

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
	<i>Dirk Schaumlöffel</i>
1.1	Introduction 3
1.2	Metallome and Metallomics in Relation to Other “-Ome” and “-Omics” Fields 3
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 10
1.7	Metallothiolomics as Example for Metallomics Studies of a Metallome Subgroup 11
1.8	Concluding Remarks 14
	References 15
2	Coupling Techniques and Orthogonal Combination of Mass Spectrometric Techniques 17
	<i>Daniel Präfrock</i>
2.1	Introduction 17

2.2	Analytical Techniques for Metallomics	19
2.2.1	Overview about Available Separation Techniques	19
2.2.1.1	Liquid Chromatography (LC)	20
2.2.1.2	Capillary Electrophoresis (CE)	25
2.2.1.3	Gel Electrophoresis (GE)	28
2.2.1.4	Gas Chromatography (GC)	30
2.3	Ionization Principles and Mass Spectrometric Detectors for Speciation	30
2.3.1	Element-Specific Detection with ICP-Based Techniques	31
2.3.1.1	Mass Analyzers for ICP-MS	34
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
2.3.3.1	TOF Mass Analyzers for MALDI-MS	45
2.4	Overview about Coupling Techniques	48
2.4.1	LC Couplings	49
2.4.1.1	Coupling of Miniaturized LC and ICP-MS	49
2.4.2	Coupling of CE and ICP-MS	52
2.4.3	Laser Ablation (LA)	55
2.4.4	Gas 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
	<i>Heidi G. Infante</i>	
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
3.3	The Role of Species-Specific Isotope Dilution in Increasing Metrological Traceability for the Quantification of Bioinorganic Species	72
3.3.1	IDMS and Speciation Analysis	72
3.3.2	Quantitative Se Speciation in Food/Supplements by Species-Specific 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

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
3.3.4.1	Inorganic Cr Quantification in Cr–Yeast Supplements	78
3.3.4.2	Inorganic Cr Species Quantification in Clean and Wastewater	79
	References	81
4	Novel Methods for Bioimaging Including LA-ICP-MS, NanoSIMS, TEM/X-EDS, and SXRF	83
	<i>Dirk Schaumlöffel, Robert Hutchinson, Julien Malherbe, Philippe Le Coustumer, Etienne Gontier, and Marie-Pierre Isaure</i>	
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
4.2.4	Proteomic Bioimaging by LA-ICP-MS	88
4.2.5	Frontiers in Bioimaging by LA-ICP-MS	90
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
4.4	Bioimaging by TEM/X-EDS	93
4.4.1	Principle	93
4.4.2	Application to Biological Samples	96
4.4.3	Preparation of Biological Samples for NanoSIMS and TEM/X-EDS	98
4.4.4	Cryofixation	101
4.4.4.1	Cryofixation by Slamming	102
4.4.4.2	Cryofixation by High-Pressure Freezing	102
4.4.5	Lyophilization	103
4.4.6	Cryosubstitution	103
4.4.7	Sectioning by Ultramicrotomy	103
4.5	Bioimaging by SXRF	104
4.5.1	Principle	104
4.5.2	Sample Preservation during Preparation and Measurements	106
4.5.3	Data Treatments	107
4.5.4	Applications	107
4.6	Conclusions and Outlook	108
	References	109

5	Electrochemistry Coupled to Mass Spectrometry for Investigating Oxidative Metabolism of Pt-Based Drug Conjugates: A Novel Approach	117
	<i>Günther Weber</i>	
5.1	Introduction	117
5.2	EC-MS Methodology	119
5.3	EC-MS of Thiols	119
5.4	Influence of Cisplatin on Thiol Oxidation	121
5.5	Conclusions	125
	References	126
	Part II Metallomics in Environment and Nutrition	129
6	Selenium and Selenium Species	131
6.1	Speciation Analysis Especially of Tin and Selenium in Environmental Matrices	131
	<i>Maria Ochsenkühn-Petropoulou and Fotios Tsopeas</i>	
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
	<i>Lena Ruzik, Katarzyna Bierła, and Joanna Szpunar</i>	
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

7	Arsenic and As Species	173
7.1	Arsenic Species in Marine Food	173
	<i>María Carmen Barciela-Alonso and Pilar Bermejo-Barrera</i>	
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
	<i>Jörg Feldmann, Andrea Raab, Helle R. Hansen, Katharina Bluemlein, and Dirk Wallschläger</i>	
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	Arsinothioly 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
	<i>Michael Stiboller, Ronald A. Glabonjat, Georg Raber, Kenneth B. Jensen, and Kevin A. Francesconi</i>	
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

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

9 Mercury Toxicity and Speciation Analysis 285

Eva M. Krupp, Zuzana Gajdosechova, Tanja Schwerdtle, and Hanna Lohren

- 9.1 Mercury Toxicity 285
 - 9.1.1 Occurrence and Human Exposure 285
 - 9.1.2 Toxicokinetic of Hg Species 286
 - 9.1.2.1 Elemental Mercury 287
 - 9.1.2.2 Inorganic Mercuric Mercury 287
 - 9.1.2.3 Methylmercury 287
 - 9.1.2.4 Thiomersal 288
 - 9.1.3 Biomarkers of Exposure 288
 - 9.1.4 Toxicity of Hg Species 289
 - 9.1.5 Concluding Remarks on Hg-Species-Induced Toxicity 290
- 9.2 Mercury Speciation Analysis 291
 - 9.2.1 Sample Preparation for Hg Analysis 291
 - 9.2.2 Hg Species Quantification Using Isotope Dilution Mass Spectrometry 293
 - 9.2.3 Analytical Techniques 293
 - 9.2.3.1 Thin-Layer Chromatography 293
 - 9.2.3.2 Capillary Electrophoresis 294
 - 9.2.3.3 High-Performance Liquid Chromatography 294
 - 9.2.3.4 Gas Chromatography 294

9.2.3.5	Particulate Hg Analysis	296
9.2.3.6	X-Ray Absorption Spectroscopy	296
9.2.4	Mercury Complexes in Life Sciences: Phytochelatins and Thimerosal	297
9.2.5	Concluding Remarks on Mercury Analysis and Speciation	297
	References	298
10	Environmental Speciation of Platinum Emissions from Chemotherapy	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
	<i>Gaëtane Lespes</i>	
11.1	Introduction	319
11.2	Nanoparticle Overview	319
11.2.1	Terminology and Classification	319
11.2.2	Environmental Fate and Biological Effects	321
11.3	Analytical Strategies	326
11.3.1	Sample Preparation	326
11.3.2	Analysis	328
11.3.2.1	On-Line Separation	328
11.3.2.2	Light-Scattering-Based Spectroscopy	331
11.3.2.3	Microscopy Imaging	331
11.3.2.4	Other Techniques	332
11.3.2.5	Coupling and Multitechnique Approach	333
11.4	Conclusion	334
	References	335
	Part III Metallomics in Medicine and Biology	339
12	Metalloproteins	341
	<i>Maria Montes-Bayón and Elisa Blanco-González</i>	
12.1	General Introduction to Metalloprotein Analysis	341

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
	<i>Jordan Sonet, Anne-Laure Bulteau, and Laurent Chavatte</i>	
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
	<i>Tamara García-Barrera, José Luis Gómez-Ariza, and Belén Callejón-Leblic</i>	
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

13.2.2.2	Interelement and Interfraction Ratios in Alzheimer's Disease and Mild Cognitive Impairment Patients	381
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
	<i>Sarah Theiner, Luis Galvez, Gunda Koellensperger, and Bernhard K. Keppler</i>	
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
13.4.1.4	Recent Developments and Future Trends in LA-ICP-MS Bioimaging	405
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
13.5	Silver Distribution in Skin during Wound Healing	420
	<i>Marco Roman and Carlo Barbante</i>	
13.5.1	Skin Physiology and Wound Healing	421

13.5.2	Silver in Wound Care	422
13.5.3	Release of Ag in Solution	424
13.5.4	Release of Ag <i>In Vivo</i>	428
13.5.5	Interaction with Skin Cells <i>In Vitro</i>	428
13.5.6	AgNPs Dissolution into the Wound Fluid	429
13.5.7	Percutaneous Permeation <i>In Vitro</i> and <i>Ex Vivo</i>	431
13.5.8	Skin Penetration <i>In Vivo</i>	434
13.5.9	Systemic Distribution	436
	References	436
13.6	Neurodegeneration with Focus on Manganese and Iron Speciation	442
	<i>Katharina Neth, Julia Bornhorst, and Bernhard Michalke</i>	
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