

Preface

- Quantitative biosciences at all scales of life
- The goal
- The structure of this book
- You can do it

xiii
xiii
xv
xvii
xxi

Acknowledgments

xxiii

I MOLECULAR AND CELLULAR BIOSCIENCES

1

1 Fluctuations and the Nature of Mutations

3

- 1.1 Chance favors the independent mutation
- 1.2 Cellular phenotypes
- 1.3 Mutations that depend on selection
- 1.4 Independent mutations: A continuous model
- 1.5 Modeling the growth of (discrete) mutants
- 1.6 Variance of mutants when mutations are independent of selection
- 1.7 On (in)direct inference
- 1.8 Take-home messages
- 1.9 Homework problems
- 1.10 Technical appendix

3
6
7
11
15
18
20
22
22
25

2 Bistability of Genetic Circuits

29

- 2.1 More is different
- 2.2 Molecular cast and scene
- 2.3 The first ingredient: Regulation of a target gene
- 2.4 Feedback and bistability—autoregulation
- 2.5 The dynamics of a genetic toggle switch
- 2.6 Take-home messages
- 2.7 Homework problems
- 2.8 Technical appendix

29
31
33
39
43
47
48
50

3	Stochastic Gene Expression and Cellular Variability	57
3.1	Living with randomness	57
3.2	Stochasticity in gene regulation	60
3.3	Characterizing dynamics of individual cells, given stochastic gene expression	64
3.4	Is gene expression bursty?	68
3.5	The geometry of bursts	72
3.6	Take-home messages	77
3.7	Homework problems	77
3.8	Technical appendix	80
4	Evolutionary Dynamics: Mutations, Selection, and Diversity	87
4.1	Evolution in action	87
4.2	Selection and the disappearance of diversity	91
4.3	Mechanisms that restore diversity	96
4.4	Stochasticity in the evolution of populations—baseline expectations	99
4.5	Evolutionary dynamics with stochasticity and selection	103
4.6	Sweeps or hitchhiking or both?	107
4.7	Take-home messages	110
4.8	Homework problems	110
4.9	Technical appendix	113
II	ORGANISMAL BEHAVIOR AND PHYSIOLOGY	119
5	Robust Sensing and Chemotaxis	121
5.1	On taxis	121
5.2	Why swim?	123
5.3	The behavior of swimming <i>E. coli</i>	125
5.4	Chemotaxis machinery	127
5.5	Signaling cascades	129
5.6	Fine-tuned adaptation	132
5.7	Buffering and robust cellular adaptation	135
5.8	Take-home messages	137
5.9	Homework problems	138
5.10	Technical appendix	142

6	Nonlinear Dynamics and Signal Processing in Neurons	145
6.1	Walking in the path of Hodgkin and Huxley	145
6.2	The brain: Memory, learning, and behavior	148
6.3	Of ions and neurons	151
6.4	Dynamical properties of excitable neuronal systems	159
6.5	From neurons to neural networks and information processing	163
6.6	Take-home messages	167
6.7	Homework problems	168
6.8	Technical appendix	170
7	Excitations and Signaling from Cells to Tissue	173
7.1	From excitable cells to excitable systems	173
7.2	Principles of oscillatory dynamics	176
7.3	Relaxation oscillations—a generalized view	180
7.4	Principles of excitability: From cardiac cells to tissue	184
7.5	Take-home messages	188
7.6	Homework problems	189
7.7	Technical appendix	191
8	Organismal Locomotion through Water, Air, and Earth	195
8.1	Movement from within	195
8.2	Movement with brief moments in air	198
8.3	Principles of slow swimming	205
8.4	Terrestrial locomotion	212
8.5	Take-home messages	215
8.6	Homework problems	215
8.7	Technical appendix	217
III	POPULATIONS AND ECOLOGICAL COMMUNITIES	223
9	Flocking and Collective Behavior: When Many Become One	225
9.1	Life is with other organisms	225
9.2	Endogenous vs. exogenous drivers of spatial ordering	228
9.3	Vicsek model: Uniting static and dynamic order	236
9.4	Collective decision making at the flock scale	241
9.5	Take-home messages	245

9.6	Homework problems	245
9.7	Technical appendix	247
10	Conflict and Cooperation Among Individuals and Populations	251
10.1	Games, relatively speaking	251
10.2	Payoffs: A classic approach	255
10.3	From payoffs to populations	259
10.4	Games that real organisms play	263
10.5	Feedback between strategies and the environment	271
10.6	Take-home messages	275
10.7	Homework problems	275
10.8	Technical appendix	277
11	Eco-evolutionary Dynamics	281
11.1	The power of exponentials	281
11.2	Canonical models of population dynamics	285
11.3	Predator-prey dynamics	289
11.4	Toward predator-prey dynamics with rapid evolution	294
11.5	Take-home messages	299
11.6	Homework problems	299
11.7	Technical appendix	302
12	Outbreak Dynamics: From Prediction to Control	309
12.1	Modeling in the age of pandemics	309
12.2	The core model of an outbreak: The SIR model	312
12.3	The shape of an outbreak	316
12.4	Principles of control	321
12.5	EVD: A case study in control given uncertainty	323
12.6	On the ongoing control of SARS-CoV-2	327
12.7	Take-home messages	330
12.8	Homework problems	330
12.9	Technical appendix	333
IV	THE FUTURE OF ECOSYSTEMS	339
13	Ecosystems: Chaos, Tipping Points, and Catastrophes	341
13.1	Ecosystems—the integrated frontier	341
13.2	Chaos in communities	344

13.3	Condorcet and catastrophes	348
13.4	Thresholds in ecosystems and the Earth system	351
13.5	The challenge continues	354
References		357
Index		369
Color plates follow page 152		

But the Italian biologist D'Ancona had a problem. D'Ancona was an Italian biologist who was puzzled by the abundance of fishes in the Adriatic Sea during World War I. The war had closed most fisheries, but rather than increasing the number of all fish, the closed fisheries seemed to have paradoxical effects on fish populations. The closed fisheries seemed to benefit some species—predators—like shark and dogfish, whose numbers went up—while other species—prey—like sea bass and sea bream, whose numbers went down. When the fisheries reopened, the effects reversed. Puzzled, D'Ancona wrote to his son-in-law, the mathematician Vito Volterra. This correspondence—published by H. Lotka and G. Sibly in *The Ecology of Numbers*—was the catalyst for a major discovery.

Volterra realized that the fishing was a source of mortality. The feedback between predator and prey was disrupted. A simple system in which prey could thrive in the absence of predators and predators could live with high mortality rates in the absence of prey. These three rules—growth, limitation and mortality—were enough to generate a wide set of conditions (Volterra 1926). First, when prey were abundant, predators would grow in number; they would deplete prey, yet as prey became scarce, predators would starve, enabling prey to regrow. Second, they realized a system can oscillate without external oscillatory pressure. Instead, the oscillations arose from endogenous and nonlinear feedback. Specifically, the fact that the rate of prey population increase is a product of the prey and predator populations. The model was applied to recreate his son-in-law's puzzle. It was predicted that prey population would drop while predator populations would go up as a function of the strength of the fishing pressure.

The model discovered and developed in parallel by the American physicist Alfred Lotka (1925) is now known as the Lotka-Volterra model of predator-prey dynamics. It was not the only model of a potentially paradoxical series of changes in the early twentieth-century fishery. It was a harbinger of a far broader phenomenon. Yet the model also had an important feature: the initial conditions mattered. That is, if one were to begin a system with a certain number of predators and prey, the model predicted whether the system would grow and then prey out to that initial point. Similarly, if the system had started with too many predators, then the model would predict oscillations that would eventually settle at a new starting point. Put simply speaking, these are termed "neutral" or "conserved" quantities in the system. Such conservation laws may be important in other contexts, but in this context they point to pathologies in the ecological model. The original form of the Lotka-Volterra model showed how predator-prey dynamics could