

Contents

List of Figures	xiii
List of Tables.....	xix
Acknowledgments.....	xxi
About the Authors.....	xxiii
Abbreviations	xxv
To the Reader	xxix

Chapter 1 An Overview	1
1.1 A Brief History	1
1.2 Definitions Concerning Instruments, Mass, <i>m/z</i> , and Ions	2
1.3 Components of Instruments and Their Functions	11
1.3.1 Sample Introduction	11
1.3.2 Ion Sources	13
1.3.3 Mass Analyzers	17
1.3.4 Ion Current Detectors.....	21
1.3.5 Vacuum Systems	22
1.3.6 Data Systems	23
1.4 Definitions Concerning Instrument Performance	23
1.5 Definitions Concerning Applications	26
1.6 Information from Mass Spectra	28
1.7 Diversity and Scope of Applications	31
Chapter 2 Instrumentation	35
2.1 Sample Introduction	37
2.1.1 Pure Samples or Simple Mixtures.....	37
2.1.1.1 Introduction of Gases and Volatile Liquids Using Batch Inlets	37
2.1.1.2 Semipermeable Polymer Membrane Inlets...	38
2.1.1.3 Direct (Static) Insertion Probes	38
2.1.2 Chromatographic Separation of Complex Mixtures ..	39
2.1.2.1 Gas Chromatography–Mass Spectrometry (GC-MS)	40
2.1.2.2 Liquid Chromatography–Mass Spectrometry (LC-MS).....	43
2.1.2.3 Capillary Electrophoresis (CE).....	45
2.2 Ion Sources and Methods of Ionization.....	45
2.2.1 Electron Ionization (EI)	49
2.2.2 Soft Ionization	52
2.2.2.1 Chemical Ionization (CI)	53
2.2.2.2 Electrospray Ionization (ESI)	56

2.2.2.3	Atmospheric Pressure Chemical Ionization (APCI)	61
2.2.2.4	Atmospheric Pressure Photo-Ionization (APPI)	63
2.2.3	Surface Ionization Methods	64
2.2.3.1	Desorption Electrospray Ionization (DESI)...	64
2.2.3.2	Direct Analysis in Real Time (DART).....	65
2.2.4	Matrix-Assisted Laser Desorption/Ionization (MALDI).....	67
2.2.4.1	Surface-Enhanced Laser Desorption Ionization (SELDI)	70
2.2.5	Alternative Ionization Methods.....	71
2.3	Mass Analyzers	71
2.3.1	Quadrupole (Q)	72
2.3.1.1	Quadrupoles as Ion Guides (q)	74
2.3.2	Ion Traps.....	74
2.3.2.1	Quadrupole Ion Trap (QIT)	74
2.3.2.2	Linear Ion Trap (LIT)	76
2.3.3	Time-of-Flight (TOF) Analyzer.....	76
2.3.4	Fourier Transform Ion Traps	83
2.3.4.1	Orbitrap.....	83
2.3.4.2	Fourier Transform–Ion Cyclotron Resonance (FT-ICR)	84
2.3.5	Ion Mobility Analyzers	87
2.3.5.1	High-Field Asymmetric Waveform Ion Mobility Spectrometer (FAIMS)	87
2.3.5.2	Ion Mobility Separator (IMS).....	89
2.3.6	Magnetic Sector Analyzers	90
2.3.7	Multianalyzer (MS/MS) Systems.....	91
2.3.7.1	Tandem MS/MS Instruments	92
2.3.7.2	Hybrid MS/MS Instruments	94
2.4	Ion Current Detectors	97
2.4.1	Electron Multipliers.....	97
2.4.2	Daly Detector	100
2.4.3	Image Currents	100
2.5	Vacuum Systems.....	102
2.5.1	Backing (Roughing) Pumps	104
2.5.1.1	Rotary Pumps	104
2.5.1.2	Scroll Pumps.....	105
2.5.2	Turbomolecular Pumps	106
2.6	Data Systems	107
Chapter 3	Methodologies and Strategies	111
3.1	Measures of Instrument Performance	111
3.1.1	Instrument Tuning and Mass Scale Calibration.....	111

3.1.2	Resolution	113
3.1.3	Accurate Mass Measurement	115
3.2	Interpretation of Mass Spectra	122
3.2.1	What Is a Mass Spectrum?	122
3.2.2	Isotope Patterns	124
3.2.3	Electron Ionization Spectra of Small Molecules.....	127
3.2.4	Spectra from Ionization by the Addition or Removal of Charges	130
3.2.4.1	Electrospray Ionization Spectra of Large Molecules	130
3.2.4.2	Atmospheric Pressure Ionization and Fragmentation	134
3.2.5	Fragmentation and Quantification.....	134
3.2.6	A Few Ions to Avoid (or at least recognize)	134
3.3	Analytical Techniques and Strategies	135
3.3.1	Techniques for Instruments with Single Analyzers	136
3.3.1.1	Techniques for Ion Activation.....	136
3.3.1.2	Ion Activation and Fragment Formation in Single-Analyzer Instruments	137
3.3.2	Mass Spectrometry/Mass Spectrometry (MS/MS)	138
3.3.2.1	Collision-Induced Dissociation (CID)	138
3.3.2.2	Infrared Multiphoton Dissociation (IRMPD)	140
3.3.2.3	Electron Transfer Dissociation (ETD) and Electron Capture Dissociation (ECD)....	141
3.3.2.4	Photodissociation and Surface-Induced Dissociation	141
3.3.3	Tandem-in-Space MS/MS	142
3.3.3.1	MS/MS Techniques Using Triple Quadrupole (QqQ) Analyzers	142
3.3.3.2	MS/MS Techniques Using Time-of- Flight/Time-of-Flight (TOF/TOF) Analyzers	146
3.3.3.3	MS/MS Techniques Using Hybrid Instruments	146
3.3.3.4	Data Dependent Acquisition (DDA) and CID Fragmentation by Voltage Switching (Data Independent Acquisition, DIA).....	147
3.3.4	MS/MS Techniques Using Tandem-in-Time (Trapped-Ion) Analyzers	149
3.3.5	Quantification of Small Molecules.....	149
3.3.5.1	Standard Deviations and Method Validation.....	157

3.4	Omics.....	157
3.4.1	Metabolomics	159
3.4.2	Lipidomics.....	160
3.5	Biopolymers.....	162
3.5.1	Proteomics.....	163
3.5.1.1	Peptide Sequencing.....	164
3.5.1.2	Bottom-Up Protein Sequencing	166
3.5.1.3	Top-Down Protein Sequencing.....	168
3.5.1.4	<i>De Novo</i> Protein Sequencing	170
3.5.1.5	Post-Translational Modification (PTM)....	171
3.5.1.6	Some Other Ions to Know About and Avoid.....	173
3.5.1.7	Protein Conformation	173
3.5.1.8	Hydrogen/Deuterium Exchange (HDX) ...	177
3.5.1.9	Quantification of Proteins.....	179
3.5.2	Nucleomics (Nucleic Acid Analysis).....	187
3.5.3	Glycomics.....	190
3.6	Imaging Mass Spectrometry	194
3.7	Bioinformatics	196
3.8	Buying a Mass Spectrometer.....	198
Chapter 4	Examples from Representative Publications.....	205
4.1	An Open-Access Mass Spectrometry Facility	205
4.2	Environmental: Organochlorines in Fish	208
4.3	Environmental: Pharmaceuticals in Surface and Wastewaters	210
4.4	Pharmacology: Lipitor Metabolism.....	213
4.5	New Techniques: Paper Spray of Pharmaceuticals	216
4.6	Petroleomics: Crude Oil Characterization	219
4.7	Metabolomics: Disease Markers for a Tropical Disease	221
4.8	Metabolomics: Chemical Defense.....	223
4.9	Lipidomics: Coronary Artery Disease	225
4.10	Proteomics: Protein Identification in a Painting.....	227
4.11	Proteomics: Protein Identification and Metastasis	230
4.12	Proteomics: Noncovalent Interactions.....	232
4.13	Tissue Imaging	235
Chapter 5	The Absolute Essentials.....	239
5.1	General	239
5.2	Instrument Components	242
5.3	Performance Parameters.....	249
5.4	Techniques and Strategies	250

Chapter 6 Resources	255
6.1 Books, Journals, Review Articles, Classical Publications	255
6.1.1 General	255
6.1.2 Formulas and Derivations	256
6.1.3 Instrumentation and Techniques	257
6.1.4 Applications.....	257
6.1.4.1 General.....	257
6.1.4.2 Proteomics	258
6.1.4.3 Other Omics.....	258
6.1.4.4 Pharmaceutical, Medical, and Clinical	258
6.1.4.5 Miscellaneous	259
6.1.5 Journals	259
6.1.6 Selected Review Articles.....	259
6.1.6.1 General and Sample Preparation	260
6.1.6.2 Instrumentation.....	260
6.1.6.3 Quantification	260
6.1.6.4 MS/MS.....	261
6.1.6.5 Data Processing and Bioinformatics	261
6.1.6.6 Applications	261
6.1.7 Classic Publications.....	262
6.2 Major Instrument Manufacturers	263
6.3 Mass Spectrometry Societies, Blogs, and Discussion Groups	263
6.4 The Mass Spectrometrist and the Internet	264
6.4.1 Wikipedia	264
6.4.2 Tutorials.....	264
6.4.3 Databases.....	265
6.4.4 Miscellaneous Resources	266
Index.....	267

FIGURE 2.7 Mass spectra of two different types of samples.

FIGURE 2.8 Mass spectra of three catalysts under different ionization conditions.

FIGURE 2.9 Electron ionization (EI) source.

FIGURE 2.10 Comparison of EI spectra for (a) an aromatic and (b) an aliphatic compound.

FIGURE 2.11 Chemical ionization (CI) source.

FIGURE 2.12 Electrospray ionization (ESI) source.

FIGURE 2.13 Taylor cone formation (source) and droplet desolvation (desolvation).