CLUSTER SECONDARY ION MASS SPECTROMETRY
WILEY SERIES ON MASS SPECTROMETRY

Series Editors

Dominic M. Desiderio
Departments of Neurology and Biochemistry
University of Tennessee Health Science Center

Nico M. M. Nibbering
Vrije Universiteit Amsterdam, The Netherlands

Joseph A. Loo
Department of Chemistry and Biochemistry
UCLA

A complete list of the titles in this series appears at the end of this volume.
1 AN INTRODUCTION TO CLUSTER SECONDARY ION MASS SPECTROMETRY (CLUSTER SIMS)

Christine M. Mahoney and Greg Gillen

1.1 Secondary Ion Mass Spectrometry in a Nutshell
  1.1.1 SIMS Imaging
  1.1.2 SIMS Depth Profiling
1.2 Basic Cluster SIMS Theory
  1.3 Cluster SIMS: An Early History
    1.3.1 Nonlinear Sputter Yield Enhancements
    1.3.2 Molecular Depth Profiling
1.4 Recent Developments
1.5 About this Book
Acknowledgment
References

2 CLUSTER SIMS OF ORGANIC MATERIALS: THEORETICAL INSIGHTS

Arnaud Delcorte, Oscar A. Restrepo, and Bartlomiej Czerwinski

2.1 Introduction
2.2 Molecular Dynamics Simulations of Sputtering with Clusters
  2.2.1 The Cluster Effect
  2.2.2 Computer Simulations and the Molecular Dynamics “Experiment”
  2.2.3 Light and Heavy Element Clusters, and the Importance of Mass Matching
  2.2.4 Structural Effects in Organic Materials
    2.2.4.1 Amorphous Molecular Solids and Polymers
    2.2.4.2 Organic Crystals
    2.2.4.3 Thin Organic Layers on Metal Substrates
    2.2.4.4 Hybrid Metal–Organic Samples
  2.2.5 Induced Chemistry
  2.2.6 Multiple Hits and Depth Profiling
  2.2.7 From Small Polyatomic Projectiles to Massive Clusters
    2.2.7.1 Light-Element Clusters
    2.2.7.2 Large Argon Clusters
    2.2.7.3 Massive Gold Clusters
2.3 Other Models
   2.3.1 Analytical Models: From Linear Collision Cascades to Fluid Dynamics
   2.3.2 Recent Developments and Hybrid Approaches
2.4 Conclusions
Acknowledgments
References

3 ION SOURCES USED FOR SECONDARY ION MASS SPECTROMETRY
   Albert J. Fahey
   3.1 Introduction
   3.2 Research Needs that have Influenced the Development of Primary Ion Sources for Sputtering
   3.3 Functional Aspects of Various Ion Sources
      3.3.1 Energy Spread in the Beam
      3.3.2 Point-Source Ionization
      3.3.3 Stable Emission
      3.3.4 Ion Reactivity
      3.3.5 Source Lifetime
      3.3.6 Penetration Depth and Surface Energy Spread of the Projectile
   3.4 Atomic Ion Sources
      3.4.1 Field Emission
      3.4.2 Radio Frequency (RF) Ionization
      3.4.3 Electron Impact
      3.4.4 Thermal Ionization
      3.4.5 DC-Glow Discharge
      3.4.6 Sputtering
   3.5 Molecular Ion Sources
      3.5.1 Field Emission
      3.5.2 Radio Frequency Discharge
      3.5.3 Electron Impact
      3.5.4 DC-Glow Discharge
      3.5.5 Sputtering
   3.6 Cluster Ion Sources
      3.6.1 Jets and Electron Impact (Massive Gas Clusters)
      3.6.2 Field Emission
   3.7 Summary
   References

4 SURFACE ANALYSIS OF ORGANIC MATERIALS WITH POLYATOMIC PRIMARY ION SOURCES
   Christine M. Mahoney
   4.1 Introduction
   4.2 Cluster Sources in Static SIMS
      4.2.1 A Brief Introduction to Static SIMS
      4.2.2 Analysis beyond the Static Limit
      4.2.3 Increased Ion Yields
      4.2.4 Decreased Charging
      4.2.5 Surface Cleaning
4.3 Experimental Considerations

4.3.1 When to Employ Cluster Sources as Opposed to Atomic Sources 83

4.3.2 Type of Cluster Source Used 84

4.3.2.1 Liquid Metal Ion Gun (LMIG) 84

4.3.2.2 \( C_{60}^+ \) for Mass Spectral Analysis and Imaging Applications 85

4.3.2.3 The Gas Cluster Ion Beam (GCIB) 86

4.3.2.4 \( Au_{4+} \) 86

4.3.2.5 Other Sources 88

4.3.3 Cluster Size Considerations 88

4.3.4 Beam Energy 90

4.3.5 Sample Temperature 92

4.3.6 Matrix-Enhanced and Metal-Assisted Cluster SIMS 92

4.3.7 Matrix Effects 95

4.3.8 Other Important Factors 96

4.4 Data Analysis Methods 96

4.4.1 Principal Components Analysis 96

4.4.1.1 Basic Principles of PCA 97

4.4.1.2 Examples of PCA in the Literature 98

4.4.2 Gentle SIMS (G-SIMS) 101

4.5 Other Relevant Surface Mass-Spectrometry-Based Methods 101

4.5.1 Desorption Electrospray Ionization (DESI) 103

4.5.2 Plasma Desorption Ionization Methods 105

4.5.3 Electrospray Droplet Impact Source for SIMS 107

4.6 Advanced Mass Spectrometers for SIMS 108

4.7 Conclusions 109

Appendix A: Useful Lateral Resolution 110

References 110
viii CONTENTS

5.5.2 Understanding the Basics of Ion Irradiation Effects in Molecular Solids 146
5.5.3 Ion Beam Irradiation and the Gel Point 147
5.5.4 The Chemistry of Cluster Ion Beams 150
5.5.5 Chemical Structure Changes and Corresponding Changes in Depth Profile Shapes 152

5.6 Optimization of Experimental Parameters for Organic Depth Profiling 156
5.6.1 Introduction 156
5.6.2 Organic Delta Layers for Optimization of Experimental Parameters 157
5.6.3 Sample Temperature 159
5.6.4 Understanding the Role of Beam Energy During Organic Depth Profiling 167
5.6.5 Optimization of Incidence Angle 171
5.6.6 Effect of Sample Rotation 174
5.6.7 Ion Source Selection
   5.6.7.1 SF$_5^+$ and Other Small Cluster Ions 178
   5.6.7.2 C$_{60}^+$ and Similar Carbon Cluster Sources 179
   5.6.7.3 The Gas Cluster Ion Beam (GCIB) 180
   5.6.7.4 Low Energy Reactive Ion Beams 188
   5.6.7.5 Electrospray Droplet Impact (EDI) Source for SIMS 189
   5.6.7.6 Liquid Metal Ion Gun Clusters (Bi$_3^+$ and Au$_3^+$) 193
5.6.8 C$_{60}^+$/Ar$^+$ Co-sputtering 195
5.6.9 Chamber Backfilling with a Free Radical Inhibitor Gas 197
5.6.10 Other Considerations for Organic Depth Profiling Experiments 197
5.6.11 Molecular Depth Profiling: Novel Approaches and Methods 198

5.7 Conclusions 198
References 200

6 THREE-DIMENSIONAL IMAGING WITH CLUSTER ION BEAMS
   207
Andreas Wucher, Gregory L. Fisher, and Christine M. Mahoney

6.1 Introduction 207
6.2 General Strategies
   6.2.1 Three-Dimensional Sputter Depth Profiling 210
   6.2.2 Wedge Beveling 216
   6.2.3 Physical Cross Sectioning 217
   6.2.4 FIB-ToF Tomography 219
6.3 Important Considerations for Accurate 3D Representation of Data 225
   6.3.1 Beam Rastering Techniques 225
   6.3.2 Geometry Effects 226
   6.3.3 Depth Scale Calibration 228
6.4 Three-Dimensional Image Reconstruction 233
6.5 Damage and Altered Layer Depth 238
6.6 Biological Samples 242
6.7 Conclusions 243
References 244
7  CLUSTER SECONDARY ION MASS SPECTROMETRY (SIMS) FOR SEMICONDUCTOR AND METALS DEPTH PROFILING  247

Greg Gillen and Joe Bennett

7.1 Introduction 247
7.2 Primary Particle–Substrate Interactions 248
  7.2.1 Collisional Mixing and Depth Resolution 248
  7.2.2 Transient Effects 249
  7.2.3 Sputter-Induced Roughening 251
7.3 Possible Improvements in SIMS Depth Profiling—The Use of Cluster Primary Ion Beams 253
7.4 Development of Cluster SIMS for Depth Profiling Analysis 255
  7.4.1 CF$_3^+$ Primary Ion Beams 255
  7.4.2 NO$_2^+$ and O$_3^+$ Primary Ion Beams 256
  7.4.3 SF$_5^+$ Polyatomic Primary Ion Beams 257
  7.4.4 CSC$_6^-$ and C$_8^-$ Depth Profiling 258
  7.4.5 Os$_3$(CO)$_{12}$ and Ir$_4$(CO)$_{12}$ Primary Ion Beams 262
  7.4.6 C$_{20}^-$ Primary Ion Beams 263
  7.4.7 Massive Gaseous Cluster Ion Beams 265
7.5 Conclusions and Future Prospects 266
References 266

8  CLUSTER TOF-SIMS IMAGING AND THE CHARACTERIZATION OF BIOLOGICAL MATERIALS  269

John Vickerman and Nick Winograd

8.1 Introduction 269
8.2 The Capabilities of TOF-SIMS for Biological Analysis 270
8.3 New Hybrid TOF-SIMS Instruments 270
  8.3.1 Introduction 270
  8.3.2 Benefits of New DC Beam Technologies 271
8.4 Challenges in the Use of TOF-SIMS for Biological Analysis 273
  8.4.1 Sample Handling of Biological Samples for Analysis in Vacuum 273
  8.4.2 Analysis is Limited to Small to Medium Size Molecules 274
  8.4.3 Ion Yields Limit Useful Spatial Resolution for Molecular Analysis to not Much Better than 1 µm 275
  8.4.4 Matrix Effects Inhibit Application in Discovery Mode and Greatly Complicates Quantification 275
  8.4.5 The Complexity of Biological Systems can Result in Data Sets that Need Multivariate Analysis (MVA) to Unravel 276
8.5 Examples of Biological Studies Using Cluster-TOF-SIMS 276
  8.5.1 Analysis of Tissue 277
  8.5.2 Drug Location in Tissue 285
  8.5.3 Microbial Mat—Surface and Subsurface Analysis in Streptomyces 289
  8.5.4 Cells 291
  8.5.5 Depth Scale Measurement 302
  8.5.6 High Throughput Biomaterials Characterization 306
8.6 Final Thoughts and Future Directions 310
Acknowledgments 310
References 310
CONTENTS

9 FUTURE CHALLENGES AND PROSPECTS OF CLUSTER SIMS 313

Peter Williams and Christine M. Mahoney

9.1 Introduction 313
9.2 The Cluster Niche 314
9.3 Cluster Types 314
9.4 The Challenge of Massive Molecular Ion Ejection 315
  9.4.1 Comparing with MALDI: The Gold Standard 316
  9.4.2 Particle Impact Techniques 317
9.5 Ionization 318
  9.5.1 “Preformed” Ions 319
  9.5.2 Radical Ions and Ion Fragments 319
  9.5.3 Ionization Processes for Massive Clusters 320
9.6 Matrix Effects and Challenges in Quantitative Analysis 321
9.7 SIMS Instrumentation 322
  9.7.1 Massive Cluster Ion Source Technology 323
9.8 Prospects for Biological Imaging 324
9.9 Conclusions 325
References 326

Index 329
CONTRIBUTORS

Albert J. Fahey, National Security Directorate, Pacific Northwest National Laboratory, Richland, WA

Andreas Wucher, Department of Physics, University of Duisburg-Essen, Campus Duisburg, Duisburg, Germany

Arnaud Delcorte, Institute of Condensed Matter and Nanosciences, Université catholique de Louvain, Louvain-la-Neuve, Belgium

Bartłomiej Czerwinski, Institute of Condensed Matter and Nanosciences, Université catholique de Louvain, Louvain-la-Neuve, Belgium

Christine M. Mahoney, Environmental Molecular Sciences Laboratory, Pacific Northwest National Laboratory, Richland, WA

Greg Gillen, Surface and Microanalysis Science Division, Materials Measurement Laboratory, National Institute of Standards and Technology, Gaithersburg, MD

Gregory L. Fisher, Physical Electronics, Incorporated, Chanhassen, Minnesota

Joe Bennett, Novati Technologies, Austin, TX

John Vickerman, Surface Analysis Research Centre, Manchester Interdisciplinary Biocentre, School of Chemical Engineering and Analytical Science, The University of Manchester, Manchester, UK

Nick Winograd, Department of Chemistry, Penn State University, University Park, PA

Oscar A. Restrepo, Institute of Condensed Matter and Nanosciences, Université catholique de Louvain, Louvain-la-Neuve, Belgium

Peter Williams, Department of Chemistry & Biochemistry, Arizona State University, Tempe, AZ
Dr. Christine M. Mahoney is a recognized expert and leader in the field of Secondary Ion Mass Spectrometry (SIMS). Throughout her career she has focused primarily on the application of SIMS to molecular targets, and has played a significant role in the development of cluster SIMS for polymer depth profiling applications. She received her Ph.D. in Analytical Chemistry from SUNY Buffalo in 1993. After which, she spent the following eight years at the National Institute of Standards and Technology (NIST), where much of her molecular depth profiling work was performed. Christine is currently employed as a senior research scientist at the Environmental and Molecular Sciences Laboratory (EMSL) at the Pacific Northwest National Laboratory (PNNL) where she continues to lead research in the field of SIMS.
Cluster secondary ion mass spectrometry (SIMS) has had a significant impact on the mass spectrometry and surface analysis communities over the past two decades, with its newfound ability to characterize surface and in-depth compositions of molecular species with minimal damage, excellent spatial (100 nm or less) and depth (5 nm) resolutions, and increased sensitivities for bioimaging applications. With the continual development of new cluster ion beam technologies, we are breaking down barriers once thought to be unbreakable, and entering into new fields once labeled as out of reach. Instrument designs are now advancing to account for these new applications, allowing for further improvements in molecular sensitivities, selectivities, and even high throughput analysis. Although we are

*Official contribution of the National Institute of Standards and Technology; not subject to copyright in the United States.
†Commercial equipment and materials are identified in order to adequately specify certain procedures. In no case does such identification imply recommendation or endorsement by the National Institute of Standards and Technology, nor does it imply that the materials or equipment identified are necessarily the best available for the purpose.
‡This document was prepared as an account of work sponsored by an agency of the US Government. Neither the US Government nor any agency thereof, nor Battelle Memorial Institute, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the US Government or any agency thereof, or Battelle Memorial Institute. The views and opinions of authors expressed herein do not necessarily state or reflect those of the US Government or any agency thereof.
only at the beginning of the growth curve toward low damage molecular SIMS, we have come a long way over the past few years, and significant discoveries have been made. This book addresses these new discoveries and describes practical approaches to SIMS analysis of samples using cluster sources, with a focus on soft sample analysis.

1.1 SECONDARY ION MASS SPECTROMETRY IN A NUTSHELL

Before we discuss cluster beam technology, it is appropriate to first review the basics of SIMS. SIMS is a mass spectrometric-based analytical technique, which is used to obtain information about the molecular, elemental, and isotopic composition of a surface. In a conventional SIMS experiment, an energetic primary ion beam, such as Ga⁺, Cs⁺, or Ar⁺ is focused onto a solid sample surface under ultra high vacuum conditions (Fig. 1.1). The interaction of the primary ion beam with the sample results in the sputtering and desorption of secondary ions from the surface of the material. These secondary ions are subsequently extracted into a mass analyzer, resulting in the creation of a mass spectrum that is characteristic of the analyzed surface (Fig. 1.2a), and yielding elemental, isotopic, and molecular information simultaneously, with sensitivities in the parts per million (ppm) to parts per billion (ppb) range. There are three basic types of SIMS instruments that are used most commonly in the field, each employing a different mass analyzer:

1. Time-of-Flight Secondary Ion Mass Spectrometers (ToF-SIMS). These spectrometers extract the secondary ions into a field-free drift tube, where the ions are allowed to travel along a known flight path to the detector. As the velocity of a given ion is inversely proportional to its mass, its flight time will vary accordingly, and heavier ions will arrive at the detector later than lighter ions. This type of mass spectrometer allows for simultaneous detection of all secondary ions of a given polarity and has excellent mass resolution. Moreover, because the design utilizes a pulsed ion beam operated at extremely low

![Figure 1.1 Illustration of the sputtering process in secondary ion mass spectrometry (SIMS).](image-url)
1.1 SECONDARY ION MASS SPECTROMETRY IN A NUTSHELL

Figure 1.2 (a) Example of negative ion mass spectral data acquired from a sample of composition-4 (C-4) plastic explosive, comprised of poly(isobutylene), RDX explosives, di-iso-octylsebacate, and other additives. (b) Example of negative ion molecular imaging (200 × 200 μm) in Semtex plastic explosive, based on RDX explosive, PETN explosive, poly(styrene-co-butadiene), and other additives; green = PETN explosive molecules (m/z 376), red = binder and oils (m/z 25), and blue = SiO$_2^-$ (m/z 60) from the Si substrate. (c) Example of positive ion elemental mapping of trace elements in plant roots; green = CN$^-$ (m/z 26), blue = Si$_2^-$ (m/z 28), and red = As (m/z 75). (d) Isotopic imaging of bacteria grown in $^{15}$N culture medium. Green regions indicate $^{15}$N-enriched bacteria, while blue regions indicate more natural isotopic abundances. Hence, the bacteria in the blue regions are not as metabolically active as the green regions. Figure 1.2c and d recreated from Moore et al.$^3$ and Kilburn,$^4$ respectively, with permission from the American Society for Plant Biology and the University of Western Australia.
currents (picoampere range), this mass spectrometer is useful for analysis of surfaces, insulators, and soft materials, which may be prone to ion-induced chemical damage.

2. **Magnetic Sector SIMS instruments.** Magnetic sector SIMS instruments typically use a combination of electrostatic and magnetic sector analyzers for velocity and mass analysis of the sputtered secondary ions. The use of a magnetic field to deflect the ion beam causes lighter ions to be deflected more than the heavier ions, which have a greater momentum. Thus, the ions of differing mass will physically separate into distinct beams. An electrostatic field is also applied to the secondary beam in order to remove any chromatic aberrations. Because of the higher operating currents and continuous beams, these instruments are very useful for depth profiling. However, they are not as ideal for surface analysis and characterization of samples that will charge and/or damage readily.

3. **Quadrupole SIMS Instruments.** These instruments are becoming increasingly rare because of the relatively limited mass resolution attributed to them (unit mass resolution—unable to resolve more than one peak per nominal mass). The quadrupole utilizes a resonating electric field, where only ions with selected masses have stable trajectories through a given oscillating field. Similar to the magnetic sector instruments, these instruments are operated under high primary ion currents and are generally thought of as “dynamic SIMS” instruments (i.e., used for sputter depth profiling and/or bulk analysis of solid samples).

Although these designs are most commonly observed in the SIMS community at present, there are many new exciting designs emerging, which may play a more prominent role in the future.\(^1\) These new designs include continuous ion beam designs with multiple mass spectrometers (e.g., quadrupole/ToF for MS-MS analysis) and even a Fourier transform ion cyclotron resonance (FT-ICR) instrument, with mass resolutions approaching 1 million or greater. These new designs will be briefly introduced in Chapters 4 and 8.

### 1.1.1 SIMS Imaging

In all SIMS instruments, mass spectrometric imaging can be achieved by focusing and rastering the ion beam over a selected area or by using secondary ion optical focusing elements (in the case of magnetic sector instruments), where the secondary ion intensity for a given mass-to-charge ratio \((m/z)\) is monitored as a function of position on the sample. Examples of molecular, elemental, and isotopic mapping of components on surfaces are given in Figure 1.2b–d.\(^3,4\)

### 1.1.2 SIMS Depth Profiling

SIMS can be utilized for both surface analysis (at low primary ion doses) and in-depth analysis (at high primary ion doses). An example of SIMS depth profiling is shown in Figure 1.3, which depicts the elemental intensities of Cr, Ni, and C.
plotted as a function on increasing primary ion sputtering time in a sample containing Ni/Cr alternating layers. Each Ni and Cr layer is readily observed using SIMS depth profiling, as indicated by the inversely alternating Cr and Ni intensities.

Unlike inorganic samples, organic, polymeric, and biological materials have historically required the use of “static SIMS” analysis conditions, where the primary ion fluence is maintained at or below a critical dose in order to retain the surface in an undamaged state. This critical dose is defined as the “static limit,” and is often reported to be at or less than $1 \times 10^{13}$ ions/cm$^2$, depending on the sample and the ion beam employed. Unfortunately, this limitation results in decreased sensitivity and precludes compositional depth profiling in soft materials. One potential solution to this limitation is to use cluster or polyatomic primary ion beams (such as C$_{60}^+$, SF$_5^+$, or Ar$_{700}^+$) in place of atomic sources in order to extend the characterization of these samples beyond the static limit.

### 1.2 BASIC CLUSTER SIMS THEORY

When a cluster ion impacts a surface, the cluster breaks apart and each atom in the cluster retains only a fraction of the initial energy of the ion as described in the relationship shown below in Equation 1.1 (where $E_c$ is the final energy of a constituent atom after collision with the surface, $E_0$ is the energy of the polyatomic ion before impact, $M_c$ is the mass of the constituent, and $M_t$ is the total mass of the polyatomic ion).

$$E_c = E_0 \left( \frac{M_c}{M_t} \right)$$

Since the penetration depth of the ion is proportional to the impact energy of the ion, cluster ion bombardment results in a significant reduction in penetration depth of the ion. This causes surface-localized damage and consequently, preserves
6  CHAPTER 1  AN INTRODUCTION TO CLUSTER SECONDARY ION MASS SPECTROMETRY

\[ SY = 297 \text{ molecules/ion} \]
\[ \text{Range} = 4.4 \text{ nm} \]

\[ SY = 8 \text{ molecules/ion} \]
\[ \text{Range} = 12.3 \text{ nm} \]

5.5 keV impact at 42° incident angle

**Figure 1.4** Graphic illustration suggesting how the high sputter yields and low penetration depths observed with polyatomic ion bombardment may reduce the accumulation of beam-induced damage in an organic thin film. The actual SRIM calculations are indicated below each illustration, where SY represents the calculated sputter yield in a PMMA sample, and the range represents the depth of the projectile into the PMMA sample. Reproduced from Gillen and Roberson \(^1\) with permission from Wiley.

the chemical structure in the subsurface region (Fig. 1.4). \(^5\) Similar energy atomic beams, however, will penetrate deeply, resulting in the breaking of molecular bonds deep into the sample and thus precluding the ability to depth profile in molecular samples. Furthermore, because there are more atoms bombarding the sample simultaneously with cluster ions, the sputtering yield can be significantly enhanced. This is in part because of the increased number of atoms per ion, but is also a result of the formation of a high energy density “collisional spike” regime that is formed with cluster ion bombardment, causing nonlinear sputtering yield enhancements (i.e., sputtering yield of \(C_n^+ \gg nC^+\)). \(^6\)

### 1.3 CLUSTER SIMS: AN EARLY HISTORY

#### 1.3.1 Nonlinear Sputter Yield Enhancements

The benefits of utilizing polyatomic ions for sputtering was shown as early as 1960, with the observation of nonlinear enhancements in sputtering yields when using polyatomic ions as opposed to atomic ions. \(^7\)–\(^10\) An example of this nonlinear sputtering effect can be seen in Figure 1.5, which compares the sputtering yield per incoming atom when employing Te\(^+\) ions as compared to Te\(_2^+\) ions under an identical \(E_c\) (Eq. 1.1). \(^9\) It can be seen from Figure 1.5, that the sputtering yield resultant from one Te\(_2^+\) diatomic ion is greater than the combined sputtering yield from two Te\(^+\) atomic ions of similar \(E_c\).

Although these nonlinear effects were observed much earlier, the benefits of cluster sources (where cluster is defined here as an ion with more than two atoms) for SIMS applications were not realized until the mid to late 1980s. One of the earliest works was published in 1982, in which the authors compared the performance
of siloxane molecular ions to Hg$^+$ ions for characterization of oligosaccharides in a glycerol matrix. The results showed a large increase in the ionization of the organic molecules when employing the siloxane cluster source as compared to the atomic Hg$^+$ ion source.

Later, Appelhans et al. used SF$_6$ neutral beams to characterize electrically insulating polymer samples such as polytetrafluoroethylene (PTFE), poly(ethylene terephthalate) (PET), poly(methyl methacrylate) (PMMA), and polyphosphazene, where the authors found that the SF$_6$ cluster beam yielded 3–4 orders of magnitude more intense secondary ion yields from these polymer samples than equivalent energy atomic beams. Similar findings were found in the mass spectra of pharmaceutical compounds.

### 1.3.2 Molecular Depth Profiling

Another unique feature of cluster ion beams as compared to their atomic ion beam counterparts is their ability to retain molecular information as a function of depth in soft materials. The combination of increased sputter yields along with decreased subsurface damage has enabled the SIMS analyst to characterize compositions as a function of depth in organic materials for the first time; a process now referred to as *molecular depth profiling*. Cornett et al. were among the first to demonstrate the feasibility of molecular depth profiling with cluster ion beams, when they discovered that continued bombardment of protein samples with massive glycerol cluster ions yielded constant molecular secondary ion signals with increasing ion fluence, while the same samples irradiated with Xe$^+$ ions yielded the characteristic rapid signal decay that is commonly associated with atomic beams.

An example of molecular depth profiling is demonstrated in Figure 1.6, which shows an early attempt at depth profiling in a thin glutamate film (180 nm) vapor...
CHAPTER 1 AN INTRODUCTION TO CLUSTER SECONDARY ION MASS SPECTROMETRY

Figure 1.6 Comparison of depth profiles obtained from a 180 nm vapor-deposited glutamate film using (a) Ar\(^+\) and (b) SF\(_5\)\(^+\) primary ions under dynamic SIMS conditions. The SF\(_5\)\(^+\) primary ion dose required to reach the silicon was \(2.4 \times 10^{15}\) ions/cm\(^2\). Reproduced from Gillen and Roberson\(^1\) with permission from Wiley.

In this example, glutamate molecular ion signal intensities \([M + H]^+\), and fragment ion intensities \((m/z\) 84 and \(m/z\) 102) are measured as a function of sputtering time, using both Ar\(^+\) (Fig. 1.6a) and SF\(_5\)\(^+\) polyatomic primary ions (Fig. 1.6b). Si\(^+\) ion intensities \((m/z\) 28) were also measured as a function of sputtering time in both examples. When employing the Ar\(^+\) monatomic ions, the molecular signals decay rapidly, as is characteristic of atomic ion bombardment in molecular films. However, when employing polyatomic primary ion sources, the molecular ion and fragment ion intensities of the glutamate remain constant throughout the entire depth of the film. In addition, while the SF\(_5\)\(^+\) source was able to profile through the entire film in the 900 s sputter time interval, as indicated by the decreasing molecular ion signal intensities with commensurate increases in the Si, the Ar\(^+\) was unable to sputter through the material during the allotted time interval.

1.4 RECENT DEVELOPMENTS

Since the advent of cluster SIMS, there has been an abundance of work on surface and in-depth characterization of soft materials ranging from simple molecular films and polymers\(^16,17\) to complex biological systems.\(^2\) Cluster primary ion sources such as C\(_{60}\)\(^+\), Au\(_3\)\(^+\), SF\(_5\)\(^+\), Bi\(_3\)\(^+\), and Ar\((x>500)\)\(^{n+1}\) have resulted in significant improvements (typically >1000-fold) in characteristic molecular secondary ion yields and decreased beam-induced damage. Furthermore, most of these sources have allowed for molecular depth profiling in samples; a feat that was unheard of with previously employed monatomic ion beam sources. With these new cluster sources, beam damage limitations have all but been removed for depth profiling in most organic
and polymeric materials. With the increased sensitivity, nanoscale depth resolution (<5 nm), and submicrometer lateral resolution, cluster SIMS is a promising new characterization tool enabling high resolution three-dimensional imaging capabilities for organic and polymeric-based materials (Fig. 1.7 and Fig. 1.8).\textsuperscript{16,18}

1.5 ABOUT THIS BOOK

This book will serve as a compendium of knowledge on the topic of cluster SIMS. In this book, in-depth discussions on the various aspects of cluster SIMS and its applications will be presented—from the details of cluster SIMS theory and erosion dynamics, to experimental parameters for optimum depth profiling in molecular samples.

Theoretical discussions regarding cluster ion beam interactions with organic materials will be discussed in Chapter 2, where important aspects of molecular dynamics simulations will be reviewed. This chapter will review the current state of the literature in this field, as well as help one to obtain a better understanding of the physics of cluster ion bombardment in organic, polymeric, and biological samples.

Chapter 3 presents a detailed overview of the myriad of sources that are available, for SIMS, cluster ion beams, or otherwise. This chapter will provide

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Positive secondary ion image maps (100 × 100 µm) of characteristic tetracycline signal (m/z 59) in a PLGA film, acquired using an SF\textsubscript{5}\textsuperscript{+} sputtering source in conjunction with a Bi\textsubscript{3}\textsuperscript{+} analysis source. (a) No sputtering, (b) 15 s sputtering with SF\textsubscript{5}\textsuperscript{+} (∼75 nm depth), (c) 75 s sputtering with SF\textsubscript{5}\textsuperscript{+} (∼375 nm depth), and (d) 3D volumetric representation of tetracycline signal (m/z 59) in PLGA film (acquired from approximately the top 2 µm) containing 15% tetracycline; 5 keV SF\textsubscript{5}\textsuperscript{+} beam energy, operated at 4 nA continuous current and a 500 × 500 µm raster.}
\end{figure}
Figure 1.8  (a–d) Two-dimensional (2D) images of NRK cells after the forty-fifth sputter cycle. Summed signals of amino acid fragment ions are represented in red (b), those of phospholipids in green (c), and substrate-derived secondary ions are depicted in blue (a). (d) An overlay of the three images. The scale bar in (d) corresponds to 20 μm. (e) and (f) Vertical \( xz \) sections through the sample. Data acquired using \( C_{60}^+ \) sputtering in conjunction with \( Bi_3^+ \) analysis. Reproduced from Breitenstein et al.\(^{18}\) with permission from Wiley.

information about how these various sources function, what they are used for, and the benefits and disadvantages of each.

Chapters 4 and 5 will provide a comprehensive review of the literature regarding the surface characterization and in-depth analysis of soft materials with cluster SIMS. Chapter 4 will describe the important aspects that need to be considered during any static SIMS experiment employing cluster sources (i.e., the best source, the experimental conditions, etc.). A similar approach will be taken in Chapter 5, which will provide a summary of molecular depth profiling. Both the physics and the chemistry of cluster ion bombardment will be discussed in detail, with the introduction of erosion dynamics theory and a brief description of ion beam irradiation chemistries.

Three-dimensional imaging in soft materials is the ultimate goal in molecular depth profiling. This topic will be introduced in Chapter 6, which will serve as both a review of the literature, and a tutorial for 3D imaging. There are, in particular, many important considerations and corrections that are required in order to obtain accurate representations of 3D SIMS image data. Many of these considerations
will be discussed here. Furthermore, this chapter serves as a guide for practical molecular depth profiling and analysis with cluster ion beams, discussing how one should make precise and accurate measurements of depth resolution, damage cross sections and efficiencies, beam conditions, and sputtering rates. The authors will discuss these measurements and more; defining the rules for different scenarios (i.e., organic/organic layers vs organic/inorganic layers), and identifying how and what should be reported in each of these scenarios.

Chapters 7 and 8 will discuss special applications of cluster SIMS for characterization of inorganic materials and biological materials, respectively. Chapter 8 will discuss in detail, the special case of biological samples. Biological materials and cells are particularly challenging and complex, and therefore need special consideration. This chapter will help the reader to better understand the successes and challenges for surface characterization and in-depth analysis of biological samples, and will serve as a detailed review of the field, displaying brilliant 3D molecular images in cells and other biological samples. Finally, all these discussions are wrapped up in Chapter 9, which briefly gives a perspective on what the future holds for the technique of cluster SIMS.

ACKNOWLEDGMENT

The authors would like to acknowledge Kenneth McDermott from the Food and Drug Administration for the provision of samples for analysis in Figure 1.7.

REFERENCES

2.1 INTRODUCTION

I am ashamed to tell you to how many figures I carried these computations, having no other business at the time.

*Sir Isaac Newton*

By definition, clusters are “small, multatom particles.” The upper size limit of clusters is reached when the number of atoms is sufficient to reproduce the physical properties of the condensed matter, such as the band structure. Clusters can be made of a collection of atoms or molecules, and of any element in the periodic table—from hydrogen or noble gases to heavy metals. Adding that to the variety of possible surfaces and energy ranges, it becomes clear that an exhaustive theoretical description of energetic cluster-surface interactions constitutes a serious endeavor, apt to mobilize the workforce of generations of researchers. Although the range of cluster sources used for secondary ion mass spectrometry (SIMS) is restricted by technological considerations, the initial domain of commercially available, relatively small heavy metal and light-element cluster sources such as $\text{Au}_n^+$ and $\text{C}_{60}^+$ is soon to be overcome and one reads more and more reports concerning other types of projectiles, such as massive noble gas (Ar), metal (Au), or molecular (water) clusters.\(^1\)

The study of kiloelectronvolt cluster impacts is deeply rooted in classical physics, as far back as Galileo and Newton, who were able to define the notions of
momentum and energy and the way these physical quantities can be exchanged or transferred in collisions. Microscopic cluster-surface interactions bear resemblances with macroscopic phenomena, such as meteoric impacts on celestial bodies, bullet penetration in a target, or even rain droplets splashing on the surface of a pond. These analogies stimulate researchers to propose phenomenological models based on similar concepts. For Au clusters impinging on Au surfaces with typical meteoroid velocities ($\sim 22$ km/s), the limit between microscopic and macroscopic impact behaviors was identified for cluster nuclearities between 1000 and 10,000.

The state-of-the-art theoretical approaches used for the explanation of cluster interactions with surfaces involve analytical models as well as computer simulations. The analytical formulas resulting from hydrodynamic models are sometimes even coupled with initial molecular dynamics (MD) simulations to predict effects that would be too long to treat with the sole use of MD computer codes (Section 2.3). Nowadays, the models provide a good description of the sputtering (or desorption) process for an ever-increasing number of systems and initial conditions (cluster nature, surface material, projectile energy, and angle). However, one must acknowledge that the detailed understanding of ionization processes of molecules and fragments upon cluster bombardment, and in turn the prediction of ionized fractions, remains out of reach. As was stated in a recent review article on the physics of surface-based organic mass spectrometry, the relatively small number of particles sputtered per impact ($10^3$ or less), combined with the low measured ion fractions ($10^{-3}$ to $10^{-5}$), make any theoretical prediction in that field very difficult. Indeed, assuming that the right physics was in the model, “hundreds of trajectories,” each of weeks to months, would have to be performed in order to make comparisons with experimental distributions.”

In this chapter, we will discuss the case of organic and related materials, with a few examples taken from other types of systems when deemed necessary. From the theoretical point of view, cluster-induced sputtering of organic materials offers a particular challenge because one wishes to correctly describe not only the overall dynamics of the bombarded systems, but also predict the fate of each and every sputtered molecule (are they ejected? do they survive or fragment?). Indeed, the ultimate result of an organic SIMS experiment is a complex collection of charged atoms, fragments, intact molecules, recombination products, and … clusters. And organics are often fragile materials that like to do chemistry. The problem worsens if one needs to model the results of multiple overlapping impacts, in which induced roughness, chemical modification and damage mechanisms, and long-term relaxation effects may play an important role, as is observed upon molecular depth profiling of polymers. The models are not yet able to handle the large complexity of the latter, but forays in the right direction exist.

Keeping the above-mentioned caveats in mind, this chapter will focus on problems of cluster–surface interactions that the theory could successfully tackle. These include several important issues for scientists working in the field of cluster

*In MD simulation terminology, a “trajectory” corresponds to the time evolution of the system for a given set of initial conditions, different trajectories corresponding in turn to different sets of initial conditions.