

Contents

	Preface	<i>xv</i>
	Acknowledgment	<i>xvii</i>
	List of Abbreviations	<i>xxiii</i>
1	Introduction	<i>1</i>
1.1	Motivation and Applications	<i>1</i>
1.2	Enzyme-Based Logic Gates and Short Logic Circuits	<i>3</i>
	References	<i>5</i>
2	Boolean Logic Gates Realized with Enzyme-Catalyzed Reactions: Unusual Look at Usual Chemical Reactions	<i>9</i>
2.1	General Introduction and Definitions	<i>9</i>
2.2	Fundamental Boolean Logic Operations Mimicked with Enzyme-Catalyzed Reactions	<i>11</i>
2.2.1	Identity (YES) Gate	<i>11</i>
2.2.2	Inverted Identity (NOT) Gate	<i>12</i>
2.2.3	OR Gate	<i>13</i>
2.2.4	NOR Gate	<i>15</i>
2.2.5	XOR Gate	<i>15</i>
2.2.6	NXOR Gate	<i>18</i>
2.2.7	AND Gate	<i>20</i>
2.2.8	NAND Gate	<i>21</i>
2.2.9	INHIB Gate	<i>22</i>
2.2.10	Summary on the Basic Boolean Gates Realized with Enzyme Systems	<i>23</i>
2.3	Modular Design of NOR and NAND Logic Gates	<i>24</i>
2.4	Majority and Minority Logic Gates	<i>28</i>
2.5	Reconfigurable Logic Gates	<i>34</i>
2.5.1	3-Input Logic Gates Switchable Between AND–OR Logic Functions Operating in a Solution	<i>34</i>
2.5.2	Enzyme-Based Logic Gates Switchable Between OR, NXOR, and NAND Boolean Operations Realized in a Flow System	<i>35</i>
2.6	Conclusions and Perspectives	<i>40</i>
	References	<i>41</i>

3	Optimization of Enzyme-Based Logic Gates for Reducing Noise in the Signal Transduction Process	47
3.1	Introduction	47
3.2	Signal Transduction Function in the Enzyme-Based Logic Systems: Filters Producing Sigmoid Response Functions	48
3.2.1	Identity (YES) Logic Gate Optimization	50
3.2.2	AND Logic Gate Optimization	52
3.2.3	OR Logic Gate Optimization	55
3.2.4	XOR Logic Gate Optimization	56
3.3	Summary	59
	References	59
4	Enzyme-Based Short Logic Networks Composed of Concatenated Logic Gates	63
4.1	Introduction: Problems in Assembling of Multistep Logic Networks	63
4.2	Logic Network Composed of Concatenated Gates: An Example System	64
4.3	Logic Networks with Suppressed Noise in the Presence of Filter Systems	66
4.4	Logic Circuits Activated with Biomolecular Signals and Magnetic Field Applied	68
4.4.1	Biocatalytic Reactions Proceeding with Bulk Diffusion of Intermediate Substrates/Products and with Their Channeling	68
4.4.2	Magneto-Controlled Biocatalytic Cascade Switchable Between Substrate Diffusion and Substrate Channeling Modes of Operation	69
4.4.3	Logic Signal Processing with the Switchable Biocatalytic System	72
4.5	The Summary: Step Forward from Single Logic Gates to Complex Logic Circuits	74
	References	75
5	Sophisticated Reversible Logic Systems	79
5.1	Introduction	79
5.1.1	Reversible Logic Gates and Their Features	79
5.1.2	Logic Reversibility vs. Physical Reversibility	80
5.1.3	Integration of Reversible Logic Gates into Biomolecular Computing Systems	81
5.1.4	Spatial Separation of Enzyme Logic Operation: The Use of Flow Devices	81
5.2	Feynman Gate: Controlled NOT (CNOT) Gate	82
5.3	Double Feynman Gate (DFG) Operation	86
5.4	Toffoli Gate Operation	90
5.5	Peres Gate Operation	94
5.6	Gates Redirecting Output Signals	99
5.6.1	Controlled-Switch Gate	99

5.6.2	Fredkin (Controlled-Swap) Gate	102
5.7	Advantages and Disadvantages of the Developed Approach	107
5.7.1	Advantages	107
5.7.2	Disadvantages	108
5.8	Conclusions and Perspectives	109
	References	109
6	Transduction of Signals Generated by Enzyme Logic Gates	113
6.1	Optical Analysis of Output Signals Generated by Enzyme-Based Logic Systems	113
6.1.1	Optical Absorbance Measurements for Transduction of Output Signals Produced by Enzyme-Based Logic Gates	114
6.1.2	Bioluminescence Measurements for Transduction of Output Signals Produced by Enzyme-Based Logic Gates	120
6.1.3	Surface Plasmon Resonance (SPR) Measurements for Transduction of Output Signals Produced by Enzyme-Based Logic Gates	121
6.2	Electrochemical Analysis of Output Signals Generated by Enzyme-Based Logic Systems	122
6.2.1	Chronoamperometric Transduction of Chemical Output Signals Produced by Enzyme-Based Logic Systems	123
6.2.2	Potentiometric Transduction of Chemical Output Signals Produced by Enzyme-Based Logic Systems	124
6.2.3	pH Measurements as a Tool for Transduction of Chemical Output Signals Produced by Enzyme-Based Logic Systems	126
6.2.4	Indirect Electrochemical Analysis of Output Signals Generated by Enzyme-Based Logic Systems Using Electrodes Functionalized with pH-Switchable Polymers	127
6.2.5	Conductivity Measurements as a Tool for Transduction of Chemical Output Signals Produced by Enzyme-Based Logic Systems	130
6.2.6	Transduction of Chemical Output Signals Produced by Enzyme-Based Logic Systems Using Semiconductor Devices	132
6.3	Macro/Micro/Nano-mechanical Transduction of Chemical Output Signals Produced by Enzyme-Based Logic Systems	134
6.3.1	Mechanical Bending of a Cantilever Used for Transduction of Chemical Output Signals Produced by Enzyme-Based Logic Systems	135
6.3.2	Quartz Crystal Microbalance (QCM) Transduction of Chemical Output Signals Produced by Enzyme-Based Logic Systems	137
6.3.3	Atomic Force Microscopy (AFM) Transduction of Chemical Output Signals Produced by Enzyme-Based Logic Systems	138
6.4	Conclusions and Perspectives	142
	References	143
7	Circuit Elements Based on Enzyme Systems	151
7.1	Enzyme-Based Multiplexer and Demultiplexer	151

7.1.1	General Definition of the Multiplexer and Demultiplexer Functions	151
7.1.2	2-to-1 Digital Multiplexer Based on the Enzyme-Catalyzed Reactions	153
7.1.3	1-to-2 Digital Demultiplexer Based on the Enzyme-Catalyzed Reactions	155
7.1.4	1-to-2 Digital Demultiplexer Interfaced with an Electrochemical Actuator	158
7.2	Biomolecular Signal Amplifier Based on Enzyme-Catalyzed Reactions	164
7.3	Biomolecular Signal Converter Based on Enzyme-Catalyzed Reactions	166
7.4	Utilization of a Fluidic Infrastructure for the Realization of Enzyme-Based Boolean Logic Circuits	167
7.5	Other Circuit Elements Required for the Networking of Enzyme Logic Systems and General Conclusions	169
	References	170
8	Enzyme-Based Memory Systems	175
8.1	Introduction	175
8.2	Enzyme-Based Flip-Flop Memory Elements	175
8.2.1	Set/Reset (SR) Flip-Flop Memory Based on Enzyme-Catalyzed Reactions	176
8.2.2	Delay (D) Flip-Flop Memory Based on Enzyme-Catalyzed Reactions	182
8.2.3	Toggle (T) Flip-Flop Memory Based on Enzyme-Catalyzed Reactions	185
8.2.4	Enzyme-Based Flip-Flop Memory Systems: Conclusions and Perspectives	186
8.3	Memristor Based on Enzyme Biocatalytic Reactions	188
8.3.1	Memristors: From Semiconductor Devices to Soft Matter and Biomolecular Materials	188
8.3.2	The Memristor Device Based on a Biofuel Cell	189
8.3.3	The Memristor Device Controlled by Logically Processed Biomolecular Signals	196
8.3.4	Enzyme-Based Memristors: Conclusions and Perspectives	198
8.4	Enzyme-Based Associative Memory Systems	198
8.4.1	Associative Memory: Biological Origin and Function	199
8.4.2	Realization of the Associative Memory with a Multienzyme Biocatalytic Cascade	201
8.4.3	Enzyme-Based Associative Memory: Challenges and Perspectives	203
8.5	Enzyme-Based Memory Systems: Challenges, Perspectives, and Limitations	204
	References	206

- 9 Arithmetic Functions Realized with Enzyme-Catalyzed Reactions 211**
 - 9.1 Molecular and Biomolecular Arithmetic Systems: Introduction and Motivation 211
 - 9.2 Half-Adder 212
 - 9.3 Half-Subtractor 216
 - 9.4 Conclusions and Perspectives 219
 - References 219

- 10 Information Security Applications Based on Enzyme Logic Systems 223**
 - 10.1 Keypad Lock Devices as Examples of Electronic Information Security Systems 223
 - 10.2 Keypad Lock Systems Based on Biocatalytic Cascades 224
 - 10.3 Other Biomolecular Information Security Systems 229
 - 10.3.1 Steganography and Encryption Methods Based on Bioaffinity Complex Formation Followed by a Biocatalytic Reaction 229
 - 10.3.2 Barcodes Produced by Bioelectrocatalytic Reactions 231
 - 10.4 Summary 233
 - References 233

- 11 Enzyme Logic Digital Biosensors for Biomedical, Forensic, and Security Applications 235**
 - 11.1 Introduction: Short Overview 235
 - 11.2 From Traditional Analog Biosensors to Novel Binary Biosensors Based on the Biocomputing Concept 235
 - 11.3 How Binary Operating Biosensors Can Benefit Biomedical Analysis: Requirements, Challenges, and First Applications 238
 - 11.4 Binary (YES/NO) Analysis of Liver Injury Biomarkers: From Test Tube Probes to Animal Research 240
 - 11.5 Further Examples of Injury Biomarker Analysis Using AND/NAND Logic Gates 245
 - 11.5.1 Soft Tissue Injury (STI) Logic Analysis 246
 - 11.5.2 Traumatic Brain Injury (TBI) Logic Analysis 247
 - 11.5.3 Abdominal Trauma (ABT) Logic Analysis 250
 - 11.5.4 Hemorrhagic Shock (HS) Logic Analysis 251
 - 11.5.5 Oxidative Stress (OS) Logic Analysis 254
 - 11.5.6 Radiation Injury (RI) Logic Analysis 258
 - 11.6 Multienzyme Logic Network Architectures for Assessing Injuries: Aiming at the Increased Complexity of the Biocomputing–Bioanalytic Systems 261
 - 11.6.1 The System Structure Based on the Complex Biocatalytic Cascade 261
 - 11.6.2 STI Operation Mode of the Logic Network 264
 - 11.6.3 TBI Operation Mode of the Logic Network 265

- 11.6.4 Switching Between the STI and TBI Modes and General Comments on the System 267
- 11.7 New Approach in Forensic Analysis: Biomolecular Computing-Based Analysis of Forensic Biomarkers 268
- 11.8 Logic Analysis of Security Threats (Explosives and Nerve Agents) Based on Biocatalytic Cascades 270
- 11.9 Integration of Biocatalytic Cascades with Microelectronics and Wearable Sensors 272
- 11.10 Conclusions and Perspectives 276
References 276

- 12 Release of Molecular Species Stimulated by Logically Processed Biomolecule Signals 283**
 - 12.1 Motivation and Experimental Background 283
 - 12.2 Fe³⁺-Cross-Linked Alginate Hydrogel is a Good Example of Matrix for Signal-Stimulated Release 284
 - 12.3 DNA Release as an Example of Signal-Stimulated Biomolecule Release 287
 - 12.4 Bioelectrochemical Systems with Sensing and Releasing Electrodes 287
 - 12.4.1 Sensing Electrodes Activated with Single Input Identity Gate 288
 - 12.4.2 Sensing Electrodes Activated with Multi-input Logic Networks 288
 - 12.4.3 Releasing Electrodes: Various Released Species for Different Applications 291
 - 12.5 Fe³⁺-Cross-Linked Alginate Hydrogel Decomposition and Entrapped Molecule Release Triggered by Enzymatically Produced H₂O₂ 294
 - 12.5.1 DNA Release from Fe³⁺-Cross-Linked Alginate Hydrogel Stimulated by Signals Processed through OR, AND, and INHIB Logic Gates 294
 - 12.5.2 DNA Release from Fe³⁺-Cross-Linked Alginate Hydrogel Stimulated by Signals Processed Through Multi-gate Network Composed of Concatenated AND Gates 304
 - 12.6 Conclusions and Perspectives 307
References 307

- 13 Biofuel Cells Controlled by Biocomputing Systems 313**
 - 13.1 Introduction: Biofuel Cells, Their Applications, and Motivation for Designing Adaptive, Signal-Controlled Devices 313
 - 13.2 Biofuel Cells Controlled by Logically Processed Biochemical Signals 315
 - 13.3 Biofuel Cells Controlled by Biomolecular Keypad Lock Systems 326
 - 13.4 Conclusions and Perspectives 328
References 330

- 14 Bioelectronic Interface Between Enzyme-Based and DNA-Based Computing Systems 335**
 - 14.1 Introduction: Interfacing Enzyme-Based and DNA-Based Computing Systems Is a Challenging Goal 335

14.2	Bioelectronic Interface Transducing Logically Processed Signals from an Enzymatic System to a DNA System	336
14.3	The Bioelectronic Interface Connecting Enzyme-Based Reversible Logic Gates and DNA-Based Reversible Logic Gates: Realization in a Flow Device	344
14.3.1	Enzyme-Based Fredkin Gate Processing Biomolecular Signals Prior to the Bioelectronic Interface	345
14.3.2	Reversible DNA-Based Feynman Gate Activated by Signals Produced by the Enzyme-Based Fredkin Gate	348
14.4	Conclusions and Perspectives	351
	References	352
15	What Is Next? Mimicking Natural Biological Information Processes	357
15.1	Motivation and Goals	357
15.2	Example and Discussion of Feed Forward Loops	358
15.3	Enzymatic Feed-Forward Loops	360
15.4	Process Design and Kinetic Modeling	364
15.5	Simpler Biocatalytic Systems: Not a Feed-Forward Loop Yet	366
15.6	Conclusion	367
	References	368
16	Conclusions and Perspectives: Where Are We Going?	371
16.1	Conclusions	371
16.2	Perspectives	373
16.2.1	Information Processing Through Complex Biological Pathways in Cells	374
16.2.2	Signal-Controlled Bioelectronic Devices and Signal-Triggered Molecular Release	375
16.2.3	Allosteric and Hybrid Enzymes	375
16.2.4	Enzyme System Controlled by Various Chemical and Physical Signals	377
16.2.5	Molecular and Nanomachines for Self-Propulsion and Logic Operation	378
16.3	Final Comments	379
	References	380
	Index	383

