Contents

1 Introduction ................................................... 1
  1.1 Epidemiology ............................................... 1
  1.2 Classification of Infectious Diseases ....................... 1
  1.3 Basic Definitions in the Epidemiology of Infectious Diseases .... 3
  1.4 Historical Remarks on Infectious Diseases and Their Modeling .... 4
  1.5 General Approach to Modeling ............................. 6

2 Introduction to Epidemic Modeling .............................. 9
  2.1 Kermack–McKendrick SIR Epidemic Model .................... 9
    2.1.1 Deriving the Kermack–McKendrick Epidemic Model ......... 9
    2.1.2 Mathematical Properties of the SIR Model ............... 12
  2.2 The Kermack–McKendrick Model: Estimating Parameters from Data ...................................................... 15
    2.2.1 Estimating the Recovery Rate .......................... 15
    2.2.2 The SIR Model and Influenza at an English Boarding School 1978 .................................................. 17
  2.3 A Simple SIS Epidemic Model ............................... 18
    2.3.1 Reducing the SIS Model to a Logistic Equation ........... 19
    2.3.2 Qualitative Analysis of the Logistic Equation .......... 21
    2.3.3 General Techniques for Local Analysis of Single-Equation Models .................................................... 23
  2.4 An SIS Epidemic Model with Saturating Treatment ............ 25
    2.4.1 Reducing the SIS Model with Saturating Treatment to a Single Equation ........................................... 26
    2.4.2 Bistability ............................................. 28
Problems ...................................................... 29

3 The SIR Model with Demography: General Properties of Planar Systems ....................................................... 33
  3.1 Modeling Changing Populations .............................. 33
    3.1.1 The Malthusian Model .................................. 33
3.1.2 The Logistic Model as a Model of Population Growth .... 35
3.1.3 A Simplified Logistic Model .......................... 36
3.2 The SIR Model with Demography ......................... 37
3.3 Analysis of Two-Dimensional Systems ..................... 39
  3.3.1 Phase-Plane Analysis ............................. 40
  3.3.2 Linearization ..................................... 44
  3.3.3 Two-Dimensional Linear Systems .................... 45
3.4 Analysis of the Dimensionless SIR Model ................. 48
  3.4.1 Local Stability of the Equilibria of the SIR Model .. 48
  3.4.2 The Reproduction Number of the Disease $R_0$ ........ 50
  3.4.3 Forward Bifurcation ............................... 51
3.5 Global Stability ....................................... 52
  3.5.1 Global Stability of the Disease-Free Equilibrium .... 52
  3.5.2 Global Stability of the Endemic Equilibrium ......... 53
3.6 Oscillations in Epidemic Models ........................ 56

Problems .................................................... 63

4 Vector-Borne Diseases ..................................... 67
4.1 Vector-Borne Diseases: An Introduction .................... 67
  4.1.1 The Vectors ..................................... 67
  4.1.2 The Pathogen .................................... 68
  4.1.3 Epidemiology of Vector-Borne Diseases ............... 68
4.2 Simple Models of Vector-Borne Diseases .................... 70
  4.2.1 Deriving a Model of Vector-Borne Disease .......... 70
  4.2.2 Reproduction Numbers, Equilibria, and Their Stability 73
4.3 Delay-Differential Equation Models of Vector-Borne Diseases 75
  4.3.1 Reducing the Delay Model to a Single Equation .... 76
  4.3.2 Oscillations in Delay-Differential Equations ....... 79
  4.3.3 The Reproduction Number of the Model with Two Delays 83
4.4 A Vector-Borne Disease Model with Temporary Immunity 85

Problems .................................................... 86

5 Techniques for Computing $R_0$ ............................. 91
5.1 Building Complex Epidemiological Models ................. 91
  5.1.1 Stages Related to Disease Progression ............... 91
  5.1.2 Stages Related to Control Strategies ................. 94
  5.1.3 Stages Related to Pathogen or Host Heterogeneity . 97
5.2 Jacobian Approach for the Computation of $R_0$ .......... 98
  5.2.1 Examples in Which the Jacobian Reduces to a $2 \times 2$ Matrix .. 99
  5.2.2 Routh–Hurwitz Criteria in Higher Dimensions ....... 100
  5.2.3 Failure of the Jacobian Approach .................... 103
5.3 The Next-Generation Approach .......................... 104
  5.3.1 Van den Driessche and Watmough Approach .......... 104
  5.3.2 Examples ......................................... 108
  5.3.3 The Castillo-Chavez, Feng, and Huang Approach .... 116

Problems .................................................... 119
# Contents

<table>
<thead>
<tr>
<th>Chapter</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Fitting Models to Data</td>
</tr>
<tr>
<td>6.1 Introduction</td>
</tr>
<tr>
<td>6.2 Fitting Epidemic Models to Data: Examples</td>
</tr>
<tr>
<td>6.2.1 Using Matlab to Fit Data for the English Boarding School</td>
</tr>
<tr>
<td>6.2.2 Fitting World HIV/AIDS Prevalence</td>
</tr>
<tr>
<td>6.3 Summary of Basic Steps</td>
</tr>
<tr>
<td>6.4 Model Selection</td>
</tr>
<tr>
<td>6.4.1 Akaike Information Criterion</td>
</tr>
<tr>
<td>6.4.2 Example of Model Selection Using AIC</td>
</tr>
<tr>
<td>6.5 Exploring Sensitivity</td>
</tr>
<tr>
<td>6.5.1 Sensitivity Analysis of a Dynamical System</td>
</tr>
<tr>
<td>6.5.2 Sensitivity and Elasticity of Static Quantities</td>
</tr>
<tr>
<td>Problems</td>
</tr>
<tr>
<td>7 Analysis of Complex ODE Epidemic Models: Global Stability</td>
</tr>
<tr>
<td>7.1 Introduction</td>
</tr>
<tr>
<td>7.2 Local Analysis of the SEIR Model</td>
</tr>
<tr>
<td>7.3 Global Stability via Lyapunov Functions</td>
</tr>
<tr>
<td>7.3.1 Lyapunov–Kasovskii–LaSalle Stability Theorems</td>
</tr>
<tr>
<td>7.3.2 Global Stability of Equilibria of the SEIR Model</td>
</tr>
<tr>
<td>7.4 Hopf Bifurcation in Higher Dimensions</td>
</tr>
<tr>
<td>7.5 Backward Bifurcation</td>
</tr>
<tr>
<td>7.5.1 Example of Backward Bifurcation and Multiple Equilibria</td>
</tr>
<tr>
<td>7.5.2 Castillo-Chavez and Song Bifurcation Theorem</td>
</tr>
<tr>
<td>Problems</td>
</tr>
<tr>
<td>8 Multistain Disease Dynamics</td>
</tr>
<tr>
<td>8.1 Competitive Exclusion Principle</td>
</tr>
<tr>
<td>8.1.1 A Two-Strain Epidemic SIR Model</td>
</tr>
<tr>
<td>8.1.2 The Strain-One- and Strain-Two-Dominance Equilibria and Their Stability</td>
</tr>
<tr>
<td>8.1.3 The Competitive Exclusion Principle</td>
</tr>
<tr>
<td>8.2 Multistain Diseases: Mechanisms for Coexistence</td>
</tr>
<tr>
<td>8.2.1 Mutation</td>
</tr>
<tr>
<td>8.2.2 Superinfection</td>
</tr>
<tr>
<td>8.2.3 Coinfection</td>
</tr>
<tr>
<td>8.2.4 Cross-Immunity</td>
</tr>
<tr>
<td>8.3 Analyzing Two-Strain Models with Coexistence: The Case of Superinfection</td>
</tr>
<tr>
<td>8.3.1 Existence and Stability of the Disease-Free and Two Dominance Equilibria</td>
</tr>
<tr>
<td>8.3.2 Existence of the Coexistence Equilibrium</td>
</tr>
<tr>
<td>8.3.3 Competitive Outcomes, Graphical Representation, and Simulations</td>
</tr>
</tbody>
</table>
8.4 Computing the Invasion Numbers Using the Next-Generation Approach ................................................................. 207
  8.4.1 General Description of the Method ............................... 207
  8.4.2 Example ..................................................... 210
Problems ........................................................................... 212

9 Control Strategies ............................................................. 215
  9.1 Introduction ................................................................ 215
  9.2 Modeling Vaccination: Single-Strain Diseases ...................... 216
    9.2.1 A Model with Vaccination at Recruitment ..................... 217
    9.2.2 A Model with Continuous Vaccination ......................... 217
  9.3 Vaccination and Genetic Diversity of Microorganisms .............. 224
  9.4 Modeling Quarantine and Isolation ...................................... 230
  9.5 Optimal Control Strategies .............................................. 234
    9.5.1 Basic Theory of Optimal Control ................................. 235
    9.5.2 Examples ....................................................... 237
Appendix .............................................................................. 242
Problems .............................................................................. 244

10 Ecological Context of Epidemiology ..................................... 249
  10.1 Infectious Diseases in Animal Populations .......................... 249
  10.2 Generalist Predator and SI-Type Disease in Prey .................... 251
    10.2.1 Indiscriminate Predation ........................................... 252
    10.2.2 Selective Predation ................................................... 253
  10.3 Generalist Predator and SIR-Type Disease in Prey ................. 254
    10.3.1 Selective Predation ................................................... 255
    10.3.2 Indiscriminate Predation ............................................. 257
  10.4 Specialist Predator and SI Disease in Prey ............................ 258
    10.4.1 Lotka–Volterra Predator–Prey Models ............................ 259
    10.4.2 Lotka–Volterra Model with SI Disease in Prey ................. 262
  10.5 Competition of Species and Disease .................................... 268
    10.5.1 Lotka–Volterra Interspecific Competition Models ............... 269
    10.5.2 Disease in One of the Competing Species ........................ 273
Problems .............................................................................. 276

11 Zoonotic Disease, Avian Influenza, and Nonautonomous Models .................. 281
  11.1 Introduction ................................................................ 281
  11.2 Modeling Avian Influenza ............................................... 282
    11.2.1 Simple Bird–Human Avian Influenza Model ..................... 282
    11.2.2 Parameterizing the Simple Avian Influenza Model ............. 283
    11.2.3 Evaluating Avian Influenza Control Strategies .................. 284
  11.3 Seasonality in Avian Influenza Modeling ............................. 286
    11.3.1 An Avian Influenza Model with Seasonality ..................... 286
    11.3.2 Tools For Nonautonomous Models ............................... 288
11.3.3 Analyzing the Avian Influenza Model with Seasonality
11.3.4 The Nonautonomous Avian Influenza Model with \( \nu_d = 0 \)
11.3.5 The Full Nonautonomous Avian Influenza Model

Appendix
Problems

12 Age-Structured Epidemic Models
12.1 Introduction
12.2 Linear Age-Structured Population Model
12.2.1 Derivation of the Age-Structured Model
12.2.2 Reformulation of the Model Through the Method of the Characteristics. The Renewal Equation
12.2.3 Separable Solutions. Asymptotic Behavior
12.3 Age-Structured SIS Epidemic Models
12.3.1 Introduction of the SIR Age-Structured Epidemic Model
12.3.2 Equilibria and Reproduction Number
12.3.3 Local Stability of the Disease-Free Equilibrium
12.4 Numerical Methods for Age-Structured Models
12.4.1 A Numerical Method for the McKendrick–von Foerster Model
12.4.2 Numerical Method for the Age-Structured SIR Model
Problems

13 Class-Age Structured Epidemic Models
13.1 Variability of Infectivity with Time-Since-Infection
13.2 Time-Since-Infection Structured SIR Model
13.2.1 Derivation of the Time-Since-Infection Structured Model
13.2.2 Equilibria and Reproduction Number of the Time-Since-Infection SIR Model
13.2.3 Local Stability of Equilibria
13.3 Influenza Model Structured with Time-Since-Recovery
13.3.1 Equilibria of the Time-Since-Recovery Model
13.3.2 Stability of Equilibria
13.3.3 Numerical Method for the Time-Since-Recovery Model
Appendix
Problems

14 Immuno-Epidemiological Modeling
14.1 Introduction to Immuno-Epidemiological Modeling
14.2 Within-Host Modeling
14.2.1 Modeling Replication of Intracellular Pathogens
14.2.2 Modeling the Interaction of the Pathogen with the Immune System
14.2.3 Combining Intracellular Pathogen Replication and Immune Response
14.3 Nested Immuno-Epidemiological Models ......................... 368
  14.3.1 Building a Nested Immuno-Epidemiological Model .......... 369
  14.3.2 Analysis of the Immuno-Epidemiological Model ............ 371
  14.3.3 Dependence of $R_0$ and Prevalence on Immunological
    Parameters ............................................. 374
  14.3.4 Sensitivity and Elasticity of $R_0$ and Prevalence
    with Respect to Immunological Parameters ................. 377
14.4 A Nested Immuno-Epidemiological Model with Immune
  Response ............................................. 379
Problems .............................................. 383

15 Spatial Heterogeneity in Epidemiological Models ............... 387
  15.1 Introduction ....................................... 387
  15.2 Metapopulation Modeling of Epidemic Spread ................. 388
    15.2.1 Lagrangian Movement Epidemic Models ............. 389
    15.2.2 Eulerian Movement Epidemic Models .............. 391
  15.3 Spatial Models with Diffusion .......................... 392
    15.3.1 Derivation of Reaction–Diffusion Equations ......... 393
    15.3.2 Equilibria and Their Local Stability .......... 396
    15.3.3 Traveling-Wave Solutions ...................... 399
    15.3.4 Turing Instability ............................ 405
Problems .............................................. 411

16 Discrete Epidemic Models .................................. 415
  16.1 Single-Species Discrete Population Models ................. 415
    16.1.1 Simple Discrete Population Models ............. 415
    16.1.2 Analysis of Single-Species Discrete Models ...... 418
  16.2 Discrete Epidemic Models ................................ 421
    16.2.1 A Discrete SIS Epidemic Model ............... 421
    16.2.2 Analysis of Multidimensional Discrete Models ..... 422
    16.2.3 Analysis of the SIS Epidemic Model ............ 424
  16.3 Discrete SEIS Model .................................. 427
  16.4 Next-Generation Approach for Discrete Models ............. 431
    16.4.1 Basic Theory .................................. 431
    16.4.2 Examples ..................................... 432
Problems .............................................. 437

References ............................................. 441

Index .................................................. 449
An Introduction to Mathematical Epidemiology
Martcheva, M.
2015, XIV, 453 p. 103 illus., 60 illus. in color., Hardcover
ISBN: 978-1-4899-7611-6