

Contents

1	Defining the Field of Sequence-Controlled Polymers	1
	<i>Jean-François Lutz</i>	
1.1	Introduction	1
1.2	Glossary	4
1.3	Sequence Regulation in Biopolymers	7
1.3.1	Nucleic Acids	7
1.3.2	Proteins	7
1.4	Bio-Inspired Sequence-Regulated Approaches	8
1.5	Sequence Regulation in Synthetic Macromolecules	9
1.5.1	Step-Growth Polymerizations	11
1.5.2	Chain-Growth Polymerizations	11
1.5.3	Multistep Growth Polymerizations	13
1.6	Characterization of SCPs	15
1.7	Impact in Materials Science	17
1.8	Some Words About the Future	19
	References	20
2	Kinetics and Thermodynamics of Sequence Regulation	27
	<i>Pierre Gaspard</i>	
2.1	Introduction	27
2.2	Generalities	28
2.2.1	Characterization of Sequences and Information	28
2.2.1.1	Single-Molecule Level of Description	28
2.2.1.2	Many-Molecule Level of Description	29
2.2.2	Precise or Loose Sequence Control during Copolymerization	30
2.2.3	Conditions for Growth or Dissolution	31
2.2.4	Kinetic Equations	32
2.3	Thermodynamics	33
2.3.1	Free Copolymerization	34
2.3.2	Template-Directed Copolymerization	35
2.3.3	Depolymerization	35
2.4	Kinetics Yielding Bernoulli Chains	36
2.5	Kinetics Yielding Markov Chains	36
2.6	Kinetics Yielding Non-Markovian Chains	40

2.7	Effect of Sequence Disorder on Ceiling and Floor Temperatures	40
2.8	Mechanical Power of Sequence Disorder	43
2.9	Template-Directed Copolymerization	44
2.10	Conclusion	45
	Acknowledgments	45
	References	46
3	Nucleic Acid-Templated Synthesis of Sequence-Defined Synthetic Polymers	49
	<i>Zhen Chen and David R. Liu</i>	
3.1	Introduction	49
3.2	Enzymatic Templated Syntheses of Non-Natural Nucleic Acids	50
3.2.1	Polymerase-Catalyzed Syntheses of Backbone-Modified Nucleic Acids	50
3.2.2	Polymerase-Catalyzed Syntheses of Nucleobase-Modified Nucleic Acids	52
3.2.3	Polymerase-Catalyzed Syntheses of Sugar-Modified Nucleic Acids	54
3.2.4	Ligase-Catalyzed Syntheses of Non-Natural Nucleic Acids	58
3.3	Ribosomal Synthesis of Non-Natural Peptides	59
3.4	Nonenzymatic Polymerization of Nucleic Acids	61
3.5	Nonenzymatic Polymerization of Non-Nucleic Acid Polymers	67
3.6	Conclusion and Outlook	71
	Acknowledgments	73
	References	73
4	Design of Sequence-Specific Polymers by Genetic Engineering	91
	<i>Davoud Mozhdehi, Kelli M. Luginbuhl, Stefan Roberts, and Ashutosh Chilkoti</i>	
4.1	Introduction	91
4.2	Design of Repetitive Protein Polymers	93
4.3	Methods for the Genetic Synthesis of Repetitive Protein Polymers	96
4.4	Expression of Repetitive Protein Polymers	100
4.5	Expanding the Chemical Repertoire of Protein Polymers	100
4.5.1	Chemo-Enzymatic Modification	101
4.5.2	Incorporation of Noncanonical Amino Acids	104
4.5.3	Post-Translational Modifications	105
4.6	Summary and Outlook	107
	References	108
5	Peptide Synthesis and Beyond the Use of Sequence-Defined Segments for Materials Science	117
	<i>Niels ten Brummelhuis, Patrick Wilke, and Hans G. Börner</i>	
5.1	Introduction	117
5.2	The History of Solid-Phase-Supported Peptide Synthesis	118
5.3	Supports for the Chemical Synthesis of Peptides	120
5.4	Synthesis of Peptide–Polymer Conjugates	122

5.5	Identification of Functional Sequences	125
5.5.1	Phage Display	125
5.5.2	Split-and-Mix Libraries and SPOT Synthesis	130
5.5.3	Applications of Libraries	134
5.5.4	Dynamic Covalent (Pseudo)Peptide Libraries	136
5.6	Sequence–Property Relationships	136
5.7	Translation of Sequence to Synthetic Precision Polymer Platforms	137
5.8	Conclusion	141
	References	141
6	Iterative Synthetic Methods for the Assembly of Sequence-Controlled Non-Natural Polymers	159
	<i>Christopher Alabi</i>	
6.1	Introduction	159
6.2	The Solid-Phase Approach	161
6.2.1	Type of Solid Supports	161
6.2.2	Iterative Assembly using Single Heterobifunctional Monomers	162
6.2.3	Iterative Assembly using Multiple Heterobifunctional Monomers	163
6.3	The Liquid-Phase Approach	164
6.3.1	Requirements for Liquid-Phase Supports	165
6.3.2	Examples of Iterative Liquid-Phase Methodologies	165
6.3.3	The Fluorous Liquid-Phase Approach	167
6.4	The Template Approach	168
6.5	A Support-Free Approach	170
6.6	Outlook	175
	References	176
7	Sequence-Controlled Peptoid Polymers: Bridging the Gap between Biology and Synthetic Polymers	183
	<i>Mark A. Kline, Li Guo, and Ronald N. Zuckermann</i>	
7.1	Introduction	183
7.1.1	Closing the Gap between Biological Polymers and Synthetic Polymers	184
7.1.2	Enhancing Synthetic Polymers with Sequence Control	184
7.2	Peptoids – Bridging the Gap	187
7.3	Polypeptoid Synthesis	189
7.3.1	Solution Polymerization Method	189
7.3.2	Solid-Phase Synthesis Method	190
7.3.2.1	Solid-Phase Peptide Synthesis	190
7.3.2.2	Solid-Phase Peptoid Synthesis	192
7.3.2.3	Solid-Phase Submonomer Synthesis Method	192
7.3.3	Combinatorial Synthesis	197
7.3.4	Polypeptoid Analysis	197
7.4	Discovering Peptoid Properties Derived from Sequence Control	198
7.4.1	Peptoids as Potential Therapeutics	199

7.4.2	Peptoids with Controlled Conformation	199
7.4.2.1	Peptoid Properties Dominated by Side Chains	201
7.4.2.2	The Effect of Bulky Side Chains	201
7.4.2.3	The Peptoid Backbone Differs from a Peptide Backbone	202
7.4.2.4	Cyclic Peptoids	205
7.4.3	Peptoids That Function as Biomaterials	205
7.4.3.1	Antimicrobial and Antifouling Peptoids	206
7.4.3.2	Lipidated Peptoids for Drug Delivery	206
7.4.4	Ordered Supramolecular Assemblies: Toward Hierarchal Structures with Function	206
7.4.4.1	Supramolecular Self-Assembly from Uncharged Amphiphilic Diblock Copolypeptoids	207
7.4.4.2	Structures from Amphiphilic, Ionic-Aromatic Diblock Copolypeptoids	207
7.4.4.3	Free-Floating Two-Dimensional Peptoid Nanosheets with Crystalline Order	211
7.5	Conclusion	214
	Acknowledgments	215
	References	215
8	Sequence and Architectural Control in Glycopolymer Synthesis	229
	<i>Yamin Abdouni, Gokhan Yilmaz, and C. Remzi Becer</i>	
8.1	Introduction: Glycopolymer–Lectin Binding	229
8.2	Sequence-Controlled Glycopolymers	230
8.2.1	Sequence-Defined Glycooligomers	231
8.2.2	Sequence Control via Time-Regulated Additions	234
8.2.3	Sequence Control via Time-Regulated Chain Extensions	235
8.2.4	Sequence Control via Orthogonal Reactions	237
8.3	Self-Assembly of Glycopolymers	238
8.3.1	Self-Assembly Based on Amphiphilicity	238
8.3.2	Temperature-Triggered Self-Assemblies	242
8.3.3	pH-Responsive Self-Assemblies	243
8.3.4	Self-Assembly Based on Electrostatic Interactions	245
8.4	Single-Chain Folding of Glycopolymers: The Future?	248
8.4.1	Selective Point Folding	249
8.4.2	Repeat Unit Folding	249
8.5	General Conclusion and Future Outlook	251
	Acknowledgments	251
	References	251
9	Sequence Regulation in Chain-Growth Polymerizations	257
	<i>Makoto Ouchi</i>	
9.1	Introduction	257
9.2	Alternating Copolymerization	259
9.2.1	Addition Polymerization	259
9.2.2	Alternating ROMP	261

9.3	Iterative Single-Unit Addition with Living Polymerization	262
9.3.1	Iterative Process along with Purification via Peak Separation	263
9.3.2	Iterative Process along with Transformation of Pendant Group	266
9.4	Template-Assisted Polymerization	267
9.4.1	Template Initiator	268
9.4.2	Template Inimer	269
9.5	Cyclopolymerization	270
9.6	Ring-Opening Polymerization of Sequence-Programmed Monomer	272
9.7	Conclusion	274
	References	274
10	Sequence-Controlled Polymers by Chain Polymerization	281
	<i>Junpo He, Jie Ren, and Erlita Mastan</i>	
10.1	Introduction	281
10.2	Sequence-Controlled Polymers by Various Polymerization Mechanisms	282
10.2.1	Anionic Polymerization	282
10.2.2	Cationic Polymerization	289
10.2.3	Ring-Opening Polymerization (ROP)	290
10.2.4	Ring-Opening Metathesis Polymerization (ROMP)	292
10.2.4.1	Regioselective ROMP of Substituted Cyclooctene	292
10.2.4.2	Regioselective ROMP of Macrocyclic Compounds	294
10.2.4.3	Alternating Copolymerization	296
10.2.4.4	Kinetic Control for Polymers with Sequence-Defined Functionalities	299
10.2.5	Radical Polymerization	300
10.2.5.1	Polymers with Alternating AB Sequence	301
10.2.5.2	Polymer with ABB (1 : 2) Sequence	305
10.2.5.3	Polymers with Site-Specific Functionalization	307
10.2.5.4	Polymers with Precisely Controlled Sequence at Monomer Level	309
10.2.5.5	Other Sequence-Controlled Polymers	312
10.2.6	Coordination Polymerization	315
10.3	Concluding Remarks	316
	References	317
11	Sequence-Controlled Polymers via Cationic Polymerization	327
	<i>Sadahito Aoshima and Arihiro Kanazawa</i>	
11.1	Introduction	327
11.2	Recent Developments in Living Cationic Polymerization	328
11.2.1	Design of Initiating Systems for Living Polymerization	328
11.2.2	Base-Assisting Living Systems with Various Metal Halides	329
11.2.3	New Monomers for Cationic Polymerization	330
11.3	Sequence-Regulated Functional Polymers	331
11.3.1	Synthesis of New Block, Gradient, and End-Functionalized Polymers	331

11.3.2	Synthesis of Various Alternating Polymers by Controlled Cationic Polymerization	334
11.3.3	Synthesis of New Ring Polymers	336
11.4	Sequence Control Based on the Cationic Copolymerization of Vinyl and Cyclic Monomers	337
11.4.1	Strategy for Sequence Control by Copolymerizing Different Types of Monomers	337
11.4.2	Concurrent Cationic Vinyl-Addition and Ring-Opening Copolymerization of VEs and Oxiranes	338
11.4.3	Terpolymerization via the Exclusive One-way Cycle of Crossover Propagation Reactions	341
11.4.4	Concurrent Cationic Vinyl-Addition and Ring-Opening Copolymerization Mediated by Long-Lived Species	344
	References	345
12	Periodic Copolymers by Step-Growth Polymerization	349
	<i>Zi-Long Li and Zi-Chen Li</i>	
12.1	Introduction	349
12.2	Carbon-Chain Periodic Polymers	352
12.2.1	Acyclic Diene Metathesis Polymerization	352
12.2.2	Atom Transfer Radical Coupling	355
12.2.3	C(sp ³)-C(sp ³) Coupling	355
12.2.4	Atom Transfer Radical Polyaddition	356
12.3	Hetero-Chain Periodic Polymers	357
12.3.1	Polycondensation or Polyaddition of Oligomonomers	357
12.3.1.1	Polycondensation	357
12.3.1.2	Polyaddition via Click Reactions	359
12.3.1.3	Radical Addition-Coupling Polymerization	362
12.3.2	One-Pot Sequential Monomer Addition and Polymerization	364
12.3.3	Multicomponent Polymerizations	364
12.4	Conclusions and Outlook	369
	References	372
13	Click and Click-Inspired Chemistry for the Design of Sequence-Controlled Polymers	379
	<i>Steven Martens, Joshua O. Holloway, and Filip E. Du Prez</i>	
13.1	Introduction to “Click” and Click-Inspired Reactions Within the Area of Sequence-Controlled Polymers	379
13.2	Click and Click-Inspired Reactions for Sequence Building	380
13.2.1	Copper(I)-Catalyzed Azide/Alkyne Cycloaddition	380
13.2.2	Thiol-X and Thiolactone Chemistries	386
13.2.3	Diels-Alder: Photo-Triggered and Thermally Induced Reactions	395
13.3	Conclusions and Outlook	400
	References	400

14	One-Pot Sequence-Controlled (SC) Multiblock Copolymers via Copper-Mediated Polymerization	417
	<i>Athina Anastasaki, Richard Whitfield, Vasiliki Nikolaou, Nghia P. Truong, Glen R. Jones, Nikolaos G. Engelis, Evelina Liarou, Michael R. Whittaker, and David M. Haddleton</i>	
14.1	Introduction	417
14.2	Criteria for the Successful Synthesis of SC Multiblock Copolymers	419
14.3	Historical Background toward the Development of One-Pot SC Multiblocks	419
14.4	Access to SC Acrylic Multiblock Copolymers	420
14.4.1	The Cu(0)-Wire-Mediated RDRP Approach	420
14.4.1.1	When to Use Cu(0)-Wire-Mediated RDRP	422
14.4.1.2	When Not to Use This Technique	422
14.4.1.3	Protocol for the Synthesis of Acrylic Multiblock Copolymers via Cu(0)-Wire-Mediated RDRP	423
14.4.2	Light-Mediated Copper Polymerization for the Synthesis of Acrylic Multiblock Copolymers	424
14.4.2.1	Attributes of the Light-Mediated Copper Polymerization Technique	426
14.4.2.2	Reasons Not to Select This Technique	426
14.4.2.3	Protocol for the Synthesis of Acrylic Multiblock Copolymers via Light-Mediated Copper Polymerization	426
14.5	Access to SC Acrylamide Multiblock Copolymers (The CuBr/Me ₆ Tren Disproportionation Technique)	427
14.5.1	Why Use the CuBr/Me ₆ Tren Disproportionation Technique	428
14.5.2	Reasons Not to Select This Technique	428
14.5.3	Protocol for the Synthesis of Acrylic Multiblock Copolymers via CuBr/Me ₆ Tren Disproportionation Technique	429
14.6	Perspective and Outlook	429
	References	430
15	Properties and Applications of Sequence-Controlled Polymers	435
	<i>Jordan H. Swisher, Jamie A. Nowalk, Michael A. Washington, and Tara Y. Meyer</i>	
15.1	Introduction	435
15.1.1	Definitions	436
15.1.2	Types of Sequence-Dependent Properties	437
15.1.3	Categories of Sequence Comparison Studies	438
15.2	Molecular Properties	439
15.2.1	Monomer Order	439
15.2.2	Electronic/Vibrational Properties and Reactivity	439
15.3	Solution-Phase Properties	439
15.3.1	Folding	441
15.3.2	Recognition	443

15.3.3	Aggregation	444
15.4	Sequence Dependence of Bulk-Phase Properties	445
15.4.1	Category I – Block Composition	446
15.4.1.1	Block Dispersity	446
15.4.1.2	Block Frequency	446
15.4.2	Category II – Monomer Distribution	449
15.4.2.1	Tacticity	449
15.4.2.2	Alternating versus Random (and Block)	453
15.4.2.3	Gradient Copolymers	454
15.4.3	Category III – Precision Placement	454
15.4.4	Category IV – Side-Chain Sequence	458
15.4.5	Category V – Complex Sequences	458
15.5	Conclusions and Outlook	461
15.5.1	Solution-Phase Properties	462
15.5.2	Bulk-Phase Properties	464
15.5.3	The Future	466
	References	466
16	Tandem Mass Spectrometry Sequencing of Sequence-Controlled and Sequence-Defined Synthetic Polymers	479
	<i>Laurence Charles</i>	
16.1	Introduction	479
16.2	MS/MS Principle	480
16.3	MS/MS of Sequence-Controlled Copolymers	482
16.4	MS/MS of Sequence-Defined Polymers	485
16.4.1	Biomimetics	485
16.4.2	Sequence-Defined Copolymers for Information Storage	490
16.5	Conclusions and Perspectives	498
	References	500
	Index	505