Contents

List of Contributors XI

1 Detection in Capillary Electrophoresis – An Introduction 1
   Gerhardus de Jong
   1.1 UV Absorption 2
   1.2 Fluorescence 2
   1.3 Conductivity 3
   1.4 Mass Spectrometry 4
   References 4

2 Electrospray Ionization Interface Development for Capillary Electrophoresis–Mass Spectrometry 7
   Jessica M. Risley, Caitlyn A.G. De Jong, and David D.Y. Chen
   2.1 A Brief Introduction to the Development of CE-MS 7
   2.2 Fundamentals of ESI and Electrochemical Reactions in CE-MS 8
   2.2.1 Principles of ESI: Converting Solvated Ions into Gaseous Ions 8
   2.2.2 Considerations and Conditions for CE-ESI-MS Methods 9
   2.2.3 Electrochemical Considerations in CE-MS 10
   2.3 Interface Designs 11
   2.3.1 Sheath-Flow Interfaces 11
   2.3.1.1 Flow-Through Microvial Interface 12
   2.3.1.2 Nanospray Sheath-Flow Interfaces 13
   2.3.1.3 Electrokinetically Pumped Sheath-Flow Nanospray Interface 13
   2.3.2 Sheathless Interfaces 15
   2.3.2.1 Porous-Tip Nanospray Sheathless Interface/CESI 8000 15
   2.3.2.2 Sheathless Porous Emitter NanoESI Interface 16
   2.3.3 Interface Applications/CE Mode of Separation 17
   2.4 Specific Interface Applications 18
   2.4.1 Capillary Isoelectric Focusing 18
   2.4.2 Glycan Analysis by CE-ESI-MS 19
   2.5 Conclusion 20
   Abbreviations 32
Acknowledgments 32
References 32

3 Sheath Liquids in CE-MS: Role, Parameters, and Optimization 41
Christian W. Klampfl and Markus Himmelsbach
3.1 Introduction 41
3.2 Sheath-Liquid Functions and Sheath-Flow Interface Design 42
3.2.1 Coaxial Sheath-Flow Interface 42
3.2.2 Liquid Junction Interface 44
3.3 Sheath-Liquid-Related Parameters and their Selection 46
3.3.1 Sheath-Liquid Composition 46
3.3.2 Effect of Sheath-Liquid Composition on Molecular Structures 51
3.3.3 Sheath-Liquid Flow Rates and their Optimization 51
3.4 Sheath Liquids for Non-ESI CE-MS Interfaces 53
3.4.1 APCI and APPI 53
3.5 Sheath-Flow Chemistry 57
3.6 Conclusions 59
References 61

4 Recent Developments of Microchip Capillary Electrophoresis Coupled with Mass Spectrometry 67
Gerard Rozing
4.1 Introduction 67
4.2 Microchip Capillary Electrophoresis 68
4.2.1 Brief Retrospective 68
4.2.2 Principle of Operation of MCE 69
4.2.3 Preparation and Availability of Microfluidic Chips for Capillary Electrophoresis 71
4.3 Reviews on MCE and MCE-MS 72
4.4 Principal Requirements for MCE-MS 74
4.4.1 Electrospray Ionization 74
4.4.2 Principle Layout of MCE-MS Devices 76
4.5 MCEMS by Direct Off-Chip Spraying 77
4.6 MCE-MS with Connected Sprayer 78
4.7 MCE-MS Devices with Integrated Sprayer 83
4.8 Multidimensional MCE-MS Devices 90
4.9 Conclusions and Perspectives 91
References 96

5 On-Line Electrophoretic, Electrochromatographic, and Chromatographic Sample Concentration in CE-MS 103
Joselito P. Quirino
5.1 Introduction 103
5.2 Electrophoretic and Electrochromatographic Sample Concentration or Stacking 104
5.2.1 Electrophoretic Stacking Techniques 104
5.2.1.1 Transient Isotachophoresis or t-ITP 105
5.2.1.2 Field-Amplified/Enhanced Stacking 107
5.2.1.3 Dynamic pH Junction 110
5.2.2 Electrochromatographic Sample Concentration 113
5.2.2.1 Sweeping 113
5.2.2.2 Analyte Focusing by Micelle Collapse or AFMC 114
5.2.2.3 Micelle to Solvent Stacking or MSS 115
5.3 On-line/In-line SPE with CE-MS 115
5.3.1 On-line SPE 116
5.3.2 In-line SPE 117
5.4 Conclusion 121
Acknowledgment 122
References 122

6 CE-MS in Drug Analysis and Bioanalysis 129
Julie Schappler, Victor González-Ruiz, and Serge Rudaz
6.1 Introduction 129
6.2 CE-MS in Drug Analysis 132
6.2.1 Impurity Profiling 134
6.2.2 Chiral Analysis 135
6.2.3 Determination of Drugs’ Physicochemical Properties 136
6.2.3.1 pK_a and log P 137
6.2.3.2 Plasma Protein Binding 140
6.3 CE-MS in Bioanalysis 141
6.3.1 Selectivity Issues and Matrix Effects 142
6.3.2 Sample Preparation 144
6.4 CE-MS in Drug Metabolism Studies 145
6.4.1 Electrophoretically Mediated Microanalysis 146
6.4.2 Targeted in vitro Metabolism Assays 147
6.5 Quantitative Aspects in CE-MS 148
6.5.1 Instrumental Aspects 148
6.5.2 Methodological Aspects 149
6.6 Conclusions 151
Abbreviations 151
References 152

7 CE-MS for the analysis of intact proteins 159
Rob Haselberg and Govert W. Somsen
7.1 Introduction 159
7.2 CE of Intact Proteins 161
7.2.1 CE Modes 161
7.2.2 Preventing Protein Adsorption 161
7.3 MS Detection of Intact Proteins 164
7.3.1 Ionization Modes 164
Contents

7.3.2 Mass Analyzers 167
7.4 Applications of Intact Protein CE-MS 168
7.4.1 Biopharmaceuticals 168
7.4.2 Glycoproteins 174
7.4.3 Protein – Ligand Interactions 177
7.4.4 Metalloproteins 180
7.4.5 Top-Down Protein Analysis 182
7.4.6 Other Selected Applications 184
7.5 Conclusions 186
Abbreviations 187
References 188

8 CE-MS in Food Analysis and Foodomics 193
Tanize Acunha, Clara Ibáñez, Virginia García-Cañas, Alejandro Cifuentes, and Carolina Simó
8.1 Introduction: CE-MS, Food Analysis, and Foodomics 193
8.1.1 CE-MS and Food Safety 194
8.1.2 CE-MS in Food Quality and Authenticity 201
8.1.3 CE-MS and Foodomics 204
8.2 Concluding Remarks 209
Acknowledgments 209
References 210

9 CE-MS in Forensic Sciences with Focus on Forensic Toxicology 217
Nadia Porpiglia, Elena Giacomazzi, Rossella Gottardo, and Franco Tagliaro
9.1 Introduction 217
9.2 Sample Preparation of Forensically Relevant Matrices 218
9.2.1 Blood 219
9.2.2 Urine 221
9.2.3 Hair 223
9.2.4 Saliva 224
9.3 Separation Modes and Analytical Conditions 225
9.3.1 Capillary Zone Electrophoresis 225
9.3.2 Capillary Isotachophoresis 226
9.3.3 Micellar Electrokinetic Chromatography 227
9.3.4 Capillary Electrochromatography 228
9.3.5 Capillary Gel Electrophoresis 228
9.3.6 Chiral Separation 228
9.3.7 Analytical Conditions 231
9.4 Applications 234
9.4.1 Forensic Toxicology 234
9.4.1.1 Drugs of Abuse 235
9.4.1.2 Alcohol Abuse Biomarkers 247
Contents

Abbreviations  339
Acknowledgments  340
References  340

Index  345