## Contents

List of Contributors XVII Preface XXV

## Part I Analytical Methods and Strategies in Metallomics 1

1	The Position of Metallomics Within Other Omics Fields 3
	Dirk Schaumlöffel
1.1	Introduction 3
1.2	Metallome and Metallomics in Relation to Other "-Ome" and "-Omics" Fields <i>3</i>
1.2.1	Genomics 4
1.2.2	Transcriptomics 4
1.2.3	Proteomics 4
1.2.4	Metabolomics 5
1.2.5	Metallomics 6
1.3	Is Metallomics Feasible as a Global Study of the Metallome 7
1.4	Approaching the Metallome: Study of Metallome Subgroups 8
1.5	Analytical Strategies in Metallomics 8
1.5.1	Element Mass Spectrometry (ICP-MS) 8
1.5.2	Coupling Techniques 8
1.5.3	Elemental Imaging Techniques 9
1.5.4	Bioinformatic Approaches 10
1.6	Functional Connections Between DNA, Proteins, Metabolites, and Metals <i>10</i>
1.7	Metallothiolomics as Example for Metallomics Studies of a Metallome Subgroup <i>11</i>
1.8	Concluding Remarks 14 References 15
2	Coupling Techniques and Orthogonal Combination of Mass
	Spectrometric Techniques 17
	Daniel Pröfrock
2.1	Introduction 17

VII

VIII Contents

- 2.2 Analytical Techniques for Metallomics 19
- 2.2.1Overview about Available Separation Techniques 19
- 2.2.1.1 Liquid Chromatography (LC) 20
- 2.2.1.2 Capillary Electrophoresis (CE) 25
- 2.2.1.3Gel Electrophoresis (GE) 28
- 2.2.1.4Gas Chromatography (GC) 30
- Ionization Principles and Mass Spectrometric Detectors for 2.3 Speciation 30
- Element-Specific Detection with ICP-Based Techniques 31 2.3.1
- Mass Analyzers for ICP-MS 34 2.3.1.1
- 2.3.2 Electrospray Ionization – Mass Spectrometry (ESI-MS) -38
- 2.3.2.1 Mass Analyzers Used for ESI-MS 39
- 2.3.3 Matrix-Assisted Laser Desorption/Ionization-Mass Spectrometry Techniques (MALDI-MS) 43
- TOF Mass Analyzers for MALDI-MS 2.3.3.1 45
- 2.4 **Overview about Coupling Techniques** 48
- 2.4.1LC Couplings 49
- 2.4.1.1Coupling of Miniaturized LC and ICP-MS 49
- Coupling of CE and ICP-MS 52 2.4.2
- Laser Ablation (LA) 55 2.4.3
- 2.4.4Gas Chromatography (GC) 57
- 2.5 Final Remarks and Outlook 58 References 58

3 Quality Control in Speciation Analysis Using HPLC with ICP-MS and ESI MS/MS: Focus on Quantitation Strategies Using Isotope Dilution Analysis 69

Heidi G. Infante

- 3.1 Introduction 69
- 3.2 Synergetic Use of Elemental and Organic Mass Spectrometry in Compound Quantitation and Quality Assurance of Food Selenium Speciation 70
- 3.2.1 Quality Assurance in Species Quantitation 70
- 3.2.2 Quality Assurance in Species Identification 72
- The Role of Species-Specific Isotope Dilution in Increasing 3.3 Metrological Traceability for the Quantification of Bioinorganic Species 72
- IDMS and Speciation Analysis 72 3.3.1
- Quantitative Se Speciation in Food/Supplements by Species-Specific 3.3.2 IDMS: Production of "Speciated" Reference Materials 74
- 3.3.3 Species-Specific Double IDMS Quantification of Plasma Selenoproteins: Advantages and Limitations in Comparison with the
  - Species-Unspecific IDMS Approach 76
- 3.3.3.1 Selenoproteins in Human Plasma 76
- 3.3.3.2 Se-Containing Proteins in Human Plasma 77

Contents IX

3.3.4 Application of Species-Specific Double Spike IDMS to Account for Redox Exchange between Cr(III) and Cr(VI) Species: Practical Considerations for Quality Assurance 78 Inorganic Cr Quantification in Cr – Yeast Supplements 3.3.4.1 78 3.3.4.2 Inorganic Cr Species Quantification in Clean and Wastewater 79 References 81 Novel Methods for Bioimaging Including LA-ICP-MS, NanoSIMS, 4 TEM/X-EDS, and SXRF 83 Dirk Schaumlöffel, Robert Hutchinson, Julien Malherbe, Philippe Le Coustumer, Etienne Gontier, and Marie-Pierre Isaure 4.1 Introduction 83 4.2 Bioimaging by LA-ICP-MS 84 4.2.1 Principle 84 4.2.2 Elemental Bioimaging by LA-ICP-MS 85 4.2.3 Quantitative Bioimaging by LA-ICP-MS 87 Proteomic Bioimaging by LA-ICP-MS 88 4.2.4 Frontiers in Bioimaging by LA-ICP-MS 90 4.2.5 4.3 Bioimaging by NanoSIMS 90 4.3.1 Principle 90 4.3.2 Ion Sources 91 4.3.3 Application Fields 92 4.3.4 Application to Biological Samples 92 4.3.5 Analysis of Metals in Biological Samples 93 Bioimaging by TEM/X-EDS 93 4.4 4.4.1 Principle 93 4.4.2Application to Biological Samples 96 Preparation of Biological Samples for NanoSIMS and 4.4.3 TEM/X-EDS 98 4.4.4 Cryofixation 101 Cryofixation by Slamming 102 4.4.4.14.4.4.2 Cryofixation by High-Pressure Freezing 102 4.4.5 Lyophilization 103 4.4.6 Cryosubstitution 103 4.4.7 Sectioning by Ultramicrotomy 103 Bioimaging by SXRF 104 4.5 Principle 104 4.5.14.5.2 Sample Preservation during Preparation and Measurements 106 4.5.3 Data Treatments 107 4.5.4 Applications 107 Conclusions and Outlook 108 4.6 References 109

X Contents

5	Electrochemistry Coupled to Mass Spectrometry for Investigating Oxidative Metabolism of Pt-Based Drug Conjugates: A Novel Approach 117 Günther Weber
51	Introduction 117
5.2	FC-MS Methodology 119
53	EC-MS of Thiols 119
5.0 5.4	Influence of Cisplatin on Thial Oxidation 121
5.5	Conclusions 125
5.5	Potoroncos 126
	References 120
	Part IIMetallomics in Environment and Nutrition129
6	Selenium and Selenium Species 131
6.1	Speciation Analysis Especially of Tin and Selenium in Environmental
	Matrices 131
	Maria Ochsenkühn-Petropoulou and Fotios Tsopelas
6.1.1	The Need for Elemental Speciation in Environmental Matrices: The
	Case of Tin and Selenium 131
6.1.2	Sample Collection and Storage 132
6.1.3	Determination of Total Tin and Selenium Content in Environmental
	Samples 135
6.1.4	Extraction Methodologies 137
6.1.5	Speciation Procedure: Separation/Preconcentration Techniques and
	Final Detection 138
6.1.6	Quality Control of Speciation Analysis Approaches – Standard
	Reference Materials 141
6.1.7	Trends and Future Developments for Elemental Speciation in
	Environmental Matrices 142
	References 143
6.2	Selenium Species Extraction and Speciation in Plants and Yeast 151
	Lena Ruzik, Katarzyna Bierła, and Joanna Szpunar
6.2.1	Introduction 151
6.2.2	Selenium Species of Interest in Plants and Yeast 152
6.2.2.1	Selenometabolites 152
6.2.2.2	Selenium-Containing Proteins 154
6.2.3	Selenium Levels Encountered in Natural and Fortified Samples 154
6.2.4	Analytical Approaches for Speciation of Selenium in Plants and
	Yeast 155
6.2.4.1	Extraction of Selenospecies 155
6.2.4.2	Instrumental Approaches for Detection of Selenium Species 164
6.2.4.3	Molecular Mass Spectrometry for Identification of
	Selenospecies 165
	References 169

Contents XI

7	Arsenic and As Species 173
7.1	Arsenic Species in Marine Food 173
	María Carmen Barciela-Alonso and Pilar Bermejo-Barrera
7.1.1	Introduction 173
7.1.2	Sample Pretreatment 173
7.1.2.1	Sample Preparation for Total Arsenic Determination 177
7.1.2.2	Extraction Methods for Arsenic Speciation Analysis 177
7.1.3	Analytical Techniques for Arsenic Species Determination 178
7.1.4	Bioavailability of Arsenic Species 192
7.1.5	Changes in Arsenic Speciation During Storage and Cooking
	Procedures 195
7.1.6	Conclusion 197
	References 198
7.2	Compounds with As–S Bonds: Analytical and Biogeochemical
	Reasons Why These Species have been Elusive in Biota and
	Environment 202
	Jörg Feldmann, Andrea Raab, Helle R. Hansen, Katharina Bluemlein,
	and Dirk Wallschläger
7.2.1	Introduction 202
7.2.2	Analytical Methods for Compounds with an As–S Bond 202
7.2.2.1	XANES/EXAFS 203
7.2.2.2	Hyphenated Techniques Featuring HPLC-ICPMS/ESI-MS 206
7.2.3	Arsinothioyl Metabolites 208
7.2.3.1	The Importance of Thio-Organoarsenicals 208
7.2.3.2	Speciation Analysis for Thio-Organoarsenicals 209
7.2.4	Thioarsenates and Thioarsenites 210
7.2.4.1	Environmental Relevance 211
7.2.4.2	Analytical Methods and Associated Challenges 214
7.2.5	Arsenic Complexed by Biothiols 216
7.2.5.1	Importance of Glutathione and Phytochelatins 216
7.2.5.2	Analysis of These Complexes and the Challenges 217
	References 218
7.3	Arsenolipids: An overview of current analytical aspects 222
	Michael Stiboller, Ronald A. Glabonjat, Georg Raber, Kenneth B. Jensen,
	and Kevin A. Francesconi
7.3.1	Introduction 222
7.3.2	Sample Preparation: Extraction/Solvent Partitioning, Cleanup, and
	Derivatization 223
7.3.2.1	Extraction and Solvent Partitioning 223
7.3.2.2	Solid-Phase Extraction 225
7.3.2.3	Derivatizations 226
7.3.3	Measurement of Arsenolipids by HPLC/MS 227
7.3.4	Overview and Future Work 231
	References 234

XII Contents

8	Analytical Procedures for Speciation of Chromium, Aluminum, and Tin
	in Environmental and Biological Samples 237
	Radmila Milačič, Tea Zuliani, Janja Vidmar, and Janez Ščančar
8.1	Speciation of Chromium 237
8.1.1	Speciation of Chromium in Environmental Samples 239
8.1.1.1	Sampling and Sample Storage 239
8.1.1.2	Sample Pretreatment 239
8.1.1.3	Instrumental Analysis 243
8.1.2	Speciation of Chromium in Biological Samples 248
8.2	Speciation of Aluminum 250
8.2.1	Speciation of Aluminum in Environmental Samples 251
8.2.1.1	Sampling, Sample Storage, and Sample Pretreatment 251
8.2.1.2	Analytical Procedures 252
8.2.2	Speciation of Aluminum in Biological Samples 255
8.2.2.1	Sampling, Sample Storage, and Cleaning Procedures 256
8.2.2.2	Analytical Procedures 256
8.3	Speciation of Tin 260
8.3.1	Sampling and Sample Storage 262
8.3.2	Extraction and Derivatization Procedures 262
8.3.2.1	Speciation of Organotin Compounds in Environmental
	Samples 263
8.3.2.2	Speciation of Organotin Compounds in Biological Samples 271
	References 275
	References 2/5
9	Mercury Toxicity and Speciation Analysis 285
9	References       275         Mercury Toxicity and Speciation Analysis       285         Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna Lohren
<b>9</b> 9.1	Keterences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285
<b>9</b> 9.1 9.1.1	References275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285
<b>9</b> 9.1 9.1.1 9.1.2	Keterences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286
<b>9</b> 9.1 9.1.1 9.1.2 9.1.2.1	Keterences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286Elemental Mercury287
<b>9</b> 9.1 9.1.1 9.1.2 9.1.2.1 9.1.2.2	Keterences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286Elemental Mercury287Inorganic Mercuric Mercury287
<b>9</b> 9.1 9.1.1 9.1.2 9.1.2.1 9.1.2.2 9.1.2.3	Keterences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286Elemental Mercury287Inorganic Mercuric Mercury287Methylmercury287
<b>9</b> 9.1 9.1.1 9.1.2 9.1.2.1 9.1.2.2 9.1.2.3 9.1.2.4	Keterences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286Elemental Mercury287Inorganic Mercuric Mercury287Methylmercury287Thiomersal288
<b>9</b> 9.1 9.1.1 9.1.2 9.1.2.1 9.1.2.2 9.1.2.3 9.1.2.4 9.1.3	Keterences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286Elemental Mercury287Inorganic Mercuric Mercury287Methylmercury287Thiomersal288Biomarkers of Exposure288
<b>9</b> 9.1 9.1.1 9.1.2 9.1.2.1 9.1.2.2 9.1.2.3 9.1.2.4 9.1.3 9.1.4	Keterences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286Elemental Mercury287Inorganic Mercuric Mercury287Methylmercury287Thiomersal288Biomarkers of Exposure288Toxicity of Hg Species289
<b>9</b> 9.1 9.1.1 9.1.2 9.1.2.1 9.1.2.2 9.1.2.3 9.1.2.4 9.1.3 9.1.4 9.1.5	Keterences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286Elemental Mercury287Inorganic Mercuric Mercury287Methylmercury287Thiomersal288Biomarkers of Exposure288Toxicity of Hg Species289Concluding Remarks on Hg-Species-Induced Toxicity290
<b>9</b> 9.1 9.1.1 9.1.2 9.1.2.1 9.1.2.2 9.1.2.3 9.1.2.4 9.1.3 9.1.4 9.1.5 9.2	Keterences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286Elemental Mercury287Inorganic Mercuric Mercury287Methylmercury287Thiomersal288Biomarkers of Exposure288Toxicity of Hg Species289Concluding Remarks on Hg-Species-Induced Toxicity290Mercury Speciation Analysis291
<b>9</b> 9.1 9.1.1 9.1.2 9.1.2.1 9.1.2.2 9.1.2.3 9.1.2.4 9.1.3 9.1.4 9.1.5 9.2 9.2.1	Keterences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286Elemental Mercury287Inorganic Mercuric Mercury287Methylmercury287Thiomersal288Biomarkers of Exposure288Toxicity of Hg Species289Concluding Remarks on Hg-Species-Induced Toxicity290Mercury Speciation Analysis291Sample Preparation for Hg Analysis291
<b>9</b> 9.1 9.1.1 9.1.2 9.1.2.1 9.1.2.2 9.1.2.3 9.1.2.4 9.1.3 9.1.4 9.1.5 9.2 9.2.1 9.2.2	Keterences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286Elemental Mercury287Inorganic Mercuric Mercury287Methylmercury287Thiomersal288Biomarkers of Exposure288Toxicity of Hg Species289Concluding Remarks on Hg-Species-Induced Toxicity290Mercury Speciation Analysis291Sample Preparation for Hg Analysis291Hg Species Quantification Using Isotope Dilution Mass
<b>9</b> 9.1 9.1.1 9.1.2 9.1.2.1 9.1.2.2 9.1.2.3 9.1.2.4 9.1.3 9.1.4 9.1.5 9.2 9.2.1 9.2.2	References275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286Elemental Mercury287Inorganic Mercuric Mercury287Thiomersal288Biomarkers of Exposure288Toxicity of Hg Species289Concluding Remarks on Hg-Species-Induced Toxicity290Mercury Speciation Analysis291Sample Preparation for Hg Analysis291Hg Species Quantification Using Isotope Dilution MassSpectrometry293
<b>9</b> 9.1 9.1.1 9.1.2 9.1.2.1 9.1.2.2 9.1.2.3 9.1.2.4 9.1.3 9.1.4 9.1.5 9.2 9.2.1 9.2.2 9.2.3	Kererences275Mercury Toxicity and Speciation Analysis285Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna LohrenMercury Toxicity285Occurrence and Human Exposure285Toxicokinetic of Hg Species286Elemental Mercury287Inorganic Mercuric Mercury287Methylmercury287Thiomersal288Biomarkers of Exposure288Toxicity of Hg Species289Concluding Remarks on Hg-Species-Induced Toxicity290Mercury Speciation Analysis291Sample Preparation for Hg Analysis291Hg Species Quantification Using Isotope Dilution MassSpectrometry293Analytical Techniques293
9          9.1         9.1.1         9.1.2         9.1.2.1         9.1.2.2         9.1.2.3         9.1.2.4         9.1.3         9.1.4         9.1.5         9.2         9.2.1         9.2.2         9.2.3         9.2.3.1	Kererences 275 Mercury Toxicity and Speciation Analysis 285 Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna Lohren Mercury Toxicity 285 Occurrence and Human Exposure 285 Toxicokinetic of Hg Species 286 Elemental Mercury 287 Inorganic Mercuric Mercury 287 Methylmercury 287 Thiomersal 288 Biomarkers of Exposure 288 Toxicity of Hg Species 289 Concluding Remarks on Hg-Species-Induced Toxicity 290 Mercury Speciation Analysis 291 Sample Preparation for Hg Analysis 291 Hg Species Quantification Using Isotope Dilution Mass Spectrometry 293 Analytical Techniques 293 Thin-Layer Chromatography 293
<ul> <li>9</li> <li>9.1</li> <li>9.1.1</li> <li>9.1.2</li> <li>9.1.2.1</li> <li>9.1.2.2</li> <li>9.1.2.3</li> <li>9.1.2.4</li> <li>9.1.3</li> <li>9.1.4</li> <li>9.1.5</li> <li>9.2</li> <li>9.2.1</li> <li>9.2.2</li> <li>9.2.3</li> <li>9.2.3.1</li> <li>9.2.3.2</li> </ul>	Kererences 275 Mercury Toxicity and Speciation Analysis 285 Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna Lohren Mercury Toxicity 285 Occurrence and Human Exposure 285 Toxicokinetic of Hg Species 286 Elemental Mercury 287 Inorganic Mercuric Mercury 287 Methylmercury 287 Thiomersal 288 Biomarkers of Exposure 288 Toxicity of Hg Species 289 Concluding Remarks on Hg-Species-Induced Toxicity 290 Mercury Speciation Analysis 291 Sample Preparation for Hg Analysis 291 Sample Preparation for Hg Analysis 291 Hg Species Quantification Using Isotope Dilution Mass Spectrometry 293 Analytical Techniques 293 Thin-Layer Chromatography 293 Capillary Electrophoresis 294
9          9.1         9.1.1         9.1.2         9.1.2.1         9.1.2.3         9.1.2.4         9.1.3         9.1.4         9.1.5         9.2         9.2.1         9.2.2         9.2.3         9.2.3.1         9.2.3.2         9.2.3.3	Kererences 275 Mercury Toxicity and Speciation Analysis 285 Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna Lohren Mercury Toxicity 285 Occurrence and Human Exposure 285 Toxicokinetic of Hg Species 286 Elemental Mercury 287 Inorganic Mercuric Mercury 287 Methylmercury 287 Thiomersal 288 Biomarkers of Exposure 288 Toxicity of Hg Species 289 Concluding Remarks on Hg-Species-Induced Toxicity 290 Mercury Speciation Analysis 291 Sample Preparation for Hg Analysis 291 Sample Preparation for Hg Analysis 291 Hg Species Quantification Using Isotope Dilution Mass Spectrometry 293 Analytical Techniques 293 Thin-Layer Chromatography 293 Capillary Electrophoresis 294 High-Performance Liquid Chromatography 294

9.2.3.4 Gas Chromatography 294

Contents XIII

9.2.3.5 9.2.3.6 9.2.4	Particulate Hg Analysis 296 X-Ray Absorption Spectroscopy 296 Mercury Complexes in Life Sciences: Phytochelatins and Thimerosal 297 Concluding Remarks on Mercury Analysis and Speciation 297
21210	References 298
10	<b>Environmental Speciation of Platinum Emissions from</b> <b>Chemotherapy</b> 305 <i>Marianna Vitkova, Gunda Koellensperger, and Stephan Hann</i>
10.1	Introduction 305
10.2	Elemental Analysis of Platinum 306
10.3	Quantification Strategies 309
10.4	Preparation of Samples for Total Platinum Analysis by ICP-MS 309
10.4.1	Preparation of Wastewater Samples 309
10.4.2	Sample Storage 310
10.5	Analysis of Platinum 310
10.6	Speciation of Platinum Emissions from Chemotherapy 311
10.7	Speciation Strategies for the Determination of CPC 312
10.8	Selected Applications 312
10.9	Conclusion 314
	References 315
11	Nanoparticles in Environment and Health Effect 319
11	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes
11 11.1	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319
11 11.1 11.2	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319
11 11.1 11.2 11.2.1	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319 Terminology and Classification 319
<b>11</b> 11.1 11.2 11.2.1 11.2.2	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319 Terminology and Classification 319 Environmental Fate and Biological Effects 321
11 11.1 11.2 11.2.1 11.2.2 11.3	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319 Terminology and Classification 319 Environmental Fate and Biological Effects 321 Analytical Strategies 326
11 11.1 11.2 11.2.1 11.2.2 11.3 11.3.1	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319 Terminology and Classification 319 Environmental Fate and Biological Effects 321 Analytical Strategies 326 Sample Preparation 326
<b>11</b> <ul> <li>11.1</li> <li>11.2</li> <li>11.2.1</li> <li>11.2.2</li> <li>11.3</li> <li>11.3.1</li> <li>11.3.2</li> </ul>	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319 Terminology and Classification 319 Environmental Fate and Biological Effects 321 Analytical Strategies 326 Sample Preparation 326 Analysis 328 On Line Sensention 228
<b>11</b> <ul> <li>11.1</li> <li>11.2</li> <li>11.2.1</li> <li>11.2.2</li> <li>11.3</li> <li>11.3.1</li> <li>11.3.2</li> <li>11.3.2.1</li> <li>11.3.2.1</li> </ul>	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319 Terminology and Classification 319 Environmental Fate and Biological Effects 321 Analytical Strategies 326 Sample Preparation 326 Analysis 328 On-Line Separation 328 Light Scattering Based Spectroscopy 221
<b>11</b> <ul> <li>11.1</li> <li>11.2</li> <li>11.2.1</li> <li>11.2.2</li> <li>11.3</li> <li>11.3.1</li> <li>11.3.2</li> <li>11.3.2.1</li> <li>11.3.2.2</li> <li>11.3.2.2</li> </ul>	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319 Terminology and Classification 319 Environmental Fate and Biological Effects 321 Analytical Strategies 326 Sample Preparation 326 Analysis 328 On-Line Separation 328 Light-Scattering-Based Spectroscopy 331
<b>11</b> <ul> <li>11.1</li> <li>11.2</li> <li>11.2.1</li> <li>11.2.2</li> <li>11.3</li> <li>11.3.1</li> <li>11.3.2</li> <li>11.3.2.1</li> <li>11.3.2.2</li> <li>11.3.2.3</li> <li>11.3.2.4</li> </ul>	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319 Terminology and Classification 319 Environmental Fate and Biological Effects 321 Analytical Strategies 326 Sample Preparation 326 Analysis 328 On-Line Separation 328 Light-Scattering-Based Spectroscopy 331 Microscopy Imaging 331 Other Tachniques 222
11         11.1         11.2         11.2.1         11.2.2         11.3         11.3.1         11.3.2         11.3.2.1         11.3.2.2         11.3.2.3         11.3.2.4	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319 Terminology and Classification 319 Environmental Fate and Biological Effects 321 Analytical Strategies 326 Sample Preparation 326 Analysis 328 On-Line Separation 328 Light-Scattering-Based Spectroscopy 331 Microscopy Imaging 331 Other Techniques 332
11 11.1 11.2 11.2.1 11.2.2 11.3 11.3.1 11.3.2 11.3.2.1 11.3.2.2 11.3.2.3 11.3.2.4 11.3.2.5 11.4	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319 Terminology and Classification 319 Environmental Fate and Biological Effects 321 Analytical Strategies 326 Sample Preparation 326 Analysis 328 On-Line Separation 328 Light-Scattering-Based Spectroscopy 331 Microscopy Imaging 331 Other Techniques 332 Coupling and Multitechnique Approach 333 Conclusion 324
11 11.1 11.2 11.2.1 11.2.2 11.3 11.3.1 11.3.2 11.3.2.1 11.3.2.3 11.3.2.4 11.3.2.5 11.4	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319 Terminology and Classification 319 Environmental Fate and Biological Effects 321 Analytical Strategies 326 Sample Preparation 326 Analysis 328 On-Line Separation 328 Light-Scattering-Based Spectroscopy 331 Microscopy Imaging 331 Other Techniques 332 Coupling and Multitechnique Approach 333 Conclusion 334 References 335
11 11.1 11.2 11.2.1 11.2.2 11.3 11.3.1 11.3.2 11.3.2.1 11.3.2.3 11.3.2.4 11.3.2.5 11.4	Nanoparticles in Environment and Health Effect 319 Gaëtane Lespes Introduction 319 Nanoparticle Overview 319 Terminology and Classification 319 Environmental Fate and Biological Effects 321 Analytical Strategies 326 Sample Preparation 326 Analysis 328 On-Line Separation 328 Light-Scattering-Based Spectroscopy 331 Microscopy Imaging 331 Other Techniques 332 Coupling and Multitechnique Approach 333 Conclusion 334 References 335
<b>11</b> 11.1 11.2 11.2.1 11.2.2 11.3 11.3.1 11.3.2 11.3.2.1 11.3.2.3 11.3.2.4 11.3.2.5 11.4	Nanoparticles in Environment and Health Effect 319Gaëtane LespesIntroduction 319Nanoparticle Overview 319Terminology and Classification 319Environmental Fate and Biological Effects 321Analytical Strategies 326Sample Preparation 326Analysis 328On-Line Separation 328Light-Scattering-Based Spectroscopy 331Microscopy Imaging 331Other Techniques 332Coupling and Multitechnique Approach 333Conclusion 334References 335Part IIIMetalloproteins 341
<pre>11 11.1 11.2 11.2.1 11.2.2 11.3 11.3.1 11.3.2 11.3.2.1 11.3.2.3 11.3.2.4 11.3.2.5 11.4</pre>	Nanoparticles in Environment and Health Effect 319Gaëtane LespesIntroduction 319Nanoparticle Overview 319Terminology and Classification 319Environmental Fate and Biological Effects 321Analytical Strategies 326Sample Preparation 326Analysis 328On-Line Separation 328Light-Scattering-Based Spectroscopy 331Microscopy Imaging 331Other Techniques 332Coupling and Multitechnique Approach 333Conclusion 334References 335Part IIIMetalloproteins 341Maria Montes-Bayón and Elisa Blanco-González

XIV Contents

12.2	Sample Preparation Methodologies to Preserve Metal–Protein
	Interactions 342
12.2.1	Metalloprotein Solubilization from Tissues 343
12.2.2	Preconcentration Strategies 343
12.2.3	Isolation by Means of Immunochemical Reactions 344
12.3	Analytical Strategies for Identification of Metalloproteins 344
12.3.1	Hyphenated Methods Based on ICP-MS Coupled to Different
	Separation Techniques (HPLC, CE): Metal-Targeted Analysis 345
12.3.1.1	Liquid Chromatography with ICP-MS Detection 345
12.3.1.2	Capillary Electrophoresis with ICP-MS Detection 348
12.3.2	Molecular MS Techniques (ESI-MS, MALDI-MS): Isotopic
	Fingerprint 348
12.4	Quantitative Strategies for the Analysis of Metalloproteins 349
12.4.1	The Use of Specific and Generic Standards 350
12.4.2	The Application of Isotopically Enriched Metal Tracers 351
	References 355
13	Biomedical and Pharmaceutical Applications 359
13.1	Selenium and Selenoproteins in Human Health and Diseases 359
	Jordan Sonet, Anne-Laure Bulteau, and Laurent Chavatte
13.1.1	Introduction 359
13.1.2	Selenium History, from a Poison to an Essential Trace Element 359
13.1.3	Selenium Levels and Tissue Distribution in Human 360
13.1.4	The Selenoproteome: Synthesis, Function, and Regulation 361
13.1.4.1	Selenoprotein Biosynthesis 361
13.1.4.2	Selenoprotein Function 361
13.1.4.3	Selenoprotein Hierarchy 362
13.1.5	Detection Strategies for Selenium and Selenoproteins 365
13.1.5.1	Total Selenium 365
13.1.5.2	Enzymatic Activities for Selenoproteins 366
13.1.5.3	Selenoprotein mRNA Levels 366
13.1.5.4	Selenoprotein Levels 367
13.1.5.5	Cellular or Tissue Imaging 368
13.1.6	Link between Selenium, Selenoproteins, and Human Diseases 368
13.1.6.1	Cancer 368
13.1.6.2	Other Diseases 369
13.1.7	Concluding Remarks 370
	Acknowledgments 370
	References 370
13.2	Metal Species as Biomarkers for Medical Diagnosis: A Case Study of
	Alzheimer's Disease 375
	Tamara García-Barrera, José Luis Gómez-Ariza, and Belén Callejón-Leblic
13.2.1	The Role of Metals in Biology 375
13.2.2	The Role of Metals in Alzheimer's Disease 378
13.2.2.1	Metal Homeostasis in the Progression of Alzheimer's Disease 378

Contents XV

	Conte
13.2.2.2	Interelement and Interfraction Ratios in Alzheimer's Disease and Mild Cognitive Impairment Patients <i>381</i>
13.2.3	Concluding Remarks 384
	References 385
13.3	Vanadium Speciation as a Means in Drug Development and
	Monitoring for Diabetes 388
	<i>Volker Nischwitz</i>
13.3.1	Introduction 388
13.3.2	Brief Overview on Abundance and Chemistry of Vanadium 389
13.3.3	Pharmaceutical Application of Vanadium Compounds 389
13.3.4	Vanadium Uptake and Metabolism 391
13.3.5	Techniques for Determination of Total Vanadium Levels in
	Biomedical Samples 393
13.3.6	Vanadium Speciation Analysis 393
13.3.6.1	Direct Techniques 394
13.3.6.2	Hyphenated Techniques 395
13.3.6.3	Model Solutions 395
13.3.6.4	Serum 396
13.3.6.5	Cells 397
13.3.7	Summary and Outlook 398
	References 398
13.4	Analysis of Pt- and Ru-Based Anticancer Drugs: New
	Developments 401

Sarah Theiner, Luis Galvez, Gunda Koellensperger, and Bernhard K. Keppler

- 13.4.1 Imaging Techniques in Metal-Based Anticancer Drug Research 401
- 13.4.1.1 Imaging of Metal-Based Anticancer Drugs at Tissue Level 402
- 13.4.1.2 State of the Art of Quantification by LA-ICP-MS 402
- 13.4.1.3 LA-ICP-MS Imaging in Metal-Based Anticancer Drug Development 403
- 13.4.1.4Recent Developments and Future Trends in LA-ICP-MS<br/>Bioimaging405
- 13.4.1.5 Imaging of Metal-Based Drugs at Cellular and Subcellular Level 406
- 13.4.1.6 NanoSIMS 407
- 13.4.1.7 X-Ray-Based Imaging Techniques 408
- 13.4.2 Elemental Speciation Analysis in Metal-Based Anticancer Drug Research 409
- 13.4.2.1 Elemental Speciation Analysis Regarding Clinically Established Metallodrugs 409
- 13.4.2.2 Elemental Speciation Analysis Regarding Metal-Based Anticancer
   Drug Candidates 416
   References 416
- 13.5Silver Distribution in Skin during Wound Healing420Marco Roman and Carlo Barbante
- 13.5.1Skin Physiology and Wound Healing421

XVI Contents

13.5.2	Silver in Wound Care 422
13.5.3	Release of Ag in Solution 424
13.5.4	Release of Ag In Vivo 428
13.5.5	Interaction with Skin Cells In Vitro 428
13.5.6	AgNPs Dissolution into the Wound Fluid 429
13.5.7	Percutaneous Permeation In Vitro and Ex Vivo 431
13.5.8	Skin Penetration In Vivo 434
13.5.9	Systemic Distribution 436
	References 436
13.6	Neurodegeneration with Focus on Manganese and Iron
	Speciation 442
	Katharina Neth, Julia Bornhorst, and Bernhard Michalke
13.6.1	Manganese in Physiology and Pathophysiology 442
13.6.2	Manganese Speciation Studies 445
13.6.2.1	Manganese Speciation in Human Samples 445
13.6.2.2	Manganese Speciation in Animal Samples 449
13.6.3	Iron (II)/(III) Species in Animal Samples Following Manganese
	Exposure 455
13.6.4	Future Perspectives and Conclusion 456
	References 457

Index 463