

Contents

1	Systems Biology of Population Cell Response	1
	High-Throughput Biology	2
	Scale-Free Property	4
	Simplifying Biological Complexity	6
	References	9
2	Perturbation-Response Approach for Biological	
	Network Analysis.....	13
	The Perturbation-Response Approach	17
	The Origins of Linear Response	20
	Limitations of Linear Response Approach	22
	References	23
3	Basics of the Mammalian Immune System.....	25
	Types of Innate and Adaptive Immune Cells and Their Roles	26
	The Link Between Innate and Adaptive Immunity	27
	Toll-Like Receptors and Their Signaling Networks	29
	References	33
4	Inferring Novel Features of the TLR4 Pathways	35
	Computational Response Model of the TLR4 Pathways	36
	Simulations of NF- κ B and MAP Kinases Activity	
	in TLR4 Signaling.....	42
	Simulating Wild-Type and MyD88 KO Conditions	43
	Determination of Time Delay Process and Crosstalk Mechanisms	44
	Simulating TRIF KO and TRAM KO Conditions	48
	Simulating TRAF 6 KO, TAK1 KO, and RIP1 KO Conditions	49
	References	51

5	Signaling Flux Redistribution	53
	Simulating TLR4-Induced Gene Transcription	53
	Experimental Demonstration of <i>SFR</i>	55
	<i>SFR</i> at Other Pathway Junctions	60
	References	64
6	Investigating the TLR3 Signaling Dynamics	65
	Characterizing TLR3 Signaling Topology in Macrophages	66
	The Prediction of Missing Intermediary Processes	66
	Identification of Novel Pathways for MAP Kinases Activation	70
	References	73
7	Understanding TNFR1 Signaling Dynamics	75
	Simulations of TNFR1 Signaling Response	77
	Analyzing TNF-Induced Gene Expression Patterns Reveals	
	Novel Transcription Process	78
	Predicting Novel Target for Regulating Proinflammatory Response	83
	References	85
8	TRAIL Signaling in Cancer	87
	Dynamic Model for TRAIL-Stimulated HT1080	
	Cell Population Response	89
	Simulations of Initial TRAIL Signaling Model	91
	Revealing Novel Features of TRAIL Signaling	93
	Investigating p38 Dynamics	93
	Investigating JNK Dynamics	93
	Identifying In Silico Targets for Enhancing Cancer Cell Death	95
	References	103
9	Stochasticity and Variability: Insights from Single-Cell	
	Dynamics	105
	Biological Noise: Stochasticity and Heterogeneity	106
	The Origins of Biological Noise	109
	Noise in a Simple Gene Regulatory Network Is Crucial	
	for Bimodal Decisions	110
	References	115
10	Investigating Single-Cell Stochasticity in TRAIL Signaling	117
	Stochastic Algorithm	117
	Stochastic TRAIL Signaling Model	118
	References	124
11	The Distinction Between Single-Cell and Population	
	Dynamics	125
	References	130

12 Finding Chaos in Biology 131

 Attractors..... 133

 Self-Similarity and Patterns 135

 Sensitivity to Initial Conditions or Noise..... 137

 References..... 139

13 Concluding Remarks 141

Index..... 143

Immuno Systems Biology

A macroscopic approach for immune cell signaling

Selvarajoo, K.

2013, IX, 146 p. 69 illus., 61 illus. in color.,

ISBN: 978-1-4614-7690-0