Contents

Preface XVII
List of Contributors XXI

Part I Polymer Surfaces 1

1 Proteins for Surface Structuring 3
   Alexander Schulz, Stephanie Hiltl, Patrick van Rijn, and Alexander Böker
   1.1 Introduction 3
   1.2 Structuring and Modification of Interfaces by Self-Assembling Proteins 3
      1.2.1 Formation and Modification of Protein Structures at Liquid Interfaces 4
         1.2.1.1 Silaffins 4
         1.2.1.2 Hydrophobins 5
      1.2.2 Formation and Modification of Protein Structures at Solid Interfaces 8
         1.2.2.1 Silicateins 8
      1.3 Structuring and Modification of Solid Surfaces via Printing of Biomolecules 11
         1.3.1 Intaglio Printing Using Nanostructured Wrinkle Substrates 11
         1.3.1.1 Wrinkling: Nanostructured Templates 11
         1.3.1.2 Assembly of Bionanoparticles on Wrinkles 12
         1.3.1.3 Intaglio Printing of Tobacco Mosaic Virus 14
      1.3.2 Microcontact Printing for Bioinspired Surface Modification 16
         1.3.2.1 Microcontact Printing onto Self-Assembled Monolayers 16
         1.3.2.2 Microcontact Printing with Wrinkle Stamps 16
         1.3.2.3 Microcontact Printing with Porous Stamps 18
         1.3.2.4 Enhanced Microcontact Printing 20
   1.4 Conclusion and Outlook 22
   References 22
2 Surface-Grafted Polymer Brushes 27
Szczepan Zapotoczny
2.1 Introduction 27
2.2 Synthesis of Polymer Brushes 28
2.3 Stimuli-Responsive Polymer Brushes 30
2.4 Polyelectrolyte Brushes 33
2.5 Bio-Functionalized Polymer Brushes 35
Acknowledgment 37
References 37

3 Inhibiting Nonspecific Protein Adsorption: Mechanisms, Methods, and Materials 45
Mojtaba Binazadeh, Hongbo Zeng, and Larry D. Unsworth
3.1 Introduction 45
3.2 Underlying Forces Responsible for Nonspecific Protein Adsorption 46
3.2.1 Protein Structure Effects on Adsorption and Adsorbed Film Properties 47
3.3 Poly(Ethylene Glycol) 48
3.4 Surface Forces Apparatus (SFA) 50
3.5 Applications of Poly(Ethylene Glycol) 53
Summary 55
References 55

4 Stimuli-Responsive Surfaces for Biomedical Applications 63
Rui R. Costa, Natália M. Alves, J. Carlos Rodríguez-Cabello, and João F. Mano
4.1 Introduction 63
4.2 Surface Modification Methodologies: How to Render Substrates with Stimuli Responsiveness 64
4.2.1 Self-Assembled Monolayers 64
4.2.2 Thin Polymer Network Films 65
4.2.3 Grafting 66
4.2.4 Layer-by-Layer 68
4.3 Exploitable Stimuli and Model Smart Biomaterials 69
4.3.1 Physical Stimuli 69
4.3.1.1 Temperature 69
4.3.1.2 Light 71
4.3.2 Chemical Stimuli 72
4.3.2.1 pH 72
4.3.2.2 Ionic Strength 73
4.3.3 Biochemical Stimuli 73
4.3.3.1 Antigens 73
4.3.3.2 Enzymes 73
4.3.3.3 Glucose 74
4.3.4 Multiple-Responsive Surfaces 74
5.1 Introduction 89
5.2 Effect of Material Surfaces on Interactions with Biological Entities 90
5.2.1 Fundamental Aspects of Biological Responses to Biomaterials 90
5.2.2 Surface Properties of Polymeric Biomaterials 92
5.3 Surface Morphology of Polymeric Biomaterials 96
5.3.1 Physical Methods 97
5.3.1.1 Physical Adsorption 97
5.3.1.2 Surface Micro- and Nanopatterning 99
5.3.1.3 Langmuir–Blodgett (LB) Film Deposition 100
5.3.2 Chemical Methods 102
5.3.2.1 Ozone Treatment 102
5.3.2.2 Silanization 103
5.3.2.3 Fluorination 104
5.3.2.4 Wet Treatments 104
5.3.2.5 Flame Treatment 105
5.3.2.6 Incorporation of Functional Groups 105
5.3.3 Biological Methods 106
5.3.3.1 Protein–Enzyme Immobilization 107
5.3.4 Radiation Methods 109
5.3.4.1 Plasma Radiation 110
5.3.4.2 Microwave and Corona Discharge 113
5.3.4.3 Photoactivation by UV 114
5.3.4.4 Laser 115
5.3.4.5 Ion Beam 115
5.3.4.6 Gamma Irradiation 115
5.3.5 Improvement of Hydrophilicity 115
5.4 Surface Modifications to Improve Biocompatibility of Biomaterials 118
5.4.1 Adsorption of Proteins 118
5.4.1.1 Patterning of the Surfaces 120
5.5 Surface Modifications to Improve Hemocompatibility of Biomaterials 126
5.5.1 Blood–Material Interaction 126
5.5.2 Factors Influencing Hemocompatibility 129
6 Polymer Vesicles on Surfaces 159
Agnieszka Jagoda, Justyna Kowal, Mihaela Delcea, Cornelia G. Palivan, and Wolfgang Meier

6.1 Introduction 159
6.2 Polymer Vesicles 160
6.2.1 Polymer Vesicles in Solution 160
6.2.1.1 Self-Assembly 160
6.2.1.2 Amphiphilic Copolymers 161
6.2.1.3 Preparation of Polymer Vesicles 161
6.2.1.4 Properties of Polymer Vesicles 162
6.2.2 Polymer Vesicles Tethered to Surfaces 164
6.2.2.1 Surface Preparation 165
6.2.2.2 Immobilization Procedures 166
6.2.3 Characterization of Vesicles, Surfaces, and Vesicles on Surfaces 168
6.2.4 Characterization of Vesicles in Solution 169
6.2.4.1 Scattering Methods 169
6.2.4.2 Microscopic Techniques 173
6.2.5 Solid Support Characterization 176
6.2.6 Vesicles on Surfaces 177
6.3 Applications of Polymer Membranes and Vesicles as Smart and Active Surfaces 180
6.3.1 Surface Functionalization of Polymeric Membranes and Vesicles 182
6.3.1.1 Insertion of Membrane Proteins in Polymeric Vesicles 182
6.3.1.2 Functionalization of Polymeric Membranes and Vesicles with Antibodies, Peptides, and Other Ligands 183
6.3.2 Polymer Membranes and Vesicles as (Bio)sensors 184
6.3.3 Polymer Vesicles as Nanoreactors for Diagnostics and Therapy 185
6.3.3.1 Encapsulation of Fluorescent Molecules 186
6.3.3.2 Encapsulation of Nanoparticles 186
6.3.3.3 Polymer Vesicles as Nanoreactors 186
6.4 Current Limitations of Polymer Vesicles and Emerging Trends 187
6.4.1 Reproducibility and Stability of Polymer Vesicles 187
6.4.2 Loading Efficiency of Polymer Vesicles 188
6.4.3 Cytotoxicity of Polymer Vesicles 188
6.4.4 Next Generation of Polymer Vesicles 189
6.5 Conclusions 190

Abbreviations and Symbols 191
References 193

Part II Hydrogel Surfaces 205

7 Protein-Engineered Hydrogels 207
Jordan Raphel, Andreina Parisi-Amon, and Sarah C. Heilshorn
7.1 Introduction to Protein Engineering for Materials Design 207
7.2 History and Development of Protein-Engineered Materials 207
7.3 Modular Design and Recombinant Synthesis Strategy 210
7.3.1 Module Design 210
7.3.2 Linker Design 212
7.3.3 Recombinant Protein Expression 214
7.4 Processing Protein-Engineered Materials 216
7.4.1 Cross-Linking Mechanisms 216
7.4.1.1 Effects of Cross-Link Density 217
7.4.1.2 Chemical Hydrogels 219
7.4.1.3 Physical Hydrogels 220
7.4.1.4 Self-Assembling Hydrogel Triggers 222
7.4.2 Protein-Engineered Hydrogel Processing Techniques 222
7.4.2.1 Thin Film Techniques 223
7.4.2.2 Bulk Protein Techniques 224
7.4.2.3 Surface Patterning Techniques 226
7.5 Conclusion 228

References 229

8 Bioactive and Smart Hydrogel Surfaces 239
8.1 Introduction 239
8.2 Mimicking the Extracellular Matrix 240
8.2.1 Importance of Mimicking ECM Structure: From 2D to 3D Culture 240
8.2.2 Patterned Surfaces 242
8.2.2.1 Lithography 242
8.2.2.2 Micromolding 243
8.2.2.3 Nano-Microfluidics 243
8.2.2.4 Biopatterning 243
8.2.2.5 Response of Cells to Patterned Surfaces 244
8.3 Hydrogels: Why Are They So Special? 245
8.3.1 Chemical versus Physical Hydrogels 247
8.3.1.1 Chemical Cross-linking 247
8.3.1.2 Bioinspired Peptidic Motifs for Physical Cross-linking 250
8.3.2 Injectable Hydrogels 251
8.3.3 Natural versus Artificial Polymers 251
8.3.3.1 Natural Polymers 251
8.3.3.2 Artificial Polymers 254
8.4 Elastin-Like Recombinamers as Bioinspired Proteins 255
8.4.1 ELR Chemical Hydrogels 258
8.4.2 ELR Physical Hydrogels 259
8.4.3 Adding Biofunctionality 260
8.4.4 Composites 260
8.5 Perspectives 261
Acknowledgments 261
References 261

9 Bioresponsive Surfaces and Stem Cell Niches 269
Miguel Angel Mateos-Timoneda, Melba Navarro, and Josep Anton Planell
9.1 General Introduction 269
9.2 Stem Cell Niches 271
9.2.1 Hematopoietic Stem Cell Niche 271
9.2.2 Epithelial Stem Cell Niche 271
9.2.3 Neural Stem Cell Niche 272
9.3 Surfaces as Stem Cell Niches 274
9.3.1 Topography Effect on Stem Cell Behavior 275
9.3.2 Importance of Mechanical Properties on Stem Cells 276
9.3.3 Engineering Chemical Microenvironments for Stem Cells 277
9.4 Conclusions 279
References 279

Part III Hybrid & Inorganic Surfaces 285

10 Micro- and Nanopatterning of Biomaterial Surfaces 287
Daniel Brodoceanu and Tobias Kraus
10.1 Introduction 287
10.2 Photolithography 287
10.3 Electron Beam Lithography 290
10.4 Focused Ion Beam 292
10.5 Soft Lithography 292
10.6 Dip-Pen Nanolithography 294
10.7 Nanoimprint Lithography 295
10.8 Sandblasting and Acid Etching 298
10.9 Laser-Induced Surface Patterning 298
10.10 Colloidal Lithography 301
10.11 Conclusions and Perspectives 303
Acknowledgments 305
References 306
11 Organic/Inorganic Hybrid Surfaces 311
Tobias Mai, Katrin Bleek, and Andreas Taubert

11.1 Introduction 311
11.2 Calcium Carbonate Surfaces and Interfaces 314
11.3 Calcium Phosphate Surfaces and Interfaces 319
11.4 Silica Surfaces and Interfaces 326
11.5 Conclusion and Outlook 327
Acknowledgments 328
References 328

12 Bioactive Ceramic and Metallic Surfaces for Bone Engineering 337
Carlos Mas-Moruno, Montserrat Espanol, Edgar B. Montufar, Gemma Mestres, Conrado Aparicio, Francisco Javier Gil, and Maria-Pau Ginebra

12.1 Introduction 337
12.2 Ceramics for Bone Replacement and Regeneration 338
12.2.1 The Concept of Bioactivity in Ceramics: Genesis and Evolution 339
12.2.2 Bioactivity as a Surface Property: Surface Reactions in Glasses and Ceramics 340
12.2.3 In vitro Evaluation of Bioactivity 344
12.2.4 Bioactivity via Functionalization of Surfaces 345
12.3 Metallic Surfaces for Bone Replacement and Regeneration 346
12.3.1 Physical Surface Modifications to Confer Functionality to Metallic Implants 348
12.3.1.1 Microrough and Nanorough Surfaces 348
12.3.1.2 Superhydrophilic Surfaces 349
12.3.2 Inorganic and Hybrid Bioactive Coatings to Improve Bone – Implant Interactions 350
12.3.2.1 Biomimetic Calcium Phosphate Coatings 351
12.3.2.2 Other Inorganic Surface Modifications 352
12.3.2.3 Hybrid Coatings 352
12.3.3 Functionalization of Metallic Materials with Biomolecules 353
12.3.3.1 Coating with Full-Length Proteins or Linear Peptides 354
12.3.3.2 Coating with Peptide Mixtures and Multiple Peptide Motifs 358
12.3.3.3 Coating with Engineered Protein Fragments 360
12.3.3.4 Coating with Cyclic Peptides 360
12.3.3.5 Coating with Peptidomimetics 361
12.3.4 Design of a Coating Molecule and Immobilization Methods 362
12.3.4.1 The Coating System 362
12.3.4.2 Immobilization Methods 363
12.4 Conclusions 364
References 365
13 Plasma-Assisted Surface Treatments and Modifications for Biomedical Applications 375
Sanjay Mathur, Trilok Singh, Mahboubeh Maleki, and Thomas Fischer
13.1 Introduction 375
13.2 Surface Requisites for Biomedical Applications 377
13.2.1 Techniques of Surface Modification 378
13.2.2 Plasma-Assisted Modification of Biomaterials 379
13.3 Surface Functionalization of Inorganic Surfaces by Plasma Techniques 383
13.3.1 Plasma-Enhanced Chemical Vapor Deposition (PECVD) 384
13.3.2 Plasma-Assisted Etching (PAE) 385
13.3.3 Plasma-Assisted Modifications (PAM) 385
13.4 Applications of Plasma-Modified Surfaces in Biology and Biomedicine 386
13.4.1 Surface Modification for Improved Blood Compatibility 386
13.4.2 Surface Modification for Promoting Cell Adhesion and Growth 389
13.4.3 Surface Modification for Improving Wear and Corrosion Resistance 395
13.4.4 Surface Modification for Targeted Drug Delivery 399
13.5 Conclusions and Outlook 401
Acknowledgments 402
References 402

14 Biological and Bioinspired Micro- and Nanostructured Adhesives 409
Longjian Xue, Martin Steinhart, and Stanislav N. Gorb
14.1 Introduction: Adhesion in Biological Systems 409
14.2 Fibrillar Contact Elements 410
14.2.1 Origin 410
14.2.2 Hierarchy 411
14.2.3 Slanted Fibrils 412
14.2.4 Tip Shape of Fibrils 413
14.3 Basic Physical Forces Contributing to Adhesion 414
14.4 Contact Mechanics 415
14.5 Larger Animals Rely on Finer Fibers 416
14.6 Peeling Theory 416
14.7 Artificial Adhesive Systems 419
14.7.1 Arrays of Micro- and Nano-Fibrils 419
14.7.2 Tip Shape 424
14.7.3 Slanted Angle 430
14.7.4 Hierarchy 432
14.7.5 Combination of Several Features 436
14.8 Toward Smart Adhesives 436
Acknowledgment 436
References 437
Part IV  Cell–Surface Interactions  441

15  Generic Methods of Surface Modification to Control Adhesion of Cells and Beyond  443
Marcus Niepel, Alexander Köwitsch, Yuan Yang, Ning Ma, Neha Aggarwal, Deepak Guduru, and Thomas Groth

15.1  General Introduction  443
15.2  Survey on Generic Methods to Modify Material Surfaces  444
15.2.1  Methods for Preparation of Nanostructured Surfaces  444
15.2.2  Layer-by-Layer Technique  445
15.2.3  Self-Assembled Monolayers  446
15.2.4  Covalent Modification by Wet Chemical Methods  448
15.3  Results and Discussion  449
15.3.1  Cell Adhesion on Nanostructured Surfaces  449
15.3.2  Cell Adhesion on PEM-Modified Surfaces  451
15.3.3  Cell Adhesion on SAMs  454
15.3.4  Chemical Modification with Glycans  457
15.4  Summary and Conclusions  461
Acknowledgments  462
References  462

16  Severe Deformations of Malignant Bone and Skin Cells, as well as Aged Cells, on Micropatterned Surfaces  469
Patricia M. Davidson, Tokuko Haraguchi, Takako Koujin, Thorsten Steinberg, Pascal Tomakidi, Yasushi Hiraoka, Karine Anselme, and Günther Reiter

16.1  Introduction  469
16.2  Experimental Methods  470
16.2.1  Substrate Preparation  470
16.2.1.1  Silicon Templates  470
16.2.1.2  PDMS Replicas  471
16.2.1.3  Hot Embossing  471
16.2.2  Cell Culture  471
16.2.2.1  Bone Cells  471
16.2.2.2  Keratinocytes  472
16.2.2.3  TIG-1 Cells  472
16.2.2.4  Sample Preparation for Cell Seeding  472
16.2.2.5  Immunohistochemical Staining and Imaging  472
16.3  The Interaction of Bone Cells with Micropillars  473
16.3.1  The Behavior of Cancerous Cells on Micropatterned Surfaces  474
16.3.2  The Deformation of Bone Cells as a Function of Their Malignancy  477
16.4  The Deformation of Skin Cells as a Function of Their Malignancy  480
16.5  The Deformation of Fibroblasts of Different Cellular Ages  481
16.6  Discussion  484
16.6.1  Comparison of Bone Cells and Skin Cells  485
16.6.2 Comparison with Aging Cells 485
16.7 Conclusions 486
Acknowledgments 487
References 487

17 Thermoresponsive Cell Culture Surfaces Designed for Cell-Sheet-Based Tissue Engineering and Regenerative Medicine 491
Jun Kobayashi and Teruo Okano
17.1 Introduction 491
17.2 Characteristics of PIPAAm-Grafted Cell Culture Surfaces 493
17.3 Mechanisms of Cell Detachment from the Thermoresponsive Cell Culture Dish 495
17.4 Cell-Sheet-Based Tissue Engineering and Its Clinical Applications 495
17.5 Next-Generation Thermoresponsive Cell Culture Dishes 498
17.5.1 Functional Thermoresponsive Cell Culture Dishes 499
17.5.2 Affinity Regulation between Cells and Surface-Immobilized Ligands on Thermoresponsive Cell Culture Dishes 500
17.5.3 Cocultured Cell Sheets Using Micropatterned Thermoresponsive Surfaces 501
17.5.4 Prevascularized Cell Sheets 502
17.5.5 Thermoresponsive Microcarriers for Large-Scale Cultivation 502
17.6 Conclusions 503
References 504

18 Cell Mechanics on Surfaces 511
Jessica H. Wen, Hermes Taylor-Weiner, Alexander Fuhrmann, and Adam J. Engler
18.1 Introduction 511
18.2 What Is Elasticity and Stiffness? 511
18.3 Measuring and Quantifying Stiffness 514
18.3.1 Measuring Linearly Elastic Properties 515
18.3.2 Measuring Nonlinearly Elastic Properties 518
18.4 Controlling Substrate Stiffness 519
18.4.1 Material Properties That Determine Stiffness 519
18.5 Naturally Derived Scaffolds 520
18.5.1 Collagen Type I 521
18.5.2 Hyaluronic Acid 523
18.5.3 Cell-Derived Extracellular Matrix 524
18.6 Synthetic Scaffolds 525
18.6.1 Polyacrylamide Hydrogels 525
18.6.2 Poly(ethylene glycol) 527
18.6.3 Polydimethylsiloxane 528
18.7 Substrate Stiffness' Impact on Cell Behavior 528
18.8 When Stiffness In vivo Goes Awry: The Impact of Fibrosis on Function 530
18.9 Novel Surface Fabrication Techniques to Improve Biomimicry 531
18.10 Conclusion 532
Acknowledgment 533
Abbreviations 533
References 533

19 Electrode–Neural Tissue Interactions: Immune Responses, Current Technologies, and Future Directions 539
Gloria Bora Kim, Pouria Fattahi, and Mohammad Reza Abidian

19.1 Introduction 539
19.2 Immune Response to Neural Implants 540
19.2.1 Cells Involved in the Immune Response of CNS 540
19.2.2 Acute Response to Implanted Electrodes 542
19.2.3 Chronic Response to Implanted Electrodes 542
19.3 Past and Current Neural Interfaces 543
19.3.1 Electrode Types 544
19.3.1.1 Microwires 544
19.3.1.2 Silicon Electrodes 544
19.3.2 Shape, Size, and Texture of Electrodes 545
19.3.3 Materials Used for the Insulating Layer 547
19.3.4 Materials Used as Electrode Connectors 547
19.4 Methods for Improvement of the Electrode–Tissue Interface 548
19.4.1 Improvement of Electrical and Mechanical Properties 548
19.4.1.1 Conducting Polymers 548
19.4.1.2 Carbon Nanotubes 549
19.4.1.3 Hydrogels 552
19.4.2 Methods of Anchoring Electrodes 555
19.4.3 Electrode Insertion and Implantation Procedure 555
19.5 Conclusions and Future Directions 557
References 558

Index 567