

Table of contents

The role of metabolomics in systems biology	1
Jens Nielsen and Michael C. Jewett.....	1
Abstract	1
1 Metabolomics	1
2 Applications of metabolomics.....	3
3 The role of metabolomics in systems biology	4
4 Outline of this book.....	6
References	8
Analytical methods from the perspective of method standardization	11
Silas G. Villas-Bôas, Albert Koulman, and Geoffrey A. Lane	11
Abstract	11
1 Introduction	11
2 Pre-analytical variability	13
2.1 Biological variability	13
2.2 Variability introduced during sampling	14
2.3 Variability introduced during sample processing	19
3 Intra-analytical variability	28
3.1 GC-MS.....	29
3.2 ESI-MS	37
3.3 Conclusions.....	43
4 Post-analytical issues.....	43
5 Final remarks.....	44
Acknowledgments	45
References	45
Abbreviations	51
Reporting standards.....	53
Nigel Hardy and Helen Jenkins	53
Abstract	53
1 Introduction	53
1.1 Data handling in metabolomics	54
2 Standards, models, and formats.....	56
3 Initiatives in metabolomics data standards.....	60
3.1 MIAMET	60
3.2 ArMet.....	61
3.3 SMRS.....	61
3.4 MSI	62
4 Reporting standards in other fields.....	62
4.1 Transcriptomics	62
4.2 Proteomics	64

5 Cross-domain standards	64
6 Issues in metabolomics standards.....	66
6.1 The detailed nature of standards	66
6.2 Controlled vocabularies and ontologies.....	68
6.3 Chemical identity.....	69
7 Conclusions.....	70
References.....	70
The Golm Metabolome Database: a database for GC-MS based metabolite profiling.....	75
Jan Hummel, Joachim Selbig, Dirk Walther, and Joachim Kopka	75
Abstract	75
1 Introduction.....	75
1.1 Pathway databases	77
1.2 Cheminformatics databases	78
1.3 Databases dedicated to metabolite profiling	79
1.4 The Golm Metabolome Database (GMD)	80
2 Database objects.....	80
3 Information exchange between databases	81
4 The main work flows of metabolite profiling.....	82
4.1 The metabolite profiling work flow: from sample to metabolite fingerprint and profile.....	83
4.2 The metabolite mapping work flow: from metabolite to specific and selective GC-MS mass fragment.....	85
5 The main database objects.....	87
5.1 Modelling the “MST” database object.....	87
5.2 Modelling the “chemical substance” database object	88
6 Outlook.....	90
References.....	91
List of abbreviations.....	95
Reconstruction of dynamic network models from metabolite measurements.....	97
Matthias Reuss, Luciano Aguilera-Vázquez, Klaus Mauch	97
Abstract	97
1 Introduction.....	97
2 Quantitative measurements of intracellular metabolites	99
3 Use of metabolite measurements for identification of dynamic models.....	103
3.1 Modular decomposition of the network.....	103
3.2 <i>In silico</i> identification of whole cell metabolite dynamics through evolutionary algorithms and parallel computing	118
3.3 Identification of kinetic rate expression from series of steady state observations.....	122
4. Summary and outlook	123
References.....	124

Toward metabolome-based ^{13}C flux analysis: a universal tool for measuring <i>in vivo</i> metabolic activity	129
Nicola Zamboni	129
Abstract	129
1 Introduction	129
2 Fundamentals of metabolic flux analysis	132
3 Principles of labeling experiments	133
4 Current practice of stationary ^{13}C flux analysis	135
4.1 Experimental design	135
4.2 From analytes to ^{13}C labeling patterns	136
4.3 From ^{13}C labeling patterns to fluxes	138
5 Toward metabolome-based ^{13}C flux analysis	144
5.1 Experimental proof-of-concept	144
5.2 Analytics: lessons from metabolomics	145
5.3 Current developments	147
6 Conclusions	151
Acknowledgements	151
References	151
List of abbreviations	157
Data acquisition, analysis, and mining: Integrative tools for discerning metabolic function in <i>Saccharomyces cerevisiae</i>	159
Michael C. Jewett, Michael A.E. Hansen, and Jens Nielsen	159
Abstract	159
1 Yeast as a model system for metabolomics	159
2 Metabolite analysis workflow	161
3 Chemical analysis	162
3.1 Quenching	162
3.2 Extraction	162
3.3 Analytical methods	163
3.4 Standardization	165
4 Data analysis	165
4.1 Pre-processing	166
4.2 Statistical analysis	169
4.3 Classification	175
4.4 Genetic programming	175
4.5 SpectConnect	176
5 Data integration	177
6 Future outlook	180
Acknowledgements	180
References	180

<i>E. coli</i> metabolomics: capturing the complexity of a “simple” model	189
Martin Robert, Tomoyoshi Soga and Masaru Tomita	189
Abstract	189
1 Introduction	189
2 Experimental methods	190
2.1 Quenching of metabolism and metabolite extraction	191
2.2 Main analytical methods tested with <i>E. coli</i>	193
3.1 Groundwork	198
3.2 Combining concentration data with enzyme activity and flux measurements	201
3.3 Emerging metabolomic studies in <i>E. coli</i>	202
4 Evaluating the size of the <i>E. coli</i> metabolome	203
4.1 Hints from genome-based models	203
4.2 Experimental clues	203
4.3 Improving metabolite identification	204
5 Architecture/anatomy of the <i>E. coli</i> metabolome	206
5.1 Metabolite architecture	206
5.2 Pathway architecture	206
6 <i>E. coli</i> metabolomics as a powerful tool for functional genomics	207
6.1 Metabolic footprinting	208
6.2 Enzyme discovery using non-targeted metabolomics	208
6.3 Deorphanizing enzymatic activities and filling-in metabolic pathway holes	212
6.4 Phenotype microarrays as reporters of metabolic phenotype	212
7 Metabolomics to facilitate metabolic engineering of <i>E. coli</i>	213
8 Metabolomics in flux analysis	215
9 Adaptive evolution in <i>E. coli</i> , metabolomics, and metabolic phenotype	215
10 Metabolic models of <i>E. coli</i> : the role of metabolomics	216
11 Databases and resources	218
12 Data integration and visualization	221
13 Future prospects and developments	222
14 Concluding remarks	223
Acknowledgement	223
References	224
Abbreviations	234
The exo-metabolome in filamentous fungi	235
Ulf Thrane, Birgitte Andersen, Jens C. Frisvad, Jørn Smedsgaard	235
Abstract	235
1 Introduction	235
2 Exo-metabolome and taxonomy	236
3 Exo-metabolome and fungal growth	237
4 Visualisation of the exo-metabolome	239
5 Extraction of the exo-metabolome	240

6 Analysis of the exo-metabolome by high performance liquid chromatography.....	242
7 Direct infusion electrospray mass spectrometry for profiling	247
8 Outlook – a polyphasic approach	248
Acknowledgements	249
References	249
The importance of anatomy and physiology in plant metabolomics.....	253
Ute Roessner and Filomena Pettolino.....	253
Abstract	253
1 Introduction	253
1.1 Importance of plants	253
1.2 Plant metabolomics	254
2 Plant anatomy.....	255
2.1 Whole plant anatomy	255
2.2 Cell anatomy	256
3 Plant physiology – Challenges for plant metabolomics.....	260
3.1 Photosynthesis	260
3.2 Photorespiration.....	260
3.3 Transpiration.....	262
3.4 Starch and other storage products	262
3.5 Cell wall synthesis	263
3.6 Secondary metabolites	266
4 Unique aspects of plant research	267
4.1 Functional genomics	267
4.2 Breeding and QTL analysis	268
4.3 Genetic engineering	270
5 Recent, current and future of plant metabolomics.....	272
5.1 Successful applications	272
6 Future	274
References	274
Index	279