質量分析法の原理と活用方法（講義・実習/日本語）
Principle and application of mass spectroscopy (Lecture and Practice in Japanese)

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質量分析法では、有機化合物や無機化合物、高分子や生体分子といった多様な化合物の分子量や分子式および化学構造などの情報を得ることができる。そのため、医薬品の開発や高分子材料の創製など、応用分野は多岐にわたる。本講義では、質量分析法の原理を概説するとともに、分析装置の構成要素（イオン化部、質量分析部、検出部等）や活用方法について説明する。

Mass spectrometry is a measurement method to determine the molecular weight, molecular formula, and chemical structure of various compounds such as organic and inorganic molecules, polymers, and biomolecules. Due to its versatility, mass spectrometry is widely applied in diverse fields such as pharmaceutical research, polymer materials development, etc. In this lecture, the principles of mass spectrometry will be introduced, followed by an explanation of the key components: the ionization unit, mass analyzer, and detector. Furthermore, examples of practical applications will be presented in detail.

Principle and Application of Mass Spectrometry

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What is the definition of mass?

Mass is an intrinsic quantity of matter that does not change with location, and is one of the most important fundamental physical properties of matter.
Atoms and molecules have intrinsic mass.

C (Carbon)	**H (Hydrogen)**	**N (Nitrogen)**
^{12}C = 12.0000	^{1}H = 1.0078	^{14}N = 14.0031
O (Oxygen)	**Cl (Chlorine)**	**Na (Sodium)**
^{16}O = 15.9949	^{35}Cl = 34.9689	^{23}Na = 22.9898
Ethanol	**Glucose**	**Glycine**
C_2H_6O	$C_6H_{12}O_6$	$C_2H_5NO_2$

Water H_2O: 18.0106
Ammonium NH_4^+: 18.0338

Mass spectrometry

Mass spectrometry is a method for analyzing the structure of substances and is a method for analyzing their mass.

In mass spectrometry, molecules are ionized and then moved in an electromagnetic field. The mass of the ions is measured based on differences in this movement.

The *m/z* (a dimensionless quantity calculated by dividing the relative mass of an ion by its charge) is directly measured in mass spectrometry since the force an ion experiences in an electromagnetic field is proportional to its charge.

$$M \xrightarrow{\text{ionization}} M^{+\cdot} \quad [M+H]^+ \quad [M-H]^-_{\text{etc}}$$

M:Molecule　　　detection

Features of mass spectrometry

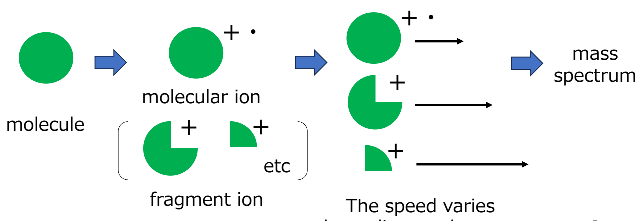
Features
・Gas, liquid, and solid samples
(Organic and inorganic compounds)
・Microanalysis
・Destructive measurement
・Combination with separation devices (GC, LC, etc).

What can be learned
・Molecular weight
・Atomic composition
・Partial molecular structure

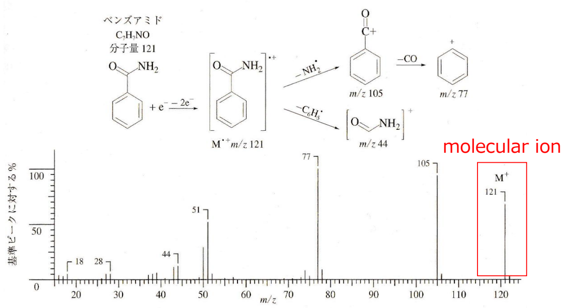
Configuration of mass spectrometer

Mass spectrometer consists of a sample introduction section, an ionization section, a mass separation section, and a detection section.

introduction section → ionization section → mass separation section → detection section



Example of mass spectrum



野村正勝ら，有機化学のためのスペクトル解析法（第2版）,化学同人，2010.

Configuration of mass spectrometer

introduction section → ionization section → mass separation section → detection section

Configuration of mass spectrometer : Introduction section

introduction section → ionization section → mass separation section → detection section

- Direct introduction: pure sample
- Gas chromatography: gaseous mixture
- Liquid chromatography: liquid mixture

  etc

Configuration of mass spectrometer : Ionization section

introduction section → ionization section → mass separation section → detection section

- Electron Impact Ionization (EI)
- Chemical Ionization (CI)
- Fast Atom Bombardment (FAB)
- Matrix-Assisted Laser Desorption/Ionization (MALDI)
- Electrospray Ionization (ESI)

  etc

Configuration of mass spectrometer : mass separation section

introduction section → ionization section → mass separation section → detection section

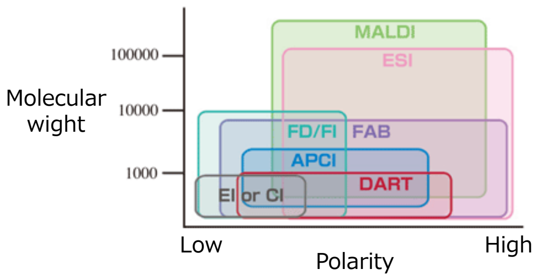
- Quadrupole type
- Time-of-flight type
- Magnetic field type
- Ion trap type
- Fourier transform type

  etc

Mass spectrometer in SUMS

- Gas Chromatograph Mass Spectrometer（GC-MS）
  ▶EI+Quadrupole type
- Matrix Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometer（MALDI-TOFMS）
  ▶MALDI+TOF type
- Inductively Coupled Plasma Mass Spectrometer（ICP-MS）

Operational scope of ionization techniques



JEOL HP: https://www.jeol.co.jp/products/scientific/lcms/DART.html

Electron Impact Ionization (EI)

Molecules can be ionized by bombarding them with a beam of electrons.

$$M + e^- \longrightarrow M^{+\cdot} + 2e^-$$

M:molecule, e^-:electron

In rare cases, divalent ions may be formed.

$$M + e^- \longrightarrow M^{2+} + 3e^-$$

Electron Impact Ionization (EI)

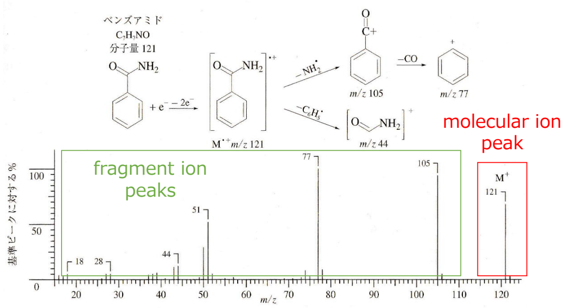
・Detected Ions: $M^{+\cdot}$, M^+

・Approximate highest integer mass measurable: 1000

・The fragment ions provide structural information.

・Ionization requires vaporization of the sample.
(Possibility of thermal decomposition, samples that do not vaporize cannot be measured)

Example of mass spectrum (EI)



野村正勝ら，有機化学のためのスペクトル解析法（第2版）,化学同人，2010.

Chemical ionization (CI)

・CI involves proton transfer or charge exchange between an ionized reactant gas and neutral molecules.

①The reactant gas (mainly hydrocarbons or NH_3) is ionized by electron impact.
②Proton transfer occurs from the ionized reactant gas, ionizing the target molecules.

*Different reactant gases are used depending on the target molecules (methane: hard ionization; isobutane and ammonia: soft ionization).

Chemical ionization (CI)

・Detected Ions: $[M+H]^+$, $[M-H]^-$, etc

・Approximate highest integer mass measurable: 1000

・Fragmentation is suppressed, resulting in a strong molecular ion signal.

・Ionization requires vaporization of the sample.
(Possibility of thermal decomposition, samples that do not vaporize cannot be measured)

Fast Atomic Bombardment (FAB)

High-speed neutral atoms (argon or xenon) are directed at a thin film of sample, ionizing the sample molecules.

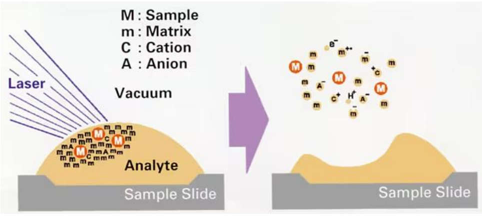
*To increase the speed of atoms such as argon, they must first be ionized in the electron gun.

Fast Atomic Bombardment (FAB)

- Detected Ions: $[M+H]^+$
- Approximate highest integer mass measurable: 3000
- Fragmentation is suppressed, resulting in a strong molecular ion signal.
- Highly polar and high molecular weight substances can be measured such as organic compounds that are difficult or impossible to vaporize.
- Disadvantages: Low solubility in the matrix (usually glycerol)

Matrix-Assisted Laser Desorption/Ionization

The matrix is excited by the laser beam.
Then, the matrix energizes the sample, causing it to be ionized and vaporized.
The external electric field removes the ionized sample from the matrix and it proceeds to the mass separation section.

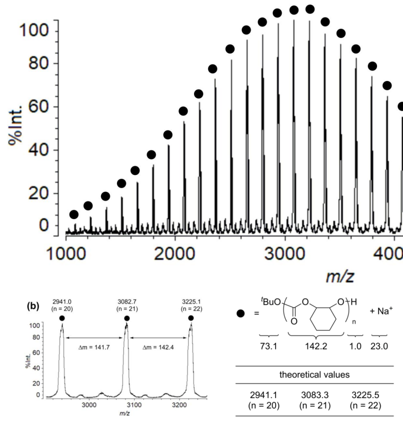


Shimadzu HP: https://www.an.shimadzu.co.jp/service-support/technical-support/analysis-basics/maldi/index.html

Matrix-Assisted Laser Desorption/Ionization

- Detected Ions: $[M+H]^+$, $[M+Na]^+$, $[M-H]^-$, etc
- Approximate maximum integer mass that can be measured: 600,000
- The optimal matrix should be used.
- Preparation of samples takes time.

Example of mass spectrum (MALDI)

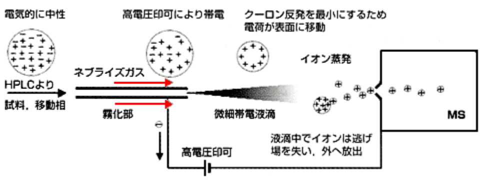


sample
1,8,9-trihydroxyanthracene : 10 mg
sodium trifluoroacetate : 10 mg
polymer : 3 mg
tetrahydrofurane : 1 mL

Y. Mori, *et al.*, *J. Polym. Sci.*, **2022**, *60*, 1416.

Electrospray ionization (ESI)

A high voltage is applied to the sample solution to generate a mist of charged droplets that are then ionized. No vaporization or heating is required.



JEOL HP: https://www.jeol.co.jp/products/scientific/lcms/DART.html

Electrospray ionization (ESI)

- Detected Ions: $[M+H]^+$, $[M+Na]^+$, etc
- Approximate maximum integer mass that can be measured: 10,000
- Samples with highly polar and high molecular weight can be measured.
- Limited types of solvents that can be used (e.g., methanol and acetonitrile).
- Less fragmentation

Application of mass spectrometry

- Low to medium molecular weight organic compounds: Pharmaceuticals, agrochemicals, natural products
- Polymeric materials: polyethylene, polyester, and etc.
- Biomolecules: nucleic acids, proteins
- Inorganic compounds

⬇

MS is used in various fields:
pharmaceuticals, pesticides, materials, food, environmental, etc.