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J. D. Murray

Mathematical Biology

With 292 Figures



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James D. Murray, FRS
Professor of Mathematical Biology
Director, Centre for Mathematical Biology
Mathematical Institute
University of Oxford
24–29 St. Giles'
Oxford OX1 3LB
Great Britain

Cover picture: A model based on a system of reaction-diffusion equations has been suggested by the author of this book to explain how the coat markings on the leopard and other mammals are generated. In this book, he gives a whole range of animal patterning examples - from the stripes on the zebra to the eyespots on the wings of butterflies - to demonstrate the wide applicability of such models.

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Preface

Mathematics has always benefited from its involvement with developing sciences. Each successive interaction revitalises and enhances the field. Biomedical science is clearly the premier science of the foreseeable future. For the continuing health of their subject mathematicians must become involved with biology. With the example of how mathematics has benefited from and influenced physics, it is clear that if mathematicians do not become involved in the biosciences they will simply not be a part of what are likely to be the most important and exciting scientific discoveries of all time.

Mathematical biology is a fast growing, well recognised, albeit not clearly defined, subject and is, to my mind, the most exciting modern application of mathematics. The increasing use of mathematics in biology is inevitable as biology becomes more quantitative. The complexity of the biological sciences makes interdisciplinary involvement essential. For the mathematician, biology opens up new and exciting branches while for the biologist mathematical modelling offers another research tool commensurate with a new powerful laboratory technique but *only* if used appropriately and its limitations recognised. However, the use of esoteric mathematics arrogantly applied to biological problems by mathematicians who know little about the real biology, together with unsubstantiated claims as to how important such theories are, does little to promote the interdisciplinary involvement which is so essential.

Mathematical biology research, to be useful and interesting, must be relevant *biologically*. The best models show how a process works and then predict what may follow. If these are not already obvious to the biologists *and* the predictions turn out to be right, then you will have the biologists' attention. Suggestions as to what the governing mechanisms are, may evolve from this. *Genuine* interdisciplinary research and the use of models can produce exciting results, many of which are described in this book.

No previous knowledge of biology is assumed of the reader. With each topic discussed I give a brief description of the biological background sufficient to understand the models studied. Although stochastic models are important, to keep the book within reasonable bounds, I deal exclusively with deterministic models. The book provides a toolkit of modelling techniques with numerous examples drawn from population ecology, reaction kinetics, biological oscillators, developmental biology, evolution, epidemiology and other areas.

The emphasis throughout the book is on the practical application of mathematical models in helping to unravel the underlying mechanisms involved in the biological processes. The book also illustrates some of the pitfalls of indiscriminate, naive or uninformed use of models. I hope the reader will acquire a practical and realistic view of biological modelling and the mathematical techniques needed to get approximate quantitative solutions and will thereby realise the importance of relating the models and results to the real biological problems under study. If the use of a model stimulates experiments – even if the model is subsequently shown to be wrong – then it has been successful. Models can provide biological insight and be very useful in summarizing, interpreting and interpolating real data. I hope the reader will also learn that (certainly at this stage) there is usually no ‘right’ model: producing similar temporal or spatial patterns to those experimentally observed is only a first step and does not imply the model mechanism is the one which applies. Mathematical descriptions are *not* explanations. Mathematics can never provide the complete solution to a biological problem on its own. Modern biology is certainly not at the stage where it is appropriate for mathematicians to try to construct comprehensive theories. A close collaboration with biologists is needed for realism, stimulation and help in modifying the model mechanisms to reflect the biology more accurately.

Although this book is titled *mathematical biology* it is not, and could not be, a definitive all-encompassing text. The immense breadth of the field necessitates a restricted choice of topics. Some of the models have been deliberately kept simple for pedagogical purposes. The exclusion of a particular topic – population genetics for example – in no way reflects my view as to its importance. However, I hope the range of topics discussed will show how exciting intercollaborative research can be and how significant a role mathematics can play. The main purpose of the book is to present some of the basic and, to a large extent, generally accepted theoretical frameworks for a variety of biological models. The material presented does not purport to be the latest developments in the various fields, many of which are constantly developing. The already lengthy list of references is by no means exhaustive and I apologise for the exclusion of many that should be included in a definitive list.

With the specimen models discussed and the philosophy which pervades the book the reader should be in a position to tackle the modelling of genuinely practical problems with realism. From a *mathematical* point of view, the art of good modelling relies on: (i) a sound understanding and appreciation of the biological problem; (ii) a realistic mathematical representation of the important biological phenomena; (iii) finding useful solutions, preferably quantitative; and what is crucially important (iv) a biological interpretation of the mathematical results in terms of insights and predictions. The mathematics is dictated by the biology and not vice-versa. Sometimes the mathematics can be very simple. Useful mathematical biology research is not judged by mathematical standards but by different and no less demanding ones.

The book is suitable for physical science courses at various levels. The level of mathematics needed in collaborative biomedical research varies from the very

simple to the sophisticated. Selected chapters have been used for applied mathematics courses in the University of Oxford at the final year undergraduate and first year graduate levels. In the U.S.A. the material has also been used for courses for students from the second year undergraduate level through graduate level. It is also accessible to the more theoretically orientated bioscientists who have some knowledge of calculus and differential equations.

I would like to express my gratitude to the many colleagues around the world who have, over the past few years, commented on various chapters of the manuscript, made valuable suggestions and kindly provided me with photographs. I would particularly like to thank Drs. Philip Maini, David Lane and Diana Woodward and my present graduate students who read various drafts with such care, specifically Daniel Bentil, Meghan Burke, David Crawford, Michael Jenkins, Mark Lewis, Gwen Littlewort, Mary Myerscough, Katherine Rogers and Louisa Shaw.

Oxford, January 1989

J. D. Murray

*If the Lord Almighty had consulted me
before embarking on creation I should have
recommended something simpler*

Alphonso X (Alphonso the Wise), 1221–1284
King of Castile and Leon (attributed)

Table of Contents

1. Continuous Population Models for Single Species	1
1.1 Continuous Growth Models	1
1.2 Insect Outbreak Model: Spruce Budworm	4
1.3 Delay Models	8
1.4 Linear Analysis of Delay Population Models: Periodic Solutions	12
1.5 Delay Models in Physiology: Dynamic Diseases	15
1.6 Harvesting a Single Natural Population	24
*1.7 Population Model with Age Distribution	29
Exercises	33
2. Discrete Population Models for a Single Species	36
2.1 Introduction: Simple Models	36
2.2 Cobwebbing: A Graphical Procedure of Solution	38
2.3 Discrete Logistic Model: Chaos	41
2.4 Stability, Periodic Solutions and Bifurcations	47
2.5 Discrete Delay Models	51
2.6 Fishery Management Model	54
2.7 Ecological Implications and Caveats	57
Exercises	59
3. Continuous Models for Interacting Populations	63
3.1 Predator-Prey Models: Lotka-Volterra Systems	63
3.2 Complexity and Stability	68
3.3 Realistic Predator-Prey Models	70
3.4 Analysis of a Predator-Prey Model with Limit Cycle Periodic Behaviour: Parameter Domains of Stability	72
3.5 Competition Models: Principle of Competitive Exclusion	78
3.6 Mutualism or Symbiosis	83
3.7 General Models and Some General and Cautionary Remarks	85
3.8 Threshold Phenomena	89
Exercises	92

* Denotes sections in which the mathematics is at a higher level. These sections can be omitted without loss of continuity.

4.	Discrete Growth Models for Interacting Populations	95
4.1	Predator-Prey Models: Detailed Analysis	96
*4.2	Synchronized Insect Emergence: 13 Year Locusts	100
4.3	Biological Pest Control: General Remarks	106
	Exercises	107
5.	Reaction Kinetics	109
5.1	Enzyme Kinetics: Basic Enzyme Reaction	109
5.2	Michaelis-Menten Theory: Detailed Analysis and the Pseudo-Steady State Hypothesis	111
5.3	Cooperative Phenomena	118
5.4	Autocatalysis, Activation and Inhibition	122
5.5	Multiple Steady States, Mushrooms and Isolas	130
	Exercises	137
6.	Biological Oscillators and Switches	140
6.1	Motivation, History and Background	140
6.2	Feedback Control Mechanisms	143
6.3	Oscillations and Switches Involving Two or More Species: General Qualitative Results	148
6.4	Simple Two-Species Oscillators: Parameter Domain Determination for Oscillations	156
6.5	Hodgkin-Huxley Theory of Nerve Membranes: FitzHugh-Nagumo Model	161
6.6	Modelling the Control of Testosterone Secretion	166
	Exercises	175
7.	Belousov-Zhabotinskii Reaction	179
7.1	Belousov Reaction and the Field-Noyes (FN) Model	179
7.2	Linear Stability Analysis of the FN Model and Existence of Limit Cycle Solutions	183
7.3	Non-local Stability of the FN Model	187
7.4	Relaxation Oscillators: Approximation for the Belousov-Zhabotinskii Reaction	190
7.5	Analysis of a Relaxation Model for Limit Cycle Oscillations in the Belousov-Zhabotinskii Reaction	192
	Exercises	199
8.	Perturbed and Coupled Oscillators and Black Holes	200
8.1	Phase Resetting in Oscillators	200
8.2	Phase Resetting Curves	204
8.3	Black Holes	208
8.4	Black Holes in Real Biological Oscillators	210
8.5	Coupled Oscillators: Motivation and Model System	215

*8.6	Singular Perturbation Analysis: Preliminary Transformation	217
*8.7	Singular Perturbation Analysis: Transformed System	220
*8.8	Singular perturbation Analysis: Two-Time Expansion	223
*8.9	Analysis of the Phase Shift Equation and Application to Coupled Belousov-Zhabotinskii Reactions	227
	Exercises	231
9.	Reaction Diffusion, Chemotaxis and Non-local Mechanisms	232
9.1	Simple Random Walk Derivation of the Diffusion Equation	232
9.2	Reaction Diffusion Equations	236
9.3	Models for Insect Dispersal	238
9.4	Chemotaxis	241
*9.5	Non-local Effects and Long Range Diffusion	244
*9.6	Cell Potential and Energy Approach to Diffusion	249
	Exercises	252
10.	Oscillator Generated Wave Phenomena and Central Pattern Generators	254
10.1	Kinematic Waves in the Belousov-Zhabotinskii Reaction	254
10.2	Central Pattern Generator: Experimental Facts in the Swimming of Fish	258
*10.3	Mathematical Model for the Central Pattern Generator	261
*10.4	Analysis of the Phase-Coupled Model System	268
	Exercises	273
11.	Biological Waves: Single Species Models	274
11.1	Background and the Travelling Wave Form	274
11.2	Fisher Equation and Propagating Wave Solutions	277
11.3	Asymptotic Solution and Stability of Wavefront Solutions of the Fisher Equation	281
11.4	Density-Dependent Diffusion Reaction Diffusion Models and Some Exact Solutions	286
11.5	Waves in Models with Multi-Steady State Kinetics: The Spread and Control of an Insect Population	297
11.6	Calcium Waves on Amphibian Eggs: Activation Waves on <i>Medaka</i> Eggs	305
	Exercises	309
12.	Biological Waves: Multi-species Reaction Diffusion Models	311
12.1	Intuitive Expectations	311
12.2	Waves of Pursuit and Evasion in Predator-Prey Systems	315
12.3	Travelling Fronts in the Belousov-Zhabotinskii Reaction	322
12.4	Waves in Excitable Media	328

12.5	Travelling Wave Trains in Reaction Diffusion Systems with Oscillatory Kinetics	336
*12.6	Linear Stability of Wave Train Solutions of λ - ω Systems . . .	340
12.7	Spiral Waves	343
*12.8	Spiral Wave Solutions of λ - ω Reaction Diffusion Systems . . .	350
	Exercises	356
*13.	Travelling Waves in Reaction Diffusion Systems with Weak Diffusion: Analytical Techniques and Results	360
*13.1	Reaction Diffusion System with Limit Cycle Kinetics and Weak Diffusion: Model and Transformed System	360
*13.2	Singular Perturbation Analysis: The Phase Satisfies Burgers' Equation	363
*13.3	Travelling Wavetrain Solutions for Reaction Diffusion Systems with Limit Cycle Kinetics and Weak Diffusion: Comparison with Experiment	367
14.	Spatial Pattern Formation with Reaction/Population Interaction Diffusion Mechanisms	372
14.1	Role of Pattern in Developmental Biology	372
14.2	Reaction Diffusion (Turing) Mechanisms	375
14.3	Linear Stability Analysis and Evolution of Spatial Pattern: General Conditions for Diffusion-Driven Instability	380
14.4	Detailed Analysis of Pattern Initiation in a Reaction Diffusion Mechanism	387
14.5	Dispersion Relation, Turing Space, Scale and Geometry Effects in Pattern Formation in Morphogenetic Models	397
14.6	Mode Selection and the Dispersion Relation	408
14.7	Pattern Generation with Single Species Models: Spatial Heterogeneity with the Spruce Budworm Model	414
14.8	Spatial Patterns in Scalar Population Interaction-Reaction Diffusion Equations with Convection: Ecological Control Strategies	419
*14.9	Nonexistence of Spatial Patterns in Reaction Diffusion Systems: General and Particular Results	424
	Exercises	430
15.	Animal Coat Patterns and Other Practical Applications of Reaction Diffusion Mechanisms	435
15.1	Mammalian Coat Patterns – ‘How the Leopard Got Its Spots’ .	436
15.2	A Pattern Formation Mechanism for Butterfly Wing Patterns .	448
15.3	Modelling Hair Patterns in a Whorl in <i>Acetabularia</i>	468

16. Neural Models of Pattern Formation	481
16.1 Spatial Patterning in Neural Firing with a Simple Activation-Inhibition Model	481
16.2 A Mechanism for Stripe Formation in the Visual Cortex	489
16.3 A Model for the Brain Mechanism Underlying Visual Hallucination Patterns	494
16.4 Neural Activity Model for Shell Patterns	505
Exercises	523
17. Mechanical Models for Generating Pattern and Form in Development	525
17.1 Introduction and Background Biology	525
17.2 Mechanical Model for Mesenchymal Morphogenesis	528
17.3 Linear Analysis, Dispersion Relation and Pattern Formation Potential	538
17.4 Simple Mechanical Models Which Generate Spatial Patterns with Complex Dispersion Relations	542
17.5 Periodic Patterns of Feather Germs	554
17.6 Cartilage Condensations in Limb Morphogenesis	558
17.7 Mechanochemical Model for the Epidermis	566
17.8 Travelling Wave Solutions of the Cytogel Model	572
17.9 Formation of Microvilli	579
17.10 Other Applications of Mechanochemical Models	586
Exercises	590
18. Evolution and Developmental Programmes	593
18.1 Evolution and Morphogenesis	593
18.2 Evolution and Morphogenetic Rules in Cartilage Formation in the Vertebrate Limb	599
18.3 Developmental Constraints, Morphogenetic Rules and the Consequences for Evolution	606
19. Epidemic Models and the Dynamics of Infectious Diseases	610
19.1 Simple Epidemic Models and Practical Applications	611
19.2 Modelling Venereal Diseases	619
19.3 Multi-group Model for Gonorrhoea and Its Control	623
19.4 AIDS: Modelling the Transmission Dynamics of the Human Immunodeficiency Virus (HIV)	624
19.5 Modelling the Population Dynamics of Acquired Immunity to Parasite Infection	630
*19.6 Age Dependent Epidemic Model and Threshold Criterion	640
19.7 Simple Drug Use Epidemic Model and Threshold Analysis	645
Exercises	649

20. Geographic Spread of Epidemics	651
20.1 Simple Model for the Spatial Spread of an Epidemic	651
20.2 Spread of the Black Death in Europe 1347-1350	655
20.3 The Spatial Spread of Rabies Among Foxes I: Background and Simple Model	659
20.4 The Spatial Spread of Rabies Among Foxes II: Three Species (SIR) Model	666
20.5 Control Strategy Based on Wave Propagation into a Non-epidemic Region: Estimate of Width of a Rabies Barrier	681
20.6 Two-Dimensional Epizootic Fronts and Effects of Variable Fox Densities: Quantitative Predictions for a Rabies Outbreak in England	689
Exercises	696
 Appendices	
1. Phase Plane Analysis	697
2. Routh-Hurwitz Conditions, Jury Conditions, Descarte's Rule of Signs and Exact Solutions of a Cubic	702
3. Hopf Bifurcation Theorem and Limit Cycles	706
4. General Results for the Laplacian Operator in Bounded Domains	720
 Bibliography	723
 Index	745