

Contents

Preface

1 Introduction

1.1 Neurons	1
1.1.1 What Is a Spike?	2
1.1.2 Where Is the Threshold?	3
1.1.3 Why Are Neurons Different, and Why Do We Care?	6
1.1.4 Building Models	6
1.2 Dynamical Systems	8
1.2.1 Phase Portraits	8
1.2.2 Bifurcations	11
1.2.3 Hodgkin Classification	14
1.2.4 Neurocomputational properties	16
1.2.5 Building Models (Revisited)	20
Review of Important Concepts	21
Bibliographical Notes	21

2 Electrophysiology of Neurons

2.1 Ions	25
2.1.1 Nernst Potential	26
2.1.2 Ionic Currents and Conductances	27
2.1.3 Equivalent Circuit	28
2.1.4 Resting Potential and Input Resistance	29
2.1.5 Voltage-Clamp and I-V Relation	30
2.2 Conductances	32
2.2.1 Voltage-Gated Channels	33
2.2.2 Activation of Persistent Currents	34
2.2.3 Inactivation of Transient Currents	35
2.2.4 Hyperpolarization-Activated Channels	36
2.3 The Hodgkin-Huxley Model	37
2.3.1 Hodgkin-Huxley Equations	37
2.3.2 Action Potential	41
2.3.3 Propagation of the Action Potentials	42

2.3.4 Dendritic Compartments	43
2.3.5 Summary of Voltage-Gated Currents	44
Review of Important Concepts	49
Bibliographical Notes	50
Exercises	50
3 One-Dimensional Systems	53
3.1 Electrophysiological Examples	53
3.1.1 I-V Relations and Dynamics	54
3.1.2 Leak + Instantaneous $I_{Na,p}$	55
3.2 Dynamical Systems	57
3.2.1 Geometrical Analysis	59
3.2.2 Equilibria	60
3.2.3 Stability	60
3.2.4 Eigenvalues	61
3.2.5 Unstable Equilibria	61
3.2.6 Attraction Domain	62
3.2.7 Threshold and Action Potential	63
3.2.8 Bistability and Hysteresis	66
3.3 Phase Portraits	67
3.3.1 Topological Equivalence	68
3.3.2 Local Equivalence and the Hartman-Grobman Theorem	69
3.3.3 Bifurcations	70
3.3.4 Saddle-Node (Fold) Bifurcation	74
3.3.5 Slow Transition	75
3.3.6 Bifurcation Diagram	77
3.3.7 Bifurcations and I-V Relations	77
3.3.8 Quadratic Integrate-and-Fire Neuron	80
Review of Important Concepts	82
Bibliographical Notes	83
Exercises	83
4 Two-Dimensional Systems	89
4.1 Planar Vector Fields	89
4.1.1 Nullclines	92
4.1.2 Trajectories	94
4.1.3 Limit Cycles	96
4.1.4 Relaxation Oscillators	98
4.2 Equilibria	99
4.2.1 Stability	100
4.2.2 Local Linear Analysis	101
4.2.3 Eigenvalues and Eigenvectors	102
4.2.4 Local Equivalence	103

4.2.5	Classification of Equilibria	103
4.2.6	Example: FitzHugh-Nagumo Model	106
4.3	Phase Portraits	108
4.3.1	Bistability and Attraction Domains	108
4.3.2	Stable/Unstable Manifolds	109
4.3.3	Homoclinic/Heteroclinic Trajectories	111
4.3.4	Saddle-Node Bifurcation	113
4.3.5	Andronov-Hopf Bifurcation	116
	Review of Important Concepts	121
	Bibliographical Notes	122
	Exercises	122
5	Conductance-Based Models and Their Reductions	127
5.1	Minimal Models	127
5.1.1	Amplifying and Resonant Gating Variables	129
5.1.2	$I_{Na,p} + I_K$ -Model	132
5.1.3	$I_{Na,t}$ -model	133
5.1.4	$I_{Na,p} + I_h$ -Model	136
5.1.5	$I_h + I_{Kir}$ -Model	138
5.1.6	$I_K + I_{Kir}$ -Model	140
5.1.7	I_A -Model	142
5.1.8	Ca^{2+} -Gated Minimal Models	147
5.2	Reduction of Multidimensional Models	147
5.2.1	Hodgkin-Huxley model	147
5.2.2	Equivalent Potentials	151
5.2.3	Nullclines and I-V Relations	151
5.2.4	Reduction to Simple Model	153
	Review of Important Concepts	156
	Bibliographical Notes	156
	Exercises	157
6	Bifurcations	159
6.1	Equilibrium (Rest State)	159
6.1.1	Saddle-Node (Fold)	162
6.1.2	Saddle-Node on Invariant Circle	164
6.1.3	Supercritical Andronov-Hopf	168
6.1.4	Subcritical Andronov-Hopf	174
6.2	Limit Cycle (Spiking State)	178
6.2.1	Saddle-Node on Invariant Circle	180
6.2.2	Supercritical Andronov-Hopf	181
6.2.3	Fold Limit Cycle	181
6.2.4	Homoclinic	185
6.3	Other Interesting Cases	190

6.3.1	Three-Dimensional Phase Space	190
6.3.2	Cusp and Pitchfork	192
6.3.3	Bogdanov-Takens	194
6.3.4	Relaxation Oscillators and Canards	198
6.3.5	Bautin	200
6.3.6	Saddle-Node Homoclinic Orbit	201
6.3.7	Hard and Soft Loss of Stability	204
	Bibliographical Notes	205
	Exercises	210
7	Neuronal Excitability	215
7.1	Excitability	215
7.1.1	Bifurcations	216
7.1.2	Hodgkin's Classification	218
7.1.3	Classes 1 and 2	221
7.1.4	Class 3	222
7.1.5	Ramps, Steps, and Shocks	224
7.1.6	Bistability	226
7.1.7	Class 1 and 2 Spiking	228
7.2	Integrators vs. Resonators	229
7.2.1	Fast Subthreshold Oscillations	230
7.2.2	Frequency Preference and Resonance	232
7.2.3	Frequency Preference in Vivo	237
7.2.4	Thresholds and Action Potentials	238
7.2.5	Threshold manifolds	240
7.2.6	Rheobase	242
7.2.7	Postinhibitory Spike	242
7.2.8	Inhibition-Induced Spiking	244
7.2.9	Spike Latency	246
7.2.10	Flipping from an Integrator to a Resonator	248
7.2.11	Transition Between Integrators and Resonators	251
7.3	Slow Modulation	252
7.3.1	Spike Frequency Modulation	255
7.3.2	I-V Relation	256
7.3.3	Slow Subthreshold Oscillation	258
7.3.4	Rebound Response and Voltage Sag	259
7.3.5	AHP and ADP	260
	Review of Important Concepts	264
	Bibliographical Notes	264
	Exercises	265

8 Simple Models	267
8.1 Simplest Models	267
8.1.1 Integrate-and-Fire	268
8.1.2 Resonate-and-Fire	269
8.1.3 Quadratic Integrate-and-Fire	270
8.1.4 Simple Model of Choice	272
8.1.5 Canonical Models	278
8.2 Cortex	281
8.2.1 Regular Spiking (RS) Neurons	282
8.2.2 Intrinsically Bursting (IB) Neurons	288
8.2.3 Multi-Compartment Dendritic Tree	292
8.2.4 Chattering (CH) Neurons	294
8.2.5 Low-Threshold Spiking (LTS) Interneurons	296
8.2.6 Fast Spiking (FS) Interneurons	298
8.2.7 Late Spiking (LS) Interneurons	300
8.2.8 Diversity of Inhibitory Interneurons	301
8.3 Thalamus	304
8.3.1 Thalamocortical (TC) Relay Neurons	305
8.3.2 Reticular Thalamic Nucleus (RTN) Neurons	306
8.3.3 Thalamic Interneurons	308
8.4 Other Interesting Cases	308
8.4.1 Hippocampal CA1 Pyramidal Neurons	308
8.4.2 Spiny Projection Neurons of Neostriatum and Basal Ganglia	311
8.4.3 Mesencephalic V Neurons of Brainstem	313
8.4.4 Stellate Cells of Entorhinal Cortex	314
8.4.5 Mitral Neurons of the Olfactory Bulb	316
Review of Important Concepts	319
Bibliographical Notes	319
Exercises	321
9 Bursting	325
9.1 Electrophysiology	325
9.1.1 Example: The $I_{Na,p} + I_K + I_{K(M)}$ -Model	327
9.1.2 Fast-Slow Dynamics	329
9.1.3 Minimal Models	332
9.1.4 Central Pattern Generators and Half-Center Oscillators	334
9.2 Geometry	335
9.2.1 Fast-Slow Bursters	336
9.2.2 Phase Portraits	336
9.2.3 Averaging	339
9.2.4 Equivalent Voltage	341
9.2.5 Hysteresis Loops and Slow Waves	342
9.2.6 Bifurcations “Resting \leftrightarrow Bursting \leftrightarrow Tonic Spiking”	344

9.3	Classification	347
9.3.1	Fold/Homoclinic	350
9.3.2	Circle/Circle	354
9.3.3	SubHopf/Fold Cycle	359
9.3.4	Fold/Fold Cycle	364
9.3.5	Fold/Hopf	365
9.3.6	Fold/Circle	366
9.4	Neurocomputational Properties	367
9.4.1	How to Distinguish?	367
9.4.2	Integrators vs. Resonators	368
9.4.3	Bistability	368
9.4.4	Bursts as a Unit of Neuronal Information	371
9.4.5	Chirps	372
9.4.6	Synchronization	373
	Review of Important Concepts	375
	Bibliographical Notes	376
	Exercises	378
10	Synchronization	385
	Solutions to Exercises	387
	References	419
	Index	435
10	Synchronization (www.izhikevich.com)	443
10.1	Pulsed Coupling	444
10.1.1	Phase of Oscillation	444
10.1.2	Isochrons	445
10.1.3	PRC	446
10.1.4	Type 0 and Type 1 Phase Response	450
10.1.5	Poincare Phase Map	452
10.1.6	Fixed points	453
10.1.7	Synchronization	454
10.1.8	Phase-Locking	456
10.1.9	Arnold Tongues	456
10.2	Weak Coupling	458
10.2.1	Winfree's Approach	459
10.2.2	Kuramoto's Approach	460
10.2.3	Malkin's Approach	461
10.2.4	Measuring PRCs Experimentally	462
10.2.5	Phase Model for Coupled Oscillators	465
10.3	Synchronization	467

10.3.1 Two Oscillators	469
10.3.2 Chains	471
10.3.3 Networks	473
10.3.4 Mean-Field Approximations	474
10.4 Examples	475
10.4.1 Phase Oscillators	475
10.4.2 SNIC Oscillators	477
10.4.3 Homoclinic Oscillators	482
10.4.4 Relaxation Oscillators and FTM	484
10.4.5 Bursting Oscillators	486
Review of Important Concepts	488
Bibliographical Notes	489
Solutions	497

tic circuits, but also on the *electrophysiological properties of neurons*. Even if two neurons in different regions of the nervous system possess identical morphological features, they may respond to the same synaptic input in very different manners because of each cell's intrinsic properties.

McCormick (2004)

Much of present neuroscientific research concerns voltage- and second-gated currents in individual cells. The goal of understanding the cell's intrinsic neurocomputational properties is widely accepted that knowing the currents suffices to determine what the cell is doing and what it's not doing. This, however, contradicts a half-century-old observation that neurons having currents can nevertheless exhibit quite different dynamics. For example, two neurons having presumably similar electrophysiology (all spikes, no rebound, no afterhyperpolarization, no rebound), Hodgkin (1948) found a DC-current of twice the size, and discovered that some preparations could exhibit repetitive spiking at extremely low frequencies, while the others discharged in a narrow frequency band. This observation was largely ignored by the neuroscience community until the seminal paper by Rinzel and Ermentrout (1989), who showed that the difference in behavior is due to different bifurcation mechanisms of excitability.

Let us treat the amplitude of the injected current in Hodgkin's experiments as a bifurcation parameter. When the amplitude is small, the cell is quiescent; when the amplitude is large, the cell fires repetitive spikes. When we change the amplitude of the injected current, the cell undergoes a transition from quiescence to repetitive spiking. From the dynamical systems point of view, the transition corresponds to a bifurcation from equilibrium to a limit cycle attractor. The type of bifurcation determines the most fundamental computational properties of neurons, such as the class of excitability, the presence or nonexistence of threshold, all-or-none spikes, subthreshold oscillations, sensitivity to generate postinhibitory rebound spikes, bistability of resting and spiking states, whether the neuron is an integrator or a resonator, and so on.

This book is devoted to a systematic study of the relationship between electrophysiology, bifurcations, and computational properties of neurons. The reader will learn why neurons having nearly identical currents may undergo distinct bifurcations, and hence they have fundamentally different neurocomputational properties. (Conversely, cells