Contents

Preface xv

1 Introduction 1
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 25
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 $I_{\mathrm{Na,p}}$ 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 $I_{\mathrm{Na,p}}+I_{\mathrm{K}}$-Model . . . 132
5.1.3 $I_{\mathrm{Na,t}}$-model . . . 133
5.1.4 $I_{\mathrm{Na,p}}+I_{\mathrm{h}}$-Model . . . 136
5.1.5 $I_{\mathrm{h}}+I_{\mathrm{Kir}}$-Model . . . 138
5.1.6 $I_{\mathrm{K}}+I_{\mathrm{Kir}}$-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 $I_{\mathrm{Na,p}}+I_{\mathrm{K}}+I_{\mathrm{K(M)}}$-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 ↔ Bursting ↔ 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