Chapter 4-SIMS

Contents:
- Introduction to mass spectrometry
  - sample introduction
  - ionization
  - mass separation
  - ion fragmentation and mass spectrum interpretation
- SIMS
  - principle and instrumentation of ToF-SIMS
- SIMS spectra, depth profiling, and imaging

What is mass spectrometry?
1) The mass to charge ratio (m/z) is used to describe ions observed in mass spectrometry.
2) $m$ is the numerical value for the mass of the ion and $z$ is the numerical value for the charge of the ion. The unified atomic mass (u) and the elementary charge units (e) are used for these values.
3) The unified atomic mass is defined as 1/12 the mass of an atom of $^{12}$C. Older terms still in use but not accepted as SI units include the atomic mass unit (amu) and the dalton (Da). The amu is no longer acceptable due to conflicting definitions. The dalton is frequently used for polymers, peptides and other large molecules.
4) Because the unified atomic mass and the charge number are pure numbers, the mass-to-charge ratio is a number and has no unit.

$$1 \text{ u} = 1/N_A \text{ (g)} \quad \text{(where } N_A \text{ is Avogadro’s number)}$$

$$1 \text{ u} \approx 1.66053886 \times 10^{-27} \text{ kg}$$

Definition of Dalton:
Measure of molecular weight or mass. One hydrogen atom has mass of 1 Da. The dalton is one twentieth of the mass of the nuclide $^{12}$C.

What is mass spectrometer?
**History of mass spectrometry?**

- 1886: E. Goldstein discovers anode rays (positive gas ions) in gas discharge
- 1897: J. J. Thomson discovers the electron and determines its m/z ratio. Nobel Prize in 1906.
- 1898: W. Wien analyzes the anode rays by magnetic deflection, and establishes that they carry a positive charge. Nobel Prize in 1911.
- 1909: R.A. Millikan & H. Fletcher determine the elementary unit of charge.
- 1912: First Mass Spectrometer (J. J. Thomson)
- 1919: Electron ionization and magnetic sector MS (A.J. Dempster)
- 1942: First commercial instrument
- 1956: First GC-MS
- 1968: First commercial quadrupole
- 1975: First commercial GC-MS
- 1990s: Explosive growth in biological MS, due to ESI & MALDI
- 2002: Nobel Prize to Fenn & Tanaka for ESI & MALDI
- 2005: Commercialization of Orbitrap MS

**Applications of mass spectrometry**

**Uses of Mass Spectrometry in Organic and Biological Chemistry**

<table>
<thead>
<tr>
<th>Application</th>
<th>Sample</th>
<th>Method</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight determination</td>
<td>Pure compounds, mixtures</td>
<td>Recognize intact molecular ion in spectrum</td>
<td>Several ionization methods can be used for confirmation</td>
</tr>
<tr>
<td>Molecular formula determination</td>
<td>Usually pure compounds</td>
<td>High resolution measurement on molecular ion</td>
<td>High resolution alone seldom gives a unique molecular formula</td>
</tr>
<tr>
<td>Molecular structure determination</td>
<td>Pure compounds or mixtures by LC-MS, GC-MS, and MS-MS</td>
<td>Spectrum-structure correlations; library comparisons</td>
<td>Confirmation of suspected structures is usual: de novo interpretations rare</td>
</tr>
<tr>
<td>Sequence determination</td>
<td>Proteins, other biopolymers</td>
<td>Tandem mass spectrometry (MS-MS)</td>
<td>Sensitive, very rapid and increasingly useful</td>
</tr>
<tr>
<td>Isotopic incorporation and fractionation</td>
<td>Naturally and artificially labeled compounds (¹³C, ¹³N, ¹⁵O, etc.)</td>
<td>Ion abundance measurements</td>
<td>Precise isotope ratio measurements require special instruments</td>
</tr>
</tbody>
</table>

**Use of mass spectrometry in inorganic materials:**

- To check the elements involved into inorganic samples
- To distinguish the isotopes of elements
- To analyze the chemical status of materials

**Great names in history of mass spectrometry**

Nobel Winners for contribution to mass spectrometry

Mass Spectrometry Hall of Fame: Great innovators

**Applications of mass spectrometry**

Mass spectrometers are used in industry and academia for both routine and research purposes. Summary of the major mass spectrometric applications:

**Materials:** to identify the chemical composition and the chemical structure

**Devices:** to study the defect, the distribution of chemical components,

**Biotechnology:** the analysis of proteins, peptides, oligonucleotides

**Pharmaceutical:** drug discovery, combinatorial chemistry, pharmacokinetics, drug metabolism

**Clinical:** neonatal screening, haemoglobin analysis, drug testing

**Environmental:** water quality, food contamination

**Geological:** oil composition, fossil sample analysis

**Archaeology:** to identify the age of rock samples

**Art conservation:** to analyze the paint composition , and identify if the art masterpieces are true or fake
Mass spectrometer – sample introduction
Vacuum environment is required for ionization and mass separation. Hence, sample introduction is to convert a sample into gas-phase molecules without loss of vacuum.

mass spectrometer-sample introduction
Batch inlet (reservoir) for sample introduction
1) Gas phase analyte is introduced directly into the source region of the mass spectrometer through a needle valve.
2) Pump out lines are usually included to remove air from the sample.
3) This inlet works well for gases, liquids, or solids with a high vapor pressure.
4) Samples with low vapor pressure are heated to increase the vapor pressure.
5) Since this inlet is limited to volatile compounds and modest temperatures, it only works for some samples.

Characteristics of reservoir:
• Used for volatile liquids or solids
• Advantage: Constant signal for a while
• Disadvantage: require large amount of sample

Direct Insertion probe for sample introduction
1) The Direct Insertion Probe (DIP) is widely used to introduce low vapor pressure liquids and solids into the mass spectrometer.
2) The sample is loaded into a short capillary tube at the end of a heated sleeve. This sleeve is then inserted through a vacuum lock so the sample is inside the source region.
3) After the probe is positioned, the temperature of the capillary tube is increased to vaporize the sample.
4) The sample is under vacuum and located close to the source so that lower temperatures are required for analysis. This is important for analyzing temperature sensitive compounds.

Direct insertion probe for sample introduction
• Used for solids with low vapor pressure
• Advantages:
  -- Small distance: efficient, can be used for low vapor pressure
• Disadvantages:
  – Increases risk of venting
  – Increases risk of contamination (large amounts of sample)
  – Separation with thermal gradient
Mass spectrometer-sample introduction

Summary of sample introduction method

<table>
<thead>
<tr>
<th>System</th>
<th>Sample Type</th>
<th>Minimum Sample</th>
<th>Characteristics</th>
<th>Ionization Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Batch (reservoir)</td>
<td>Gas, liquid, low</td>
<td>&lt;1 mg</td>
<td>Steady sample delivery</td>
<td>EI, CI</td>
</tr>
<tr>
<td>Direct insertion probe</td>
<td>Melting solid</td>
<td>&lt;1 μg</td>
<td>Sample delivery varies with temperature</td>
<td>EI, CI, DI</td>
</tr>
<tr>
<td>Membrane</td>
<td>Mixtures in solution</td>
<td>&lt;10^-6 M</td>
<td>Volatiles only</td>
<td>EI, CI</td>
</tr>
<tr>
<td>Chromatography: GC, SFC</td>
<td>Mixtures in solution</td>
<td>&lt;1 μg</td>
<td>More volatile compounds</td>
<td>EI, CI</td>
</tr>
<tr>
<td>Chromatography: LC, CE</td>
<td>Mixtures in solution</td>
<td>&lt;1 μg</td>
<td>Less volatile compounds</td>
<td>SI</td>
</tr>
</tbody>
</table>

Note:
- EI: electron impact
- CI: chemical ionization
- SI: spray ionization
- DI: desorption ionization

Mass spectrometer-ionization method

Mass spectrometers measure the mass-to-charge (m/z) ratios of gas phase ions. **Ionization is to create gas phase ions**

- Electron Impact (EI)
- Chemical Ionization (CI)
- Spray ionization (SI) such as Electrospray
- Desorption ionization (DI)
  - Fast Atom Bombardment (FAB)
  - Matrix Assisted Laser Desorption (MALDI)
  - Secondary ion mass spectrometry (SIMS)

Mass spectrometer- Electron ionization (EI)

The EI is for the formation of positive ions:
- The sample is thermally vaporized.
- Electrons ejected from a heated filament are accelerated through an electric field at 70 V to form a continuous electron beam.
- The sample molecule is passed through the electron beam.
- The electrons, containing 70 V of kinetic energy, transfer some of their kinetic energy to the molecule. This transfer results in ionization (electron ejection) with the ion internally retaining no more than 6 eV excess energy.

\[ M + e^- (70 \text{ eV}) \rightarrow M^+ (~5 \text{ eV}) + 2e^- (~65 \text{ eV}) \]

- Excess internal energy (6 eV) in the molecule leads to fragmentation:
  \[ M^+ \rightarrow \text{molecular ions} + \text{fragment ions} + \text{neutral fragments} \]
Mass spectrometer- Electron ionization (EI)

**Time Scales of Ionization**
- What happens to the molecule during EI?
  - 70 eV electron $\Rightarrow$ $5 \times 10^6$ m/s
  - Molecule size $<$ 1 nm
- Transit time $= 2 \times 10^{-16}$ s
- Molecular vibrations $> 10^{-12}$ s
- Electronic time scale $\sim 10^{-16}$ s
- Nuclei remain frozen in position

**Ionization efficiency vs. electron energy**

**Time Scales of electron ionization,**

By Jeremaus

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**Mass spectrometer-Chemical ionization (CI)**

**Chemical ionization (CI)** is applied to samples similar to those analyzed by EI and is primarily used to enhance the abundance of the molecular ion. Chemical ionization uses gas phase ion-molecule reactions within the vacuum of the mass spectrometer to produce ions from the sample.

A possible mechanism for ionization in CI occurs:

$\text{Reagent (R)} + e^- \rightarrow R^+ + 2 e^-$

$R^+ + RH \rightarrow RH^+ + R$

$RH^+ + \text{Analyte (A)} \rightarrow AH^+ + R$

For example (Ar+, CH₅⁺ as ionization agents):

- Charge exchange: $M + Ar^+ \rightarrow M^+ + Ar$
- Electron capture: $M + e^- \text{ (slow)} \rightarrow M^-$
- Proton transfer: $M + CH_4 \rightarrow (M+H)^+ + CH_4$
- Adduct formation: $M + TiCl_4^+ \rightarrow (M+TiCl_4)^+$

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**Mass spectrometer-Electron ionization (EI)**

**Advantages of electron ionization**
- Reproducible method,
- Extensive fragmentation occurs. Molecular structure information is deduced,
- Ionization efficiency high,
- Method is sensitive: 1 in 1000 molecules is ionized,
- Ionization is non-selective (All vaporized molecules can be ionized).

**Disadvantages of electron ionization**
- Only positive ions formed
- Radical cations formed. Re-arrangement complicate mass spectra
- Large internal energy method (hard ionization). Limit value in molecular weight determination
- Sample must be volatile
- Limited to low molecular weight compounds $<$ 600 Da

The utility of EI decreases significantly for compounds above a molecular weight of 600 Da, because the required thermal desorption of the sample often leads to thermal decomposition before vaporization is able to occur.

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**Mass spectrometer-Chemical ionization (CI)**

**Example of chemical ionization: Methane as Reagent Species**

The reagent ions are produced by introducing a large excess of methane into an electron impact (EI) ion source. Electron collisions produce CH₄⁺ and CH₃⁺ which further react with methane to form CH₅⁺ and C₂H₅⁺:

$CH_4^+ + CH_4 \rightarrow CH_5^+ + CH_3$

$CH_3^+ + CH_4 \rightarrow C_2H_5^+ + H_2$

- Good for most organic compounds
- Usually produces [M+H]⁺, [M+CH₃]⁺ adducts

$M + CH_5^+ \rightarrow CH_3 + [M + H]^+$ (protonation)

$M + CH_5^+ \rightarrow [M + CH_3]^+$ (adduct formation)

- Adducts are not always abundant
- Extensive fragmentation
Mass spectrometer-Chemical ionization (CI)

<table>
<thead>
<tr>
<th>Reagent Gas</th>
<th>Reagent Ion</th>
<th>Analyte Ion</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₂</td>
<td>H₂⁺</td>
<td>(M+H)⁺</td>
<td>Very energetic protonating agent; produces considerable fragmentation</td>
</tr>
<tr>
<td>CH₃</td>
<td>CH₃⁺, CH₃⁺⁺</td>
<td>(M+H)⁺, (M+CH₃)⁺⁺</td>
<td>Energetic protonating agent, forms adduct ions</td>
</tr>
<tr>
<td>C₂H₄</td>
<td>C₂H₄⁺⁺</td>
<td>(M+H)⁺, (M+CH₂)⁺⁺</td>
<td>Mild protonating agent; ionizes all nitrogen bases</td>
</tr>
<tr>
<td>NH₃</td>
<td>NH₃⁺, NH₃⁺⁺</td>
<td>(M+H)⁺, (M+NH₃)⁺⁺</td>
<td>Selective ionization, little fragmentation</td>
</tr>
<tr>
<td>NH₄OH</td>
<td>NH₄⁺</td>
<td>(M+H)⁺</td>
<td>Selective protonating agent</td>
</tr>
<tr>
<td>CH₃OH</td>
<td>CH₃OH⁻</td>
<td>(M−H)⁻</td>
<td>Mild proton abstraction reagent</td>
</tr>
<tr>
<td>NF₃</td>
<td>F⁻</td>
<td>(M−H)⁻</td>
<td>Proton abstraction reagent</td>
</tr>
</tbody>
</table>

Example of Mass spectra derived from chemical ionization

[Graph showing mass spectra for Butyl methacrylate]

Characteristics of chemical ionization

- Sample must be volatile. Limited to sample with molecular weight less than 800 Da
- Hard or soft ionization. Fragmentation for molecular structure information or molecular weight determination.
- Universal or selective method. Either is available, depending on the choice of reagent gases.
- Negative ions are available.

Ionization effect on spectra

Effects of ionization method and the reagent

EI

Butyl methacrylate

Molecular weight = 142

Cl, R= Methane (PA=5.7 eV)

Cl, R= Isobutane (PA=8.5 eV)

The EI (top), methane CI (middle) and isobutane CI (bottom) mass spectra of butyl methacrylate. The ionization techniques (EI vs. CI) and the reagent gases (methane vs. isobutane) influence the amount of fragmentation and the prominence of the protonated molecular ions detected at 143 Th
Desorption ionization (DI) includes:

-- Fast Atom Bombardment (FAB)
Use neutral atoms (e.g., Ar, Xe) as primary beam

-- Secondary ion mass spectrometry (SIMS)

-- Matrix Assisted Laser Desorption (MALDI)

Desorption ionization-MALDI

MALDI is designed to enhance mass spectra by solving two main problems:
– Thermal instability and low volatility
– Large and heavy biomolecules

Characteristics of MALDI:
• Analyte molecules are embedded in a crystalline matrix composed of a low molecular weight organic species.
• Dried mixture is struck with a short, intense laser pulse that is strongly absorbed by the matrix (often UV or IR).
• Rapid heating of matrix causes sublimation and expansion into gas phase. Intact analyte molecules carried with little internal energy.
• Most widely accepted ionization mechanism is gas phase proton transfer.
• Efficient, "soft," and relatively universal (wavelength independent of analyte). Matrix isolates analyte molecules, preventing clusters.

MALDI-MS was first introduced in 1988 by Tanaka, Karas, and Hillenkamp.


MALDI is a widespread analytical tool for peptides, proteins, and most other biomolecules (oligonucleotides, carbohydrates, natural products, and lipids). The efficient and directed energy transfer during a matrix-assisted laser-induced desorption event provides high ion yields of the intact analyte, and allows for the measurement of compounds with sub-picomole sensitivity.

J. Kimmel http://www.chm.bris.ac.uk/ms/theory/maldi-ionisation.html

Desorption ionization-MALDI

Ionization mechanism of MALDI
MALDI matrix - A nonvolatile solid material facilitates the desorption and ionization process by absorbing the laser radiation.
• The analyte is highly diluted in the matrix, often 10^-6 or less, to prevent from the analyte-analyte interaction.
• Both the matrix and the sample embedded in the matrix are vaporized.
• The matrix also minimizes the sample damage from laser radiation by absorbing most of the incident energy.

Several theories have been developed to explain desorption by MALDI.
• The thermal-spike model proposes that the ejection of intact molecules is attributed to poor vibrational coupling between the matrix and analyte, which minimizes vibrational energy transfer from the matrix to the vibrational modes of the analyte molecule, thereby minimizing fragmentation.
• The pressure pulse theory proposes that a pressure gradient from the matrix is created normal to the surface. Desorption of large molecules is enhanced by momentum transfer from collisions with these fast moving matrix molecules. Ionization occurs through proton transfer or cationization during the desorption process.
**Desorption ionization-MALDI**

**Role of MALDI matrix:**

1) Isolation of analyte molecule to prevent aggregation
2) Absorption of energy from the laser
3) Energy transfer to allow des-integration without destruction of the molecule (soft desorption/soft ionization)
4) Stimulation of analyte ionization

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**Desorption ionization-MALDI**

**Commonly used MALDI matrices:**

- Nicotinic acid (NA)
- Caaffeic acid (CA)
- Sinapinic acid (SA)
- 3,4-Dihydroxyphenylalanine (DHPA)
- n-Cyano-4-hydroxycinnamic acid (CHCA)

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**MALDI-Laser Source**

- IR 10.6 microns, CO2
- IR 2.94 microns, Er:YAG
- IR 1.06 microns, Nd:YAG
- VIS 532 nm, Nd:YAG (2nd harmonic)
- UV 355 nm, Nd:YAG (3rd harmonic)
- UV 337 nm, Nd:YAG (4th harmonic)
- UV 266 nm, Nd:YAG (4th harmonic)

Laser optics usually includes:
- variable attenuator, generally rotating optical density filter
- mirror
- lens (material dependent on wavelength) with 1-5 inch focal length
- window to vacuum chamber (material dependent on wavelength)

Laser pulse width: 300 ps to 3 nanoseconds

Laser energy: 10 micro-joules to 10 milli-joules (depending on pulse width)

Laser power density: $10^6$ – $10^7$ watts/cm$^2$

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**Desorption ionization-MALDI**

- Spectra contain mostly single-charged ions.
- Fragmentation due to excess energy imparted on analyte during ionization process is possible

**UV MALDI mass spectrum of bovine serum albumin (MW=66,429 Da)**

[Image](http://www.hopkinsmedicine.org/mams/)
Desorption ionization-MALDI

**Advantages of MALDI**
- practical mass range of up to 500 kDa;
- typical sensitivity on the order of low femtomole to low picomole. Attomole sensitivity is possible;
- soft ionization with little to no fragmentation observed;
- tolerance of salts in millimolar concentrations;
- suitable for the analysis of complex mixtures.
- The utility of MALDI for biomolecule analysis lies in its ability to provide molecular weight information on intact molecules. The ability to generate accurate information can be useful for protein identification.

**Disadvantages of MALDI**
- matrix background, which can be a problem for compounds below a mass of 700 Da. This background interferences is highly dependent on the matrix material;
- possibility of photo-degradation by laser desorption;
- acidic matrix used in MALDI may cause degradation of some compounds.

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Spray ionization

**Electrospray Ionization (ESI)** is one of the Atmospheric Pressure Ionization (API) techniques.

A small volume (1-4 mL) of the sample dissolved in a suitable volatile solvent, at a concentration of ca. 1 - 10 pmol/mL, is transferred into a miniature sample vial. A reasonably high voltage (ca. 700 - 2000 V) is applied to the specially manufactured gold-plated vial resulting in sample ionisation and spraying. The flow rate of solute and solvent using this procedure is very low, 30 - 1000 nL/min.

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**Spray ionization**

**Characteristics of spray ionization**
- sample is solution, usually aqueous, including non-volatile
- thermal and electrical forces are used for ionization
- solvent acts the matrix
- usually multi protonated (M+H)n+ or deprotonated (M-H)n−, lower charges in thermal spray, higher in electrospray
- soft ionization, relatively little fragmentation
- mass range < 10^6 Da
- sensitivity is in the attomole range (pg/ul) and above
**Spray ionization**

**Comparison between MALDI and electrospray (ESI)**

**MALDI:** singly-charged ions best used with a high mass range analyzer such as the TOF mass analyzer. Singly-charged ions are an advantage.

**ESI:** multiply charged ions; can be used with quadrupoles and quadrupole ion traps. These instruments are more readily configured as tandem mass spectrometers for mass-selecting and fragmenting single components of a mixture.

**MALDI:** a solid-phase technique that will be utilized for high throughput microarrays on silicon chips, imaging of tissue or selection of individual cells or microorganisms.

**ESI:** a liquid techniques compatible with on-line chromatographic (reversed phase HPLC, anion exchange, etc.) chromatography and capillary electrophoresis.

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**Mass spectrometry-ionization summary**

<table>
<thead>
<tr>
<th>Ionization method</th>
<th>Typical Analytes</th>
<th>Sample Introduction</th>
<th>Mass Range</th>
<th>Method Highlights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electron Impact (EI)</td>
<td>Relatively small volatile</td>
<td>GC or liquid/solid probe</td>
<td>&lt;800 Daltons</td>
<td>Hard method versatile provides structure info</td>
</tr>
<tr>
<td>Chemical Ionization (CI)</td>
<td>Relatively small volatile</td>
<td>GC or liquid/solid probe</td>
<td>&lt;800 Daltons</td>
<td>Soft method molecular ion peak [M+H]⁺</td>
</tr>
<tr>
<td>Electrospray (ESI)</td>
<td>Peptides, Proteins non-volatile</td>
<td>Liquid Chromatography or syringe</td>
<td>&lt;200,000 Daltons</td>
<td>Soft method ions often multiple charged</td>
</tr>
<tr>
<td>Fast Atom Bombardment (FAB)</td>
<td>Carbohydrates, Organometallics, Peptides, non-volatile</td>
<td>Sample mixed in viscous matrix</td>
<td>&lt;6,000 Daltons</td>
<td>Soft method but harder than ESI or MALDI</td>
</tr>
<tr>
<td>Matrix assisted Laser Desorption (MALDI)</td>
<td>Peptides, Proteins, Nucleotides</td>
<td>Sample mixed in solid matrix</td>
<td>&lt;500,000 Daltons</td>
<td>Soft method very high mass</td>
</tr>
</tbody>
</table>

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**Mass Analyzer**

The mass analyzer separates these ions according to their m/z value.

The selection of a mass analyzer depends upon the mass resolution, mass range, scan rate, and detection limits required for an application.

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**Mass spectrometer-mass analysis**

- Magnetic Sector or Electrostatic Sector
- Time-of-Flight (TOF)
- Quadrupole
- Ion trap
- Ion Cyclotron Resonance (ICR)
Mass Analyzer - Magnetic Sector

- In magnetic analysis, the ions are accelerated into a magnetic field using an electric field.
- A charged particle traveling through a magnetic field will travel in a circular orbit with a radius that depends on the speed of the ion, the magnetic field strength, and the ion's m/z.
- A mass spectrum is obtained by scanning the magnetic field and monitoring ions as they strike a fixed point detector.

Magnetic Sector Mass Analyzer

Advantages:

- Very high reproducibility
- High resolution
- High sensitivity
- Linked scan MS/MS does not require another analyzer

Disadvantages:

- Not well-suited for pulsed ionization methods (e.g. MALDI)
- Usually larger and higher cost than other mass analyzers
- Linked scan MS/MS gives either limited precursor selectivity with unit product-ion resolution, or unit precursor selection with poor product-ion resolution

Mass analyzer - magnetic sector

- Ions possess the kinetic energy when leaving source
- Travel of ions is affected by the magnetic field
- Trajectory of ion is determined by equilibration of magnetic force and centripetal acceleration
- Ions with the same momentum (mv) have the same R. This is a momentum analyzer.

An ion beam m/z in the KeV range of kinetic energy 0.5mv^2, passes at right angle through a magnetic field B, experiences a deflection with radius r. In this example, the balances of force is given by:

\[ Bzv = \frac{mv^2}{r} \]

\[ \frac{mv}{z} = Br \]

In the special case, all the ions are accelerated through a constant potential difference, V, have the same energy, we eliminate velocity, v:

\[ \frac{1}{2}mv^2 = zV \]

\[ v = \left( \frac{2zV}{m} \right)^{1/2} \]

\[ \frac{m}{z} = \frac{B^2r^2}{2V} \]

Mass analyzer - Time-of-flight (ToF) analyzer

The ions are electrostatically accelerated into a field-free drift region with a nominal kinetic energy of:

\[ E_k = eV_0 = \frac{m}{2}v^2 \]

Where \( V_0 \) is the accelerating voltage, m the mass of ion, v the flight velocity of ion, e its charge. It is seen from the above formula that the ion with lower mass has higher flight velocity than one with higher mass. Thus they will reach the ion detector earlier. As a result, the mass separation is obtained in the flight time, t, from the sample to the detector. The flight time t is expressed by:

\[ t = \frac{L}{2eV_0/m}^{1/2} \]

Where L is the effective length of the mass spectrometer. A variety of mass ions are recorded by the detector with the time sequence to give the mass spectrum.
TOF Mass analyzer

**Advantages of reflection TOF mass analyzer:**
- High Resolution (> 20,000 in some models)
- High Accuracy (< 5 ppm)
- Highest practical mass range of all MS analyzers (>10,000 Mass Range)
- Fastest MS analyzer
- Suitable for pulsed ionization methods such as MALDI or some models of IMS

**Limitations:**
- Requires pulsed ionization method or ion beam switching

Mass analyzer- Quadrupole mass filter

- Quadrupole consists of four parallel rods; Precise dimensions and spacing; Rods connected diagonally in pairs.
- Quadrupole mass analyzers are connected in parallel to a radio frequency (RF) generator and a DC potential.
- At a specific RF field, only ions of a specific m/z can pass through the quadrupoles as shown in Figure, where only the ion of m/z 100 is detected.
- Scanning the RF field can be achieved in approximately one second (m/z 20-800).

Mass analyzer- Quadrupole mass filter

Under the certain AC and RF field, only the ions that have an appropriated m/z ratio will be stable and drift through the quadrupole mass filter.

**stability diagram:** Stability conditions for ion traps and quadrupole mass filters in terms of applied DC ($a_z$) and RF voltage ($q_z$, dimensionless parameters). The size of the symbols represent the m/z value of ions that occur at the indicated points along the scan line.

Mass analyzer- Quadrupole

**Characteristics of quadrupole-MS**
- Tolerate relatively high pressures
- Maximum m/z ~ 4,000, which is useful because electrospray ionization of proteins and other biomolecules commonly produce charge distributions from m/z 1000 to 3500.
- Resolution ~ 3,000
  - Quadrupoles are low resolution instruments
  - Usually operated at 'Unit Mass Resolution'
- Small, lightweight
- Relatively low cost;
- Easy to couple with chromatography
Mass analyzer- Quadrupole mass filter

In order to perform tandem mass analysis with a quadrupole instrument, it is necessary to place three quadrupoles in series.
- The first quadrupole (Q1) is used to scan across a preset m/z range and select an ion of interest.
- The second quadrupole (Q2), also known as the collision cell, focuses and transmits the ions while introducing a collision gas (argon or helium) into the flight path of the selected ion, in which fragments are formed.
- The third quadrupole (Q3) serves to analyze the fragment ions generated in the collision cell (Q2).

http://masspec.scripps.edu/MSHistory/whatisms.php#quadrupoles

Mass analyzer- Quadrupole ion trap

RF fields induce oscillations in r and z directions. A “trapped” ion is stable along both axes.

Quadrupole
- RF fields yield m/z band of stability
- 2D RF fields
- Detect those ions that are selectively transmitted with stable trajectories

Quadrupole ion trap
- RF fields yield m/z band of stability
- 3D RF Fields
- Detect those ions that are selectively ejected due to destabilized trajectory

Characteristics of quadrupole ion trap:
- Inexpensive
- Operated at relatively high pressure (~10⁻³ Torr)
- Robust - used for bench-top instruments
- Small size, good portable device for field analysis
- Spectra less reproducible due to reactions of trapped ions

Recommended paper:

http://www.ionsource.com/links/iontrap.htm
Mass analyzer - Quadrupole

File_24956.exe

Mass analyzer - Ion Cyclotron Resonance

Ion Cyclotron Resonance: Fourier Transform MS
- Ions with motion normal to a magnetic field have circular trajectories with a characteristic angular frequency, \( \omega \).
- For a strong magnetic field, this is a radio frequency, e.g., \( B = 4.7 \) Tesla, 72 MHz for \( H^+ \).
- At room temperature the orbits are about 1 mm in diameter.
- Ions absorb energy from a resonant RF electric field and move in phase with it to higher radii.

Ions moves in circular orbits with a cyclotron angular frequency, which is expressed by:

\[
\omega = \frac{Bz}{m} = 2\pi f \\
m / z = B / 2\pi f
\]

From M. Guilhaus

Mass analyzer- Ion Cyclotron Resonance

1) At certain frequencies, RF electric field is in resonance with the frequency of the ions.
2) At Resonance, the ions absorb energy from a resonant RF electric field and move in phase with it to higher radii, causing the ions with the same mass to move coherently.
3) The coherently moving ions give the image currents (time-domain signal) from the circulating charge are made up of one or more high frequencies-one for each m/z.
4) Fourier transformation of this "transient" yields a power spectrum or frequency-domain signal - a mass spectrum.

Ion Cyclotron Resonance: Fourier Transform MS

Advantages of ICR MS:
- They give extremely high resolutions (>10⁶), The highest recorded mass resolution of all mass spectrometers
- High mass accuracy
- Bio FTMS - a quadrupole (linear ion trap precursor ion selection and collision induced dissociation) with the FTMS giving extremely high resolution on the precursor ions.
- Well-suited for use with pulsed ionization methods such as MALDI
- Powerful capabilities for ion chemistry and MS/MS experiments

Disadvantages of ICR MS:
- FTMS larger and very expensive to maintain (superconducting magnet – cryogenic fluids) than most other MS.
- Artifacts such as harmonics and sidebands are present in the mass spectra.
- Many parameters (excitation, trapping, detection conditions) comprise the experiment sequence that defines the quality of the mass spectrum

Good paper on ICR-MS:
Definition of Mass Resolution

Mass resolution represents the ability to separate two adjacent masses. It measures the "sharpness" of the MS peak.

Single Ion method:
Full Width at Half Maximum (FWHM)
or at 50% of the peak height

\[ R = \frac{m}{\Delta m} \]

Double Ion method:
2 adjacent ion peaks with a 10% valley max

Summary of mass analyzer

A general comparison of mass analyzers typically used for electrospray.

<table>
<thead>
<tr>
<th></th>
<th>Quadrupole</th>
<th>Ion Trap</th>
<th>Time-of-Flight</th>
<th>Time-of-Flight</th>
<th>Magnetic Sector</th>
<th>Ion cyclotron FTMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy</td>
<td>100 ppm</td>
<td>100 ppm</td>
<td>200 ppm</td>
<td>&lt;5 ppm</td>
<td>&lt;5 ppm</td>
<td>&lt;5 ppm</td>
</tr>
<tr>
<td>Resolution</td>
<td>4,000</td>
<td>4,000</td>
<td>8,000</td>
<td>15,000</td>
<td>30,000</td>
<td>100,000</td>
</tr>
<tr>
<td>m/z Range</td>
<td>4,000</td>
<td>4,000</td>
<td>&gt;300,000</td>
<td>10,000</td>
<td>10,000</td>
<td>10,000</td>
</tr>
<tr>
<td>Scan Speed</td>
<td>~a second</td>
<td>~a second</td>
<td>ms</td>
<td>ms</td>
<td>~a second</td>
<td>~a second</td>
</tr>
<tr>
<td>General Comments</td>
<td>Low cost</td>
<td>Low cost</td>
<td>Low cost</td>
<td>Low cost, high through-put</td>
<td>Good accuracy</td>
<td>High resolution, MS high vacuum, super conducting magnet, expense</td>
</tr>
<tr>
<td></td>
<td>Ease of switching pos/neg ions</td>
<td>Ease of switching pos/neg ions, Small size</td>
<td>Good accuracy, Good resolution</td>
<td>Instrument is massive</td>
<td>Capable of high resolution</td>
<td></td>
</tr>
</tbody>
</table>
Chapter 4-SIMS

Contents:
- Introduction to mass spectroscopy
  -- ionization
  -- mass separation
  -- ion fragmentation
  -- interpretation of mass spectrum
- SIMS
  -- principle and instrumentation of ToF-SIMS
- SIMS spectra, depth profiling, and imaging

Interpretation of mass spectra
General information which will aid mass spectra interpretation:

**Molecular ion (M⁺):** If the molecular ion appears, it will be the highest (or second highest) mass in a spectrum. This peak will represent the molecular weight of the compound. Its appearance depends on the stability of the compound. Double bonds, cyclic structures and aromatic rings stabilize the molecular ion and increase the probability of its appearance.

**Reference Spectra:** Mass spectral patterns are reproducible. The mass spectra of many compounds have been published. Instrument computers generally contain spectral libraries which can be searched for matches.

**Isotopes:** Isotopes occur in compounds analyzed by mass spectrometry in the same abundances that they occur in nature. This approach is very useful for identifying metal associated ion cluster.

**Fragmentation:** General rules of fragmentation exist and are helpful to predict or interpret the fragmentation pattern produced by a compound. Functional groups and overall structure determine how some portions of molecules will resist fragmenting, while other portions will fragment easily. A detailed discussion of those rules is beyond the scope of this introduction, and further information may be found in your organic textbook or in mass spectrometry reference books.

Interpretation of MS - molecular ion

**Molecular ion (M⁺):** If the molecular ion appears, typically it will be the highest mass in a spectrum if no additional chemical reagent or matrix is involved into the ionization. This peak will represent the molecular weight of the compound.

A mass spectrum of methanol (CH₃OH) is shown below. CH₃OH⁺ (the molecular ion) and the fragment ions appear in this spectrum.

![Mass spectrum of methanol](http://www.chem.arizona.edu/massspec/intro_html/intro.html)
**Interpretation of MS-molecular ion**

- Molecular weight = 93
- Molecular weight = 135

Mass spectrum of aromatic amines, obtained by electron ionization

**Effect of ionization method on the mass spectra**

- Laser desorption mass spectrum (CO₂ laser, 0.1 J pulse, 0.15us pulse period)
- Fast atom bombardment mass spectrum (Ar, 5kV, sample in glycerol)
- Chemical ionization (NH₄⁺ as reagent)

**Interpretation of MS-Isotopes**

<table>
<thead>
<tr>
<th>Element</th>
<th>Isotope</th>
<th>Relative Abundance</th>
<th>Isotope</th>
<th>Relative Abundance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon</td>
<td>¹²C</td>
<td>100</td>
<td>¹³C</td>
<td>1.11</td>
</tr>
<tr>
<td>Hydrogen</td>
<td>¹H</td>
<td>100</td>
<td>²H</td>
<td>0.016</td>
</tr>
<tr>
<td>Chlorine</td>
<td>³⁵Cl</td>
<td>100</td>
<td>³⁷Cl</td>
<td>32.5</td>
</tr>
<tr>
<td>Bromine</td>
<td>⁷⁹Br</td>
<td>100</td>
<td>⁸¹Br</td>
<td>98.0</td>
</tr>
</tbody>
</table>

The ratio of peaks containing ⁷⁹Br and its isotope ⁸¹Br (100/98) confirms the presence of bromine in the compound.

**Mass spectrum of methyl bromide**

m/z = 15
(⁷⁹BrCH₃ m/z = 94)
(⁸¹BrCH₃ m/z = 96)

**Mass spectrum of Li-doped ZnO film**

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Atomic mass</th>
<th>abundance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>⁶⁵Zn</td>
<td>65.9</td>
<td>48.63</td>
</tr>
<tr>
<td>⁶³Zn</td>
<td>65.9</td>
<td>27.90</td>
</tr>
<tr>
<td>⁶⁷Zn</td>
<td>66.9</td>
<td>4.10</td>
</tr>
<tr>
<td>⁶⁹Zn</td>
<td>67.9</td>
<td>18.75</td>
</tr>
<tr>
<td>⁷⁴Zn</td>
<td>69.9</td>
<td>0.62</td>
</tr>
</tbody>
</table>
**mass spectrometry-ion fragmentation**

The output of the mass spectrometer shows a plot of relative intensity vs m/z. The most intense peak in the spectrum is termed the base peak and all others are reported relative to it's intensity. The peaks themselves are typically very sharp, and are often simply represented as vertical lines.

The process of fragmentation follows simple and predictable chemical pathways and the ions which are formed will reflect the most stable cations and radical cations which that molecule can form.

**Interpretation of MS- ion fragmentation**

**Ion fragmentation of Alkanes:**
1) Simple alkanes tend to undergo fragmentation by the initial loss of a methyl group to form a (m/z=15) species.
2) This carbocation can then undergo stepwise cleavage down the alkyl chain, expelling neutral two-carbon units (ethene).
3) Branched hydrocarbons form more stable secondary and tertiary carbocations, and these peaks will tend to dominate the mass spectrum.

**Fragments of alkanes**

<table>
<thead>
<tr>
<th>m/z</th>
<th>ions</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>CH₃</td>
</tr>
<tr>
<td>27</td>
<td>C₂H₅</td>
</tr>
<tr>
<td>28</td>
<td>C₂H₄</td>
</tr>
<tr>
<td>29</td>
<td>C₂H₆</td>
</tr>
<tr>
<td>39</td>
<td>C₃H₇</td>
</tr>
<tr>
<td>41</td>
<td>C₄H₉</td>
</tr>
<tr>
<td>43</td>
<td>C₅H₁₁</td>
</tr>
<tr>
<td>57</td>
<td>C₆H₁₃</td>
</tr>
</tbody>
</table>

**Ion fragmentation of Aromatic Hydrocarbons:**
1) The fragmentation of the aromatic nucleus is, generating a series of characteristic peaks having m/z =91, 77, 65, 63, etc.
2) These characteristic peaks are difficult to describe in simple terms, they do form a pattern (the "aromatic cluster").
3) If the molecule contains a benzyl unit, the major cleavage will be to generate the benzyl carbocation, which rearranges to form the tropylium ion.
4) Expulsion of acetylene (ethyne) from this generates a characteristic m/e = 65 peak.

**Example**

- For dodecane, the base peak is CH₃, and the other peaks are reported relative to this intensity.

**Intensities**

- m/z = 71 (pentyl, m/z = 71),
- m/z = 57 (butyl, m/z = 57),
- m/z = 43 (propyl, m/z = 43),
- m/z = 29 (ethyl, m/z = 29),
- m/z = 15 (methyl, m/z = 15).

**Diagrams**

- Aromatic cluster diagram showing characteristic peaks.
- Benzyl and tropylium ion formation.
- Mass spectrum of dodecane with base peak and other characteristic peaks.

---

From Paul R. Young.
Interpretation of MS- ion fragmentation

Ion fragmentation of Aldehydes:
1) In addition to losing a proton and hydroxy radical, alcohols tend to lose one of the α-alkyl groups (or hydrogens) to form the oxonium ions seen below.
2) For primary alcohols, this generates a peak at m/e = 31;
3) Secondary alcohols generate characteristic peaks with m/z = 45, 59, and 73 besides 31, according to substitution.

Ion fragmentation of Ketones:
Major fragmentation peaks result from cleavage of the C-C bonds adjacent to the carbonyl.

Ion fragmentation of Alcohols:
1) In addition to losing a proton and hydroxy radical, alcohols tend to lose one of the α-alkyl groups (or hydrogens) to form the oxonium ions seen below.
2) For primary alcohols, this generates a peak at m/e = 31;
3) Secondary alcohols generate characteristic peaks with m/z = 45, 59, and 73 besides 31, according to substitution.
Interpretation of MS- ion fragmentation

C₅H₈O₂, MW = 100.12

The spectrum shows a small molecular ion peak.
- A pair of peaks at m/z = 57 and 58. The peak at m/z = 57 corresponds to loss of m/z = 43, which is the base peak and corresponds to the acylium ion (CH₃CO⁺).
- The m/z = 57 fragment corresponds to C₃H₅O, suggesting the original compound was an allyl (-O-CH₂CH=CH) or methylvinyl (-O-CH=CHCH₃) ester. Either of these would generate the peak observed at m/z = 41.
- The peak at m/z = 58 corresponds to the protonated m/z = 57 cation radical.

Interpretation of mass spectra

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Interpretation of mass spectrum

Useful websites:
A library of spectra can be found in the NIST WebBook a data collection of the National Institute of Standards and Technology. (http://webbook.nist.gov/)

Useful tools such as an exact mass calculator and a spectrum generator can be found in the MS Tools section of Scientific Instrument Services webpage. (http://elchem.kaist.ac.kr/vl/index.htm)

The JEOL Mass Spectrometry website contains tutorials, reference data and links to other sites (http://www.jeol.com/tabid/96/Default.aspx)

References:
J. B. Lambert, organic structural spectroscopy, Prentice Hall, 1998
Paul R. Young, University of Illinois at Chicago, http://www.chem.uic.edu/web1/ocol/spec/MS.htm
What is SIMS?
1) SIMS is one type of mass spectrometer
2) SIMS needs UHV
3) Only solid samples are used in SIMS
4) Primary beam is ion beam
5) SIMS (SSIMS) is surface-sensitive technique, sampling depth is 1-2 monolayer
6) SIMS is capable of high-resolution chemical imaging


What is mass spectrometer?
• SIMS is a instrument operated in ultrahigh vacuum environment
• Static SIMS (SSIMS) is a surface sensitive instrument that has a sampling depth of 1-2 monolayers

Chapter 4-SIMS
Contents:
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• SIMS
  -- principle and instrumentation of ToF-SIMS
• SIMS spectra, depth profiling, and imaging
SIMS- ion sputtering effects

- The collision cascade model quantitatively explains how the primary beam interacts with the sample atoms.
- In this model, a fast primary ion transfer energy to target atoms in a series of binary collisions.
- Energetic target atoms (called recoil atoms) collide with more target atoms.
- Target atoms that recoil back through the sample surface constitute sputtered material. Atoms from the sample's outer monolayer can be driven in about several nanometers generating surface mixing.

Data courtesy of Pennsylvania State University

SIMS- ion beam sputtering

The bombarding primary ion beam produces particles of sample material and resputtered primary ions, along with electrons and photons. The secondary particles carry negative, positive, and neutral charges and they have kinetic energies that range from zero to several hundred eV.

- Primary beam species include Au+, Ga+, Cs+, O2+, and Ar+ at energies between 1 and 30 keV. Primary ions are implanted and mix with sample atoms to depths of 1 to 10 nm.
- Sputter rates typically vary between 0.1 and 5 nm/s. Sputter rates depend on primary beam intensity, sample material, and crystal orientation.
- The sputter yield is the ratio of the number of atoms sputtered to the number of impinging primary ions. Typically, sputter yields fall in a range from 5 to 15.


SIMS- ion beam sputtering

The sputter yield is the ratio of the number of atoms sputtered to the number of impinging primary ions. Typically, SIMS sputter yields fall in a range from 5 to 15.

Figure 5.2: Experimental sputter yield data for aluminium as a function of primary ion energy for a number of different primary ions: △, He; ○, Xe; □, Ar; +, Xe (theoretical); x, Ar (theoretical)
The SIMS ionization efficiency is called ion yield, defined as the fraction of sputtered atoms that become ionized. Ion yields vary over many orders of magnitude for the various elements.

Many factors affect the ion yield. The most obvious are:
- Intrinsic tendency to be ionized
  - Positive ion: Ionization potential (IP)
  - Negative ion: Electron affinity (EA)
- Matrix effect
- Primary beam

The most obvious influences on ion yield are ionization potential for positive ions and electron affinity for negative ions. For example, the following figure shows the logarithm of positive ion yields plotted as a function of ionization potential. The ion yields are relative to silicon in a silicon matrix with oxygen sputtering.

Other factors affecting the secondary ionization efficiencies in SIMS:
- Oxygen bombardment increases the yield of positive ions
- Cesium bombardment increases the yield of negative ions.

The increases can range up to four orders of magnitude.
Oxygen enhancement occurs as a result of metal-oxygen bonds in an oxygen rich zone. When these bonds break in the ion emission process, the oxygen becomes negatively charged because its high electron affinity favors electron capture and its high ionization potential inhibits positive charging. The metal is left with the positive charge. Oxygen beam sputtering increases the concentration of oxygen in the surface layer.

The enhanced negative ion yields produced with cesium bombardment can be explained by work functions that are reduced by implantation of cesium into the sample surface. More secondary electrons are excited over the surface potential barrier. Increased availability of electrons leads to increased negative ion formation.

Secondary Ion Yields- Primary Beam Effects

Secondary Ion Yields- Matrix effect

Absolute secondary ion yields as a function of atomic number, (a) under high vacuum conditions; (b) under oxygen saturation 3 keV Ar⁺, incident angle 60°, beam density 10⁻³ μA/cm², pressure 10⁻¹⁰ Torr. The presence of oxygen enhances the ion yield; The ion yield decrease with the atomic number.

SIMS- Instrumentation

Three major components in UHV chamber
(1). Primary Ion Sources
- Ion sources with electron impact ionization: Duoplasmatron Ar⁺, O₂⁺, O⁻
- Ion sources with surface ionization: Cs⁺ ion source.
- Ion sources with field emission: Ga⁺ Liquid metal ion source.

(2). Mass Analyzers for secondary ion mass separation
- Magnetic sector analyzer
- Quadrupole mass analyzer
- Time-of-flight analyzer

(3). Secondary ion detectors
- Faraday cup
- Dynode electron multiplier
- Ion imaging detector

SIMS- primary ion source

The duoplasmatron can operate with virtually any gas, but oxygen is the most common because oxygen implantation into the sample surface enhances ionization efficiency for electropositive elements. The oxygen plasma within the duoplasmatron source contains both O⁻ and O₂⁺, and either can be extracted.
The cesium surface ionization source produces Cs⁺ ions as Cs atoms vaporize through a porous tungsten plug.

**Cesium Surface Ionization Source**

- Cesium Reservoir
- Focus Electrode
- Extraction Electrode (+ground)
- Porous Tungsten Plug
- Cs⁺

(0 to 20 kV)

The electrostatic lenses and the apertures control the intensity and width of the primary ion beam.

Electrostatic deflectors steer the primary beam in a raster pattern onto the sample.

The combination of a magnetic and an electrostatic sector produces a double focusing instrument.

In a series arrangement of one electrostatic and one magnetic sector, the energy dispersion of the electrostatic sector can just compensate the energy dispersion of the magnet.

**Primary Ion Source**

**Primary Ion Gun**

This mass filter eliminates impurity species in the beam. For example, Cr, Fe, and Ni ions sputter from stainless steel surfaces within a duoplasmatron.

**Primary Ion Column**

- Cesium Gun
- Mass Filter
- Apertures
- Electrostatic Deflectors
- Sample

**SIMS- Mass Analyzer**

- Electrosstatic Sector
- Spectrometer Lens
- Magnetic Sector
- Energy Slt
- Field Aperture
- Entrance Slt
- Exit Slt

The electrostatic lenses and the apertures control the intensity and width of the primary ion beam.

Electrostatic deflectors steer the primary beam in a raster pattern onto the sample.
SIMS- ion detector

**Secondary Ion Detectors**
- Ion counting electron multiplier. The ion counting electron multipliers are the most sensitive detectors. They must be protected from intense ion beams.
- Faraday cup. The Faraday cup detector moves on a solenoid to cover the electron multiplier when the incoming ion signal is too high.
- Ion image detectors.

- High energy neutral species form by charge exchange when an ion beam strikes a surface. These neutrals contribute noise to the ion signal.
- If an electrostatic sector precedes the electron multiplier, the neutrals can be eliminated from the ion signal.
- Quadrupole mass analyzers also use electrostatic sectors or deflectors to minimize the contributions of high energy neutral species to the ion signal.

**Faraday Cups**
1) A Faraday cup is just an electrode from which electrical current is measured while a charge particle beam (electrons or ions) impinges on it.
2) The shape helps minimize loss of secondary electrons that would alter the current measurement. A deep cup with an electron repeller plate minimizes secondary electron loss.
Ion Image Detectors

- Ion image detectors depend on microchannel plate electron multiplier arrays.
- These plates consist of large arrays of small channel electron multipliers.
- SIMS instruments typically use round arrays with about 2000 channels across a diameter.
- Each channel is 10 microns in diameter. Channels are located on 12 micron centers and the total array is 25 mm in diameter.

Surface charge on insulate sample

The surface potential of an insulator is determined by its dielectric constant \((k)\) and its thickness.

In the PHI TRIFT, the sample potential is adjusted to bring the surface potential back to 3 kV.

Total Ion Yields are typically \(10^{-2} \sim 10^{-3}\). Therefore, the secondary ion induced negative charge is very small.

The positive charge originates from implantation of positive primary beam.

Positive Charge Build-up in positive mode

Positive Charge Build-up in Negative SIMS Analysis
Effect of surface charge on mass spectra

- Loss of mass resolution — peak broaden
- Loss of spatial resolution — imaging fuzzy
- Loss of signal — peak intensity reduce

SIMS analytical modes - static and dynamic SIMS

**Static SIMS (SSIMS):**
- Typically, the low primary ion dose in the SSIMS mode is \( \leq 10^{12} \text{ ions/cm}^2 \) for mass analysis.
- Outmost surface (1-2 monolayers) affected
- Pulse mode of primary beam (short pulses of \(<1\text{ ns})
- Complete analysis before loss of surface integrity
- Elemental analysis
- Molecular information

**Dynamic SIMS (DSIMS):**
- Large primary ion dose
- Continuous mode of primary beam
- Material removal during analysis
- Elemental analysis
- No molecular information available

Charge compensation by electron flood gun

- Electron beam must be well focused
- Electron beam must be aimed at the spectrometer acceptance area

Material removal during SIMS analysis

<table>
<thead>
<tr>
<th>Magnification</th>
<th>Image width (µm)</th>
<th>Atoms (per monolayer)</th>
<th>Monolayers removed in 100s under primary ion current (nA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>1200</td>
<td>(1.4 \times 10^{13})</td>
<td>0.00005 0.0005 0.05 0.5 0.5</td>
</tr>
<tr>
<td>200</td>
<td>600</td>
<td>(3.6 \times 10^{12})</td>
<td>0.0002 0.002 0.02 0.2</td>
</tr>
<tr>
<td>500</td>
<td>300</td>
<td>(5.8 \times 10^{11})</td>
<td>0.0015 0.015 0.15 1.5</td>
</tr>
<tr>
<td>1000</td>
<td>120</td>
<td>(1.4 \times 10^{11})</td>
<td>0.005 0.05 0.5 5 5</td>
</tr>
<tr>
<td>2000</td>
<td>60</td>
<td>(3.6 \times 10^{10})</td>
<td>0.02 0.2 2 20</td>
</tr>
<tr>
<td>5000</td>
<td>30</td>
<td>(5.8 \times 10^{9})</td>
<td>0.12 1.2 12.5 125</td>
</tr>
<tr>
<td>10 000</td>
<td>12</td>
<td>(1.4 \times 10^{9})</td>
<td>0.5 5 50 500</td>
</tr>
<tr>
<td>20 000</td>
<td>6</td>
<td>(3.6 \times 10^{8})</td>
<td>2.0 20 200 2000</td>
</tr>
<tr>
<td>50 000</td>
<td>3</td>
<td>(5.8 \times 10^{7})</td>
<td>12.5 125 1250 12 500</td>
</tr>
</tbody>
</table>

Note: for a 256 x 256 pixel image with a beam spot size optimized to 100 nm diameter there is no beam spot overlap until \( \approx 5000 \) magnification. Therefore ‘damage’ occurs in the beam impact zone alone and this will be constant in that area with magnification up to \( \times 5000 \). Each damaged area will be separated by increasingly large undamaged areas as the magnification is reduced. With a 1 µm beam spot overlap occurs above magnification \( \times 500 \).
• During acquisition each primary ion should hit an undamaged area.
• Surface atomic densities are $10^{15}$ atoms/cm$^2$.
• Only 0.1% of the atomic sites should be bombarded during the measurement.
• Primary ion dose should be below $10^{15}$ ions/cm$^2$. 

SIMS analytical modes- static SIMS
Chapter 4 - Secondary Ion Mass Spectrometry (SIMS)

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- SIMS spectra, depth profiling, and imaging

Capability of SIMS
1) Identifying the elemental composition and the chemical status near the surface (1-2 monolayers) with high sensitivity (~1ppm) and high mass resolution (~9000).
2) Distinguishing the different isotopes of the same element.
3) Imaging the topography of surface using the secondary electrons.
4) Line-scanning of chemical species.
5) Mapping chemical species on the submicron scale.
6) Ultra-thin depth profiling.

SIMS can be used for surface analysis of inorganic, organic materials and biological cells, applied to conductors, insulators and semiconductors.

SIMS Spectra
High-sensitivity SIMS spectra, 40 ppm Si in the GaN film
SIMS is capable of detecting trace elements
### Detection limit for elements in Si

**Primary Ion Beam O\textsuperscript{2+} or Cs\textsuperscript{+}**

<table>
<thead>
<tr>
<th>Element</th>
<th>Detected Ion</th>
<th>Element Detection Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>1\textsuperscript{11}B\textsuperscript{+}</td>
<td>0.002 ppm, &lt;10\textsuperscript{14} atom/cm\textsuperscript{2}</td>
</tr>
<tr>
<td>P</td>
<td>3\textsuperscript{1}P/3\textsuperscript{1}P\textsuperscript{−}</td>
<td>0.1 ppm, &lt;5 \times 10\textsuperscript{15}</td>
</tr>
<tr>
<td>As</td>
<td>75\textsuperscript{As}</td>
<td>0.2 ppm, &lt;10\textsuperscript{15}</td>
</tr>
<tr>
<td>Sb</td>
<td>12\textsuperscript{1}Sb\textsuperscript{+}</td>
<td>1.0 ppm, 5 \times 10\textsuperscript{16}</td>
</tr>
<tr>
<td>C</td>
<td>12\textsuperscript{C}</td>
<td>1.0 ppm, 5 \times 10\textsuperscript{16}</td>
</tr>
<tr>
<td>O</td>
<td>16\textsuperscript{O}</td>
<td>10 ppm, 5 \times 10\textsuperscript{17}</td>
</tr>
<tr>
<td>N</td>
<td>Si\textsubscript{2}N\textsuperscript{−}</td>
<td>10 ppm, 5 \times 10\textsuperscript{17}</td>
</tr>
<tr>
<td>H</td>
<td>H\textsuperscript{−}</td>
<td>100 ppm, 5 \times 10\textsuperscript{18}</td>
</tr>
</tbody>
</table>

### Detection limit for elements in GaAs

**Primary Ion Beam: O\textsuperscript{2+} or Cs\textsuperscript{+}**

<table>
<thead>
<tr>
<th>Element</th>
<th>Detected Ion</th>
<th>Element Detection Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>H\textsuperscript{+}</td>
<td>100 ppm, 5 \times 10\textsuperscript{18} atom/cm\textsuperscript{2}</td>
</tr>
<tr>
<td>B</td>
<td>1\textsuperscript{11}B\textsuperscript{+}</td>
<td>0.01 ppm, 6 \times 10\textsuperscript{14}</td>
</tr>
<tr>
<td>Be</td>
<td>9\textsuperscript{Be}</td>
<td>0.002 ppm, 8 \times 10\textsuperscript{13}</td>
</tr>
<tr>
<td>Al</td>
<td>27\textsuperscript{Al}</td>
<td>0.2 ppm, 10\textsuperscript{18}</td>
</tr>
<tr>
<td>Si</td>
<td>30\textsuperscript{Si}</td>
<td>0.5 ppm, 2 \times 10\textsuperscript{16}</td>
</tr>
<tr>
<td>S</td>
<td>32\textsuperscript{S}</td>
<td>1.0 ppm, 5 \times 10\textsuperscript{16}</td>
</tr>
<tr>
<td>Cr</td>
<td>52\textsuperscript{Cr}</td>
<td>0.002 ppm, 8 \times 10\textsuperscript{13}</td>
</tr>
<tr>
<td>Mn</td>
<td>55\textsuperscript{Mn}</td>
<td>0.002 ppm, 10\textsuperscript{14}</td>
</tr>
<tr>
<td>Cu</td>
<td>63\textsuperscript{Cu}</td>
<td>0.2 ppm, 10\textsuperscript{18}</td>
</tr>
<tr>
<td>Zn</td>
<td>65\textsuperscript{Zn}</td>
<td>0.2 ppm, 10\textsuperscript{18}</td>
</tr>
<tr>
<td>Sn</td>
<td>113\textsuperscript{Sn}</td>
<td>0.5 ppm, 2 \times 10\textsuperscript{16}</td>
</tr>
<tr>
<td>Ge</td>
<td>68\textsuperscript{Ge}</td>
<td>0.5 ppm, 2 \times 10\textsuperscript{16}</td>
</tr>
</tbody>
</table>

---

**High resolution SIMS spectrum**

**SIMS spectrum of as-received TiO\textsubscript{2} particles**

**SIMS spectrum of silane-coated TiO\textsubscript{2} particles**
SIMS spectra - analysis of peptide

List of ion fragments [1]

<table>
<thead>
<tr>
<th>Mass/Charge</th>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hydrogen</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Oxygen</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>Silicon</td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>Carbon</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Nitrogen</td>
<td></td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td></td>
</tr>
</tbody>
</table>

SIMS spectra of peptide film, sample provided by H. Jiang

Depth profiling of SiO₂ film on the Si substrate, showing the sharp SiO₂/Si interface

SIMS Imaging

Depth profiling of the ZnO:Al/ZnO multilayers with the wavelength of 37nm, showing variation of Al content with periodic wavelength, sample provided by D. Cohen

SIMS Imaging

Chemical imaging by SIMS

25 kV Ga⁺ FIB to Prepare Metal for Imaging.
Chemical Imaging by SIMS

Example: Multilayer Cross Section TiO$_2$/SiO$_2$
- high lateral resolution < 100 nm
- parallel mapping of all elements and isotopes
- applicable to insulators

Secondary ion mass spectrometry (SIMS) images
- Chemical map of Mg$_2$MgB$_2$ composite, left: B$^+$ map, right: Mg$^+$ map; scale: 100 um; sample provided by J. Defouw
- SIMS image of organic film pattern, left: Ti$^+$ map, right: C$_2$H$_5$O$^+$ map showing the distribution of poly ethylene glycol (PEG); scale: 100um, by courtesy of J. Dalsin
- SIMS image of H modified pattern on Si substrate, scale: 10um, by courtesy of X. Chen
- SIMS image of organic film pattern (the fatty acid/thiol/Au sample), left: total ion image, middle: OH$^-$ map showing the fatty acid film; right: S$^-$ map showing the thiol film; scale: 1mm, sample provided by A. Pannier
- SIMS image of surface-modified AFM cantilever, scale: 100um, sample provided by M. Su
SIMS images

TOF-SIMS spectroscopy and imaging

• Chemical images are generated by collecting a mass spectrum at every pixel (256 x 256) as the primary ion beam is rastered across the sample surface.

• Example: elemental and molecular imaging of a cross-section of a time-release drug pellet. The map on the left is of the peak intensity at 268 Da, the molecular ion of the drug Metoprolol.

Application of SIMS in biology

Activating the Polymer Surface

A. Belu and S. Bryan, PHI
**TOF-SIMS Imaging of PET-Biotin**

Biotin
- **CN⁻**
  - m/z 26

**PFP**
- **C₆F₅O⁻**
  - m/z 183

Biotin
- **C₆H₅N₂SO₂⁺**
  - m/z 227

**PET**
- **C₇H₄O⁺**
  - m/z 104

---

**Application of SIMS in biology**

SIMS images of bio-material, showing the distribution of calcium phosphate and protein, sampled provided by B. Gotliv

- **Map of calcium phosphate**
- **Map of protein**
3D SIMS imaging

Three-dimensional map of impurities in Si matrix

3D SIMS imaging

Depth Profile of a CMOS Device

25μm x 25μm, Depth Profile

What is mass spectrometry?

Images as a Function of Depth

Acquisition Beam: 25keV Ga⁺, 25μm raster
Unbunched: 60pA
10 sec./cycle
-SIMS

Sputter Beam: 2 keV Cs⁺
300μm raster
20 sec./cycle
What is mass spectrometry?

Analytical Capabilities

<table>
<thead>
<tr>
<th>Analytical Requirements</th>
<th>XPS</th>
<th>TOF-SIMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small area analysis</td>
<td>10 µm</td>
<td>60 nm</td>
</tr>
<tr>
<td>Surface penetration</td>
<td>1-10nm</td>
<td>1Å – 3nm</td>
</tr>
<tr>
<td>Elemental identification</td>
<td>All except H, He</td>
<td>All</td>
</tr>
<tr>
<td>Quantification</td>
<td>Excellent without standard</td>
<td>Standard Required</td>
</tr>
<tr>
<td>Molecular Information</td>
<td>Functional Group Bonding</td>
<td>Some Functional Groups Molecular weight Polymer Repeat Unit Unique mass fragments</td>
</tr>
<tr>
<td>Detection Limit</td>
<td>0.1%</td>
<td>ppb - ppm</td>
</tr>
</tbody>
</table>

*No one analytical technique provides all the answers.*