Chapter 9

Mass Spectrometry

1. Introduction

Mass spectrum is obtained by converting components of sample into gaseous ions and separating them on basis of their mass-to-charge ratios. Discriminate among masses of isotopes, e.g., exact masses are quoted to three to four figures to right of decimal point.

Sequence of taking mass spectrum:
1. Introduce/prepare sample;
2. Ionize sample (usually positive ions);
3. Select kinetic energy of ions;
4. Select mass (actually mass/charge);
5. Detect ions;
6. Record spectrum, intensity data.
II. Instrumentation in Mass Spectrometry

(A) Instrument Components

**FIGURE 9-1.** “Skoog” Fig. 18-1 (p. 422).

(B) Sample Inlet Systems

i/. Batch Inlet Systems

**FIGURE 9-2.** “Skoog” Fig. 18-2a (p. 424).
Applicable to gaseous and liquid samples with boiling points up to ca. 500°C.

ii/. Direct Probe Inlet

**FIGURE 9-2.** “Skoog” Fig. 18-2b (p. 424).
Applicable to solids and nonvolatile liquids, thermally unstable samples, or when quantity of sample is limited.

iii/. Chromatographic Inlet Systems

(C) Ionization Sources

i/. Classifications

1. *Gas-phase sources vs. desorption sources.*

2. *Hard* (e.g., electron impact) vs. *soft* (e.g., chemical ionization, desorption) sources.

ii/. Gas-Phase Sources
Restricted to thermally stable compounds that have boiling points ≤ 500°C; volatilization of sample may cause thermal degradation.
Applicable only to compounds with molecular weight < 10³ dalton.
a) Electron Impact Source

**FIGURE 9-3a.** “Skoog” Fig. 18-19 (p. 440).
Not very efficient.

\[ M + e^- \rightarrow M^+ + 2e^- \]
where \( M \) = analyte molecule
Relaxation usually takes place by extensive fragmentation.

**TABLE 9-3b.** “Skoog” Table 18-3 (p. 441).
Additional disadvantages: Molecular ion peak may disappear;

b) Chemical Ionization Source

Analyte XH ionized by collision with ions of reagent gas.
e.g.,
\[ \text{CH}_4 + e^- \rightarrow \text{CH}_4^+ + 2e^- \]
\[ \text{CH}_4^+ \rightarrow \text{CH}_3^+ + \text{H} \]
\[ \text{CH}_4^+ + \text{CH}_3^- \rightarrow \text{CH}_4^+ + \text{CH}_3^+ \]
\[ \text{CH}_3^+ + \text{CH}_4 \rightarrow \text{CH}_3^+ + \text{CH}_4 \]
\[ \text{CH}_3^+ + \text{CH}_4 \rightarrow \text{C}_2\text{H}_5^+ + \text{H}_2 \]
\[ \text{CH}_4^+ + \text{XH} \rightarrow \text{XH}_2^+ + \text{CH}_4 \text{ proton transfer} \]
\[ \text{C}_2\text{H}_5^+ + \text{XH} \rightarrow \text{XH}_2^+ + \text{C}_2\text{H}_4 \text{ proton transfer} \]
\[ \text{C}_2\text{H}_5^+ + \text{XH} \rightarrow \text{X}^+ + \text{C}_3\text{H}_5 \text{ hydride transfer} \]
Little fragmentation and contain well-defined (M + 1)^+ or (M - 1)^+ peaks.

c) Field Ionization Source

**FIGURE 9-4.** “Bauer” Fig. 16.16 (p. 477).
High electric field (10^8 V/cm) induces electron tunneling and ionization.
Little fragmentation.
Lower sensitivity.
iii/. Desorption Sources
Possible for some species having molecular weights > 10,000 dalton.
Simplified spectra, often consist of only molecular ion or protonated molecular ion.

a) Field Desorption
Ionization takes place by application of high potential.

b) Fast Atom Bombardment (FAB)
Ionized by bombardment with energetic (several KeV) xenon or argon atoms.
Both positive and negative analyte ions are sputtered from surface.

c) Spray Ionization Methods
Also make use of high electric fields to desorb ions.
Desorption is from small charged droplets of solution into an ambient gas instead of into vacuum.

   FIGURE 9-5. “Science1989.v.246.pp.64-71” Fig. 1.(p. 65).
   High field at needle tip charges surface of emerging liquid, dispersing it by Coulomb forces into fine sprays of charged droplets.
   Evaporation of solvent from each droplet decreases its diameter.
   Increased charge density on its surface tears the droplet apart, producing charged daughter droplets.
   This sequence repeats until daughter droplet becomes small enough that surface charge density is strong enough to desorb ions from droplet into ambient gas.

d) Other Desorption Methods
e.g., Secondary ion, laser desorption, plasma desorption.

(D) Mass Analyzers

i/. Introduction
Analogous to optical monochromator.
For separating ions with different mass-to-charge ratio.
Ideally, should be capable of distinguishing between minute mass differences.

ii/. Resolution of Mass Spectrometers
Resolution is defined as
\[ R = \frac{m}{\Delta m} \]
where \( m \) = nominal mass of first peak
\( \Delta m \) = mass difference between two adjacent peaks that are just resolved

For commercial spectrometers, R ranges from ca. 500 to 500,000.
iii/. Types of Mass Analyzers

a) Magnetic Sector Analyzers (Single-Focusing Spectrometers)

FIGURE 9-6. “Skoog” Fig. 18-5 (p. 427).

Kinetic energy of ion of mass m and charge z upon exiting slit B is given by

\[ KE = z e V = \frac{mv^2}{2} \]  

where \( V \) = voltage between A and B

\( v \) = velocity of ion after acceleration

\( e \) = charge of ion (1.60 x 10^{-19} C)

Magnetic force in sector,

\[ F_M = B z e v \]  

where \( B \) = magnetic field strength

Centripetal force in sector,

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

where \( r \) = radius of curvature of magnetic sector

For ion to transverse circular path to collector,

\[ B z e v = \frac{mv^2}{r} \]  

i.e., \( v = \frac{B z e r}{m} \)  

From equations (1) and (2),

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

Obtain mass spectra by varying one of three variables (B, V, or r) while holding other two constant.

Problem:

Resolving power is limited by initial spread of translational energies of ions (due to Boltzmann distribution and field inhomogeneity in source and angular divergence).

i.e., Magnetic field does not produce true mass separation but rather momentum separation (from equation (2), \( r = \frac{mv}{B z e} \)).

As a result, \( R \leq 5,000 \).

b) Double Focusing Spectrometers

To counteract effect of velocity dispersion, ion beam is first passed through electrostatic analyzer (ESA) to limit kinetic energy of ions reaching magnetic sector to closely defined range.

\[ V z e = \frac{mv^2}{r} \]  

i.e., \( r = \frac{mv^2}{E z e} \Rightarrow \text{energy separation} \).

FIGURE 9-7. “Skoog” Fig. 18-6 (p. 429).

Directional focusing in magnetic sector occurs along focal plane.
Directional focusing in magnetic sector occurs along focal plane \( d \); energy focusing occurs along focal plane \( e \).
i.e., Only ions of one m/z are double focus at intersection of \( d \) and \( e \).
High resolution \((R \leq 150,000)\).

Another double-focusing design,
FIGURE 9-8. “Skoog” Fig. 18-27 (p. 456).
Energy and directional focal planes coincide.

C) Quadrupole Mass Filters

More compact, less expensive, and more rugged.
Low scan time \(< 100 \text{ ms}\).
FIGURE 9-9. “Skoog” Fig. 18-7 (p. 430).
FIGURE 9-10. “Skoog” Fig. 18-10 (p. 432).
AC potentials, \( V \) (180° out-of-phase at each pair of rods) - cause oscillation of ion between each pair of electrodes, trajectory depending on frequency and magnitude of AC signal.
FIGURE 9-11. “Skoog” Fig. 18-8 (p. 430).
DC potentials, \( U \) - function as mass filters, since momentum of ions of equal kinetic energy \( \propto \sqrt{m} \) (or \( v \propto \sqrt{m} \)), more difficult to deflect heavier ion than lighter ion.
FIGURE 9-12. “Skoog” Fig. 18-9 (p. 431).

Resolution determined by \( U/V \) ratio and is maximum when \( U/V = 0.168 \).
Pole length \( \uparrow \Rightarrow \) Resolution \( \uparrow \).
Work up to 3,000-4,000 m/z and resolve ions that differ in mass by one unit.

D) Ion Trap Analyzers

Gaseous anions or cations can be formed and confined for extended periods by electric and/or magnetic fields.
FIGURE 9-13. “Skoog” Fig. 18-14 (p. 435).
Ions with cyclotron frequency, \( \omega_c \), equal to AC electric-field frequency (usually in radio-frequency region) will absorb energy and begin to spiral (i.e., increases in \( r \) and hence \( v \)), called ion cyclotron resonance.
\[
\omega_c = \frac{v}{r} = \frac{zeB}{m} \quad \text{(from equation (2))}
\]
Image current observed after termination of AC electric-field.

FIGURE 9-14. “Skoog” Fig. 18-13 (p. 434).
Magnitude of current depends upon number of ions; frequency of current is characteristic of m/z value of ions.
Decay of current through collisions between ions provides time domain signal.
Basis of Fourier transform mass spectrometers (FT-MS).

**FIGURE 9-15.** “Skoog” Fig. 18-15a & 18-16 (p. 436).

SubJECTED to short rf pulse that increases linearly in frequency.

Expensive, but high resolution (> 10⁶ possible).

e) Time-Of-Flight (TOF) Analyzers

Positive ions are produced as pulses and are then accelerated by electric field of 10³ to 10⁴ V.

**FIGURE 9-16.** “Skoog” Fig. 18-12 (p. 433).

In field-free drift region (length = l), all ions have same kinetic energy, but their velocities, v, vary inversely with their masses, m.

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

Flight time,

\[ t = \left( \frac{m^2l}{2zeV} \right)^{1/2} \]

\[ \therefore \quad \frac{m}{z} = 2eVt^2/l \]

Resolution, \( R < 1,000 \).

Advantages: simplicity, ruggedness, ease of accessibility of ion source, virtually unlimited mass range.

(E) Detectors

i/. Electron Multipliers

**FIGURE 9-17.** “Skoog” Fig. 18-3 (p. 425).

Rugged, reliable, and capable of providing high current gain (typically 10⁷) and nanosecond response.

Low-kinetic-energy ion beams (i.e., quadrupoles) require acceleration to several thousand eV.

ii/. The Faraday Cup

**FIGURE 9-18.** “Skoog” Fig. 18-4 (p. 426).

Response is independent of energy, mass, and chemical nature of ion.

Advantages: inexpensive and simple.

Disadvantages: longer response time and lower sensitivity.

iii/. Other Types of Detectors

e.g., Photographic plates, scintillation-type detectors.
III. Atomic Mass Spectrometry

i/ Types of Atomic Mass Spectrometry

**TABLE 9-19. “Skoog” Table 11-1 (p. 255).**

ii/. Inductively Coupled Plasma Mass Spectrometry (ICPMS)

An ICP torch serves as an atomizer and ionizer.

**FIGURE 9-20. “Skoog” Fig. 11-10 (p. 262).**

Typical performance specifications:
1. A mass range of 3 to 300;
2. Ability to resolve ions differing in m/z by 1;
3. A dynamic range of 6 orders of magnitude.

Advantages:
1. Simpler and easier to interpret than corresponding optical spectra;
2. Detection limits better than optical methods by as great as 3 orders of magnitude;
3. Ability to measure atomic isotopes.

Disadvantages:
1. Instrument costs higher than optical atomic instruments by 2 to 3 times;
2. Instrument drift can be as high as 5% to 10% per hour;
3. Interference effects.

Interferences:

1. Isobaric ions
   Isobaric ions are two elements that have isotopes having substantially the same mass.
   e.g., 40Ar⁺ with 40Ca⁺
   Because isobaric overlaps are exactly predictable from abundance tables, corrections for the problem can be carried out with appropriate software.

2. Polymeric or adduct ions
   More serious than isobaric interferences.
   e.g., 14N₂⁺ with 28Si⁺, NOH⁺ with 31P⁺, 16O₂⁺ with 32S⁺.
   A different analyte isotope may have to be used.

3. Doubly charged ions
4. Refractory oxide ions

Aries form oxides and hydroxides of the analytes and of the matrix components.

**TABLE 9-22. “Skoog” Table 11-2 (p. 266).**

Matrix Effects:
Noticeable at concomitant concentrations of greater than about 500 to 1000 µg/mL.
IV. Hyphenated Mass Spectral Methods

Mass spectrometers are coupled to efficient separatory devices.

i/. Chromatography/Mass Spectrometry

Problem: Sample in chromatographic column is highly diluted by gas or liquid carrying through column.

i.e., Require removal of diluent before introducing sample into mass spectrometer.

a) Gas Chromatography/Mass Spectrometry (GC/MS)

1. For capillary columns, column output can be fed directly into ionization chamber of mass spectrometer.

2. For packed columns, use jet separator to remove most of carrier gas from analyte.

FIGURE 9-23a. “Skoog” Fig. 25-11 (p. 621)

b) Liquid Chromatography/Mass Spectrometry (LC/MS)

Problem: Mismatch between relatively large solvent volumes from LC and vacuum requirements of MS.

Solution: Develop interfaces.

1. Effluent from column is split, with only tiny fraction being introduced directly into mass spectrometer.

2. Effluent is deposited on moving belt or wire to transport to heated chamber for removal of solvent. Analyte residues are then passed into ion source area.

3. Thermospray (TS)

Effluent is vaporized as it passes through heated capillary tube to form superheated aerosol jet. Droplets are charged by statistical fluctuations in distribution of cations and anions among droplets. Analyte is ionized through charge exchange mechanism with salt (e.g., ammonium acetate).

FIGURE 9-23b. “Anal Chem 1983, v.5, pp.750-757” Fig. 1. (p. 751)

Simple spectra, often provide only molecular weight data.
Applicable only to thermally stable compounds, polar analyte molecules, and mobile phases that dissolve salt.
Varying response to different analytes.
Need for different temperature settings for different experimental conditions.
4. Aerospray (AS)
Droplets produced by pneumatic nebulization and charged by statistical fluctuations in distribution of cations and anions among droplets, called atmospheric pressure ionization (API).
Sampling of ions into vacuum region for mass spectrometer with extensive clustering with water and other polar molecules, causing fragmentation of sample ions.

5. Electrospray (ES)
FIGURE 9-23c. "Science 1989, v.246, pp.64-71" Fig. 1. (p.65).
In TS and AS, droplet-charging results from atomization of liquid. In ES, atomization results from charging, resulting in much higher droplet charge-to-mass ratios for ES than for TS or AS, with consequent substantial increases in analytical sensitivity. ES also produces ions with more extensive multiple charging, makes possible mass analysis of high molecular weight compounds.

6. Ionspray (IS)
The API source equipped with curtain gas and declustering region is well suited for incorporation of electrospray ionization, so-called ionspray.
Permits high-flow mass analysis.

7. Matrix-Assisted Laser Desorption/Ionization (MALDI)
Desorption of proteinaceous ions in excess of 60,000Da.
Energy from laser pulse is absorbed by chromophoric matrix, which rapidly expands gas phase, entraining analyte molecules as well. UV-absorbing aromatic compounds are most commonly used as matrices, and various aromatic acids provide excellent sensitivity for forming protonated ions.

ii/. Tandem Mass Spectrometry (MS/MS)
First spectrometer serves to isolate molecular ions of various components of mixture, ordinarily equipped with soft ionization source.
These ions are then introduced one at a time into second spectrometer for further fragmentation to give daughter ions.
Or, first spectrometer is scanned while second spectrometer is set to mass of one daughter ion.
Instrumentation:
Made up of various combinations of mass separators: magnetic sectors (designated by B),
electrostatic sectors (designated by E), and quadrupole filter (designated by Q).
Most widely used tandem mass spectrometer has configuration QQQ.

**FIGURE 9-24.** “Skoog” Fig. 18-26 (p. 454).
Offer same advantages as GC/MS and LC/MS but is significantly faster.
Potentially more sensitive than hyphenated chromatographic techniques.
High cost.

V. Applications

i/. Identification and Structural Elucidation of Compounds

ii/. Determination of Molecular Concentrations

iii/. Determination of Element Concentrations
a) Based upon spark sources
b) Based upon inductively coupled plasma sources
c) Based upon glow discharge sources (by sputtering)

iv/. Isotope Abundance Studies

v/. Surface Analysis

a) Secondary Ion Mass Spectrometry (SIMS)
When focused beam of primary ion is used, called *ion microprobe analyzer*.

**FIGURE 9-25.** “Bauer” Fig. 16.18 (p. 479).
Surface layer of atoms are sputtered off by ion beam, e.g., Ar⁺, Cs⁺, N₂⁺, or O₂⁺.
Small fraction forms as positive or negative ions for mass analysis.
Surface areas between 1 mm² to 1 µm² can be investigated, depending on width of
primary-ion beam.
Depth profiling possible (depth resolution = 50 to 100 Å).
Typically, sensitivity of 10⁻¹⁵ g or better.
Applicable to nonvolatile and thermally unstable samples.

b) Laser Microprobe Mass Spectrometry
Ionization and volatilization by pulsed Nd-YAG laser.
High sensitivity (down to 10⁻²⁰ g).
Spatial resolution = ca. 1 µm²
Applicable to both inorganic and organic (including biological) samples.
FIGURE 9-1. "Skoog" Fig. 18-1 (p. 422).

FIGURE 9-2. "Skoog" Fig. 18-2 (p. 424).
FIGURE 9-3a. “Skoog” Fig. 18-19 (p. 440).

TABLE 9-3b. “Skoog” Table 18-3 (p. 441).
**FIGURE 16.16.** Schematic diagram of a typical field-ionization source.

**FIGURE 9-4.** "Bauer" Fig. 16.16 (p. 477).

**FIGURE 9-5.** "Science1989,v.246,pp.64-71" Fig. 1.(p. 65).
FIGURE 9-6. "Skoog" Fig. 18-5 (p. 427).

FIGURE 9-7. "Skoog" Fig. 18-6 (p. 429).
FIGURE 18-27. Mattacuh-Henzog type double-focusing mass spectrometer. Resolution $> 10^6$ has been achieved with more recent instruments based on this design.

FIGURE 9-8. “Skoog” Fig. 18-27 (p. 456).

FIGURE 18-7. A quadrupole mass spectrometer.

FIGURE 9-9. “Skoog” Fig. 18-7 (p. 430).

\[ U + V \cos(2\pi\omega t) \]

\[ -U - V \cos(2\pi\omega t) \]
Whether or not a positive ion strikes the rod depends upon its rate of movement along z-axis, its m/z, and frequency and magnitude of AC potential.

**FIGURE 9-10.** “Skoog” Fig. 18-10 (p. 432).

**FIGURE 9-11.** “Skoog” Fig. 18-8 (p. 430).

**FIGURE 18–10.** Voltage relationships during a mass scan with a quadrupole analyzer.

**FIGURE 18–8.** Operation of a quadrupole in the xz plane. A: Ions are focused toward z-axis; B: ions are attracted toward x-rods.
FIGURE 9-12. “Skoog” Fig. 18-9 (p. 431).

Three ions:
1. Too light
2. Just right m/z
3. Too heavy

Heavier ion is more difficult to deflect and will not respond to AC potential significantly but largely to DC potential.

FIGURE 9-13. “Skoog” Fig. 18-14 (p. 435).

FIGURE 18–14 Quadrupole acts as (a) a high-pass mass filter in the yz plane; (b) a low-pass mass filter in the yz plane; and (c) a narrow-band filter when high-pass and low-pass filters are both in operation.
FIGURE 9-14. "Skoog" Fig. 18-13 (p. 434).

FIGURE 9-15. "Skoog" Fig. 18-15a & 18-16 (p. 436).
FIGURE 9-16. “Skoog” Fig. 18-12 (p. 433).

FIGURE 9-17. “Skoog” Fig. 18-3 (p. 425).
FIGURE 18–4  Faraday cup detector. (The potential on the ion suppressor plates is adjusted to minimize differential response as a function of mass.)


<table>
<thead>
<tr>
<th>Name</th>
<th>Acronym</th>
<th>Atomic Ion Sources</th>
<th>Typical Mass Analyser</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inductively coupled plasma</td>
<td>ICPMS</td>
<td>High-temperature argon plasma</td>
<td>Quadrupole</td>
</tr>
<tr>
<td>Direct current plasma</td>
<td>DC-MS</td>
<td>High-temperature argon plasma</td>
<td>Quadrupole</td>
</tr>
<tr>
<td>Microwave-induced plasma</td>
<td>MIPMS</td>
<td>High-temperature argon plasma</td>
<td>Quadrupole</td>
</tr>
<tr>
<td>Spark source</td>
<td>SSMS</td>
<td>Radio-frequency electric spark</td>
<td>Double-focusing</td>
</tr>
<tr>
<td>Thermal ionization</td>
<td>TIMS</td>
<td>Electrically heated plasma</td>
<td>Double-focusing</td>
</tr>
<tr>
<td>Glow discharge</td>
<td>GDMS</td>
<td>Glow-discharge plasma</td>
<td>Double-focusing</td>
</tr>
<tr>
<td>Laser microprobe</td>
<td>LMMS</td>
<td>Focused laser beam</td>
<td>Time-of-flight</td>
</tr>
<tr>
<td>Secondary ion</td>
<td>SIMS</td>
<td>Accelerated ion bombardment</td>
<td>Double-focusing</td>
</tr>
</tbody>
</table>
Figure 11-10. Schematic of an ICPMS system. Dotted lines show introduction of gaseous samples; solid lines show introduction of liquid samples. (From N. J. Vola, I. R. Olson, and J. A. Claeys, Anal. Chem., 1993, 65, 3576. With permission.)

**FIGURE 9-20.** "Skoog" Fig. 11-10 (p. 262).

**FIGURE 9-21.** "Skoog" Fig. 11-12 (p. 264).

Figure 11-12. Comparison of an optical ICP spectrum for 200 ppm cerium and (b) mass ICP spectrum for 10 ppm cerium.
### TABLE 11-2 Calcium Oxide and Hydroxide Species and Other Potential Interferences in the Mass Region for Ni Determination

<table>
<thead>
<tr>
<th>m/z</th>
<th>Element</th>
<th>Interferences</th>
</tr>
</thead>
<tbody>
<tr>
<td>56</td>
<td>Fe(91.66)</td>
<td>$^{40}$ArO, $^{40}$CaO</td>
</tr>
<tr>
<td>57</td>
<td>Fe(2.19)</td>
<td>$^{40}$ArOH, $^{40}$CaOH</td>
</tr>
<tr>
<td>58</td>
<td>Ni(67.77), Fe(0.33)</td>
<td>$^{40}$CaO, NaCl</td>
</tr>
<tr>
<td>59</td>
<td>Cu(100)</td>
<td>$^{40}$CaO, $^{40}$CuOH</td>
</tr>
<tr>
<td>60</td>
<td>Ni(26.16)</td>
<td>$^{40}$CaOH, $^{40}$CaO</td>
</tr>
<tr>
<td>61</td>
<td>Ni(1.25)</td>
<td>$^{40}$CaOH</td>
</tr>
<tr>
<td>62</td>
<td>Ni(3.66)</td>
<td>$^{40}$CaO, $^{40}$NaO, NaK</td>
</tr>
<tr>
<td>63</td>
<td>Cu(69.1)</td>
<td>$^{40}$CaOH, $^{40}$ArNa</td>
</tr>
<tr>
<td>64</td>
<td>Ni(1.16), Zn(68.48)</td>
<td>$^{35}$SO$_2$, $^{34}$S, $^{40}$CaO</td>
</tr>
<tr>
<td>65</td>
<td>Cu(30.9)</td>
<td>$^{35}$SO$_2$, $^{34}$SO$_2$, $^{40}$CuOH</td>
</tr>
</tbody>
</table>


### FIGURE 9-23a. "Skoog" Fig. 25-11 (p. 621)

**FIGURE 25-11 Schematic of a jet separator.**

FIGURE 9-24. "Skoog" Fig. 18-26 (p. 454).

FIGURE 9-25. "Bauer" Fig. 16.18 (p. 479).