# Table of Contents

CONTENTS, VOLUME II

Preface to the Third Edition vii
Preface to the First Edition xi

1. Multi-Species Waves and Practical Applications 1
   1.1 Intuitive Expectations 1
   1.2 Waves of Pursuit and Evasion in Predator–Prey Systems 5
   1.3 Competition Model for the Spatial Spread of the Grey Squirrel in Britain 12
   1.4 Spread of Genetically Engineered Organisms 18
   1.5 Travelling Fronts in the Belousov–Zhabotinskii Reaction 35
   1.6 Waves in Excitable Media 41
   1.7 Travelling Wave Trains in Reaction Diffusion Systems with Oscillatory Kinetics 49
   1.8 Spiral Waves 54
   1.9 Spiral Wave Solutions of \( \lambda-\omega \) Reaction Diffusion Systems 61
   Exercises 67

2. Spatial Pattern Formation with Reaction Diffusion Systems 71
   2.1 Role of Pattern in Biology 71
   2.2 Reaction Diffusion (Turing) Mechanisms 75
   2.3 General Conditions for Diffusion-Driven Instability: Linear Stability Analysis and Evolution of Spatial Pattern 82
   2.4 Detailed Analysis of Pattern Initiation in a Reaction Diffusion Mechanism 90
   2.5 Dispersion Relation, Turing Space, Scale and Geometry Effects in Pattern Formation Models 103
   2.6 Mode Selection and the Dispersion Relation 113
   2.7 Pattern Generation with Single-Species Models: Spatial Heterogeneity with the Spruce Budworm Model 120
2.8 Spatial Patterns in Scalar Population Interaction Diffusion Equations with Convection: Ecological Control Strategies .................................................. 125
2.9 Nonexistence of Spatial Patterns in Reaction Diffusion Systems: General and Particular Results ................................................................. 130
Exercises ........................................................................................................... 135

3. Animal Coat Patterns and Other Practical Applications of Reaction Diffusion Mechanisms ................................................................. 141
3.1 Mammalian Coat Patterns—‘How the Leopard Got Its Spots’ .............................................................................................................. 142
3.2 Teratologies: Examples of Animal Coat Pattern Abnormalities .... 156
3.3 A Pattern Formation Mechanism for Butterfly Wing Patterns ....... 161
3.4 Modelling Hair Patterns in a Whorl in *Acetabularia* ................. 180

4. Pattern Formation on Growing Domains: Alligators and Snakes 192
4.1 Stripe Pattern Formation in the Alligator: Experiments ............... 193
4.2 Modelling Concepts: Determining the Time of Stripe Formation .... 196
4.3 Stripes and Shadow Stripes on the Alligator ................................ 200
4.4 Spatial Patterning of Teeth Primordia in the Alligator: Background and Relevance .............................................................. 205
4.5 Biology of Tooth Initiation ................................................................. 207
4.6 Modelling Tooth Primordium Initiation: Background .................. 213
4.7 Model Mechanism for Alligator Teeth Patterning ..................... 215
4.8 Results and Comparison with Experimental Data ....................... 224
4.9 Prediction Experiments ................................................................. 228
4.10 Concluding Remarks on Alligator Tooth Spatial Patterning ... 232
4.11 Pigmentation Pattern Formation on Snakes ............................... 234
4.12 Cell-Chemotaxis Model Mechanism ........................................... 238
4.13 Simple and Complex Snake Pattern Elements ......................... 241
4.14 Propagating Pattern Generation with the Cell-Chemotaxis System . 248

5. Bacterial Patterns and Chemotaxis ...................................................... 253
5.1 Background and Experimental Results ........................................... 253
5.2 Model Mechanism for *E. coli* in the Semi-Solid Experiments .... 260
5.3 Liquid Phase Model: Intuitive Analysis of Pattern Formation ......... 267
5.4 Interpretation of the Analytical Results and Numerical Solutions . 274
5.5 Semi-Solid Phase Model Mechanism for *S. typhimurium* ............ 279
5.6 Linear Analysis of the Basic Semi-Solid Model ......................... 281
5.7 Brief Outline and Results of the Nonlinear Analysis ................. 287
5.8 Simulation Results, Parameter Spaces and Basic Patterns .......... 292
5.9 Numerical Results with Initial Conditions from the Experiments . 297
5.10 Swarm Ring Patterns with the Semi-Solid Phase Model Mechanism ..... 299
5.11 Branching Patterns in *Bacillus subtilis* ..................................... 306

6. Mechanical Theory for Generating Pattern and Form in Development 311
6.1 Introduction, Motivation and Background Biology ............................ 311
6.2 Mechanical Model for Mesenchymal Morphogenesis .......................... 319
6.3 Linear Analysis, Dispersion Relation and Pattern Formation Potential .......................................................... 330
6.4 Simple Mechanical Models Which Generate Spatial Patterns with Complex Dispersion Relations ................................................. 334
6.5 Periodic Patterns of Feather Germs .................................................. 345
6.6 Cartilage Condensations in Limb Morphogenesis and Morphogenetic Rules ................................................................. 350
6.7 Embryonic Fingerprint Formation ..................................................... 358
6.8 Mechanochemical Model for the Epidermis ........................................ 367
6.9 Formation of Microvilli .................................................................... 374
6.10 Complex Pattern Formation and Tissue Interaction Models .................... 381
Exercises .............................................................................................. 394

7. Evolution, Morphogenetic Laws, Developmental Constraints and Teratologies 396
7.1 Evolution and Morphogenesis .......................................................... 396
7.2 Evolution and Morphogenetic Rules in Cartilage Formation in the Vertebrate Limb ................................................................. 402
7.3 Teratologies (Monsters) .................................................................... 407
7.4 Developmental Constraints, Morphogenetic Rules and the Consequences for Evolution ................................................................. 411

8. A Mechanical Theory of Vascular Network Formation 416
8.1 Biological Background and Motivation .............................................. 416
8.2 Cell–Extracellular Matrix Interactions for Vasculogenesis ....................... 417
8.3 Parameter Values ............................................................................. 425
8.4 Analysis of the Model Equations ....................................................... 427
8.5 Network Patterns: Numerical Simulations and Conclusions ..................... 433

9. Epidermal Wound Healing 441
9.1 Brief History of Wound Healing ....................................................... 441
9.2 Biological Background: Epidermal Wounds ........................................ 444
9.3 Model for Epidermal Wound Healing ............................................... 447
9.4 Nondimensional Form, Linear Stability and Parameter Values ................. 450
9.5 Numerical Solution for the Epidermal Wound Repair Model .................. 451
9.6 Travelling Wave Solutions for the Epidermal Model ............................ 454
9.7 Clinical Implications of the Epidermal Wound Model ......................... 461
9.8 Mechanisms of Epidermal Repair in Embryos ..................................... 468
9.9 Actin Alignment in Embryonic Wounds: A Mechanical Model ............... 471
9.10 Mechanical Model with Stress Alignment of the Actin Filaments in Two Dimensions ................................................................. 482

10. Dermal Wound Healing 491
10.1 Background and Motivation—General and Biological .......................... 491
10.2 Logic of Wound Healing and Initial Models ........................................ 495
10.3 Brief Review of Subsequent Developments ........................................ 500
10.4 Model for Fibroblast-Driven Wound Healing: Residual Strain and 
Tissue Remodelling ............................................................... 503
10.5 Solutions of the Model Equations and Comparison with 
Experiment ................................................................. 507
10.6 Wound Healing Model of Cook (1995) ........................................... 511
10.7 Matrix Secretion and Degradation ................................................. 515
10.8 Cell Movement in an Oriented Environment .................................. 518
10.9 Model System for Dermal Wound Healing with Tissue Structure .... 521
10.10 One-Dimensional Model for the Structure of Pathological Scars ...... 526
10.11 Open Problems in Wound Healing .............................................. 530
10.12 Concluding Remarks on Wound Healing ..................................... 533

11. Growth and Control of Brain Tumours .............................................. 536
11.1 Medical Background ................................................................. 538
11.2 Basic Mathematical Model of Glioma Growth and Invasion ............ 542
11.3 Tumour Spread In Vitro: Parameter Estimation .............................. 550
11.4 Tumour Invasion in the Rat Brain ................................................. 559
11.5 Tumour Invasion in the Human Brain ............................................ 563
11.6 Modelling Treatment Scenarios: General Comments ...................... 579
11.7 Modelling Tumour Resection in Homogeneous Tissue .................... 580
11.8 Analytical Solution for Tumour Recurrence After Resection ............ 584
11.9 Modelling Surgical Resection with Brain Tissue Heterogeneity ......... 588
11.10 Modelling the Effect of Chemotherapy on Tumour Growth ............ 594
11.11 Modelling Tumour Polyclonality and Cell Mutation ....................... 605

12. Neural Models of Pattern Formation ................................................. 614
12.1 Spatial Patterning in Neural Firing with a 
Simple Activation–Inhibition Model ........................................... 614
12.2 A Mechanism for Stripe Formation in the Visual Cortex ............... 622
12.3 A Model for the Brain Mechanism Underlying Visual 
Hallucination Patterns .......................................................... 627
12.4 Neural Activity Model for Shell Patterns ..................................... 638
12.5 Shamanism and Rock Art .......................................................... 655
Exercises ............................................................................... 659

13. Geographic Spread and Control of Epidemics .................................. 661
13.1 Simple Model for the Spatial Spread of an Epidemic ....................... 661
13.2 Spread of the Black Death in Europe 1347–1350 .......................... 664
13.3 Brief History of Rabies: Facts and Myths ...................................... 669
13.4 The Spatial Spread of Rabies Among Foxes I: Background and 
Simple Model ................................................................. 673
13.5 The Spatial Spread of Rabies Among Foxes II: 
Three-Species (SIR) Model .................................................... 681
<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.6</td>
<td>Control Strategy Based on Wave Propagation into a Nonepidemic Region: Estimate of Width of a Rabies Barrier</td>
<td>696</td>
</tr>
<tr>
<td>13.7</td>
<td>Analytic Approximation for the Width of the Rabies Control Break</td>
<td>700</td>
</tr>
<tr>
<td>13.8</td>
<td>Two-Dimensional Epizootic Fronts and Effects of Variable Fox Densities: Quantitative Predictions for a Rabies Outbreak in England</td>
<td>704</td>
</tr>
<tr>
<td>13.9</td>
<td>Effect of Fox Immunity on the Spatial Spread of Rabies</td>
<td>710</td>
</tr>
<tr>
<td></td>
<td>Exercises</td>
<td>720</td>
</tr>
<tr>
<td>14.1</td>
<td>Introduction and Wolf Ecology</td>
<td>722</td>
</tr>
<tr>
<td>14.2</td>
<td>Models for Wolf Pack Territory Formation:</td>
<td>729</td>
</tr>
<tr>
<td></td>
<td>Single Pack—Home Range Model</td>
<td></td>
</tr>
<tr>
<td>14.3</td>
<td>Multi-Wolf Pack Territorial Model</td>
<td>734</td>
</tr>
<tr>
<td>14.4</td>
<td>Wolf–Deer Predator–Prey Model</td>
<td>745</td>
</tr>
<tr>
<td>14.5</td>
<td>Concluding Remarks on Wolf Territoriality and Deer Survival</td>
<td>751</td>
</tr>
<tr>
<td>14.6</td>
<td>Coyote Home Range Patterns</td>
<td>753</td>
</tr>
<tr>
<td>14.7</td>
<td>Chippewa and Sioux Intertribal Conflict c1750–1850</td>
<td>754</td>
</tr>
</tbody>
</table>

Appendix

A. General Results for the Laplacian Operator in Bounded Domains 757

Bibliography 761

Index 791
CONTENTS, VOLUME I

J.D. Murray: *Mathematical Biology, I: An Introduction*

Preface to the Third Edition vii

Preface to the First Edition xi

1. Continuous Population Models for Single Species 1
   1.1 Continuous Growth Models................................. 1
   1.2 Insect Outbreak Model: Spruce Budworm .................. 7
   1.3 Delay Models........................................... 13
   1.4 Linear Analysis of Delay Population Models: Periodic Solutions . 17
   1.5 Delay Models in Physiology: Periodic Dynamic Diseases ....... 21
   1.6 Harvesting a Single Natural Population .................. 30
   1.7 Population Model with Age Distribution .................. 36
   Exercises.................................................. 40

2. Discrete Population Models for a Single Species 44
   2.1 Introduction: Simple Models............................ 44
   2.2 Cobwebbing: A Graphical Procedure of Solution .......... 49
   2.3 Discrete Logistic-Type Model: Chaos ..................... 53
   2.4 Stability, Periodic Solutions and Bifurcations ............. 59
   2.5 Discrete Delay Models .................................. 62
   2.6 Fishery Management Model............................... 67
   2.7 Ecological Implications and Caveats ...................... 69
   2.8 Tumour Cell Growth.................................... 72
   Exercises.................................................. 75

3. Models for Interacting Populations 79
   3.1 Predator–Prey Models: Lotka–Volterra Systems ............ 79
   3.2 Complexity and Stability ................................ 83
3.3 Realistic Predator–Prey Models ........................................ 86
3.4 Analysis of a Predator–Prey Model with Limit Cycle
   Periodic Behaviour: Parameter Domains of Stability ............... 88
3.5 Competition Models: Competitive Exclusion Principle ............ 94
3.6 Mutualism or Symbiosis .............................................. 99
3.7 General Models and Cautionary Remarks ............................ 101
3.8 Threshold Phenomena .................................................. 105
3.9 Discrete Growth Models for Interacting Populations ............... 109
3.10 Predator–Prey Models: Detailed Analysis .......................... 110
Exercises .................................................................. 115

4. Temperature-Dependent Sex Determination (TSD) .............. 119
   4.1 Biological Introduction and Historical Aside on the Crocodilia .. 119
   4.2 Nesting Assumptions and Simple Population Model ............. 124
   4.3 Age-Structured Population Model for Crocodilia ............... 130
   4.4 Density-Dependent Age-Structured Model Equations ............ 133
   4.5 Stability of the Female Population in Wet Marsh Region I .... 135
   4.6 Sex Ratio and Survivorship ......................................... 137
   4.7 Temperature-Dependent Sex Determination (TSD) Versus
       Genetic Sex Determination (GSD) .................................. 139
   4.8 Related Aspects on Sex Determination ............................ 142
Exercises .................................................................. 144

5. Modelling the Dynamics of Marital Interaction: Divorce Prediction
   and Marriage Repair ..................................................... 146
   5.1 Psychological Background and Data: Gottman and Levenson Methodology .................. 147
   5.2 Marital Typology and Modelling Motivation ....................... 150
   5.3 Modelling Strategy and the Model Equations ..................... 153
   5.4 Steady States and Stability ......................................... 156
   5.5 Practical Results from the Model .................................. 164
   5.6 Benefits, Implications and Marriage Repair Scenarios .......... 170

6. Reaction Kinetics ........................................................... 175
   6.1 Enzyme Kinetics: Basic Enzyme Reaction ......................... 175
   6.2 Transient Time Estimates and Nondimensionalisation .......... 178
   6.3 Michaelis–Menten Quasi-Steady State Analysis .................. 181
   6.4 Suicide Substrate Kinetics ........................................... 188
   6.5 Cooperative Phenomena .............................................. 197
   6.6 Autocatalysis, Activation and Inhibition .......................... 201
   6.7 Multiple Steady States, Mushrooms and Isolas .................. 208
Exercises .................................................................. 215

7. Biological Oscillators and Switches ................................. 218
   7.1 Motivation, Brief History and Background ........................ 218
   7.2 Feedback Control Mechanisms ................................... 221
7.3 Oscillators and Switches with Two or More Species: General Qualitative Results ........................................... 226
7.4 Simple Two-Species Oscillators: Parameter Domain Determination for Oscillations ................................ 234
7.5 Hodgkin–Huxley Theory of Nerve Membranes: FitzHugh–Nagumo Model ............................................. 239
7.6 Modelling the Control of Testosterone Secretion and Chemical Castration ............................................. 244
Exercises ........................................................................... 253

8. BZ Oscillating Reactions ............................................. 257
8.1 Belousov Reaction and the Field–Körös–Noyes (FKN) Model ................................................................. 257
8.2 Linear Stability Analysis of the FKN Model and Existence of Limit Cycle Solutions ............................... 261
8.3 Nonlocal Stability of the FKN Model ........................................................................................................... 265
8.4 Relaxation Oscillators: Approximation for the Belousov–Zhabotinskii Reaction ...................................... 268
8.5 Analysis of a Relaxation Model for Limit Cycle Oscillations in the Belousov–Zhabotinskii Reaction ............ 271
Exercises ............................................................................. 277

9. Perturbed and Coupled Oscillators and Black Holes ................................................................. 278
9.1 Phase Resetting in Oscillators .......................................................... 278
9.2 Phase Resetting Curves ................................................................ 282
9.3 Black Holes .............................................................................. 286
9.4 Black Holes in Real Biological Oscillators ......................................................................................... 288
9.5 Coupled Oscillators: Motivation and Model System ............................................................................... 293
9.6 Phase Locking of Oscillations: Synchronisation in Fireflies .............................................................. 295
9.7 Singular Perturbation Analysis: Preliminary Transformation .............................................................. 299
9.8 Singular Perturbation Analysis: Transformed System ........................................................................... 302
9.9 Singular Perturbation Analysis: Two-Time Expansion ........................................................................... 305
9.10 Analysis of the Phase Shift Equation and Application to Coupled Belousov–Zhabotinskii Reactions .... 310
Exercises ............................................................................. 313

10. Dynamics of Infectious Diseases .................................................... 315
10.1 Historical Aside on Epidemics ............................................................. 315
10.2 Simple Epidemic Models and Practical Applications ........................................................................... 319
10.3 Modelling Venereal Diseases ................................................................................................................. 327
10.4 Multi-Group Model for Gonorrhea and Its Control ............................................................................ 331
10.5 AIDS: Modelling the Transmission Dynamics of the Human Immunodeficiency Virus (HIV) ............. 333
10.6 HIV: Modelling Combination Drug Therapy ....................................................................................... 341
10.7 Delay Model for HIV Infection with Drug Therapy ............................................................................... 350
10.8 Modelling the Population Dynamics of Acquired Immunity to Parasite Infection ............................. 351
10.9 Age-Dependent Epidemic Model and Threshold Criterion .......... 361
10.10 Simple Drug Use Epidemic Model and Threshold Analysis ....... 365
10.11 Bovine Tuberculosis Infection in Badgers and Cattle ............. 369
10.12 Modelling Control Strategies for Bovine Tuberculosis in Badgers and Cattle ................................................. 379
Exercises ................................................................. 393

11. Reaction Diffusion, Chemotaxis, and Nonlocal Mechanisms 395
11.1 Simple Random Walk and Derivation of the Diffusion Equation ... 395
11.2 Reaction Diffusion Equations ...................................... 399
11.3 Models for Animal Dispersal ......................................... 402
11.4 Chemotaxis ........................................................... 405
11.5 Nonlocal Effects and Long Range Diffusion ....................... 408
11.6 Cell Potential and Energy Approach to Diffusion and Long Range Effects ......................................................... 413
Exercises ................................................................. 416

12. Oscillator-Generated Wave Phenomena 418
12.1 Belousov–Zhabotinsky Reaction Kinematic Waves .................. 418
12.2 Central Pattern Generator: Experimental Facts in the Swimming of Fish ................................................................. 422
12.3 Mathematical Model for the Central Pattern Generator ............ 424
12.4 Analysis of the Phase Coupled Model System ..................... 431
Exercises ................................................................. 436

13.1 Background and the Travelling Waveform .......................... 437
13.2 Fisher–Kolmogoroff Equation and Propagating Wave Solutions ... 439
13.3 Asymptotic Solution and Stability of Wavefront Solutions of the Fisher–Kolmogoroff Equation ................................. 444
13.4 Density-Dependent Diffusion-Reaction Diffusion Models and Some Exact Solutions .............................................. 449
13.5 Waves in Models with Multi-Steady State Kinetics: Spread and Control of an Insect Population ........................................ 460
13.6 Calcium Waves on Amphibian Eggs: Activation Waves on Medaka Eggs ............................................................... 467
13.7 Invasion Wavespeeds with Dispersive Variability .................... 471
13.8 Species Invasion and Range Expansion ............................. 478
Exercises ................................................................. 482

14. Use and Abuse of Fractals 484
14.1 Fractals: Basic Concepts and Biological Relevance .................. 484
14.2 Examples of Fractals and Their Generation .......................... 487
14.3 Fractal Dimension: Concepts and Methods of Calculation ........ 490
14.4 Fractals or Space-Filling? ............................................. 496
Appendices

A. Phase Plane Analysis

B. Routh-Hurwitz Conditions, Jury Conditions, Descartes’ Rule of Signs, and Exact Solutions of a Cubic

   B.1 Polynomials and Conditions ........................................ 507
   B.2 Descartes’ Rule of Signs ........................................... 509
   B.3 Roots of a General Cubic Polynomial ............................ 510

Bibliography

Index
Mathematical Biology
I. An Introduction
Murray, J.D.
2002, XXIII, 551 p. 35 illus., Hardcover