

# Contents

<b>Preface</b>	<b>xv</b>
<b>1 Introduction</b>	<b>1</b>
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
<b>2 Electrophysiology of Neurons</b>	<b>25</b>
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
<b>3</b>	<b>One-Dimensional Systems</b>	<b>53</b>
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
<b>4</b>	<b>Two-Dimensional Systems</b>	<b>89</b>
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
<b>5</b>	<b>Conductance-Based Models and Their Reductions</b>	<b>127</b>
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
<b>6</b>	<b>Bifurcations</b>	<b>159</b>
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
<b>7</b>	<b>Neuronal Excitability</b>	<b>215</b>
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

<b>8</b>	<b>Simple Models</b>	<b>267</b>
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
<b>9</b>	<b>Bursting</b>	<b>325</b>
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
	<b>10 Synchronization</b>	<b>385</b>
	<b>Solutions to Exercises</b>	<b>387</b>
	<b>References</b>	<b>419</b>
	<b>Index</b>	<b>435</b>
	<b>10 Synchronization (www.izhikevich.com)</b>	<b>443</b>
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	Winfrey'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