Frank C. Hoppensteadt Charles S. Peskin

Modeling and Simulation in Medicine and the Life Sciences

Second Edition

With 93 Illustrations

Springer

Frank C. Hoppensteadt
Center for Systems Science
and Engineering
Arizona State University
Tempe, AZ 85287-7606
USA
fchoppen@asu.edu

Charles S. Peskin
Department of Mathematics
Courant Institute of
Mathematical Sciences
New York University
New York, NY 10012
USA
peskin@cims.nyu.edu

Series Editors

J.E. Marsden
Control and Dynamical Systems,
107-81
California Institute of Technology
Pasadena, CA 91125
USA

L. Sirovich
Division of Applied Mathematics
Brown University
Providence, RI 02912
USA

M. Golubitsky
Department of Mathematics
University of Houston
Houston, TX 77204-3476
USA

S.S. Antman
Department of Mathematics
and
Institute for Physical Science
and Technology
University of Maryland
College Park, MD 20742-4015
USA

Cover illustration: cover art by Charles S. Peskin and Peter H. Carrington.

Mathematics Subject Classification (2000): 92-01, 92B05, 92D99

Library of Congress Cataloging-in-Publication Data
Hoppensteadt, F.C.
Modeling and simulation in medicine and the life sciences / Frank C. Hoppensteadt, Charles S. Peskin.–2nd ed.
p. cm. – (Texts in applied mathematics ; 10)
Original title: Mathematics in medicine and the life sciences.
Includes bibliographical references and index.
ISBN 978-1-4419-2871-9
1. Biomathematics. 2. Population biology–Mathematics. 3. Physiology–Mathematics. I. Peskin, Charles S. II. Hoppensteadt, F.C. Mathematics in medicine and the life sciences. III. Title. IV. Series.
QH323.5 .H67 2001
570'.1'51—dc21 2001032010

MATLAB and Simulink are registered trademarks of The MathWorks, Inc.

ISBN 978-1-4419-2871-9 ISBN 978-0-387-21571-6 (eBook)
DOI 10.1007/978-0-387-21571-6

© 2002, 1992 Springer-Verlag New York, Inc.
Softcover reprint of the hardcover 2nd edition 1992

All rights reserved. This work may not be translated or copied in whole or in part without the written permission of the publisher (Springer-Verlag New York, Inc., 175 Fifth Avenue, New York, NY 10010, USA), except for brief excerpts in connection with reviews or scholarly analysis. Use in connection with any form of information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed is forbidden.
The use in this publication of trade names, trademarks, service marks, and similar terms, even if they are not identified as such, is not to be taken as an expression of opinion as to whether or not they are subject to proprietary rights.

9 8 7 6 5 4 3 2 (Corrected printing, 2004) SPIN 10965207

Springer-Verlag is part of *Springer-Sciences+Business Media*

springeronline.com

Contents

Series Preface vii
Preface ix

Introduction 1

1 The Heart and Circulation 5
1.1 Plan of the Circulation 5
1.2 Volume, Flow, and Pressure 7
1.3 Resistance and Compliance Vessels 8
1.4 The Heart as a Pair of Pumps 10
1.5 Mathematical Model of the Uncontrolled Circulation . . 14
1.6 Balancing the Two Sides of the Heart and the Two Circulations 18
1.7 The Need for External Circulatory Control Mechanisms . 20
1.8 Neural Control: The Baroreceptor Loop 21
1.9 Autoregulation 25
1.10 Changes in the Circulation Occurring at Birth 28
1.11 Dynamics of the Arterial Pulse 33
1.12 Computer Simulation of Pulsatile Blood Flow 39
1.13 Suggestions for Computing Projects Concerning the Circulation 63
1.14 Annotated References 68
Exercises 69

2 Gas Exchange in the Lungs **75**
2.1 The Ideal Gas Law and the Solubility of Gases 76
2.2 The Equations of Gas Transport in One Alveolus 78
2.3 Gas Transport in the Lung 82
2.4 Optimal Gas Transport 83
2.5 Mean Alveolar and Arterial Partial Pressures 85
2.6 Transport of O_2 87
2.7 Computer Solution of the Equations for O_2 Transport in the Lung 91
2.8 Computing Projects Concerning Oxygen Transport by the Lung 104
2.9 Annotated References 107
Exercises 107

3 Control of Cell Volume and Electrical Properties of Cell Membranes **109**
3.1 Osmotic Pressure and the Work of Concentration 109
3.2 A Simple Model of Cell Volume Control 113
3.3 The Movement of Ions Across Cell Membranes 115
3.4 The Interaction of Electrical and Osmotic Effects 118
3.5 The Hodgkin–Huxley Equations for the Nerve Action Potential 124
3.6 Computer Simulation of the Nerve Action Potential . . . 132
3.7 Suggestions for Computing Projects Concerning the Nerve Impulse 139
3.8 Annotated References 143
Exercises 144

4 The Renal Countercurrent Mechanism **147**
4.1 The Nephron 147
4.2 Dynamics of Na^+ and H_2O: Transport along the Renal Tubules 150
4.3 The Loop of Henle 152
4.4 The Juxtaglomerular Apparatus and the Renin–Angiotensin System 155
4.5 The Distal Tubule and Collecting Duct: Concentrating and Diluting Modes 157
4.6 Remarks on the Significance of the Juxtaglomerular Apparatus 158
4.7 How Nephrons Do Better Than a Factor of e 159
4.8 Computing Project on the Interacting Nephron Population Model 166
4.9 Annotated References 168
Exercises 169

5 Muscle Mechanics **171**
5.1 The Force–Velocity Curve 171
5.2 Crossbridge Dynamics 173
5.3 Computer Simulation of Crossbridge Attachment and Detachment 179
5.4 Suggested Computing Projects on Crossbridge Dynamics 188
5.5 Annotated References 190
Exercises 190

6 Neural Systems **193**
6.1 Guttman's Experiments on Phase Locking 195
6.2 Biological Rhythms 197
6.2.1 Modulating the Clock on the Wall 198
6.2.2 Biological Clocks 199
6.2.3 Electronic Clocks: Voltage–Controlled Oscillators 200
6.3 Model Neural Networks 200
6.3.1 A Thalamocortical Circuit. 201
6.3.2 Hippocampus 203
6.4 Annotated References 207
Exercises 208

7 Population Dynamics **215**
7.1 Bacterial Cultures 216
7.1.1 Batch Culture Growth 217
7.1.2 Least-Squares Estimation of the Growth Rate . . 221
7.2 Age Structures 222
7.2.1 Cohort Analysis 223
7.2.2 Birth Rates 224
7.2.3 Age Distributions 228
7.3 Microbial Ecology 230
7.3.1 Uptake of Nutrients 230
7.3.2 Growth and Quiescence 232
7.3.3 Biofilms and Growth in a Continuous Flow 234
7.3.4 A Solutivory Food Chain 236
7.4 Nonlinear Reproduction Curves 237
7.4.1 Compensatory Growth: Verhulst's Model 238
7.4.2 Chaos 243
7.5 Controlling Populations 248
7.5.1 Cell Synchronization 249
7.5.2 Cohort Dynamics near the Limits of Growth . . . 250
7.5.3 Harvesting: Economics of Populations 252
7.6 Annotated References 256
Exercises 257

8 Genetics **267**
8.1 Population Genetics 269
8.1.1 Natural Selection 269
8.1.2 Slow Selection 272
8.1.3 Genotype Frequencies 273
8.1.4 Random Genetic Drift 275
8.2 Biotechnology 277
8.2.1 Plasmids 277
8.2.2 Control of Plasmid Replication 281
8.2.3 Regulation of Gene Expression 286
8.2.4 Stoichiometry of Metabolic Pathways 290
8.3 Annotated References 291
Exercises 292

9 A Theory of Epidemics **295**
9.1 Spread of Infection Within a Family 296
9.2 The Threshold of an Epidemic 300
9.3 Predicting the Severity of an Epidemic 303
9.4 Annotated References 306
Exercises 306

10 Patterns of Population Growth and Dispersal **311**
10.1 Random Walks and the Process of Diffusion 312
10.1.1 Random Walks 313
10.1.2 Boundary Conditions 314
10.1.3 Sample Paths 316
10.1.4 Diffusion Approximation 317
10.1.5 Two Dimensional Diffusion 318
10.1.6 Sample Paths in Two–Dimensions 319
10.1.7 Numerical Solutions: The Method of Lines 320
10.2 Bacterial Growth on a Petri Plate 321
10.2.1 Diffusion of a Drop of Substrate 321
10.2.2 Bacterial Growth Due to Diffusing Nutrition . . . 323
10.2.3 Growth Patterns Due to Two Nutrients 323
10.3 Concluding Remarks 325
10.4 Annotated References 326
Exercises 326

Appendix A Getting Started with Matrices and MATLAB **335**

Appendix B Background on Random Processes **343**

Index **349**