

## Contents

	<i>Preface</i>	page xvii
	<i>Reserved Physical Symbols and Quantities</i>	xx
	<i>List of Abbreviations</i>	xxii
<b>1</b>	<b>Introduction</b>	<b>1</b>
	1.1 Forward Modeling of Extracellular Signals	4
	1.2 Overview of the Contents of This Book	6
	1.3 Guide to Reading This Book	8
	1.4 Guide to Simulations, Codes, and Figures	9
<b>2</b>	<b>Charges, Currents, Fields, and Potentials in the Brain</b>	<b>11</b>
	2.1 Electric Charge	12
	2.2 Electric Fields and Potentials	14
	2.2.1 Reference Point for Potentials	15
	2.2.2 Electroneutrality and Debye Shielding	17
	2.3 Coarse-Graining	19
	2.3.1 Coarse-Graining 1: From Individual Atoms and Charges to Concentrations and Currents	19
	2.3.2 Coarse-Graining 2: From a Mishmash of Entangled Neurites to Smooth Neural Tissue	20
	2.4 Electric Currents and Current Conservation	21
	2.4.1 Conductive Currents	22
	2.4.2 Capacitive Currents	24
	2.4.3 Diffusive Currents	26
	2.4.4 Other Currents	27
	2.5 Electric Currents in the Brain	28
	2.6 Extracellular Potentials in the Brain	29
	2.6.1 Neurons as Current Sources	30
	2.6.2 Two-Step (MC+VC) Scheme for Modeling Extracellular Potentials	31
	2.6.3 Alternative Schemes for Modeling Extracellular Potentials	32
	2.6.4 Bi- and Tri-domain Models	34
	2.7 Foundations of Electromagnetism	35
	2.7.1 Maxwell's Equations	35
	2.7.2 Quasi-static Approximations of Maxwell's Equations	37
	2.7.3 The Lorentz Force	39

<b>3</b>	<b>Neural Dynamics</b>	<b>41</b>
3.1	Membrane Currents	43
3.1.1	Capacitive Current	44
3.1.2	Leakage Current	45
3.1.3	Active Ion Channels	46
3.1.4	Synapses	50
3.1.5	External Current Injections	52
3.2	Multicompartment Models	53
3.2.1	Multicompartment Formalism	53
3.2.2	Endpoint Boundary Conditions	56
3.2.3	Passive Multicompartment Models	56
3.2.4	Two-Compartment Model	57
3.2.5	Biophysically Detailed Cell Models	57
3.2.6	The Hay Model	58
3.3	Cable Theory	58
3.3.1	Steady-State Solutions of the Cable Equation	59
3.3.2	Ball-and-Stick Neuron Model	60
3.3.3	Intrinsic Dendritic Filtering	61
3.4	Ion-Concentration Dynamics and Reversal Potentials	64
3.4.1	Nernst Potential	66
3.4.2	Goldman-Hodgkin-Katz Current Equation	67
3.4.3	Reversal Potential of a Non-specific Ion Channel	68
3.4.4	Leakage-Reversal Potential	68
3.4.5	Resting Membrane Potential	69
3.4.6	Intracellular Calcium Dynamics	70
3.4.7	Intracellular Dynamics of Other Ion Species	71
3.5	Neural Network Models	72
3.5.1	Networks of Biophysically Detailed Neurons	72
3.5.2	Spiking Point-Neuron Network Models	74
3.5.3	Neural Population Models	76
3.6	Discussion: From Neurodynamics to Electric Brain Signals	78
<b>4</b>	<b>Volume-Conductor Theory</b>	<b>79</b>
4.1	Point-Source Approximation	80
4.2	Line-Source Approximation	81
4.3	Current-Source Density Description	83
4.3.1	Use of the Current-Source Density Equation	84
4.3.2	Derivation of the Current-Source Density Equation	86
4.3.3	Tissue Currents versus Extracellular Currents	90
4.4	Dipole Approximation	91
4.4.1	Distance-Decay of Potential from Dipole	93
4.4.2	Multi-dipole Approximation	96

4.5	Modeling Recording Electrodes	97
4.5.1	Point-Electrode Contacts	98
4.5.2	Spatially Extended Electrode Contacts	99
4.5.3	Effect of Electrode Shanks	101
4.5.4	Effect of Position of Reference Electrode	102
4.6	Electric and Magnetic Brain Stimulation	102
4.6.1	Electric Stimulation	102
4.6.2	Magnetic Stimulation	103
<b>5</b>	<b>Conductivity of Brain Tissue</b>	<b>105</b>
5.1	Conductivity $\sigma_{ef}$ of the Extracellular Fluid	105
5.2	Conductivity $\sigma_e$ of the Extracellular Medium	107
5.2.1	Porous-Medium Approximation	107
5.2.2	Estimate of $\sigma_e$	109
5.3	Conductivity $\sigma_t$ of Brain Tissue	110
5.4	Frequency Dependence of the Tissue Conductivity	112
5.4.1	Complex Conductivity	115
5.4.2	Estimates of the Capacitive Effects in the Brain	118
5.5	Spatial Frequency Dependence of the Tissue Conductivity	123
5.6	Anisotropic Conductivity	123
5.7	Inhomogeneous Conductivity	124
5.7.1	Planar Boundaries: Tissue Interfaces and In Vitro Slice Recordings	126
<b>6</b>	<b>Schemes for Computing Extracellular Potentials</b>	<b>129</b>
6.1	Forward-Model Predictions from MC Neuron Models	130
6.2	Computing Axial and Membrane Currents	131
6.2.1	Axial and Membrane Currents in the Continuum Limit	131
6.2.2	Axial Currents in Discretized Cables	131
6.2.3	Membrane Currents in Discretized Cables	135
6.2.4	Matrix Formalism for Computing Currents	135
6.3	Application to Extracellular Potentials and Magnetic Fields	137
6.3.1	Point Sources	137
6.3.2	Line Sources	138
6.3.3	Finite-Sized Contacts	138
6.3.4	Ground-Truth Current-Source Density (CSD)	138
6.3.5	Magnetic Fields in an Infinite Homogeneous Conductor	139
6.3.6	Forward Models for Dipole Moments	139
6.3.7	Forward-Model Predictions from Population and Network Models Using the MC+VC Scheme	141
6.4	Extracellular Signal Predictions from Network Models	142
6.4.1	Case Study I: An MC Neuron Network with Extracellular Signal Predictions	144
6.4.2	Case Study II: The Hybrid Scheme for Computing Extracellular Signals	146

6.4.3	Case Study III: Predicting Kernels for Computing Extracellular Signals	151
6.4.4	Case Study IV: Proxies for Heuristic Signal Approximations	153
<b>7</b>	<b>Spikes</b>	<b>158</b>
7.1	Properties of Spikes	159
7.2	Modeling Spikes	162
7.2.1	Spikes from Morphologically Detailed Neuron Models	162
7.2.2	Spikes from Two-Compartment Neuron Model	164
7.2.3	Spikes from Ball-and-Stick Neuron Model	164
7.3	Analysis of Spike Shapes and Sizes	165
7.3.1	Approximate Spike Formulas	167
7.3.2	Distance-Dependence of Spike Amplitudes	169
7.3.3	Spike-Amplitude Dependence on Neuronal Parameters	170
7.3.4	Spike-Shape Dependence on Distance	171
7.3.5	Proxies for Spike Shapes	171
7.3.6	Generalization of Findings to Other Neuron Morphologies	172
7.4	Spikes from Action Potentials (APs) Initiated in the Axon	173
7.5	Spikes from Neurons with Active Dendrites	174
7.6	Axonal Spikes	175
7.7	Effects of Measurement Device on Spike Recordings	177
7.7.1	Physical Sizes of Contacts and Shafts of the Recording Electrode	178
7.7.2	Spikes Recorded in Micro-electrode Arrays (MEAs)	179
7.8	Spikes from Many Neurons	180
7.8.1	Synchronous Spikes	180
7.8.2	Benchmarking Data for Spike Sorting	184
7.8.3	Population Firing-Rate Estimation from MUA	184
<b>8</b>	<b>Local Field Potentials (LFPs)</b>	<b>187</b>
8.1	Neural Sources of LFPs	188
8.2	LFP from Single Postsynaptic Neuron	189
8.2.1	Single Synaptic Input	189
8.2.2	Multiple Synaptic Inputs	192
8.2.3	Correlations in Synaptic Input	195
8.2.4	Decay of LFP with Distance	198
8.2.5	Single-Neuron Shape Function	200
8.3	LFP from Neural Populations	201
8.3.1	Spatial Reach of LFPs	202
8.3.2	Spatial Decay of LFPs	210
8.3.3	LFP from Single Presynaptic Neurons: Unitary LFPs	213
8.4	Frequency Content of LFPs	215
8.4.1	Intrinsic Dendritic Filtering	215
8.4.2	LFP Filtering and Power Laws	218
8.4.3	Frequency Content of Population LFPs	222

8.5	LFP Contributions from Active Ion Channels	228
8.5.1	Subthreshold Active Ion Channels	229
8.5.2	Sodium Spikes	234
8.5.3	Calcium Spikes	235
8.5.4	NMDA Spikes	237
8.6	Slow Potentials	237
8.7	Network LFPs	239
<b>9</b>	<b>Electroencephalography (EEG)</b>	<b>241</b>
9.1	Forward Modeling of EEG Signals	242
9.2	Head Models	244
9.2.1	Simplified Head Models	244
9.2.2	Detailed Head Models	245
9.3	Effect of Head Models on EEG Signals	247
9.3.1	Effect of Dipole Position on EEG Signals	248
9.3.2	Effect of Dipole Orientation on EEG Signals	250
9.3.3	Comparison of Simple and Detailed Head Models	251
9.4	Effect of Dipole Correlations on EEG Signals	251
9.4.1	Uncorrelated Dipoles	253
9.4.2	Correlated Dipoles	255
9.4.3	Analytical Theory	256
9.5	Biophysically Detailed Modeling of Neural Activity for EEG Signals	258
9.5.1	From Membrane Currents to Dipoles	259
9.5.2	Differences and Similarities between LFP and EEG Signals	262
9.5.3	Cell-Type Specific EEG Contributions	262
9.5.4	Applications of MC+VC Scheme to EEG Signals	264
9.6	Simulating Large-Scale Neural Activity and Resulting EEG Signals	264
9.6.1	Kernel-Based Approaches	265
9.6.2	EEG Proxies	267
9.6.3	Minimally Sufficient Biophysical Models	267
9.6.4	Neural Mass and Neural Field Approaches to Modeling EEG Signals	268
<b>10</b>	<b>Electrocorticography (ECoG)</b>	<b>270</b>
10.1	Method of Images (MoI)	271
10.2	Dipole Approximation	272
10.3	Electrode Effects	274
<b>11</b>	<b>Magnetoencephalography (MEG)</b>	<b>276</b>
11.1	From Currents in the Brain to Magnetic Fields outside the Head	277
11.2	Sources of the MEG Signal	279
11.2.1	Impressed Current Density	279
11.2.2	Impressed versus Primary Currents	279
11.2.3	Dipole Sources	280

11.3	Head Models	281
11.3.1	Infinite Homogeneous Head Model	281
11.3.2	Spherically Symmetric Head Model	281
11.3.3	Detailed Head Models	282
11.4	MEG for Infinite Homogeneous and Spherically Symmetric Head Models	283
11.4.1	Radial Dipoles	284
11.4.2	Tangential Dipoles	285
11.4.3	Summary of Findings	285
11.5	Applications of the MC+VC scheme to MEG Signals	285
11.6	Magnetic Fields inside the Brain	286
<b>12</b>	<b>Diffusion Potentials in Brain Tissue</b>	<b>289</b>
12.1	What Is a Diffusion Potential?	290
12.2	Theory for Computing Diffusion Potentials	293
12.2.1	General Mathematical Frameworks	293
12.2.2	Analytical Estimates of the Diffusion Potential	295
12.3	Can Diffusion Potentials Be Seen in Recorded LFPs?	298
12.3.1	Magnitude of Diffusion Potentials	300
12.3.2	Temporal Development of Diffusion Potentials	302
12.3.3	Power Spectra of Diffusion Potentials	303
12.4	Extracellular Volume Conduction versus Electrodiffusion	305
<b>13</b>	<b>Final Comments and Outlook</b>	<b>309</b>
13.1	Common Misconceptions about Extracellular Potentials	309
13.2	Applicability of the MC+VC Scheme	310
13.2.1	Specification of Parameters	311
13.2.2	Experimental Comparison	311
13.2.3	Ephaptic Interactions	312
13.3	Outlook	313
13.3.1	Areas of Application of Forward Modeling	313
13.3.2	Future of Large-Scale Network Simulations	315
<b>Appendix A</b>	<b>Frequency-Dependent Length Constant</b>	<b>317</b>
<b>Appendix B</b>	<b>Derivation of the Current-Dipole Approximation</b>	<b>319</b>
<b>Appendix C</b>	<b>Electric Stimulation</b>	<b>324</b>
<b>Appendix D</b>	<b>Derivation of the Point-Source Equation for Anisotropic Medium</b>	<b>327</b>
<b>Appendix E</b>	<b>Statistical Measures</b>	<b>329</b>
<b>Appendix F</b>	<b>Fourier-Based Analyses</b>	<b>331</b>
<b>Appendix G</b>	<b>Derivation of Formulas for Population Signals</b>	<b>335</b>

<b>Appendix H</b>	<b>Equations for Computing Magnetic Fields</b>	<b>338</b>
<b>Appendix I</b>	<b>Derivation of the MC+ED Scheme</b>	<b>341</b>
	<i>References</i>	343
	<i>Index</i>	375