Contents

Preface XI	
List of Contributors	XIII

1	Principles of Microprocess Technology 1
	Wladimir Reschetilowski
1.1	Introduction 1
1.2	History 2
1.3	Basic Characteristics 3
1.3.1	Microfluidics and Micromixing 4
1.3.2	Temperature and Pressure Control 5
1.3.3	Safety and Ecological Impact 7
1.4	Industrial Applications 8
1.5	Concluding Remarks 9
	References 10
2	Effects of Microfluidics on Preparative Chemistry Processes 13
•	Madhvanand Kashid, Albert Renken, and Lioubov Kiwi-Minsker
2.1	Introduction 13
2.2	Mixing 15
2.3	Heat Management 18
2.3.1	Heat Transfer in Continuous-Flow Devices 19
2.3.2	Heat Control of Microchannel Reactors 22
2.4	Mass Transfer and Chemical Reactions 26
2.4.1	Fluid-Solid Catalytic Systems 26
2.4.2	Fluid-Fluid Systems 31
2.4.2.1	Flow Regimes 32
2.4.2.2	Mass Transfer 34
2.4.3	Three-Phase Systems 36
2.4.3.1	Gas-Liquid-Solid Systems 36
2.4.3.2	Gas-Liquid-Liquid Systems 40
2.5	Flow Separation 40
2.5.1	Geometrical Modifications 41
2.5.2	Wettability-Based Flow Splitters 42



'	Contents	
	2.5.3	Conventional Separator Adapted for Microstructured Reactors 44
	2.6	Numbering-Up Strategy 45
	2.7	Practical Exercise: Experimental Characterization of Mixing in
		Microstructured Reactors 46
		References 50
	3	Modular Micro- and Millireactor Systems for Preparative Chemical
	,	Synthesis and Bioprocesses 55
		Frank Schael, Marc-Oliver Piepenbrock, Jörn Emmerich, and Joachim Heck
	3.1	Introduction 55
	3.2	Modular Microreaction System 57
	3.3	Examples for Microreactor Applications 60
	3.3.1	Synthesis of Vitamin A Acetate 60
	3.3.2	Screening of Process Parameters for a Suzuki–Miyaura Reaction 62
		·
	3.3.3	Scale-Up of Thermal Rearrangement of Furfuryl Alcohol 64
	3.3.4	Online Reaction Monitoring and Automation of Chemical Synthesis and Bioprocesses 66
	3.4	Laboratory Exercise: Suzuki Reaction in a Modular Microreactor
	3.4	•
		Setup 70 References 73
		References 73
	4	Potential of Lab-on-a-Chip: Synthesis, Separation, and Analysis
		of Biomolecules 77
		Martin Bertau
	4.1	Introduction 37
	4.2	Learning from Nature: Analogies to Living Cells 77
	4.3	Microenzyme Reactors 79
	4.3.1	Enzyme Immobilization on the Microchannel Surface 80
	4.3.2	Enzyme Immobilization on Supports 81
	4.3.3	Modes of Operation 81
	4.3.4	Enzymatic Conversions 81
	4.3.5	Enzymatic Cleavage of Peptides 84
	4.3.6	Determination of Inhibitor Properties 84
	4.3.7	Cytotoxicity Assessment 87
	4.4	Microchip Electrophoresis 87
	4.4.1	Peptide Analysis 88
	4.4.2	Chiral Separation 88
	4.4.3	Coupling Biocatalysis and Analysis 88
	4.4.4	Determination of Amino Acids in Goods and Foods 89
	4.5	Microenzyme Membrane Reactor/Micromembrane
		Chromatography 89
	4.6	Nucleic Acid Analysis in Microchannels 91
	4.7	Saccharide Analyses in Microdevices 94
	4.8	Practical Exercise: Lipase-Catalyzed Esterification Reaction 96
		References 97

5	Bioprocessing in Microreactors 101
c 1	Fridolin Okkels and Dorota Kwasny
5.1	Introduction 101
5.2	Background 101
5.2.1	Basic Elements of a Biosensor 101
5.2.2	Different Sensing Methods 103
5.2.3	The Effect of Reducing Dimensionality and Length Scales of Biosensors 103
5.2.4	Biosensors Based on Field-Effect Transistors 104
5.2.4.1	The Main Working Principle of FET Sensors 105
5.2.4.2	Fabrication of SiNW FET Sensors 106
5.2.4.3	Functionalization of SiNW FET Sensors Using APTES 107
5.2.5	Shielding by the Buffer. Combined Influence from Ions and Charge Carriers 107
5.3	Practical Exercise: Functionalization of Silicon Surface 108 References 113
6	Synthesis of Fine Chemicals 115
	Sandra Hübner, Norbert Steinfeldt, and Klaus Jähnisch
6.1	Introduction 115
6.2	Organic Synthesis in Liquid and Liquid–Liquid Phases 116
6.2.1	Fluorination Reactions 116
6.2.2	Reactions with Diazomethane 127
6.2.3	Ultrasound-Assisted Liquid-Liquid Biphasic and Liquid Reactions 134
6.3	Gas-Liquid Biphasic Organic Synthesis 141
6.3.1	Ozonolysis Reactions 141
6.3.2	Photooxygenation Reactions 151
6.4	Practical Exercise: Photochemical Generation of Singlet Oxygen and Its $[4+2]$ Cycloaddition to Cyclopentadiene 159 References 161
7	Synthesis of Nanomaterials Using Continuous-Flow Microreactors 165 Chih-Hung Chang
7.1	Introduction 165
7.2	Microfluidic Devices 165
7.3	Synthesis of Nanomaterials Using Microreactors 166
7.4	Kinetic Studies 180
7.5	Process Optimization 183
7.6	Point-of Use Synthesis and Deposition 185
7.6.1	Deposition of Nanomaterials 185
7.7	Practical Exercises: Synthesis of Nanocrystals 187
7.7.1	Synthesis of ZnO Nanocrystals 187
7.7.2	Synthesis of CdS Nanoparticles 190 References 192

VIII	Contents

8	Polymerization in Microfluidic Reactors 197
	Jesse Greener and Eugenia Kumacheva
8.1	Introduction 197
8.2	Practical Considerations 198
8.2.1	Control Over Reaction Conditions 198
8.2.1.1	Batch Reactors 198
8.2.1.2	Microreactors 199
8.2.2	Control of Mixing 199
8.2.3	Control of Reagent Concentrations 200
8.2.4	Distance-to-Time Transformation 200
8.2.5	Potential Negative Impacts of Polymerization Reactions on Reactor
	Operation 201
8.2.5.1	Buildup in Solution Viscosity 201
8.2.5.2	Precipitation 202
8.2.5.3	Adsorption 202
8.2.6	Selection of Materials for Fabrication of MF Reactors 203
8.2.6.1	Polymer Materials 203
8.2.6.2	Metals 205
8.2.6.3	Glass 205
8.3	Single-Phase Polymerization 205
8.4	Multiphase Polymerization 208
8.4.1	Formation of Polymer Particles 209
8.4.1.1	Formation of Precursor Droplets 209
8.4.1.2	Transformation of Precursor Droplets into Polymer Particles 213
8.4.2	Review of Demonstrated Applications 214
8.4.2.1	Controlled Encapsulation 214
8.4.2.2	Encapsulation and Delivery 215
8.4.2.3	Cell Encapsulation 217
8.4.2.4	Microgels as Model Cells 219
8.5	Beyond Synthesis: New Developments for Next-Generation MF
	Polymerization 220
8.5.1	Scaled-Up MF Synthesis of Polymer Particles 220
8.5.2	In Situ Characterization of Polymerization in MF Reactors 223
8.5.3	Automated Systems for Polymerization Microreactors 223
8.6	Practical Exercise: MF Polymerization Reactor Kinetics Studies Using
	In Situ Characterization 224
	References 227
9	Electrochemical Reactions in Microreactors 231
	Jun-ichi Yoshida and Aiichiro Nagaki
9.1	Introduction 231
9.2	Electrode Configuration 232
9.2.1	Serial Electrode Configuration 232
9.2.2	Interdigitated Electrode Configuration 233

9.2.3	Parallel Electrode Configuration 233
9.3	Electrolysis without Supporting Electrolytes 234
9.4	Generation and Reactions with Unstable Intermediates 235
9.5	Practical Exercise: Electrochemical Reactions in Flow
	Microreactors 239
	References 241
10	Heterogeneous Catalysis in Microreactors 243
•	Evgeny V. Rebrov
10.1	Introduction 243
10.2	Bulk Catalysts 244
10.3	Supported Catalysts 246
10.3.1	Macroporous Supports 247
10.3.1.1	ZnO Support 247
10.3.1.2	γ-Al ₂ O ₃ Support 247
10.3.1.3	Catalysts Immobilized onto Polymeric Particles 249
10.3.1.4	Silica-Supported Catalysts 251
10.3.1.5	Carbon-Supported Catalysts 253
10.4	Mesoporous Supports 256
10.4.1	Mesoporous Titania 258
10.4.2	Mesoporous Silica 260
10.4.3	Mesoporous Alumina 261
10.5	Microporous Supports 261
10.6	Practical Exercise: PdZn/TiO ₂ -Catalyzed Selective
	Hydrogenation of Acetylene Alcohols in a Capillary
	Microreactor 263
	References 265
11	Chemical Intensification in Flow Chemistry through Harsh Reaction
•	Conditions and New Reaction Design 273
	Timothy Noël and Volker Hessel
11.1	Introduction 273
11.2	High-Temperature Processing in Microflow 273
11.3	High-Pressure Processing in Microflow 278
11.4	Solvent Effects in Microflow 280
11.5	Ex-Regime Processing and Handling of Hazardous Compounds in
11.5	Microflow 283
11.6	New Chemical Transformations in Microflow 284
11.7	Process Integration in Microflow 286
11.8	Practical Exercises 288
11.8.1	Claisen Rearrangement at Elevated Temperatures 288
11.8.2	Copper(I)-Catalyzed Azide-Alkyne Cycloaddition with Integrated
	Copper Scavenging Unit 290
	References 292

x۱	Contents	
	12	Modeling in Microreactors 297
		Ekaterina S. Borovinskaya
	12.1	Introduction 297
	12.2	Processes in Microreactors and the Role of Mixing 298
	12.3	Modeling of Processes in Microreactors Based on General Balance
		Equation 300
	12.3.1	Plug Flow Tube Reactor Model 300
	12.3.2	Laminar Flow Model 302
	12.4	Computation of Reaction Flows in Microreactors 308
	12.4.1	Computational Fluid Dynamics 308
	12.4.2	Single-Phase Modeling 309
	12.4.3	Two-Phase Modeling 310
	12.4.3.1	Liquid-Liquid Flow with Chemical Reaction 310
	12.4.3.2	Liquid-Gas Flow with Chemical Reaction 312
	12.4.4	Three-Phase Modeling 315
	12.5	Practical Exercise: Alkylation of Phenylacetonitrile 320
		References 323

Index 327