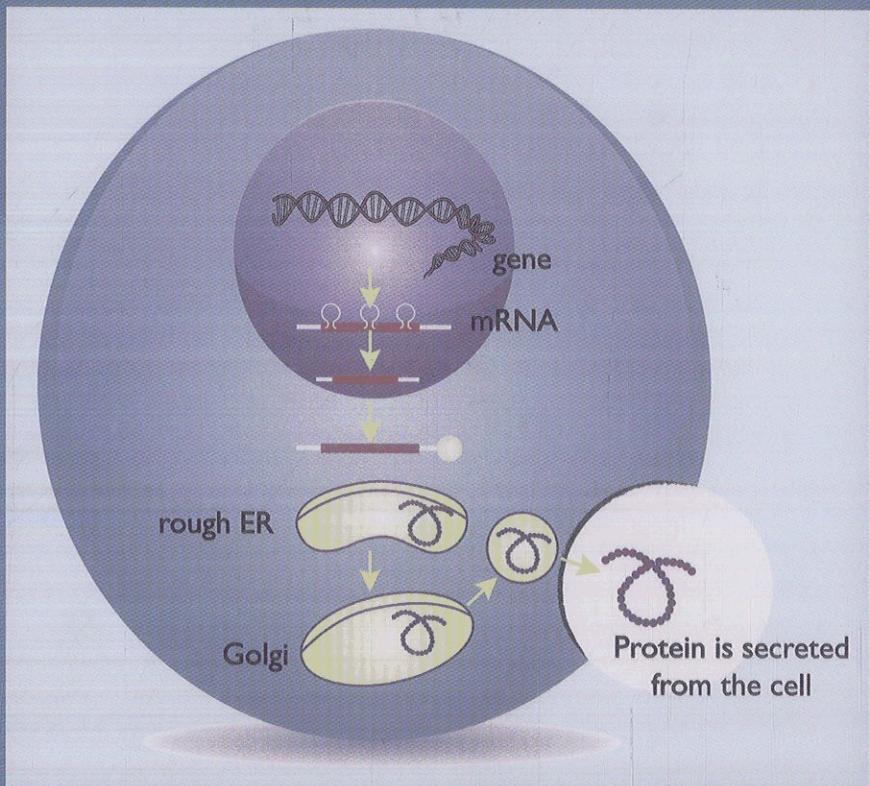


Series in
Mathematical Biology
and Medicine

Vol. 11

TOWARDS A MATHEMATICAL THEORY OF COMPLEX BIOLOGICAL SYSTEMS

C Bianca
N Bellomo



World Scientific

Contents

<i>Preface</i>	v
<i>Acknowledgments</i>	vii
<i>List of Figures</i>	xiii
<i>List of Tables</i>	xvii
1. Looking for a Mathematical Theory of Biological Systems	1
1.1 Introduction	1
1.2 On the Concept of Mathematical Theory	2
1.3 Plan of the Monograph	3
2. On the Complexity of Biological Systems	7
2.1 Ten Common Features of Living Systems	7
2.2 Some Introductory Concepts of Systems Biology	10
2.3 Reducing Complexity	13
Immune System, Wound Healing Process, and System Biology	15
3. The Immune System: A Phenomenological Overview	17
3.1 Introduction	17
3.2 Bacteria and Viruses	18
3.3 The Immune System Components	19
3.3.1 The Lymphatic System	19
3.3.2 The White Blood Cells	21

3.3.3	Antibodies and Hormones	24
3.4	The Immune Response	25
3.4.1	Innate Immunity	26
3.4.2	Adaptive Immunity	29
3.5	Immune System Diseases	32
3.6	Critical Analysis	35
4.	Wound Healing Process and Organ Repair	37
4.1	Introduction	37
4.2	Genes and Mutations	38
4.3	The Phases of Wound Healing	43
4.3.1	Hemostasis Phase	44
4.3.2	Inflammation Phase	47
4.3.3	Proliferation Phase	48
4.3.4	Maturation or Remodeling Phase	49
4.4	The Fibrosis Disease	50
4.5	Critical Analysis	54
5.	From Levels of Biological Organization to System Biology	55
5.1	Introduction	55
5.2	From Scaling to Mathematical Structures	56
5.3	Guidelines to the Modeling Approach	60

Mathematical Tools	65	
6.	Mathematical Tools and Structures	67
6.1	Introduction	67
6.2	Mathematical Frameworks of the Kinetic Theory of Active Particles	68
6.3	Guidelines Towards Modeling at the Molecular and Cellular Scales	78
6.4	Additional Analysis Looking at the Immune Competition	80
6.5	Critical Analysis	85
7.	Multiscale Modeling: Linking Molecular, Cellular, and Tissues Scales	89
7.1	Introduction	89

7.2	On the Phenomenological Derivation of Macroscopic Tissue Models	91
7.3	Cellular-Tissue Scale Modeling of Closed Systems	94
7.3.1	Asymptotic Methods for a Single Subsystem	95
7.3.2	Asymptotic Methods for Binary Mixtures of Subsystems	99
7.4	Cellular-Tissue Scale Modeling of Open Systems	108
7.5	On the Molecular-Cellular Scale Modeling	111
7.6	Critical Analysis	113
Applications and Research Perspectives		117
8.	A Model for Malign Keloid Formation and Immune System Competition	119
8.1	Introduction	119
8.2	The Mathematical Model	121
8.3	Simulations and Emerging Behaviors	131
8.3.1	Sensitivity Analysis of the Progression Rate α	132
8.3.2	Sensitivity Analysis of the Proliferation Rate β_I	144
8.3.3	Sensitivity Analysis of the Initial Distributions	147
8.4	Critical Analysis and Perspectives	154
9.	Macroscopic Models of Chemotaxis by KTAP Asymptotic Methods	157
9.1	Introduction	157
9.2	Linear Turning Kernels: Relaxation Models	159
9.2.1	The Case of a Single Subsystem	160
9.2.2	The Case of a Binary Mixture of Subsystems	162
9.3	Cellular-Tissue Scale Models of Chemotaxis	163
9.3.1	Classical Keller-Segel Type Models	165
9.3.2	Optimal Drift Following the Chemoattractant	165
9.3.3	Nonlinear Flux-Limited Model by the Mixed Scalings .	166
9.4	Critical Analysis	168
10.	Looking Ahead	171
10.1	Introduction	171
10.2	Some Challenges for Applied Mathematicians and Biologists .	172
10.3	How Far is the Mathematical Theory for Biological Systems .	173
10.4	Closure	177

Dependent Systems	179
A.1 Introduction	179
A.2 Mathematical Tools for Homogeneous Activity Systems	179
A.3 Mathematical Tools for Heterogeneous Activity Systems	182
<i>Glossary</i>	187
<i>Bibliography</i>	195
<i>Index</i>	205