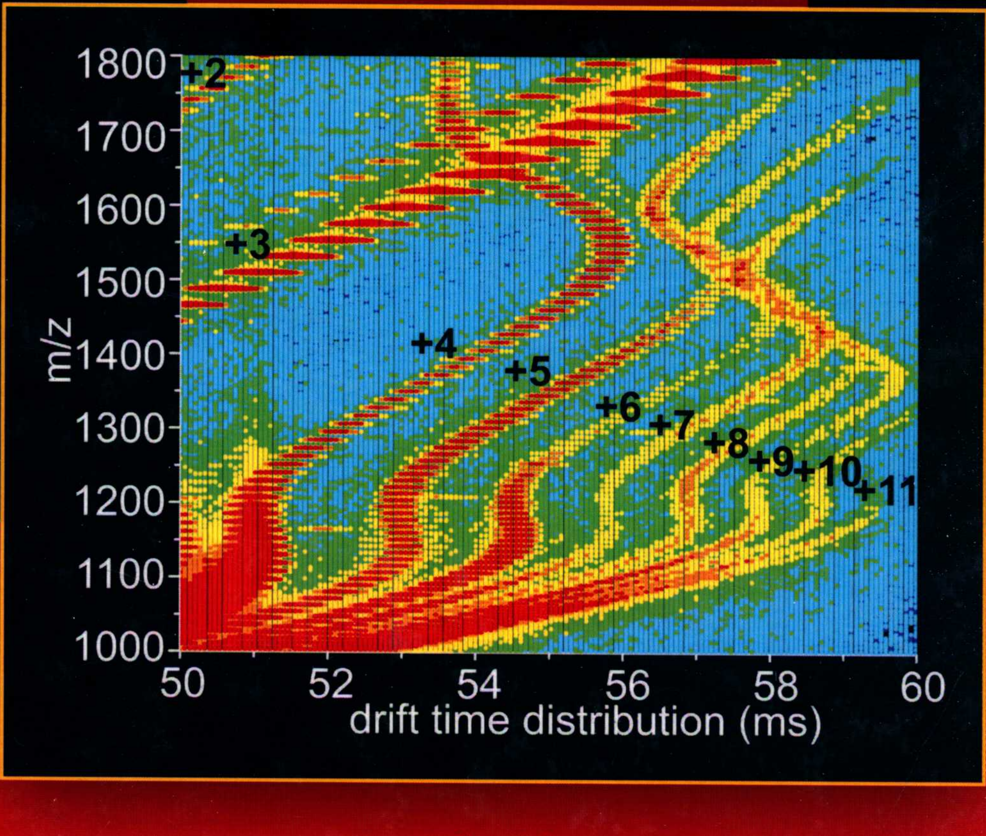
Ion Mobility Spectrometry-Mass Spectrometry

Theory and Applications



Edited by

Charles L. Wilkins and Sarah Trimpin

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Preface

Rapid advances in ion mobility spectrometry–mass spectrometry (IMS-MS) are beginning to have significant impact on biological and materials research and in analytical laboratories worldwide. Although the history of ion mobility spectrometry goes back at least 40 years, when it was more commonly known as plasma chromatography, the more recent hyphenation of ion mobility with mass spectrometers has greatly expanded its scope. Thus, IMS is a gas-phase separation method that is applicable for a wide variety of substances. For example, many airport explosives detectors are currently based upon IMS. However, it can also be used for biomedical applications, such as understanding the factors associated with Alzheimer's disease or cancer, as will be seen in several of the chapters.

Introduction of more or less turnkey commercial IMS-MS instruments are just now making this technology generally available. The analytical power afforded by IMS-MS instruments is certain to drive the technology from research to analytical laboratories. Thus, this book appears at a critical time and presents contributions from developers, as well as more recent users of this technology. It is a goal of this work to provide key information in a single location to help readers appreciate the value of having molecular size and shape information combined with the well-known analytical advantages of high-performance mass spectrometry. Armed with this understanding, it is expected that some of the readers will develop sufficient appreciation of the possible analytical uses of IMS-MS that they will become interested in further exploring the power of the method.

To this end, both fundamentals and applications are presented. Accordingly, the book begins with an overview chapter and fundamentals (Chapters 1 to 3) followed by sections emphasizing instrumentation (Chapters 4 to 7) and ionization sources (Chapters 8 and 9). In the subsequent applications (Chapters 10 to 16), homebuilt and commercial instrumentation using electrospray ionization and matrix-assisted laser desorption/ionization methods are employed to solve biological and synthetic motivated questions. In this way, it is the intent of the editors to cover the current status of IMS-MS in such a way as to make it convenient for those readers unacquainted with this technique to understand its fundamental theory and practical applications. As a consequence, it is expected that this volume could serve as a useful specialized textbook for an advanced course on IMS-MS.

Sarah Trimpin
Detroit, Michigan

Charles L. Wilkins
Fayetteville, Arkansas

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The Editors

Charles l. Wilkins is currently a Distinguished Professor in the Department of Chemistry and Biochemistry at the University of Arkansas (Fayetteville). His interests include mass spectrometry of polymer and copolymer materials, Fourier transform mass spectrometry, and the development of new methods to improve the utility of analytical mass spectrometry. Past research has dealt with applications of laboratory computers in chemistry, graph theoretic analysis of chemical problems, and research in chemometrics. Investigations of hyphenated analytical systems such as gas chromatography–infrared mass spectrometry and HPLC-NMR have also been of interest. He is the author of more than 235 scientific papers and 21 book chapters, in addition to editing eight books on a variety of chemistry topics.

He has received a number of honors recognizing his research contributions. Among them are the Tolman Medal of the Southern California American Chemical Society, the New York Section of the Society for Applied Spectroscopy Gold Medal, the American Chemical Society Franklin and Field Award for Outstanding Achievement in Mass Spectrometry, the Eastern Analytical Symposium Award for Outstanding Achievements in the Field of Analytical Chemistry, the Pittsburgh Analytical Award, and the University of Oregon Alumni Award for Outstanding Achievement in Pure Chemistry. He is a Fellow of the American Association for the Advancement of Science, a Fellow of the Society for Applied Spectroscopy, and a Fellow of the American Chemical Society. He is a lifetime Honorary Member of the Society of Applied Spectroscopy.

Professor Wilkins has served the chemistry profession through membership on numerous editorial advisory boards, including those of *Analytical Chemistry*, the *Journal of the American Society for Mass Spectometry*, *Applied Spectroscopy Reviews*, and *Mass Spectrometry Reviews*, among others. He currently serves as a contributing editor for *Trends in Analytical Chemistry*, a position that he has held for almost 20 years.

Sarah Trimpin is an assistant professor at Wayne State University with interest in improving and applying mass spectrometry to difficult problems involving both complexity and insolubility. She obtained the PhD equivalent from the Max-Planck-Institute for Polymer Research, Mainz, Germany, where she pioneered the development of the solvent-free matrix-assisted laser desorption (MALDI) method demonstrating its potential with insoluble materials. After completing a postdoctoral joint position between Oregon State University, Corvallis, and the Oregon Health & Science University, Portland, Oregon, she joined David Clemmer's laboratory at Indiana University, Bloomington, IN, as a senior research associate to study ion mobility spectroscopy–mass spectrometry (IMS-MS) instrumentation and methods. Combining solvent-free MALDI and IMS-MS has led to a total solvent-free analysis approach to analyze solubility-restricted materials. She recently discovered a new ionization method she named laserspray ionization, which combines the attributes of MALDI and electrospray ionization. The long-term goals of her research are to develop methods and instrumentation for the structural characterization and imaging of the soluble *and* insoluble components in single cells.

Dr. Trimpin has over 40 publications, including four book chapters, four reviews, and one perspective article, and has given numerous invited lectures at national and international meetings. She has received a number of honors including the German Society for Mass Spectrometry Wolfgang-Paul-Studienpreis and the Wolfgang-Paul-Promotionspreis. She was highlighted as one of *Genome Technology* magazine's Rising PIs and recently received the NSF CAREER award, the American Society for Mass Spectrometry Research Award, and the DuPont Company Young Investigator Award.

Contributors

Peter B. Armentrout
Department of Chemistry
University of Utah
Salt Lake City, Utah

Perdita E. Barran
School of Chemistry
University of Edinburgh
Edinburgh, United Kingdom

Gökhan Baykut
Bruker Daltonik GmbH
Bremen, Germany

Michael T. Bowers
Department of Chemistry and Biochemistry
University of California Santa Barbara
Santa Barbara, California

Richard M. Caprioli
Mass Spectrometry Research Center
Departments of Chemistry and Biochemistry
Vanderbilt University School of Medicine
Nashville, Tennessee

Emmanuelle Claude
Waters Corporation
Manchester, United Kingdom

David E. Clemmer
Department of Chemistry
Indiana University
Bloomington, Indiana

Claudia Cozma
Laboratory of Analytical Chemistry and Biopolymer Structure Analysis
Department of Chemistry
University of Konstanz
Konstanz, Germany

Juan Fernandez de la Mora
Mechanical Engineering Department
Yale University
New Haven, Connecticut

Michael Desor
Waters Corporation-MS Technologies Centre
Manchester, United Kingdom
and
Waters GmbH
Eschborn, Germany

Peter A. Faull
LGC Ltd.
Teddington
Middlesex, United Kingdom

Facundo M. Fernández
School of Chemistry and Biochemistry
Georgia Institute of Technology
Atlanta, Georgia

Jochen Franzen
Bruker Daltonik GmbH
Bremen, Germany

Jennifer Gidden
Arkansas Statewide Mass Spectrometry Facility
University of Arkansas
Fayetteville, Arkansas

Kevin Giles
University of the Sciences in Philadelphia
Philadelphia, Pennsylvania

Martin Green
Waters Corporation
Manchester, United Kingdom

Glenn A. Harris
School of Chemistry and Biochemistry
Georgia Institute of Technology
Atlanta, Georgia

Herbert H. Hill, Jr.
Department of Chemistry
Washington State University
Pullman, Washington

Ellen D. Inutan
Department of Chemistry
Wayne State University
Detroit, Michigan

Marius-Ionuţ Iuraşcu
Laboratory of Analytical Chemistry and Biopolymer Structure Analysis
Department of Chemistry
University of Konstanz
Konstanz, Germany

Shelley N. Jackson
NIDA IRP, NIH
Baltimore, Maryland

Kimberly Kaplan
Department of Chemistry
Washington State University
Pullman, Washington

Mark Kwasnik
School of Chemistry and Biochemistry
Georgia Institute of Technology
Atlanta, Georgia

James Langridge
Waters Corporation-MS Technologies Centre
Manchester, United Kingdom
and
Waters GmbH
Eschborn, Germany

Barbara S. Larsen
DuPont Corporate Center for Analytical Sciences
Wilmington, Delaware

Hilary Major
Waters Corporation
Manchester, United Kingdom

Jody C. May
Laboratory for Biological Mass Spectrometry
Department of Chemistry
Texas A&M University
College Station, Texas

Bryan J. McCullough
LGC Ltd.
Teddington
Middlesex, United Kingdom

Charles N. McEwen
University of the Sciences in Philadelphia
Philadelphia, Pennsylvania

John A. McLean
Department of Chemistry
Vanderbilt Institute of Chemical Biology
Vanderbilt Institute for Integrative Biosystems Research and Education
Vanderbilt University
Nashville, Tennessee

Jasna Peter-Katalinić
Institute for Medical Physics and Biophysics
Westfalian Wilhelms University Muenster
Muenster, Germany
and
Department of Biotechnology
University of Rijeka
Rijeka, Croatia

Michael Przybylski
Laboratory of Analytical Chemistry and Biopolymer Structure Analysis
Department of Chemistry
University of Konstanz
Konstanz, Germany

Oliver Raether
Bruker Daltonik GmbH
Bremen, Germany

Whitney B. Ridenour
Mass Spectrometry Research Center
Departments of Chemistry and Biochemistry
Vanderbilt University School of Medicine
Nashville, Tennessee

David H. Russell
Laboratory for Biological Mass Spectrometry
Department of Chemistry
Texas A&M University
College Station, Texas

J. Albert Schultz
Ionwerks Inc.
Houston, Texas

Nick Tomczyk
Waters Corporation-MS Technologies Centre
Manchester, United Kingdom
and
Waters GmbH
Eschborn, Germany

Sarah Trimpin
Department of Chemistry
Wayne State University
Detroit, Michigan

Sergey Y. Vakhrushev
Copenhagen Center for Glycomics
Department of Cellular and Molecular Medicine
Panum Institute
University of Copenhagen
Copenhagen, Denmark

Oliver von Halem
Bruker Daltonik GmbH
Bremen, Germany

Amina S. Woods
NIDA IRP, NIH
Baltimore, Maryland

Thomas Wyttenbach
Department of Chemistry and Biochemistry
University of California Santa Barbara
Santa Barbara, California

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Fundamentals

1 Developments in Ion Mobility *Theory, Instrumentation, and Applications*

Thomas Wyttenbach, Jennifer Gidden, and Michael T. Bowers

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1.1 INTRODUCTION

In this chapter we focus on ion mobility spectrometry (IMS) employed to obtain structural information of polyatomic ions. In these applications—reviewed by Clemmer and Jarrold,[1] Wyttenbach and Bowers,[2] Creaser et al.,[3] Weis,[4] and

Bohrer et al.[5]—IMS always occurs in combination with mass spectrometry (MS). We divide the chapter into three sections covering theory, instrumental aspects, and research applications from our lab. In the theoretical section we cover some of the basic theory of IMS, how ions exposed to an electric field move in a buffer gas, and how this motion relates to the structure of the ion. In the instrumentation section we present basic hybrid IMS-MS setups and their components and discuss issues to consider in the design of such an instrument. And finally, in the applications section we present a few instructive application examples from our lab to illustrate the concepts outlined in the theory and instrument sections and to demonstrate the potential of the method to solve biochemically relevant problems.

1.2 THEORY

1.2.1 Ion Mobility

Ions exposed to an electric field experience a force and are accelerated along the field lines. Upon addition of a buffer gas, the motion of the ions becomes more complicated as collisions with the gas scatter the ions in random directions as it diffuses. However, if an ion cloud is given enough time to reach equilibrium and the electric field is uniform throughout, the ion cloud will travel with constant velocity parallel to the field lines and simultaneously grow in size due to diffusion. This constant equilibrium velocity is the result of forward acceleration by the field and decelerating friction by collisions. Following Mason and McDaniel,[6] for weak electric fields of magnitude E, the drift velocity v is directly proportional to E with the proportionality constant K called ion mobility

$$v = K E \tag{1.1}$$

Since v is inversely proportional to the buffer gas number density N, the mobility K is also inversely proportional to N. Here N (in units of molecules per volume) is used as the relevant quantity to express pressure because N is, in contrast to pressure p, decoupled from the temperature T. Because K depends on N it is practical to convert K into the pressure-independent quantity $K_o \propto NK$, where K_o is termed the reduced mobility

$$K_o = \frac{p}{p_o} \frac{T_o}{T} K \tag{1.2}$$

with the constants $p_o = 760$ Torr and $T_o = 273.15$ K.

A field is considered weak if the average ion energy acquired from the field is small compared to the thermal energy of the buffer gas molecules. This ion field energy is proportional to v^2 or $(KE)^2$. However, for a given ion with given $K_o \propto NK$ it is the ratio E/N which determines whether a field is weak or strong, and collisional heating due to the field is given by Equation (1.3):

$$T_{eff} - T = (M/3k_B)\,(NK)^2\,(E/N)^2 \tag{1.3}$$