .....	623
4.4. Improving the protocol for dynamic cardiomyoplasty .....	625
5. Other Approaches to Cardiac Bio-Assist .....	627
6. Conclusion .....	628
References .....	628

### 4.2 PERIPHERAL NERVE AND MUSCLE STIMULATION

J. Thomas Mortimer and Narendra Bhadra

1. Introduction .....	638
2. Basic Concepts .....	639
3. Electrodes Placed on the Skin Surface .....	642
3.1. Introduction .....	642
3.2. Applications to the motor system .....	642
4. Electrodes Placed In or On the Muscle .....	644
4.1. Intramuscular electrodes .....	645
4.2. Epimysial electrodes .....	652
5. Electrodes Placed On or In the Nerve .....	654
5.1. Cuff electrodes .....	655
5.2. Intraneural electrodes .....	673
6. Summary .....	674
7. Addendum: Electrode Cleaning Instructions .....	675
7.1. Objective .....	675
7.2. Consumables .....	676
7.3. Equipment .....	676
7.4. Preparation .....	676

7.5. Precautions .....	676
7.6. Procedure.....	676
References .....	677

### 4.3 PERIPHERAL NERVE RECORDING ELECTRODES AND TECHNIQUES

Ken Yoshida and Ron Riso

1. Introduction .....	683
1.1. What place do peripheral nerve electrodes and recordings have in Functional Neuromuscular Stimulation systems?.....	683
1.2. Functional neuromuscular stimulation systems .....	684
1.3. Implanted electrodes.....	685
1.4. The peripheral nervous system .....	686
1.5. Methods of recording nerve activity .....	686
2. Electrodes.....	687
2.1. The ideal electrode .....	687
2.2. Overview of current electrode technologies .....	690
2.3. Intracellular electrodes .....	691
2.4. Intranural penetrating electrodes.....	695
2.5. Extranural electrodes .....	699
2.6. Miscellaneous electrodes.....	705
3. Design Considerations.....	712
3.1. Materials.....	713
3.2. Mechanical stabilization .....	714
3.3. Electrical considerations.....	717
4. Applications of Peripheral Nerve Recording for Feedback Control in FNS Systems .....	720
4.1. Heel strike detection for foot-drop FNS systems .....	721
4.2. Tactile sensing in grasp neuroprostheses .....	721
4.3. Cutaneous responses to contacting objects .....	724
4.4. Natural sensors for determining joint angle in FNS systems .....	727
4.5. Obtaining afferent signals from DRG cells.....	731
4.6. Evoked EMG as a sensory control signal in FNS systems .....	731
4.7. Use of FNS in the correction of sleep apnea.....	732
4.8. Feedback for FNS assisted micturition and continence.....	732
5. Trends .....	734
References.....	736

## V: CENTRAL STIMULATION AND RECORDING

745

### 5.1 NEURAL STIMULATION ELECTRODES: GEOMETRIC FACTORS

David J. Anderson and James Weiland

1. Introduction.....	747
2. The Electrochemistry of Conductive Media and the Tissue Interface.....	748
2.1. Conduction in the bulk electrolyte.....	748
2.2. Aqueous diffuse charge layer .....	749

2.3. The Helmholtz compact layer.....	750
2.4. The composite capacitance.....	751
2.5. Redox reactions.....	751
3. Tools for Electrochemical Analysis of Interfaces.....	751
3.1. Electrochemical Impedance Spectroscopy (EIS).....	752
3.2. Cyclic voltammograms.....	753
4. Dynamic Models of Electrodes.....	754
5. Large Scale Geometric Factors.....	754
5.1. Classical models.....	755
5.2. Geometries found in practical electrodes.....	755
6. Intermediate Scale Geometrical Factors.....	758
7. Summary and Conclusions.....	760
References.....	760

## 5.2 CNS RECORDING ELECTRODES AND TECHNIQUES

Daryl R. Kipke, David S. Pellinen and Patrick J. Rousche

1. Introduction.....	761
2. Microelectrode-Based Neural Recordings.....	763
2.1 Operating principles of recording microelectrodes.....	765
2.2 Microelectrode electrical characteristics.....	769
2.3 Effects of size, position, and shape of recording sites.....	773
2.4 Sources of noise.....	776
2.5 Signal conditioning, sampling, and signal processing.....	777
2.6 Microelectrode materials.....	777
3. Neural Implant Systems.....	778
4. Conclusions.....	781
Acknowledgements.....	781
References.....	782

## 5.3 SPINAL CORD AND ROOTLETS

Arthur Prochazka and Vivian K. Mushahwar

1. Introduction.....	786
2. Electrical Stimulation of the Nervous System.....	787
3. Electrical Stimulation of Peripheral Nerves.....	788
4. Basic Functional Anatomy of the Spinal Cord.....	789
5. Pacemaker Technology.....	790
6. Dorsal Column Stimulators.....	791
7. Sacral Root Stimulation for Bladder Control.....	791
8. Intraspinal Microstimulation (ISMS).....	793
9. Multi-Channel ISMS for Coordinated Control of Micturition.....	794
10. ISMS for Locomotion.....	796
11. Microelectrode Recordings in Spinal Roots and Spinal Cord.....	796
12. Concluding Remarks.....	799
Acknowledgements.....	800
References.....	800

## VI: EXISTING FES SYSTEMS

## 6.1 CONTROL ISSUES FOR MOTOR NEUROPROSTHESES

Dejan B. Popovic	
1. Introduction .....	809
2. Model Based Control.....	811
3. Mathematical Models for Simulation .....	813
4. Modeling of Skeletal Systems .....	814
5. Modeling of Muscles.....	816
6. Identification of Model Parameters .....	818
7. Nonanalytical Modeling of Movement.....	819
8. Controlling Movement of a Single Joint.....	824
9. Control of Standing .....	827
10. Control of Walking.....	828
11. Control of Grasping and Reaching .....	829
12. Conclusion .....	834
References.....	834

## 6.2 UPPER AND LOWER EXTREMITY MOTOR NEUROPROSTHESES

Kevin L. Kilgore and Robert F. Kirsch	
1. Introduction .....	844
2. Motor Neuroprosthesis Components .....	846
3. Clinical Objectives of Motor Neuroprostheses .....	848
3.1. Lower extremity .....	848
3.2. Upper extremity.....	848
4. Targeted Disabilities and Candidate Selection .....	849
4.1. Lower extremity .....	849
4.2. Upper extremity.....	850
5. Motor System Requirements .....	851
5.1. Lower extremity .....	851
5.2. Upper extremity.....	852
6. Stimulation Patterns .....	853
6.1. Lower extremity .....	853
6.2. Upper extremity.....	854
7. User Generated Control Signals .....	855
7.1. Lower extremity .....	855
7.2. Upper extremity.....	855
8. Neuroprosthesis Feedback .....	857
8.1. Lower extremity .....	857
8.2. Upper extremity.....	857
9. Clinically Deployed Motor Neuroprostheses .....	858
9.1. Lower extremity .....	858
9.2. Upper extremity.....	864
10. Current Challenges and Status of Motor Neuroprostheses.....	867
References.....	868

## 6.3 COCHLEAR IMPLANTS

P. M. Seligman and R. K. Shepherd

1. Introduction .....	878
2. Deafness Induced Changes Within the Auditory System.....	879
3. Overview of a Cochlear Implant System .....	880
3.1. The speech processor.....	882
3.2. The receiver-stimulator.....	882
3.3. The electrode array .....	882
4. Speech Processor Details.....	883
4.1. Pre-amplification and front end processing .....	883
4.2. Signal analysis.....	883
4.3. Frequency mapping.....	884
4.4. Amplitude mapping.....	884
4.5. Output encoding .....	885
4.6. Coil driver and transmitting coil.....	885
5. The Receiver-Stimulator .....	886
5.1. The receiver coil.....	886
5.2. Implant electronics .....	886
5.3. Stimulation regime .....	886
5.4. Charge recovery techniques.....	888
5.5. Electrode configurations.....	889
5.6. Receiver-stimulator packaging .....	889
5.7. Control of charge.....	890
6. System Issues .....	891
6.1. Speech processing strategies.....	891
6.2. Reverse telemetry.....	892
6.3. Power consumption .....	892
6.4. Power sources.....	893
6.5. Programming systems .....	894
6.6. The role of the audiologist.....	894
6.7. Current hardware .....	895
6.8. Upgrades .....	895
6.9. Bilateral implantation.....	895
7. Future Developments .....	896
7.1. Hardware.....	896
7.2. Speech processing .....	896
7.3. Combined electric/acoustic stimulation .....	896
7.4. Pre-processing .....	897
7.5. Non-speech sounds.....	897
7.6. Other technologies.....	898
8. Conclusions.....	898
9. Web Addresses.....	898
Acknowledgements .....	898
References.....	898

## 6.4 NEUROMODULATION AND OTHER ELECTROSTIMULATORY TECHNIQUES

Philip E.V. Van Kerrebroeck

1. Introduction .....	905
2. Electrical Stimulation in Spinal Cord Injury .....	906
3. Electrical Stimulation for Chronic Lower Urinary Tract Dysfunction .....	909
References .....	912

## 6.5 DEEP BRAIN STIMULATION

Erwin B. Montgomery Jr. and Kenneth B. Baker

1. Introduction .....	915
2. What is DBS? .....	917
3. Current Development of DBS .....	918
4. Parkinson's Disease — Prototypical Example of a DBS Therapy .....	919
5. Mechanisms of DBS .....	921
5.1. Neuronal level .....	922
5.2. Mechanisms of STN DBS .....	927
5.3. Implications for the current theory of PD pathophysiology .....	929
5.4. Alternative hypothesis from stochastic resonance .....	929
6. Advances in Systems Physiology and Pathophysiology .....	933
7. Future Applications of DBS .....	933
References .....	934

## 6.6 NEURAL RECORDING ON CLOSE SPACED ARRAYS

David J. Anderson

1. Introduction .....	936
2. Types of Close-Spaced-Arrays .....	938
2.1. Single and multishank planer arrays .....	939
3. Distribution of Activity Over an Array .....	939
3.1. The observation model .....	941
4. Discovery of the Steering Matrix and the Signals .....	942
4.1. The example .....	942
4.2. Solving the example .....	945
5. Using the Array Potential Distribution Information for Spatial Location .....	947
6. Summary and Conclusions .....	949
References .....	950

## 6.7 RESPIRATORY MUSCLE STIMULATION IN PATIENTS WITH SPINAL CORD INJURY

Anthony F. DiMarco

1. Introduction .....	951
2. Diaphragm Pacing via Phrenic Nerve Stimulation .....	952
2.1. Stimulation devices .....	954
2.2. Patient evaluation .....	958
2.3. Surgical implantation .....	960
2.4. Initial pacing regimes .....	961

2.5. Complications.....	963
2.6. Patient outcomes.....	966
3. Diaphragm Pacing via Intramuscular Diaphragm Electrodes .....	967
4. Intercostal Muscle Pacing.....	968
5. Expiratory Muscle Stimulation to Produce Cough .....	971
References.....	973

## VII: FUTURE FES SYSTEMS

979

### 7.1 THE FUTURE OF MOTOR NEUROPROSTHESES

Robert F. Kirsch and Kevin L. Kilgore<sup>2</sup>

1. Introduction.....	981
2. Activation.....	982
3. Command and Control .....	985
3.1. Command sources .....	985
3.2. Control .....	987
4. Devices.....	989
5. Targeted Populations.....	992
6. Alternative and Complementary Approaches .....	993
7. Commercialization Issues.....	994
8. Conclusions.....	995
References.....	995

### 7.2 CHALLENGES TO DEVELOPING A NEURALLY CONTROLLED UPPER LIMB PROSTHESIS

Gurpreet S. Dhillon and Sanford Meek

1. Introduction.....	1005
2. Peripheral Nerve Anatomy.....	1006
3. Nerve Injuries.....	1008
3.1. Neurolysis .....	1010
4. Mechanical Properties of Peripheral Nerves.....	1011
4.1. Nerve response to stretch.....	1012
4.2. Nerve response to compression .....	1013
5. Desired Properties for a Neural Interface .....	1013
6. Changes in the Peripheral Nerves Postaxotomy .....	1014
6.1. Neuroma formation .....	1014
6.2. Proximal stump degeneration .....	1015
6.3. Differential atrophy of fibers and electrophysiological changes .....	1015
6.4. Conduction velocity changes .....	1018
7. Central Nervous System Plasticity .....	1018
8. Sensory Feedback.....	1018
8.1. Electrocutaneous and electromechanical stimulation.....	1019
8.2. Extraneural stimulation.....	1020
8.3. Intraneural stimulation.....	1020
9. Motor Control.....	1021
9.1. Cuff electrodes .....	1021
9.2. LIFEs.....	1021
10. Information Transfer Between Electrodes and the Prosthesis.....	1022

11. The Artificial Arm.....	1022
11.1. Control.....	1022
11.2. Computation.....	1023
11.3. Sensory feedback.....	1024
11.4. Fault detection.....	1025
11.5. Fitting and training.....	1025
11.6. Hybrid systems.....	1025
11.7. Day-to-Day use.....	1026
12. Summary.....	1026
References.....	1027

### 7.3 SPINAL CORD STIMULATION FOR RESTORING LOWER EXTREMITY FUNCTION

Vivian K. Mushahwar and Arthur Prochazka

1. Introduction.....	1035
2. Summary of Currently Available FES Systems for the Lower Extremities.....	1035
3. Future FES Systems for the Lower Extremities.....	1037
3.1. Leadless intramuscular BION™ implants.....	1037
3.2. Intraspinal microstimulation (ISMS).....	1039
3.3. Boosting residual descending drive in incomplete SCI.....	1046
4. Concluding Comments on ISMS.....	1048
Acknowledgements.....	1048
References.....	1048

### 7.4 EMERGING FES APPLICATIONS FOR CONTROL OF THE URINARY BLADDER

Nico J. M. Rijkhoff

1. Introduction.....	1054
2. Bladder Emptying by Sacral Nerve Root Stimulation in Spinal Cord Injury.....	1055
3. An Injectable Stimulator to Manage Detrusor Overactivity.....	1057
4. Closed Loop Control for Management of Neurogenic Detrusor Overactivity.....	1059
5. Management of Mixed Urinary Incontinence by Electrical Stimulation.....	1062
References.....	1064

### 7.5 CAN VISION BE RESTORED BY ELECTRICAL STIMULATION?

Eyal Margalit, Gislin Dagnelie, James D. Weiland, Eugene de Juan Jr.,

Mark S. Humayun

1. Introduction.....	1067
2. Visual Cortex Prostheses.....	1068
3. Retinal Prostheses.....	1070
4. Optic Nerve Prosthesis.....	1074
5. Electrical Excitation of Neurons Along the Visual Pathways.....	1075
5.1. Threshold parameters for electrical stimulation.....	1075
5.2. <i>In-vitro</i> retinal excitation.....	1077
5.3. <i>In-vivo</i> retinal excitation.....	1078
5.4. The target cell of epiretinal electrical stimulation.....	1079



6. Safety of Visual Prostheses .....	1081
6.1. Damage caused by electrical current .....	1081
6.2. Infection and inflammation .....	1082
6.3. Heat damage .....	1083
6.4. Electrodes .....	1083
6.5. Safety of device implantation .....	1086
6.6. Attachment methods .....	1087
6.7. Hermetic sealing of the electronics .....	1087
7. Efficacy of the Visual Prosthesis .....	1088
7.1. Psychophysical experiments .....	1088
7.2. Power supply .....	1090
8. Summary .....	1091
Acknowledgments .....	1092
References .....	1093

## 7.6 CENTRAL AUDITORY PROSTHESES

R. K. Shepherd

1. Introduction .....	1103
2. Electrical Stimulation of the Auditory Nerve Using Modiolar Electrodes .....	1104
3. Auditory Brainstem Implants .....	1106
4. Electrical Stimulation of the Central Auditory Pathway .....	1110
5. Conclusions .....	1111
Acknowledgements .....	1111
References .....	1112

## 7.7 VESTIBULAR PROSTHETICS

Daniel M. Merfeld and Richard D. Rabbitt

1. Introduction .....	1115
2. Vestibular Physiology .....	1117
2.1. Neurophysiologic responses .....	1117
2.2. Electrochemical regulation .....	1118
2.3. Electrical stimulation of the vestibular system. ....	1119
3. Design of Vestibular Prostheses .....	1131
3.1. Hair cell support approaches .....	1131
3.2. Compensatory approaches .....	1131
4. Neural Prosthetic Challenges .....	1134
Acknowledgements .....	1137
References .....	1138

## 7.8 BRAIN-COMPUTER INTERFACES FOR VERBAL COMMUNICATION

Niels Birbaumer, Ute Strehl and Thilo Hinterberger

1. Introduction .....	1146
2. Brain-Computer Interfaces (BCIs) for Complete Paralysis: The Locked-in Syndrome .....	1146
3. Slow Brain Potentials and Behavior .....	1147
4. Structure of the Thought Translation Device .....	1149
4.1. Signal processing .....	1151
4.2. The language support program .....	1151
4.3. Learning progress .....	1152

4.4. Results .....	1153
5. Training.....	1153
5.1. Step 1: basic training .....	1153
5.2. Step 2: copy spelling .....	1154
5.3. Step 3: free spelling .....	1154
6. Conclusions .....	1154
Acknowledgements .....	1155
References .....	1156

## 7.9 DESIGN PRINCIPLES OF A NEUROMOTOR PROSTHETIC DEVICE

Mijail Serruya and John Donoghue

1. Introduction .....	1159
2. Control Signals .....	1160
2.1. Field potentials .....	1161
2.2. Event related potentials .....	1162
2.3. Cortical surface recordings .....	1163
2.4. Intracortical recordings .....	1164
2.5. Extracellular unit activity .....	1164
3. Recording Devices .....	1166
3.1. Surface and subdural recording .....	1166
3.2. Intracortical recording .....	1166
3.3. Physical constraints of an NMP interface .....	1169
4. Decoding Algorithms: Principles .....	1170
4.1. Two learning machines .....	1171
4.2. Discrete and continuous signals .....	1171
4.3. Mapped variables .....	1173
4.4. Control and meta-control .....	1174
4.5. Human calibration .....	1174
4.6. Error measures .....	1176
5. Decoding Algorithms: Examples .....	1176
5.1. Population vector .....	1176
5.2. Principle component analysis .....	1177
5.3. Maximum likelihood estimation: discrete control .....	1178
5.4. Linear filters .....	1178
5.5. Adaptive neural networks .....	1180
5.6. Feedback-driven models .....	1181
5.7. Number of cells .....	1181
5.8. Summary of decoding algorithms .....	1182
6. Output Devices .....	1182
6.1. Assistive devices .....	1183
6.2. Computer cursors .....	1184
6.3. Robotic assistants .....	1184
6.4. Functional electrical stimulation .....	1185
6.5. Appliances and vehicles .....	1186
6.6. Sensory feedback .....	1186
7. Integrated Control .....	1187
References .....	1190

## 7.10 NEXT GENERATION OF CORTICAL DEVICES

Patrick J. Rousche and Daryl R. Kipke

1. Introduction .....	1197
2. Neural Implant Failure Modes: Known and Postulated .....	1199
2.1. Host responses .....	1199
2.2. Material, device and system responses .....	1200
2.3. Surgical and insertion issues .....	1202
3. Successful Implant Strategies .....	1205
3.1. Improving neurocompatibility: immediate focus areas .....	1205
3.2. Advanced improvement: critical future developments .....	1209
References .....	1214

## VIII: REGULATORY ISSUES

1217

### 8.1 BIOCOMPATIBILITY OF NEUROPROTHESES

Jeffery R. Nelson and Jerry R. Nelson

1. Introduction .....	1219
2. History .....	1219
3. Investigational Device Exemption .....	1221
4. PMAs .....	1223
5. Design Control .....	1224
6. Device Tracking .....	1225
7. Biocompatibility .....	1225
7.1. GLP .....	1228
7.2. Animal tests .....	1229
7.3. Extraction media .....	1229
7.4. Cytotoxicity .....	1230
7.5. Sensitization .....	1231
7.6. Irritation tests .....	1231
7.7. Systemic toxicity tests .....	1232
7.8. Subchronic toxicity .....	1232
7.9. Genotoxicity .....	1233
7.10. Implantation .....	1233
7.11. Hemocompatibility .....	1234
7.12. Chronic toxicity .....	1234
7.13. Carcinogenicity .....	1235
7.14. Immunotoxicity .....	1236
7.15. Sterilization .....	1236
7.16. Composite testing .....	1237
8. Resource Materials .....	1237
References .....	1238

## INDEX

1241