Contents

Preface xiii

- 1 DNA Computing: Origination, Motivation, and Goals – Illustrated Introduction 1 Evgeny Katz
- 1.1 Motivation and Applications *1*
- 1.2 DNA- and RNA-Based Biocomputing Systems in Progress 3

|v

- 1.3 DNA-Based Information Storage Systems 8
- 1.4 Short Conclusions and Comments on the Book *10* References *11*

2 DNA Computing: Methodologies and Challenges 15

Deepak Sharma and Manojkumar Ramteke

- 2.1 Introduction to DNA Computing Methodologies 15
- 2.2 Key Developments in DNA Computing 16
- 2.2.1 Adleman Model 16
- 2.2.2 Lipton's Model 18
- 2.2.3 Smith's Model 19
- 2.2.4 Sakamoto's Model 21
- 2.2.5 Ouyang's Model 22
- 2.2.6 Chao's Model 24
- 2.2.7 DNA Origami 24
- 2.2.8 DNA-Based Data Storage 26
- 2.3 Challenges 26 Acknowledgment 27 References 28

3 DNA Computing and Circuits 31

Chuan Zhang

- 3.1 From Theory to DNA Implementations 31
- 3.2 Application-Specific DNA Circuits 35
 - Acknowledgments 41 References 41

vi Contents

4	Connecting DNA Logic Gates in Computational Circuits 45
4.1	Dmitry M. Kolpashchikov and Aresenij J. Kalnin
4.1	DNA Logic Gates in the Context of Molecular Computation 45
4.2	Connecting Deoxyribozyme Logic Gates 46
4.3	Connecting Gates Based on DNA Strand Displacement 47
4.4	Logic Gates Connected Via DNA Four-Way Junction (4WJ) 50
4.5	Conclusion 53 References 53
5	Development of Logic Gate Nanodevices from Fluorogenic RNA Aptamers 57 Trinity Jackson, Rachel Fitzgerald, Daniel K. Miller, and Emil F. Khisamutdinov
5.1	Nucleic Acid: The Material of Choice for Nanotechnology 57
5.2	RNA Aptamers are Modular and Programmable Biosensing Units 58
5.3	Construction of RNA Nanoparticles with Integrated Logic Gate
	Operations Using Light-Up Aptamers 64
5.3.1	Implementation of MG-Binding RNA Aptamer to Design Binary Logic Gates 65
5.3.2	Implementation of MG-Binding RNA Aptamer and Broccoli RNA Aptamer to Design Half-Adder Circuit 68
5.4	Conclusion 70
	Acknowledgments 70
	References 70
6	Programming Molecular Circuitry and Intracellular Computing
	with Framework Nucleic Acids 77
	Jiang Li and Chunhai Fan
6.1	Framework Nucleic Acids 77
6.2	A Toolbox for Biomolecular Engineering of Living Systems 80
6.2.1	Biomolecular Scaffolds 80
6.2.2	Logic Units 81
6.2.3	Cell Entry Vehicles 82
6.2.4	Isothermal Construction 83
6.2.5	Targeting and Editing 83
6.2.6	Signal Readout 84
6.2.7	Triggers and Switches 84
6.2.8	Error Correction and Resilience 84
6.3	Targeted Applications 85
6.3.1	Drug Delivery 85
6.3.2	Cellular Imaging 85
6.3.3	Metabolic Engineering and Cellular Pathway Investigation 86
6.4	Nucleic Acid Nanotechnology-Enabled Computing Kernel 86
6.5	I/O and Human–Computer Interfacing 89
6.6	Information Storage 90
6.7	Perspectives 91
6.8	Conclusion 95
6.8.1	Terminology 96
0.011	References 97

7 Engineering DNA Switches for DNA Computing Applications 105

Dominic Lauzon, Guichi Zhu, and Alexis Vallée-Bélisle

- 7.1 Introduction 105
- 7.2 Selecting Recognition Element Based on Input 107
- 7.3 Engineering Switching Mechanisms 108
- 7.4 Engineering Logic Output Function Response 116
- 7.5 Optimizing Switch Response 117
- 7.6 Perspective 120 Acknowledgments 120 References 121
- 8 Fluorescent Signal Design in DNA Logic Circuits 125
 - Dan Huang, Shu Yang, and Qianfan Yang
- 8.1 Basic Signal Generation Strategies Based on DNA Structures *126*
- 8.1.1 Strategies Based on Watson–Crick Hydrogen Bond 127
- 8.1.1.1 Signal Derived from Hairpin Structure/Molecular Beacon 127
- 8.1.1.2 Signal Derived from DNAzyme Activity 128
- 8.1.1.3 Signal Derived from Strand Displacement Reaction 129
- 8.1.2 Strategies Based on Hoogsteen Hydrogen Bond 132
- 8.1.2.1 Signal Derived from G-Quadruplex 132
- 8.1.2.2 Signal with the Help of i-Motif 135
- 8.1.3 Signal Derived from Aptamer–Ligand Interaction 138
- 8.2 Designs for Constructing Multi-output Signals 138
- 8.2.1 Selecting Individual Signal Transducers 138
- 8.2.2 Designing Multifunctional Probes 141
- 8.3 Summary and Outlook 147
 - References 149
- 9 Nontraditional Luminescent and Quenching Materials for Nucleic Acid-Based Molecular Photonic Logic 155 Rehan Higgins, Melissa Massey, and W. Russ Algar
- 9.1 Introduction 155
- 9.2 DNA Molecular Photonic Logic Gates 156
- 9.3 Nontraditional Luminescent Materials 158
- 9.4 Semiconductor "Quantum Dot" Nanocrystals 159
- 9.4.1 Quantum Dots 159
- 9.4.2 Logic Gates with QDs 160
- 9.5 Lanthanide-Based Materials 161
- 9.5.1 Luminescent Lanthanide Complexes 161
- 9.5.2 Coupling Lanthanide Complexes with Energy Transfer 163
- 9.5.3 Logic Gates with LLCs and Lanthanide Ions 163
- 9.5.4 Upconversion Nanoparticles 165
- 9.5.5 Logic Gates with UCNPs 165
- 9.6 Gold Nanoparticles 166
- 9.6.1 Gold Nanoparticles 166

- 9.6.2 Logic Gates with AuNPs and Colorimetric Output 166
- 9.6.3 Logic Gates with AuNPs and PL Quenching 168
- 9.7 Metal Nanoclusters 169
- 9.7.1 Metal Nanoclusters 169
- 9.7.2 Logic Gates with Metal Nanoclusters 170
- 9.8 Carbon Nanomaterials 171
- 9.8.1 Graphene and Graphene Oxide 171
- 9.8.2 Logic Gates with Graphene and GO 172
- 9.8.3 Carbon Dots 174
- 9.8.4 Logic Gates with CDs 175
- 9.9 Conjugated Polymers 175
- 9.9.1 Conjugated Polymers 175
- 9.9.2 Logic Gates with CPs 176
- 9.10 Conclusions and Perspective 177 References 178

10 Programming Spatiotemporal Patterns with DNA-Based Circuits 185 Mars Van Day Hofstadt Cuillauma Cines, Joan Christopha Calas, and

Marc Van Der Hofstadt, Guillaume Gines, Jean-Christophe Galas, and André Estevez-Torres

- 10.1 Introduction 185
- 10.1.1 What is Spatial Computing? 185
- 10.1.2 Digital vs. Analog Computing 186
- 10.1.3 Computing Consumes Energy 186
- 10.1.4 Molecules Compute in Space Through Reaction–Diffusion Primitives 187
- 10.2 Experimental Implementation of DNA Analog Circuits 188
- 10.2.1 DNA Strand Displacement Oscillators 189
- 10.2.2 DNA/Enzyme Oscillators 189
- 10.2.2.1 Genelets 190
- 10.2.2.2 PEN Reactions 191
- 10.3 Time-Dependent Spatial Patterns 193
- 10.3.1 Edge Detection 194
- 10.3.2 Traveling Patterns 195
- 10.3.2.1 Fronts 196
- 10.3.2.2 Go-Fetch Fronts 197
- 10.3.2.3 Waves and Spirals 198
- 10.3.3 Controlling Spatio-Temporal Patterns 199
- 10.3.3.1 Controlling Diffusion Coefficients 199
- 10.3.3.2 Initial and Boundary Conditions 200
- 10.4 Steady-State Spatial Patterns 202
- 10.4.1 Colony Formation 202
- 10.4.2 Patterns with Positional Information 203
- 10.5 Conclusion and Perspectives 206 Acknowledgments 207 References 208

- 11Computing Without Computing: DNA Version213Vladik Kreinovich and Julio C. Urenda
- 11.1 Introduction 213
- 11.2 Computing Without Computing Quantum Version: A Brief Reminder 214
- 11.3 Computing Without Computing Version Involving Acausal Processes: A Reminder 215
- 11.4 Computing Without Computing: DNA Version 217
- 11.4.1 Main Idea 217
- 11.4.2 It Is Not Easy to Stop Biological Processes 218
- 11.4.3 Towards Describing Ligation Prevention in Precise Terms 218
- 11.4.4 What Is Given 219
- 11.4.5 What We Want to Find 219
- 11.4.6 Let Us Prove that the Ligation Prevention Problem Is NP-Hard 219
- 11.4.7 How NP-Hardness Is Usually Proved 219
- 11.4.8 How We Will Prove NP-Hardness 220
- 11.4.9 The Actual Proof by Reduction 220
- 11.5 DNA Computing Without Computing Is Somewhat Less Powerful than Traditional DNA Computing: A Proof 222
- 11.5.1 Which of the Two DNA Computing Schemes is More Powerful? 222
- 11.5.2 W-hierarchy: A Brief Reminder 222
- 11.5.3 Conclusion 224
- 11.6 First Related Result: Security Is More Difficult to Achieve than Privacy 224
- 11.6.1 What We Plan to do in this Section 224
- 11.6.2 How to Describe Privacy in Graph Terms 224
- 11.6.3 How to Describe Security in Graph Terms 225
- 11.6.4 Conclusion: Security Is More Difficult to Maintain than Privacy 226
- 11.7 Second Related Result: Data Storage Is More Difficult than Data Transmission 226
- 11.7.1 Application to Information Science 226
- 11.7.2 Data Storage 226
- 11.7.3 Data Transmission 227
- 11.7.4 Conclusion: Data Storage Is More Difficult than Data Transmission 228
 Acknowledgments 228
 References 228
- 12 DNA Computing: Versatile Logic Circuits and Innovative Bio-applications 231
 - Daoqing Fan, Erkang Wang, and Shaojun Dong
- 12.1 Definition, Logical Principle, and Classification of DNA Computing 231
- 12.2 Advanced Arithmetic DNA Logic Devices 232
- 12.2.1 Half-Adder, Half-Subtractor 232
- 12.2.2 Full-Adder, Full-Subtractor 234
- 12.3 Advanced Non-arithmetic DNA Logic Devices 235

x Contents

- 12.3.1 Data Conversion: Encoder/Decoder, Multiplexer/Demultiplexer 235
- 12.3.2 Distinguishing Even/Odd Natural Numbers: The Parity Checker 236
- 12.3.3 DNA Voter and Keypad Lock 236
- 12.3.4 Parity Generator/Checker (pG/pC) for Error Detection During Data Transmission 237
- 12.3.5 Non-Boolean Ternary Logic Gates 239
- 12.4 Concatenated Logic Circuits 239
- 12.5 Innovative Multifunctional DNA Logic Library 241
- 12.6 Intelligent Bio-applications 241
- 12.7 Prospects 244 Acknowledgment 244 References 244

13Nucleic Acid-Based Computing in Living Cells Using Strand
Displacement Processes247

Lukas Oesinghaus and Friedrich C. Simmel

- 13.1 Nucleic Acid Strand Displacement 247
- 13.1.1 Basics 247
- 13.1.2 Computing with Strand Displacement Processes 248
- 13.1.3 Computing with Nucleic Acid Strand Displacement In Vivo 250
- 13.2 Synthetic Riboregulators 251
- 13.2.1 First-Generation Riboregulators 251
- 13.2.2 Toehold Switch Riboregulators 252
- 13.2.3 Other Transcriptional and Translational Regulators 254
- 13.3 Combining Strand Displacement and CRISPR Mechanisms 255
- 13.3.1 A Brief Introduction to CRISPR 255
- 13.4 Computing Via Nucleic Acid Strand Displacement in Mammalian Cells 258
- 13.5 Outlook 260
- 13.5.1 Interfacing Nucleic Acid Computing with Synthetic Biology 260 References 262

14 Strand Displacement in DNA-Based Nanodevices and Logic 265

- Antoine Bader and Scott L. Cockroft
- 14.1 An Introduction to Strand Displacement Reactions 265
- 14.1.1 External Control of Strand Displacement Reactions 265
- 14.1.2 The Toehold Exchange Mechanism 268
- 14.2 Dynamic Reconfiguration of Structural Devices 268
- 14.3 Stepped and Autonomous DNA Walkers 271
- 14.4 Early Breakthroughs in DNA Computing 274
- 14.4.1 Hamiltonian Paths 275
- 14.4.2 Satisfiability (SAT) Problem 277
- 14.5 DNA-Based Molecular Logic 279
- 14.5.1 Computing with Boolean Logic 279
- 14.5.2 Deoxyribozyme Logic Gates 280

Contents xi

- 14.5.3 Autonomous DNA Translators 282
- 14.5.4 Catalytic Systems for Signal Amplification 285
- 14.6 Future Prospects for Strand Displacement-Based Devices 286
- 14.6.1 DNA Chemical Reaction Networks 286
- 14.6.2 DNA Nanotechnology Goes In Vivo 287 Acknowledgment 289 References 289
- 15 Development and Application of Catalytic DNA in Nanoscale Robotics 293
 - David Arredondo, Matthew R. Lakin, Darko Stefanovic, and Milan N. Stojanovic
- 15.1 Introduction 293
- 15.2 Brief History of DNAzymes 293
- 15.3 Experimental Implementations 296
- 15.4 DNAzyme Walkers 298
- 15.5 Statistical Mechanics and Simulation 300
- 15.6 Conclusions 302 References 304

16 DNA Origami Transformers 307

Reem Mokhtar, Tianqi Song, Daniel Fu, Shalin Shah, Xin Song, Ming Yang, and John Reif

- 16.1 Introduction 307
- 16.2 Design 312
- 16.3 Experimental Demonstrations 316
- 16.4 Applications 318
- 16.5 Conclusion 322 Acknowledgment 322 References 322
- 17 Nanopore Decoding for DNA Computing 327
 - Hiroki Yasuga, Kan Shoji, and Ryuji Kawano
- 17.1 Introduction 327
- 17.2 Application of Nanopore Technology for Rapid and Label-Free Decoding *330*
- 17.3 Application of Nanopore Decoding in Medical Diagnosis 335
- 17.4 Conclusions 339 References 339
- 18 An Overview of DNA-Based Digital Data Storage 345

Xin Song, Shalin Shah, and John Reif

- 18.1 Introduction 345
- 18.1.1 Durability and Energy Efficiency 345
- 18.1.2 Density and Coding Capacity 345
- 18.1.3 Availability of Supporting Technologies 346
- 18.2 Components of a DNA Storage System 346

xii Contents

- 18.2.1 Data Encoding 346
- 18.2.2 Data Writing 346
- 18.2.3 Data Storage 348
- 18.2.4 Data Retrieval 348
- 18.2.5 Data Decoding 349
- 18.3 Conclusions and Outlook 350 Acknowledgments 350 References 350

19 Interfacing Enzyme-Based and DNA-Based Computing Systems: From Simple Boolean Logic to Sophisticated Reversible Logic Systems 353 Evgeny Katz

- 19.1 Interfacing Enzyme-Based and DNA-Based Computing Systems is a Challenging Goal: Motivations and Approaches 353
- 19.2 Bioelectronic Interface Transducing Logically Processed Signals from an Enzymatic System to a DNA System 354
- 19.3 The Bioelectronic Interface Connecting Enzyme-Based Reversible Logic Gates and DNA-Based Reversible Logic Gates: Realization in a Flow Device 362
- 19.4 Enzyme-Based Fredkin Gate Processing Biomolecular Signals Prior to the Bioelectronic Interface *363*
- 19.5 Reversible DNA-Based Feynman Gate Activated by Signals Produced by the Enzyme-Based Fredkin Gate 368
- 19.6 Conclusions and Perspectives 371
- 19.A Appendix 373
- 19.A.1 Oligonucleotides Used in the System Mimicking Feynman Gate 373 References 374

20 Conclusions and Perspectives: Further Research Directions and Possible Applications 379 Evgeny Katz

Index 383