

Contents

Preface XIII

List of Contributors XV

1	Biomolecular Computing: From Unconventional Computing to “Smart” Biosensors and Actuators – Editorial Introduction	1
	<i>Evgeny Katz</i>	
	References	5
2	Peptide-Based Computation: Switches, Gates, and Simple Arithmetic	9
	<i>Zehavit Dadon, Manickasundaram Samiappan, Nathaniel Wagner, Nurit Ashkenasy, and Gonen Ashkenasy</i>	
2.1	Introduction	9
2.2	Peptide-Based Replication Networks	10
2.2.1	Template-Assisted Replication	10
2.2.2	Theoretical Prediction of the Network Connectivity	11
2.2.3	<i>De novo</i> Designed Synthetic Networks	12
2.3	Logic Gates within Ternary Networks	13
2.3.1	Uniform Design Principles of All Two-Input Gates	13
2.3.2	OR Logic	14
2.3.3	AND Logic	15
2.3.4	NAND Logic	15
2.3.5	XOR Logic	15
2.4	Symmetry and Order Requirements for Constructing the Logic Gates	16
2.4.1	Symmetry and Order in Peptide-Based Catalytic Networks	16
2.4.2	How Symmetry and Order Affect the Replication of RNA Quasispecies	17
2.5	Taking the Steps toward More Complex Arithmetic	19
2.5.1	Arithmetic Units	19
2.5.2	Network Motifs	20

2.6	Experimental Logic Gates	21
2.6.1	OR Logic	21
2.6.2	NOT, NOR, and NOTIF Logic	21
2.6.3	Additional Logic Operations	23
2.7	Adaptive Networks	24
2.7.1	Chemical Triggering	24
2.7.2	Light Triggering	24
2.7.3	Light-Induced Logic Operations	25
2.8	Peptide-Based Switches and Gates for Molecular Electronics	28
2.9	Summary and Conclusion	29
	Acknowledgments	30
	References	30
3	Biomolecular Electronics and Protein-Based Optical Computing	33
	<i>Jordan A. Greco, Nicole L. Wagner, Matthew J. Ranaghan, Sanguthevar Rajasekaran, and Robert R. Birge</i>	
3.1	Introduction	33
3.2	Biomolecular and Semiconductor Electronics	34
3.2.1	Size and Speed	34
3.2.2	Architecture	36
3.2.3	Nanoscale Engineering	37
3.2.4	Stability	38
3.2.5	Reliability	38
3.3	Bacteriorhodopsin as a Photonic and Holographic Material for Bioelectronics	40
3.3.1	The Light-Induced Photocycle	40
3.3.2	The Branched Photocycle	42
3.4	Fourier Transform Holographic Associative Processors	42
3.5	Three-Dimensional Optical Memories	45
3.5.1	Write, Read, and Erase Operations	46
3.5.2	Efficient Algorithms for Data Processing	48
3.5.3	Multiplexing and Error Analysis	50
3.6	Genetic Engineering of Bacteriorhodopsin for Device Applications	51
3.7	Future Directions	53
	Acknowledgments	54
	References	54
4	Bioelectronic Devices Controlled by Enzyme-Based Information Processing Systems	61
	<i>Evgeny Katz</i>	
4.1	Introduction	61
4.2	Enzyme-Based Logic Systems Producing pH Changes as Output Signals	62

4.3	Interfacing of the Enzyme Logic Systems with Electrodes Modified with Signal-Responsive Polymers	64
4.4	Switchable Biofuel Cells Controlled by the Enzyme Logic Systems	68
4.5	Biomolecular Logic Systems Composed of Biocatalytic and Biorecognition Units and Their Integration with Biofuel Cells	70
4.6	Processing of Injury Biomarkers by Enzyme Logic Systems Associated with Switchable Electrodes	74
4.7	Summary and Outlook	77
	Acknowledgments	78
	References	78
5	Enzyme Logic Digital Biosensors for Biomedical Applications	81
	<i>Evgeny Katz and Joseph Wang</i>	
5.1	Introduction	81
5.2	Enzyme-Based Logic Systems for Identification of Injury Conditions	82
5.3	Multiplexing of Injury Codes for the Parallel Operation of Enzyme Logic Gates	85
5.4	Scaling Up the Complexity of the Biocomputing Systems for Biomedical Applications – Mimicking Biochemical Pathways	89
5.5	Application of Filter Systems for Improving Digitalization of the Output Signals Generated by Enzyme Logic Systems for Injury Analysis	94
5.6	Conclusions and Perspectives	96
	Acknowledgments	98
	Appendix	98
	References	99
6	Information Security Applications Based on Biomolecular Systems	103
	<i>Guinevere Strack, Heather R. Luckarift, Glenn R. Johnson, and Evgeny Katz</i>	
6.1	Introduction	103
6.2	Molecular and Bio-molecular Keypad Locks	104
6.3	Antibody Encryption and Steganography	108
6.4	Bio-barcode	113
6.5	Conclusion	114
	Acknowledgments	114
	References	114
7	Biocomputing: Explore Its Realization and Intelligent Logic Detection	117
	<i>Ming Zhou and Shaojun Dong</i>	
7.1	Introduction	117
7.2	DNA Biocomputing	119

7.3	Aptamer Biocomputing	121
7.4	Enzyme Biocomputing	124
7.5	Conclusions and Perspectives	128
	References	129
8	Some Experiments and Models in Molecular Computing and Robotics	133
	<i>Milan N. Stojanovic and Darko Stefanovic</i>	
8.1	Introduction	133
8.2	From Gates to Programmable Automata	133
8.3	From Random Walker to Molecular Robotics	139
8.4	Conclusions	142
	Acknowledgments	143
	References	143
9	Biomolecular Finite Automata	145
	<i>Tamar Ratner, Sivan Shoshani, Ron Piran, and Ehud Keinan</i>	
9.1	Introduction	145
9.2	Biomolecular Finite Automata	146
9.2.1	Theoretical Models of a Molecular Turing Machine	146
9.2.2	The First Realization of an Autonomous DNA-Based Finite Automaton	150
9.2.3	Three-Symbol-Three-State DNA-Based Automata	155
9.2.4	Molecular Cryptosystem for Images by DNA Computing	157
9.2.5	Molecular Computing Device for Medical Diagnosis and Treatment <i>In Vitro</i>	159
9.2.6	DNA-Based Automaton with Bacterial Phenotype Output	161
9.2.7	Molecular Computing with Plant Cell Phenotype	163
9.3	Biomolecular Finite Transducer	167
9.4	Applications in Developmental Biology	172
9.5	Outlook	176
	References	178
10	<i>In Vivo</i> Information Processing Using RNA Interference	181
	<i>Yaakov Benenson</i>	
10.1	Introduction	181
10.1.1	Regulatory Pathways as Computations	181
10.1.2	A Computation Versus a Computer	182
10.1.3	Prior Work on Synthetic Biomolecular Computing Circuits	182
10.2	RNA Interference-Based Logic	183
10.2.1	General Considerations	183
10.2.2	Logic Circuit Blueprint	184
10.2.3	Experimental Confirmation of the Computational Core	188
10.3	Building the Sensory Module	189
10.3.1	Direct Control of siRNA by mRNA Inputs	191

10.3.2	Complex Transcriptional Regulation Using RNAi-Based Circuits	194
10.4	Outlook	195
	References	197
11	Biomolecular Computing Systems	199
	<i>Harish Chandran, Sudhanshu Garg, Nikhil Gopalkrishnan, and John H. Reif</i>	
11.1	Introduction	199
11.1.1	Organization of the Chapter	199
11.2	DNA as a Tool for Molecular Programming	200
11.2.1	DNA Structure	200
11.2.2	Review of DNA Reactions	200
11.3	Birth of DNA Computing: Adleman's Experiment and Extensions	203
11.3.1	NP-Complete Problems	203
11.3.2	Hamiltonian Path Problem via DNA Computing	204
11.3.3	Other Models of DNA Computing	204
11.3.4	Shortcomings and Nonscalability of Schemes Using DNA Computation to Solve NP-Complete Problems	204
11.4	Computation Using DNA Tiles	205
11.4.1	TAM: an Abstract Model of Self-Assembly	205
11.4.2	Algorithmic Assembly via DNA Tiling Lattices	206
11.4.2.1	Source of Errors	206
11.4.3	Algorithmic Error Correction Schemes for Tilings	207
11.5	Experimental Advances in Purely Hybridization-Based Computation	209
11.6	Experimental Advances in Enzyme-Based DNA Computing	212
11.7	Biochemical DNA Reaction Networks	217
11.8	Conclusion: Challenges in DNA-Based Biomolecular Computation	218
11.8.1	Scalability of Biomolecular Computations	218
11.8.2	Ease of Design and Programmability of Biomolecular Computations	220
11.8.3	<i>In Vivo</i> Biomolecular Computations	220
11.8.4	Conclusions	220
	Acknowledgments	221
	References	221
12	Enumeration Approach to the Analysis of Interacting Nucleic Acid Strands	225
	<i>Satoshi Kobayashi and Takaya Kawakami</i>	
12.1	Introduction	225
12.2	Definitions and Notations for Set and Multiset	226
12.3	Chemical Equilibrium and Hybridization Reaction System	227
12.4	Symmetric Enumeration Method	230

12.4.1	Enumeration Graph	230
12.4.2	Path Mappings	231
12.4.3	Enumeration Scheme	232
12.4.4	An Example of Enumeration Scheme – Folding of an RNA Molecule	233
12.4.5	Convex Programming Problem for Computing Equilibrium	235
12.5	Applying SEM to Nucleic Acid Strands Interaction	236
12.5.1	Target Secondary Structures	237
12.5.2	Introducing Basic Notations	237
12.5.3	Definition of Enumeration Graph Structure	239
12.5.4	Associated Weight Functions	241
12.5.5	Symmetric Properties	242
12.5.6	Complexity Issues	242
12.6	Conclusions	243
	References	244
13	Restriction Enzymes in Language Generation and Plasmid Computing	245
	<i>Tom Head</i>	
13.1	Introduction	245
13.2	Wet Splicing Systems	246
13.3	Dry Splicing Systems	249
13.4	Splicing Theory: Its Original Motivation and Its Extensive Unforeseen Developments	252
13.5	Computing with Plasmids	253
13.6	Fluid Memory	254
13.7	Examples of Aqueous Computations	255
13.8	Final Comments about Computing with Biomolecules	260
	References	261
14	Development of Bacteria-Based Cellular Computing Circuits for Sensing and Control in Biological Systems	265
	<i>Michaela A. TerAvest, Zhongjian Li, and Largus T. Angenent</i>	
14.1	Introduction	265
14.2	Cellular Computing Circuits	267
14.2.1	Genetic Toolbox	267
14.2.1.1	Engineered Gene Regulation	267
14.2.1.2	Quorum Sensing	269
14.2.2	Implementations	269
14.2.2.1	Oscillators	269
14.2.2.2	Switches	270
14.2.2.3	AND Logic Gates	270
14.2.2.4	Edge Detector	271
14.2.2.5	Complex Logic Functions with Multiple Strains	272
14.2.3	Transition to <i>In Silico</i> Rational Design	273

14.2.4	Transition from Enzyme Computing to Bacteria-Based Biocomputing	274
14.3	Conclusion	276
	Acknowledgments	277
	References	277
15	The Logic of Decision Making in Environmental Bacteria	279
	<i>Rafael Silva-Rocha, Javier Tamames, and Víctor de Lorenzo</i>	
15.1	Introduction	279
15.2	Building Models for Biological Networks	281
15.3	Formulation and Simulation of Regulatory Networks	283
15.3.1	Stochastic Versus Deterministic Models	284
15.3.2	Graphical Models	285
15.4	Boolean Analysis of Regulatory Networks	285
15.4.1	Translating Biological Networks into Logic Circuits	286
15.4.2	Integration of Regulatory and Metabolic Logic in the Same Boolean Circuit	287
15.4.3	From Digital Networks to Workable Models	288
15.5	Boolean Description of m-xylene Biodegradation by <i>P. putida</i> mt-2: the TOL logicome	289
15.5.1	Narrative Description of the TOL Regulatory Circuit	291
15.5.2	Deconstruction of the Ps–Pr Regulatory Node into Three Autonomous Logic Units	292
15.5.3	Formalization of Regulatory Events at the Upper and Lower TOL Operons	294
15.5.4	3MB Is the Endogenous Signal Carrier through the Domains of the TOL Network	296
15.5.5	The TOL Logicome	296
15.6	Conclusion and Outlook	298
	Acknowledgments	299
	References	299
16	Qualitative and Quantitative Aspects of a Model for Processes Inspired by the Functioning of the Living Cell	303
	<i>Andrzej Ehrenfeucht, Jetty Kleijn, Maciej Koutny, and Grzegorz Rozenberg</i>	
16.1	Introduction	303
16.2	Reactions	304
16.3	Reaction Systems	305
16.4	Examples	307
16.5	Reaction Systems with Measurements	310
16.6	Generalized Reactions	312
16.7	A Generic Quantitative Model	315
16.8	Approximations of Gene Expression Systems	316

16.9	Simulating Approximations by Reaction Systems	318
16.10	Discussion	319
	Acknowledgments	321
	References	321
17	Computational Methods for Quantitative Submodel Comparison	323
	<i>Andrzej Mizera, Elena Czeizler, and Ion Petre</i>	
17.1	Introduction	323
17.2	Methods for Model Decomposition	324
17.2.1	Knockdown Mutants	324
17.2.2	Elementary Flux Modes	325
17.2.3	Control-Based Decomposition	325
17.3	Methods for Submodel Comparison	327
17.3.1	Mathematically Controlled Model Comparison	327
17.3.2	An Extension of the Mathematically Controlled Comparison	328
17.3.3	Local Submodel Comparison	329
17.3.4	A Quantitative Measure for the Goodness of Model Fit Against Experimental Data	329
17.3.5	Quantitative Refinement	330
17.3.6	Parameter-Independent Submodel Comparison	331
17.3.7	Model Comparison for Pathway Identification	332
17.4	Case Study	332
17.4.1	A Biochemical Model for the Heat Shock Response	332
17.4.2	Control-Based Decomposition	334
17.4.3	The Knockdown Mutants	335
17.4.4	Local Comparison of the Knockdown Mutants	336
17.4.5	Parameter-Independent Comparison of the Mutant Behavior	337
17.4.6	Pathway Identification for the Phosphorylation-Driven Control of the Heat Shock Response	341
17.5	Discussion	342
	Acknowledgments	343
	References	343
18	Conclusions and Perspectives	347
	<i>Evgeny Katz</i>	
	References	349
	Index	351