Mass Spectrometry Basics
Christopher G. Herbert and Robert A. W. Johnstone
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Book Review by O. David Sparkman
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According to the preface, “This book began as a small series of brief articles designed to assist (Micromass) engineers and salesmen in understanding some aspects of ion chemistry and mass spectrometry.” And, that is what the book remains. The authors further state that the articles provide a quick explanation of fundamental concepts with a minimum of text but rapidly understood pictures, and the omission of equations, not in an effort to dumb-down the subject, but to make esoteric concepts with a minimum of text but rapidly understood pictures. The book’s 49 chapters cover an eclectic group of topics which include ionization aspects readily comprehensible. The book’s 49 chapters effort to dumb-down the subject, but to make esoteric pictures, and the omission of equations, not in an effort to dumb-down the subject, but to make esoteric aspects readily comprehensible. The book’s 49 chapters cover an eclectic group of topics which include ionization techniques and interfaces to \(m/z\) analyzers, inorganic ionization and analysis techniques employing mass spectrometry, some types of mass spectrometers (especially those that have been associated with high-visibility Micromass products like the Q/TOF, “hybrid hexapole time-of-flight”, sector/TOF, etc.), ion detection, metastable ions (MS/MS), GC/MS, LC/MS, high-resolution/accurate mass measurements/elemental composition, analysis of peptides and proteins, environmental protocols, mass spectrometry computer hardware and function, isotopes for elemental composition and in archaeology and geology, and even a chapter entitled Introduction to Biotechnology. There are no references to the scientific literature in any of the chapters. These articles were originally intended for internal Micromass use; however, as outsiders became aware of them, Micromass was continually inquired as to how they could be obtained. These individual articles are intended to provide a “brief (but not superficial) explanation of various areas of mass spectrometry” so that the “nonexpert” will have enough information to understand major aspects of the field. According to the preface, the articles were originally distributed free in a ring-binder format. Later, the collection was offered as a CD-ROM (circa December 2000, Version 2). Again, according to the book’s preface, there were over 600 requests for the CD-ROM the day after its announcement on the Internet. The collection was then made available as an Internet-accessible tool and is now in its present book form.

In addition to the 49 chapters, which range in length from 4 to about 13 pages with most being 6 to 7 pages, there are 5 appendices. Appendix A (44 pages) is a collection of summaries for each of the chapters, sort of a quick study guide for the test. Appendix B is a 15-page glossary and 3 pages of “Common Abbreviations.” It appears this glossary may have been taken as a direct copy of the IUPAC Nomenclature rules, which appear in the International Union of Pure and Applied Chemistry, Physical Chemistry Division, Commission on Molecular Structure and Spectroscopy [sic], Subcommittee on Mass Spectroscopy [sic], “Recommendations For Nomenclature And Symbolism For Mass Spectroscopy” [sic] (including an appendix of terms used in vacuum technology) Todd, JF, Int. J. of Mass Spectrom. Ion Proc. 1995, 142(3), 211–240 because the same error of showing a double-barred arrow for indicating the movement of two electrons is duplicated. Appendix C is a three-and-a-half-page list of books on mass spectrometry and related topics. This list is somewhat curious in that it contains Bill Budde’s Analytical Mass Spectrometry (© 2001) but has the first edition of Jack Watson’s Introduction to Mass Spectrometry (© 1976) when the third edition has been in print since 1997. The last two appendices are “Regular Publications in Mass Spectrometry” (Appendix D) and “Publications Containing Occasional Papers Related to Mass Spectrometry” (Appendix E). Interestingly, both lists contain a reference to Mass Spectrometry Reviews. Appendix D does list three out-of-print publications which will often appear in a reference list associated with an article. These out-of-print journal titles are often missing from lists of current publications.

Looking at the title and the preface, it appears this book could have potential as a tool for those interested in the topics of mass spectrometry but do not have either the time or the inclination for a detailed study. This book could have provided a peripatetic approach to dealing with the subject. As such, the lack of references is not an issue. However, much of the technology is circa early 1990s; and, as such, important topics are omitted. As an example, the 8-page chapter entitled Analysis of Peptides and Proteins by Mass Spectrometry places initial emphasis on fast-atom bombardment (FAB). The term laser desorption mass spectrometry (LDMS) is used and it says, “...technique uses solid matrices (e.g., cinnamic acid derivatives)...”, but it makes no reference to MALD/I (matrix-assisted laser desorption/ionization). This is then followed by a section on electrospray (ES). The text found in the “Conclusion” heading reads, “Intact peptides and proteins can be examined by a variety of new techniques, including MS/MS dynamic FAB, APCI, and electro-
pray." This is the first mention of atmospheric pressure chemical ionization (APCI), which is a gas-phase ion/molecule reaction technique, and would be very difficult to use in the ionization of peptides and proteins because it would require putting neutral molecules of these substances into the gas phase. With respect to APCI, there is no chapter with this title. The chapter entitled Electrospray Ionization (ESI) states, "The electrospray inlet should be compared with the APCI inlet, which is described in Chapter 9." Chapter 9 is entitled Atmospheric-pressure Ionization (API). In the opening of the API chapter, the authors state, "API is important in thermospray, Plasmaspray, and electrospray ionization." The description of the API in this chapter is essentially the same as the description of ES. In the ES chapter, the authors say, "In effect, the device [ES interface] is a momentum separator between solvent and solute (sample) molecules." The API chapter is followed by a chapter entitled Z-Spray Combined Inlet/Ion Source. This is a chapter on Micromass-specific API (using the term correctly to mean either an ES or an APCI interface), which may or may not be appropriate for a general book on mass spectrometry. The Z-Spray chapter is followed by a chapter entitled Thermospray and Plasmaspray Interfaces. This chapter has large blocks of text that are identical to the text in the ES chapter; however, the word electrospray has been replaced with the word thermospray. The final sentence of the first page of this chapter states, "Thermospray alone is now absolute, having given way to plasmaspray (atmospheric-pressure chemical ionization—APCI) and electrospray." This is a correct statement; however, the technique of thermospray is not an atmospheric pressure technique as implied and described in this chapter. If this chapter is read alone, it appears that thermospray and ES are the same, other than the names. The ES and API chapters both conclude with a statement that APCI "...works well with solutions of thermally sensitive polar molecules, such as peptides, proteins, sugars, and oligonucleotides [sic]." What do you think the results will be if you put a solution of table sugar into an APCI interface?

As stated above, much of the material comes from circa early 1990s; but, not all. The Z-Spray and some of the analyzer chapters are much later (late 1990s and early 2000s). There are references to "The National Institutes of Health (NIH)—EPA" [sic] and NIST libraries of EI mass spectra. In the chapter entitled Environmental Protection Agency Protocol, the size of the "NIH—EPA" library is said to be over 44,000 spectra, which would date this article to circa 1986. In the GC/MS and LC/MS chapters, the size of the NIST library is said to be 50,000 to 60,000 spectra, which would be circa 1990. In the LC/MS chapter, it states, "If the ions [produced as protonated molecules] are given extra energy so that they fragment—or if the particle beam or moving-belt inlets are in place so that electron ionization can be used—then the resulting mass spectra can be compared with those held in a large library of spectra of known compounds (e.g., the NIST library)." Implicit in this statement is that spectra resulting from fragmentation due to collisional activation of protonated molecules and spectra resulting from the fragmentation of molecular ions formed by electron ionization are the same.

There is no discussion of ionization efficiency in the Electron Ionization chapter. The wording, however, would easily allow for a conclusion that the efficiency is 100%. In the CI chapter, there is the statement, "Negative-ion CI is a useful sensitive technique for substances having a high electron affinity such as halo compounds and polycyclic aromatic hydrocarbons." The only discussion in this chapter on formation of negative ions by chemical ionization has to do with the use of negative-charge reagent ions, which results in deprotonated molecules. The technique that produces high sensitivity with electrophilic compounds, which is resonance electron capture ionization and results in negative-charge molecular ions, is not covered in any of the book’s 49 chapters.

The analyzer chapters are a curious collection. Chapter 20, Hybrid Orthogonal Time-of-Flight (oa-TOF) Instruments, describes three Micromass instruments: the Q/TOF and the AutoSpec-TOF, which are instruments used for MS/MS that have an orthogonally pulsed ion beam into a TOF analyzer as its second stage of m/z analysis; and the LCT, an electrospray interface followed by two in-line hexapole ion guides that has a TOF m/z analyzer orthogonal to the ion beam emanating from the atmospheric region. Chapter 20 is followed by three chapters, each describing one of these three different instruments. In the Hybrid Hexapole Time-of-Flight (Hexapole/TOF) Instruments, the authors incorrectly describe the operation of a transmission quadrupole filter as, "...two opposed poles have an applied radio-frequency (RF) voltage applied [sic] with the other two opposed poles having a constant DC voltage." This is especially egregious because the Quadrupole Ion Optics chapter states the operation correctly and is well done. Other parts of these analyzer-specific chapters are more accurate and give a fairly representative picture. The Ion Optics of Magnetic/Electric-Sector is very good and accomplishes the goal of providing a lay-view of the subject. One shortcoming of both the magnetic and the quadrupole ion optics chapters is that neither states why there is an upper m/z limit imposed on these analyzers. These upper limits, of course, are due to the maximum field strength obtainable with the variable field magnet and the maximum amplitude obtainable for the RF voltage while still maintaining a stable frequency. One other small problem with the quadrupole chapter is the impression that all quadrupole filters are constructed with round rods. Whereas this is true for those manufactured by Micromass, it is not true for all manufacturers. The chapter entitled Time-of-Flight Ion Optics is very descriptive and, like the other ion optics chapters, accomplishes its intended purpose. However, neither the Orthogonal Time-of-Flight (oa-TOF) Ion Optics nor the Hybrid Orthogonal Time-of-
Flight (oa-TOF) Instruments chapters really describe the advantages of orthogonal ion injection with respect to variations in initial kinetic energy or spatial distributions of ions. These chapters keep repeating that orthogonal injection is good but do not go into important details of its benefits.

There is no coverage of ion traps, quadrupole or magnetic. There are a couple of references to “ion traps” and “Fourier-transform ion cyclotron resonance (FTICR) mass spectrometers” but never any explanation of the functions, presentation of advantages and disadvantages, or comparison to the other instrument types. Of course, Micromass does not produce any ion traps.

Another area that is treated in a somewhat bizarre fashion is MS/MS. Chapters 32, 33, and 34 entitled Origin and Use of Metastable Ions, Linked Scanning and Metastable Ions in Quadrupole Mass Spectrometry, and Linked Scanning and Metastable Ions in Magnetic-Sector Mass Spectrometry, respectively, appear to be the primary treatment of the topic. For a mass spectrometry novice looking for information on MS/MS, these chapter titles would make the subject somewhat elusive in this book. The book’s last chapter Transmission of Ions through Inhomogeneous RF Fields is also a treatment of the MS/MS technique and acts just as well in presenting the subject in a stealth fashion.

Throughout the book, the authors use the term protonated molecular ion although the glossary, which is Appendix B, clearly states, “The widely used term protonated molecular ion to describe MH+ ion [sic] is not recommended….” When not talking about the protonated molecular ion, the authors like to use the term quasimolecular ion, which is another term that is “not recommended” by IUPAC.

The three chapters entitled Sample Inlets for Plasma Torches, Part A: Gases; Part B: Liquid Inlets; and Part C: Solid Inlets may be considered excessive. The Nebulizer chapter is primarily directed toward ICP mass spectrometry with a little on electrospray and APCI. The conclusion of this chapter does direct the reader to the other chapters that may be more applicable to mass spectrometry analysis of organic compounds. The authors have done a good job of referencing relevant chapters in each article. The three chapters entitled Computers and Transputers in Mass Spectrometry, Part A; Part B; and Part C are well written and informative although Parts A and B may be outside of the scope of a mass spectrometry book in some respects. However, for the stated intended audience, these two chapters are a very interesting read. Many of the other chapters contain generally useful information but often present some misleading viewpoints.

Not everything in this book is incorrect; however, there is enough that is misleading and incorrect that if the book is used to get an overview of mass spectrometry, then the time to correct the erroneous conclusions would be greater than the time to read the book. This book has limited value in offering some simplified explanations for those who are already well versed in the subject of mass spectrometry. As a supporting text for a general mass spectrometry course or as a vehicle for understanding this popular subject by the laity, it falls far short. Because of the misleading information, the incompleteness with respect to different types of m/z analyzers, and the esoteric presentations to MS/MS, atmospheric pressure ionization (using the term in the generic sense, not as a synonym for APCI), and MALD/I, it is probably best that this book remain the property of the publisher.