Components of a Mass Spectrometer

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Mass spectrometer is an instrument that measures the mass-to-charge ratio (m/z) values and their relative abundances of ions.
Mass

Mass unit

\[ 1 \text{ u} = 1 \text{ Da} = 1.660\,540 \times 10^{-27} \text{ kg}. \]

**Molecular mass**: Exact mass of an ion or molecule calculated using the mass of the most abundant isotope of each element

**Molar mass**: Mass of one mole (6x10^{23} atoms or molecules) of a molecule/compound (i.e. isotope-averaged atomic mass for the constituent elements)
MS principle

\[ M - 2e^- \rightarrow M^+ \]

\[ M^+ \rightarrow D^+ + R^- \]
\[ M^+ \rightarrow D^+ + N \]

M$^+$ - Molecular ion; D$^+$ - Daughter ion or product ion

Only charged species are detected in MS

\[ [\text{M+nH}]^{n+}; [\text{M-nH}]^{n-}; [\text{M+Na}]^+ \]
Components of a Mass Spectrometer

**Sample Inlet**
- HPLC
- GC
- Syringe Plate
- Capillary

**Ion Source**
- Electron Ionization (EI)
- Chemical (CI)
- APCI
- APPI
- Electrospray (ESI)
- Fast Atom Bombardment (FAB)
- MALDI

**Analyzer**
- Sector
- Quadrupole
- TOF
- Orbitrap
- FTICR

**Detector**
- Photoplate
- Faraday cup
- Electron multipliers (MCP)
- Solid-State Image current

**Data collector and processor**
Sample Inlet

HPLC
GC
Syringe
Plate
Capillary
Ion source

The role of the ion source is to create gas phase ions

1) Analyte atoms and molecules are transferred into gas phase
2) Ionization

Hard (high energy) ionization and Soft (low energy) ionization

Electron Ionization (EI)
Chemical (CI)
Spray Ionization (APCI, APPI, ESI)
Desorption Ionization (FAB, MALDI, SALDI)
Gas discharge ion sources (e.g. Inductively Couple Plasma)
Ambient Ionization (DESI, LAESI)
Electron impact ionization (EI)

High energy (70 eV) ionization – fragmentation of molecules

Chemical Ionization (CI) is similar to EI except that a reagent gas is ionized first which in turn transfers charge to analyte molecules or an atom
Electrospray ionization

The exact mechanism of ion formation is still not clear
Multiple charged ions are produced
Sensitivity depends upon the flow rate of analyte solution

Very soft ionization – less fragmentation, non-covalent complex
Fast atom bombardment (FAB)

Liquid sample (matrix is mixed with sample) is bombarded with energetic atoms (Xe or Ar atoms of 10KeV); ions are generated through sputtering

Predominantly singly charged ions are formed

Chemical background due to matrix cluster ions and fragments are disadvantages

Soft ionization – fragmentation gives partial sequence information
Matrix Assisted Laser Desorption Ionization (MALDI)

Very soft ionization – good ion source for biomolecules

Sample is mixed with a matrix (light-absorbing, low-mass molecules) and excited with UV laser pulse (ns)

Different matrix molecules are used for different classes of analytes

Ionization is done at very low pressure ($<10^{-6}$ torr)
A mass analyzer is a device that can separate atoms and molecules according to their mass.

The five main characteristics for measuring the performance of a mass analyzer are:
1) the mass range limit or dynamic range
2) the analysis speed \([\text{u (mS}^{-1}]\)
3) the transmission \( = \text{No. of ion reaching the ions/No. of ions entering mass analyzer} \)
4) the mass accuracy
5) the resolution

Analyzers:
- Sector
- Quadrupole
- TOF
- Orbitrap
- FTICR
Resolution and Mass accuracy

Resolution = FWHM = $\delta m/m$

Mass accuracy = theoretical $m/z$ vs measured $m/z$ (ppm)
Sector analyzer

\[ m/z = B^2 r^2 / 2V \]

\[ F = q(E + v \times B), \]
Benefits
Double focusing magnetic sector mass analyzers are the "classical" model against which other mass analyzers are compared.

- Classical mass spectra
- Very high reproducibility
- Best quantitative performance of all mass spectrometer analyzers
- High resolution
- High sensitivity
- High dynamic range
- Linked scan MS/MS does not require another analyzer
- High-energy CID MS/MS spectra are very reproducible

Limitations

- 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
Quadrupole analyzer

\[ 2r_0 \]

Source - Lenses - Quadrupole - Detector

\[ -10 \text{ V} - 100 \text{ V} - 10 \text{ V} \ (U - V \cos \omega t) \]

\[ (U - V \cos \omega t) \]

\[ z \ x \ y \ z \]

\[ X \ \Phi_0 = U - V \cos \omega t \]

\[ xz \ plane \]

\[ yz \ plane \]

Stable along both \( x \) and \( y \)

Stable along \( y \), unstable along \( x \)
Quadrupole analyzer

Benefits

- Classical mass spectra
- Good reproducibility
- Relatively small and low-cost systems
- Low-energy collision-induced dissociation (CID) MS/MS spectra in triple quadrupole and hybrid mass spectrometers have efficient conversion of precursor to product

Limitations

- Limited resolution
- Peak heights variable as a function of mass (mass discrimination). Peak height vs. mass response must be 'tuned'.
- Not well suited for pulsed ionization methods
- Low-energy collision-induced dissociation (CID) MS/MS spectra in triple quadrupole and hybrid mass spectrometers depend strongly on energy, collision gas, pressure, and other factors.
Time-of-flight (TOF) analyzer


t^2 = \frac{m}{z} \left( \frac{L^2}{2eV_s} \right)

\begin{align*}
&\text{SOURCE} & \text{ANALYZER} & \text{DETECTOR} \\
&\text{grid} & \text{Flight tube} & \text{Positive ions} \\
&\text{matrix/sample} & & \\
&S\text{ampler holder} & V_s & +20000 \text{ V} \\
&E = \frac{V_s}{d_s} & \text{Acceleration region} & E = 0 & \text{Field-free region} \\
&d_s & L & \text{Drift path} \\
&-30000 \text{ V} & \text{Source} && \text{Detector linear mode} \\
&\text{Reflectron on} && \\
&\text{Detector reflectron mode} &
\end{align*}
Time-of-flight (TOF) analyzer

Benefits

- Fastest MS analyzer
- Well suited for pulsed ionization methods (method of choice for majority of MALDI mass spectrometer systems)
- High ion transmission
- MS/MS information from post-source decay
- Highest practical mass range of all MS analyzers

Limitations

- Requires pulsed ionization method or ion beam switching (duty cycle is a factor)
- Fast digitizers used in TOF can have limited dynamic range
- Limited precursor-ion selectivity for most MS/MS experiments
Ions of specific mass-to-charge ratio move in rings which oscillate along the central spindle. The frequency of these harmonic oscillations is independent of the ion velocity and is inversely proportional to the square root of the mass-to-charge ratio ($m/z$ or $m/q$).

Comparison of various analyzers

<table>
<thead>
<tr>
<th></th>
<th>Quadrupole</th>
<th>Ion trap</th>
<th>TOF</th>
<th>TOF reflectron</th>
<th>Magnetic</th>
<th>FTICR</th>
<th>Orbitrap</th>
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<tbody>
<tr>
<td>Mass limit</td>
<td>4000 Th</td>
<td>6000 Th</td>
<td>&gt;1000000 Th</td>
<td>10000 Th</td>
<td>20000 Th</td>
<td>30000 Th</td>
<td>50000 Th</td>
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<td>Resolution</td>
<td>2000</td>
<td>4000</td>
<td>5000</td>
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<td>FWHM (m/z 1000)</td>
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<td>Accuracy</td>
<td>100 ppm</td>
<td>100 ppm</td>
<td>200 ppm</td>
<td>10 ppm</td>
<td>&lt;10 ppm</td>
<td>&lt;5 ppm</td>
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<td>10^{-3} Torr</td>
<td>10^{-6} Torr</td>
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<td>10^{-10} Torr</td>
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<td>Tandem mass</td>
<td>Triple quadrupoles</td>
<td>MS/MS</td>
<td>—</td>
<td>PSD or TOF/TOF</td>
<td>Consecutive sectors</td>
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<td>spectrometry fragments</td>
<td>MS&lt;sup&gt;a&lt;/sup&gt;</td>
<td>MS/MS</td>
<td>—</td>
<td>MS/MS</td>
<td>MS/MS</td>
<td>MS&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>Low-energy</td>
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<td>Low-energy</td>
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<sup>a</sup> MS<sub>a</sub> stands for MS/MS combined with an additional collision step.
The role of the detectors is to convert the energy of the incoming ions into a current signal that is registered by the electronic devices and transferred to the acquisition system of MS.

- Photoplate
- Faraday cup
- Electron multipliers (MCP)
- Solid-State
- Image current (Orbitrap and FT ICR)
Electron multipliers (MCP)
MALDI or ES IONISATION

COLLISIONAL ACTIVATION

MS

MS/MS
Tandem MS ($MS^n$)

- Ion Source
- Analyzer
- Analyzer
- Detector
- Collision Cell
- Data collector and processor
Hybrid Tandem MS Instruments

Tribrid Fusion Orbitrap (Thermofisher)

Q-Tof

MALDI-TOF/TOF

Applied Biosystems, USA

C-CAMP

Centre for Cellular and Molecular Platforms
1) Mass spectrometry – Principles and applications by Edmond de Hoffmann

2) Mass spectrometry – Instrumentation, interpretation and applications by R. Ekman, J. Silberring, A. W- Brinkmalm and A. Karj