

Chemistry 4631

Instrumental Analysis

Lecture 34



Mass Spectrometry (MS)

Instrumentation

Principle components:

- Inlet
- Ion source
- Mass analyzer
- Ion transducer
- Pumps
- Signal processor

Mass Spectrometry (MS)

Instrumentation

Transducers

Discrete dynode electron multiplier

- **Most common**
- **Designed for detection of positive ions**
- **Similar to PMT**
- **Rugged**
- **High Current gain**
- **Nanosecond response times**

Mass Spectrometry (MS)

Instrumentation

Transducers

Discrete dynode electron multiplier

Continuous dynodes held at successively higher voltages.

The cathode and dynode surfaces are coated with Cu/Be which emit electrons when struck by energetic ions or electrons.

Typically have ~ 20 dynodes with an overall gain of ~ 10^7 .

Mass Spectrometry (MS)

Discrete dynode electron multiplier

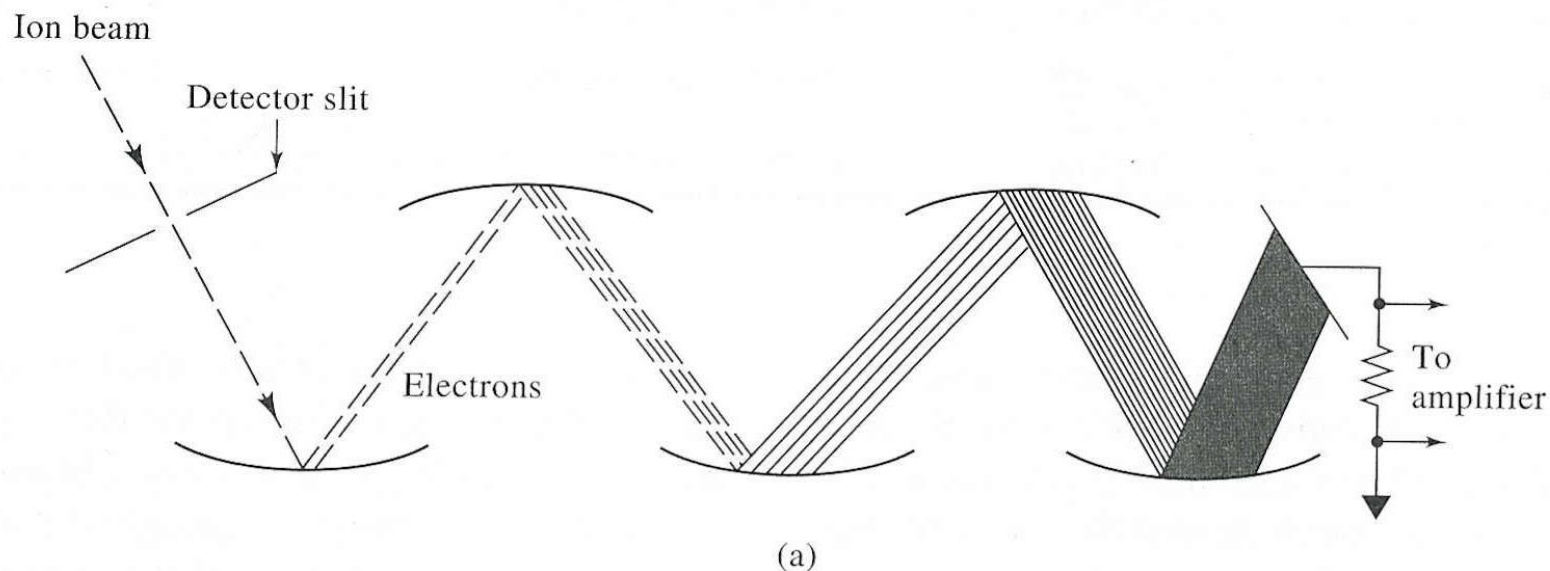


Figure 11-2 (a) Discrete dynode electron multiplier. Dynodes are kept at successively higher potentials via a multistage voltage divider. (b) Continuous dynode electron multiplier. (Adapted from J. T. Watson, *Introduction to Mass Spectrometry*, p. 247. New York: Raven Press, 1985. With permission.)

Mass Spectrometry (MS)

Instrumentation

Transducers

Continuous-dynode electron multiplier

Trumpet-shaped device made of glass doped with lead.

Ions emerging from mass analyzer are directed by a charge deflector plate into the detector.

A progressive potential of 1.8 - 2 kV is applied across the length of transducer.

Mass Spectrometry (MS)

Instrumentation

Transducers

Continuous-dynode electron multiplier

When an ion collides with the lead oxide coating on the detector walls, electrons are emitted.

With each strike on the detector walls the total emitted electrons are multiplied (amplification) and accelerated down the tube.

Gain $\sim 10^5$

Mass Spectrometry (MS)

Continuous-dynode electron multiplier

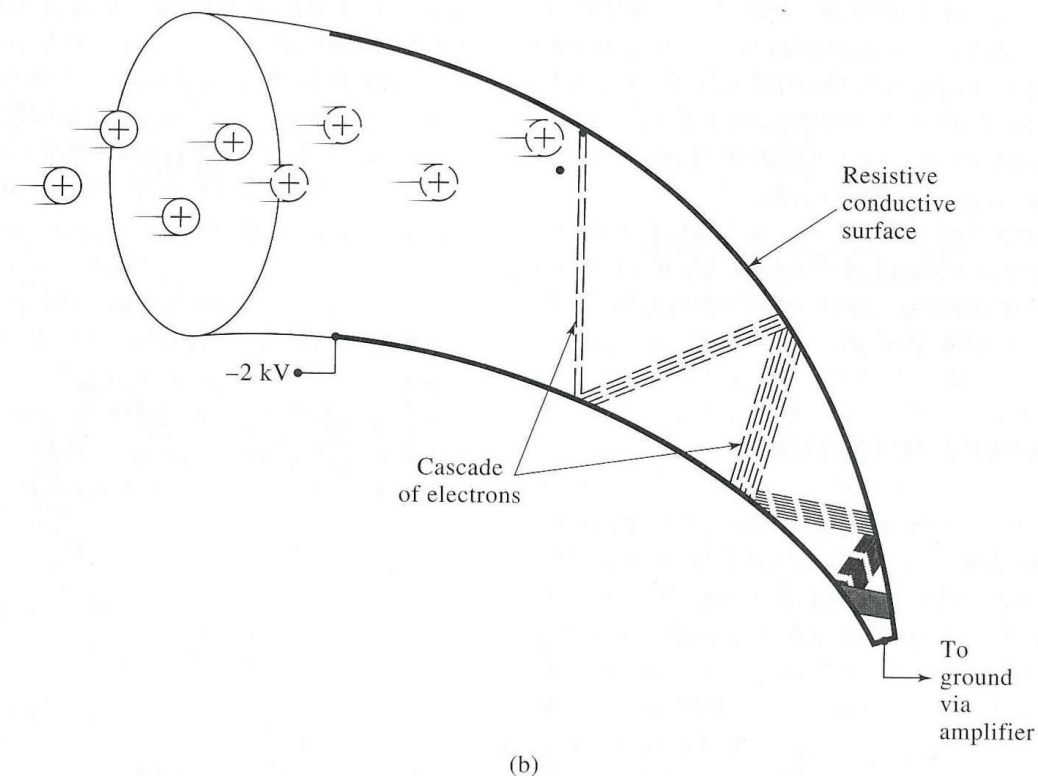


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Mass Spectrometry (MS)

Instrumentation

Transducers

Faraday Cup

Ions strike a collector electrode surrounded by a cage to prevent escape of reflected ions or secondary electrons.

The collector and cage are connected to ground through a large resistor.

Charge of positive ions striking plate is neutralized by flow of electrons from ground through the resistor.

The resulting potential drop across the resistor is amplified.

Mass Spectrometry (MS)

Faraday Cup

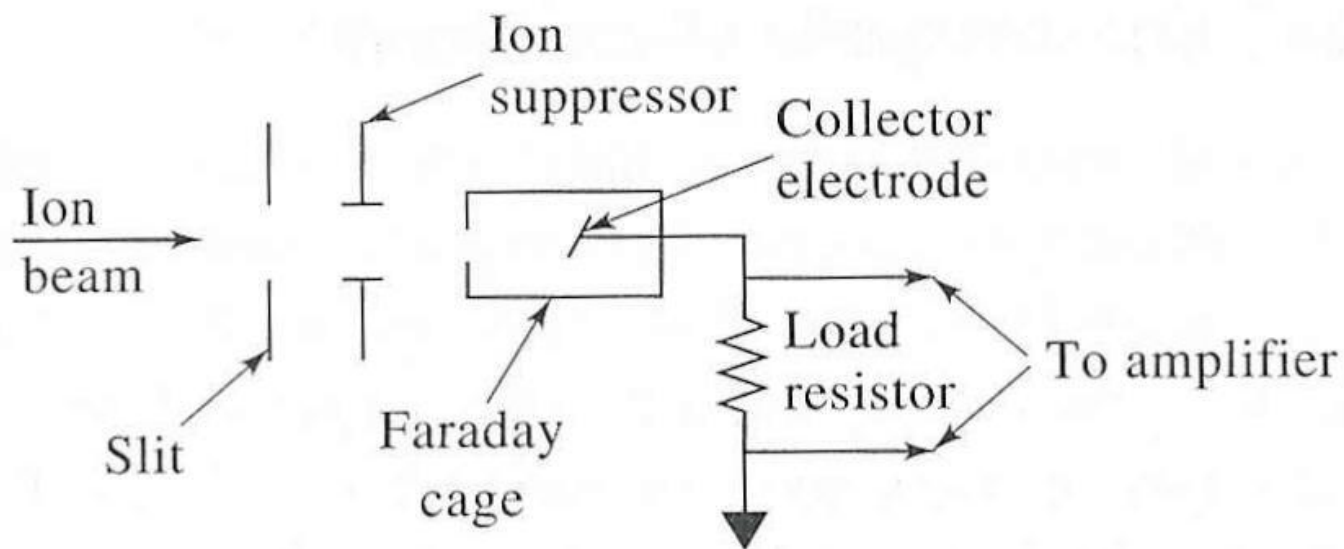


Figure 11-3 Faraday cup detector. The potential on the ion suppressor plates is adjusted to minimize differential response as a function of mass.

Mass Spectrometry (MS)

Instrumentation

Transducers

Faraday Cup

Response is independent of energy, mass, chemical nature of the ions.

Advantages

- Inexpensive
- Simple mechanically and electrically

Disadvantages

- Speed is limited by high-impedance amplifier
- Less sensitive since no internal amplification

Mass Spectrometry (MS)

Instrumentation

Principle components:

- Inlet
- Ion source
- Mass analyzer
- Ion transducer
- Pumps
- Signal processor

Mass Spectroscopy (MS)

Mass Spectrum

The pattern of ion intensities is characteristic (fingerprint) of the original molecule.

Mass Spectroscopy (MS)

Definitions

Resolving power is defined as $M/\Delta M$, where M is an m/z value and ΔM is the difference between M and the next highest m/z that can be distinguished from M .

Resolution is defined as $\Delta M/M$, the inverse of resolving power. It is usually expressed as ΔM at M in parts-per-million units.

Sensitivity is the ability of the system to measure small quantities of materials. Most MS can detect less than 10^{-11} g of a compound.

Mass Spectroscopy (MS)

Definitions

Scan Rate – typically 10 scans per second over the selected m/z range.

Scan range – the range of m/z values selected.

Mass range – the range of m/z over which data can be acquired.

Mass accuracy – typically 0.3 m/z units.

Mass Spectroscopy (MS)

Definitions

Molecular ions – the ion produced by removing an electron from the molecule.

Mass is equal to the sum of the atomic masses of the most abundant isotope of each element that makes up the molecule.

The peak with the highest m/z value may not be the molecular ion peak.

Ion addition reactions or isotopes can produce ions with higher m/z .

Mass Spectroscopy (MS)

Definitions

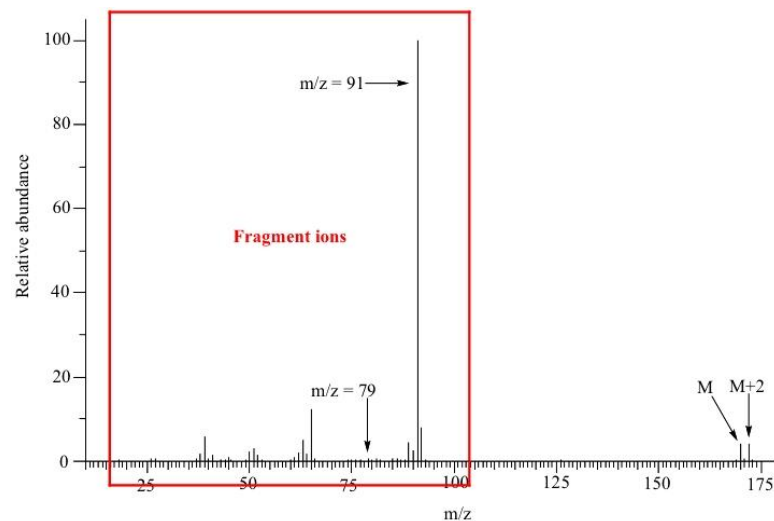
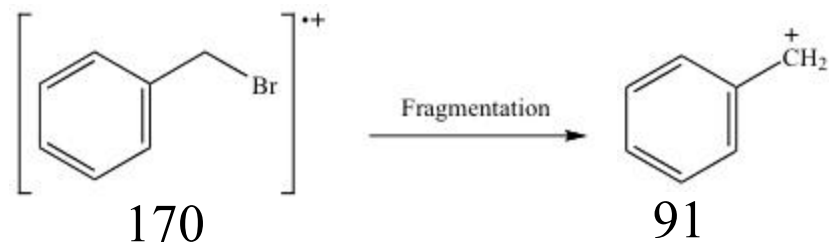
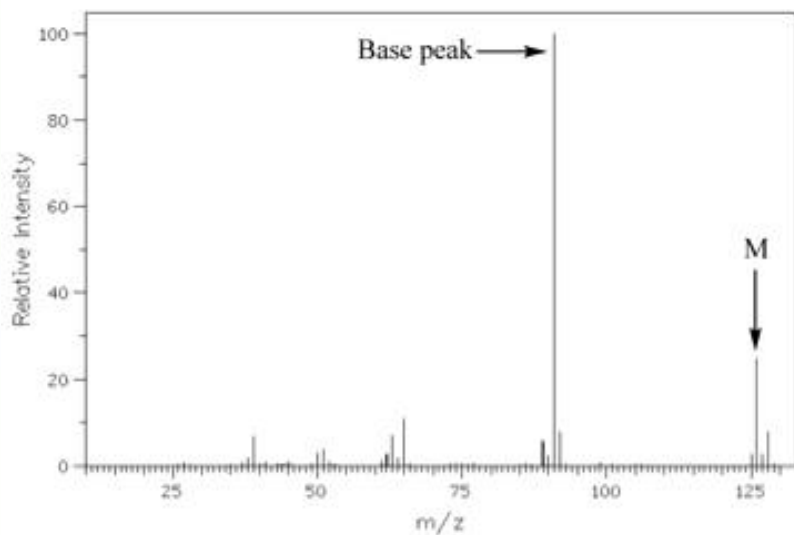
Base peak – the most intense peak in the spectrum. Represent stable ions that retain much of the structure of the original compound. The mass spectrum is normalized to the base peak (0 – 100).

Neutral fragment – does not appear in the spectrum, but its mass can be implied by the difference in mass between the molecular ion and the product ion.

Characteristic ions – ions produced for compound classes that guide interpretation.

Mass Spectroscopy (MS)

Definitions



Mass Spectroscopy (MS)

Definitions

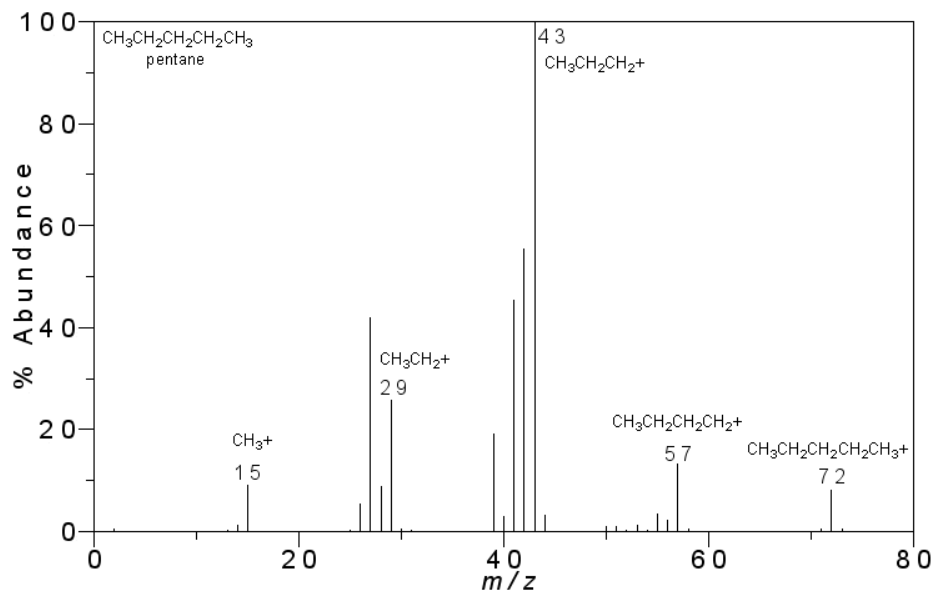


Table 5. Typical fragments lost from straight chain alkanes.

Mass Lost	Fragment Lost
1	$\text{H}\cdot$
2	$2 \text{H}\cdot$
15	$\text{CH}_3\cdot$
29	$\text{C}_2\text{H}_5\cdot$
43	$\text{C}_3\text{H}_7\cdot$ -or- C_2H_4 & $\text{CH}_3\cdot$
57	$\text{C}_4\text{H}_9\cdot$ -or- C_2H_4 & $\text{C}_2\text{H}_5\cdot$
71	$\text{C}_5\text{H}_{11}\cdot$ -or- C_3H_6 & $\text{C}_2\text{H}_5\cdot$

Mass Spectrometry (MS)

Applications of MS

- **MW determination**
- **Isotope ratios** (determining the relative abundance of the isotopes and measure of their exact masses)
- **Structural determination**
- **Compound identification**
- **Quantitative analysis**

Mass Spectrometry (MS)

Applications of MS

- **Quantitative analysis** (For small amounts – as little as 10^{-12} g, 10^{-15} moles; compounds identified at very low concentrations (one part in 10^{12}) in chemically complex mixtures) (Within an accuracy of 0.01% of total weight of sample and within 5 ppm for small organic molecules)

Mass Spectrometry (MS)

Since Tandem MS involves three distinct steps of selection-fragmentation-detection, the separation of these three steps can be realized in space or in time.

Tandem MS in space

Typical Tandem MS in space instruments include QqQ, QTOF, and hybrid ion trap/FTMS, etc.

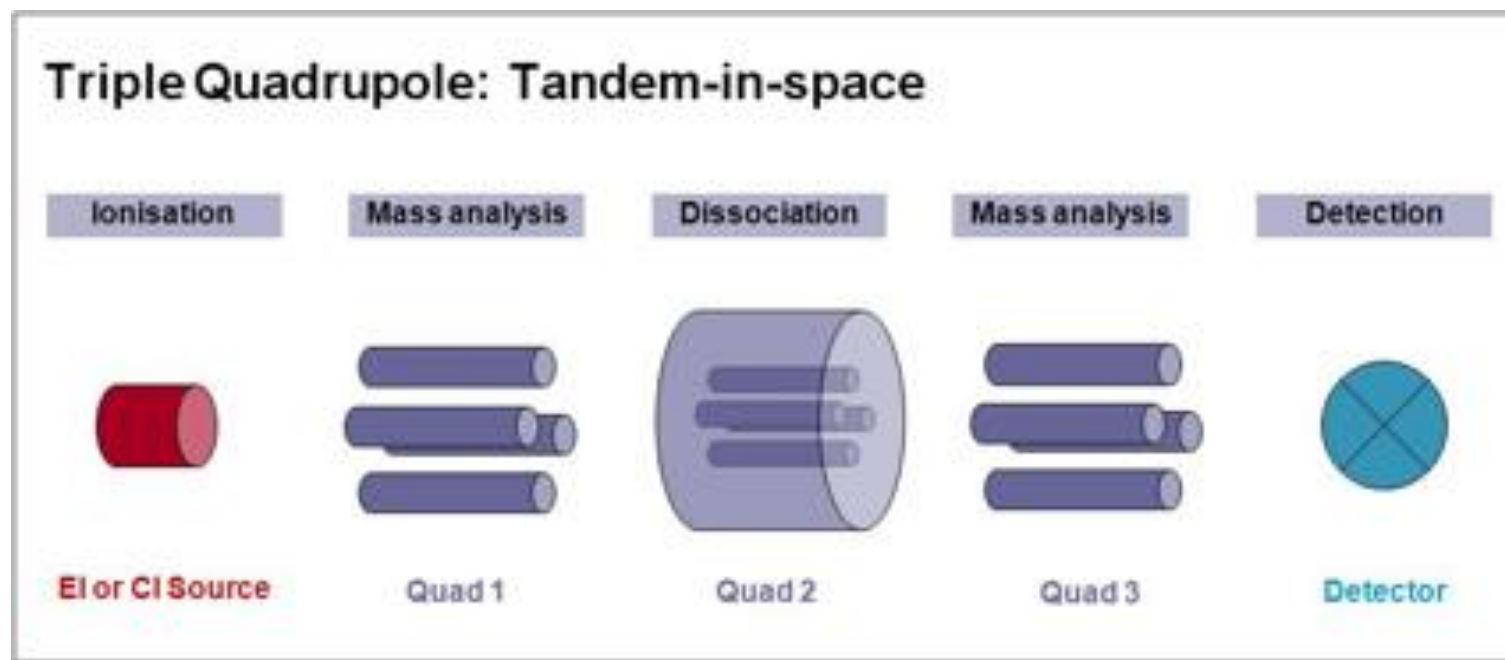
Tandem-in-Time MS/MS

Typical Tandem-in-Time MS/MS instruments include ion trap and FT-ICR MS.

Mass Spectrometry (MS)

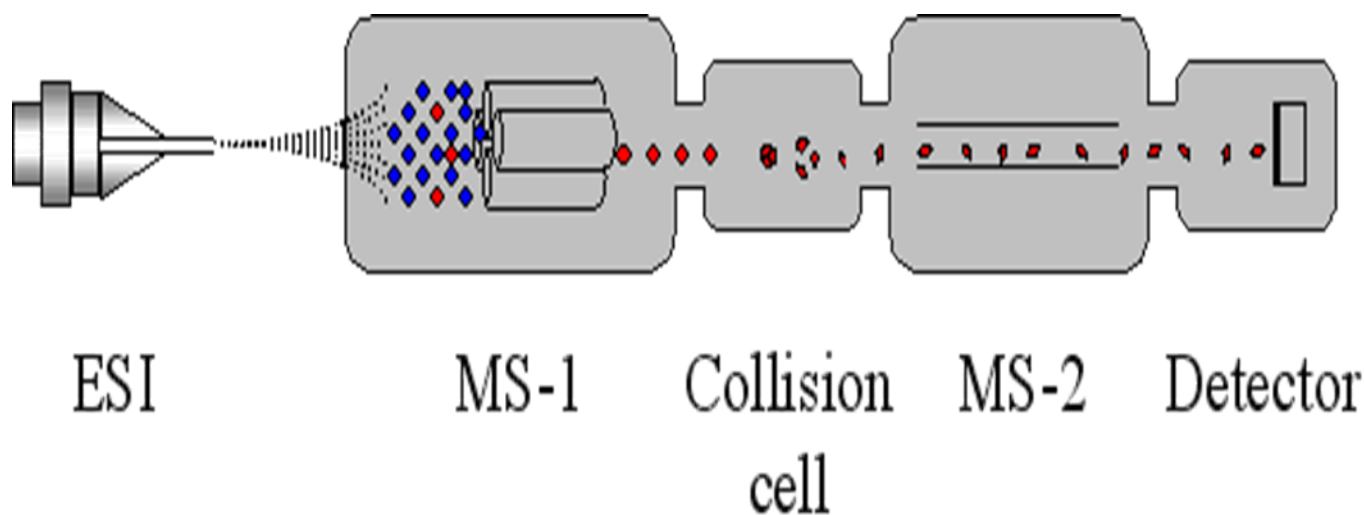
Tandem MS in space

QqQ (Triple Quadrupole)



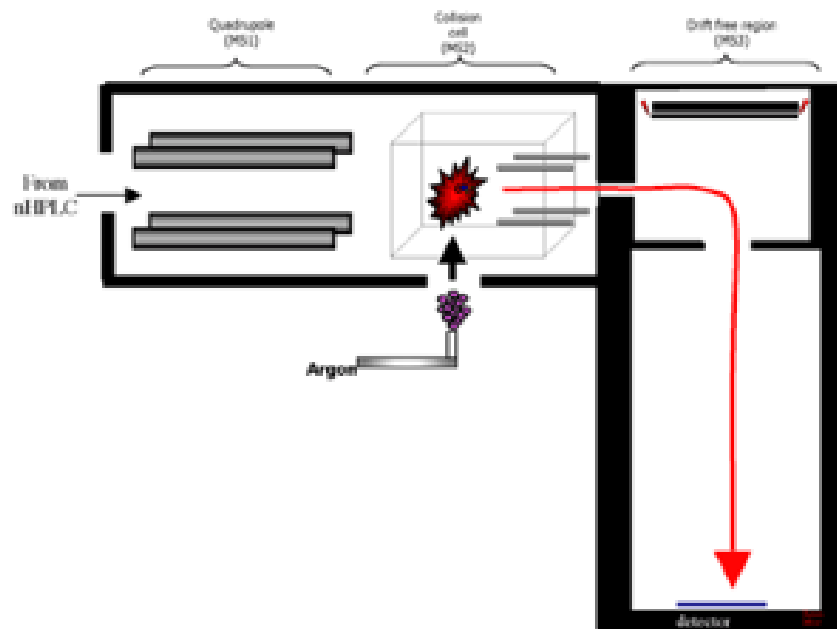
Mass Spectrometry (MS)

Three Quadrupoles (Quad 1, Quad 2, and Quad 3) are lined up in a row. Precursor ions are selected in Quad 1 and sent to Quad 2 for dissociation (fragmentation). The generated product ions are sent to Quad 3 for mass scanning.



Mass Spectrometry (MS)

QTOF (Quadrupole Time-of-flight)



In the QTOF, precursor ions are selected in the Quadrupole and sent to the Collision Cell for fragmentation. The generated product ions are detected by time-of-flight (TOF) mass spectrometry.

Mass Spectrometry (MS)

Tandem Mass Spectrometry (MS–MS)

Collision-Induced Dissociation (CID)

To obtain structural information, analyte ions are fragmented by colliding them with neutral molecules (CID).

Voltages are applied to the analyte ions to add energy to the collisions and create more fragments.

Mass Spectrometry (MS)

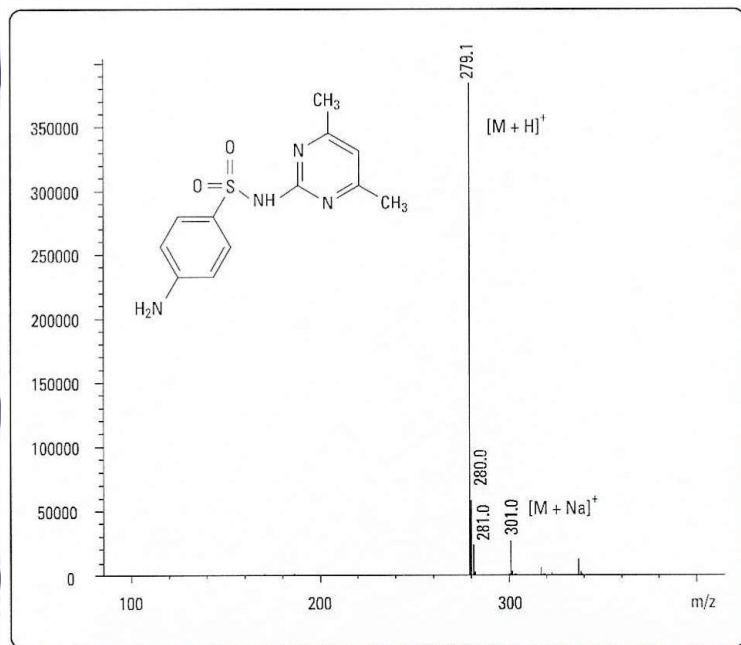


Figure 13. Mass spectrum of sulfamethazine acquired without collision-induced dissociation exhibits little fragmentation

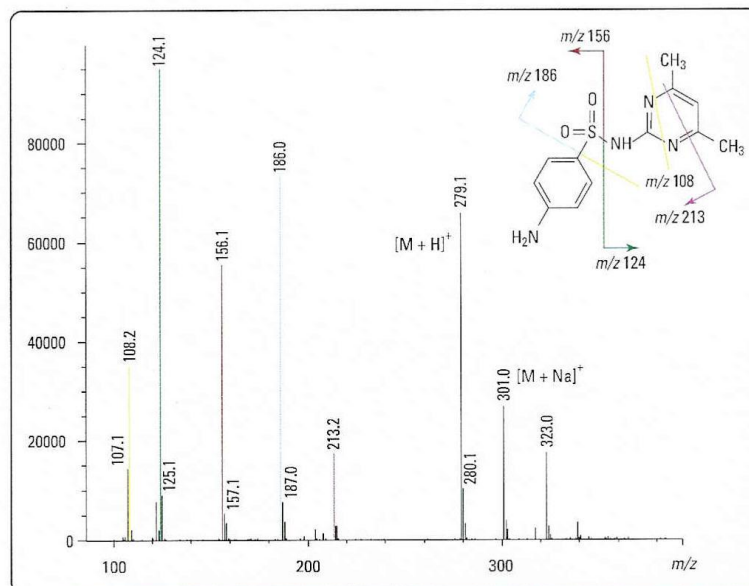


Figure 14. Mass spectrum of sulfamethazine acquired with collision-induced dissociation exhibits more fragmentation and thus more structural information

Mass Spectrometry (MS)

Tandem Mass Spectrometry (MS–MS)

The Triple Quadrupole

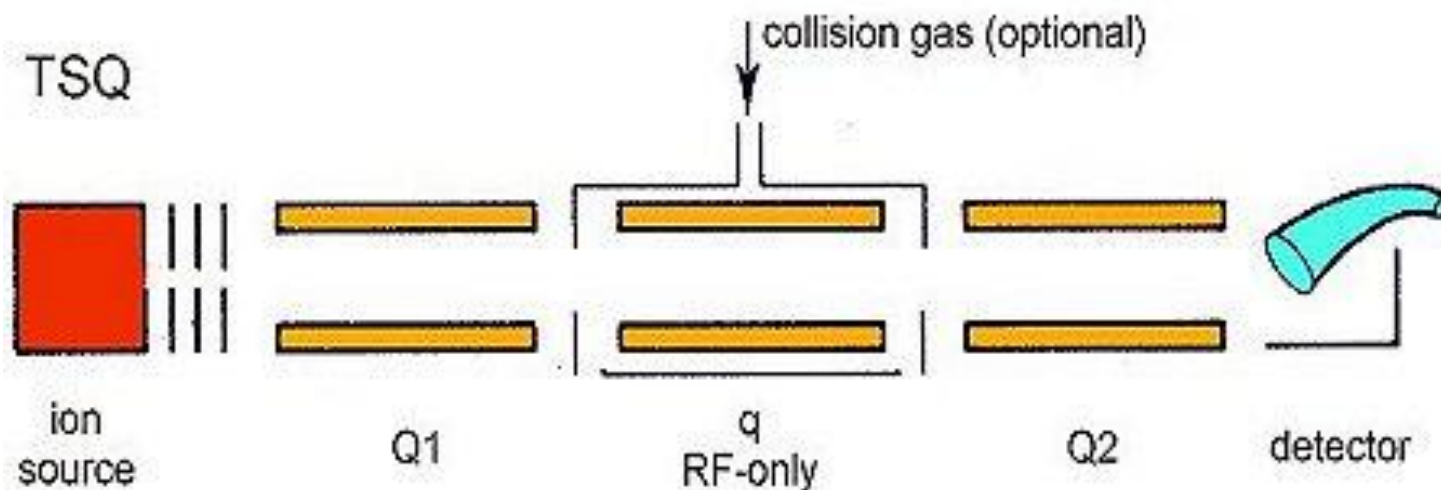
This is probably the most widely used MS–MS instrument.

The hardware, as the name suggests, consists of three sets of quadrupole rods in series.

Mass Spectrometry (MS)

The Triple Quadrupole

Triple quadrupole instruments allow MS/MS experiments to be made with ease. For this purpose, Q1 is used for mass analysis, q for fragmentation (RF-only quadrupole) and Q2 for mass analysis of ions produced within the q region.



Mass Spectrometry (MS)

Triple Quadrupole

The second set of rods is not used as a mass separation device but as a collision cell, where fragmentation of ions transmitted by the first set of quadrupole rods is carried out, and as a device for focusing any product ions into the third set of quadrupole rods.

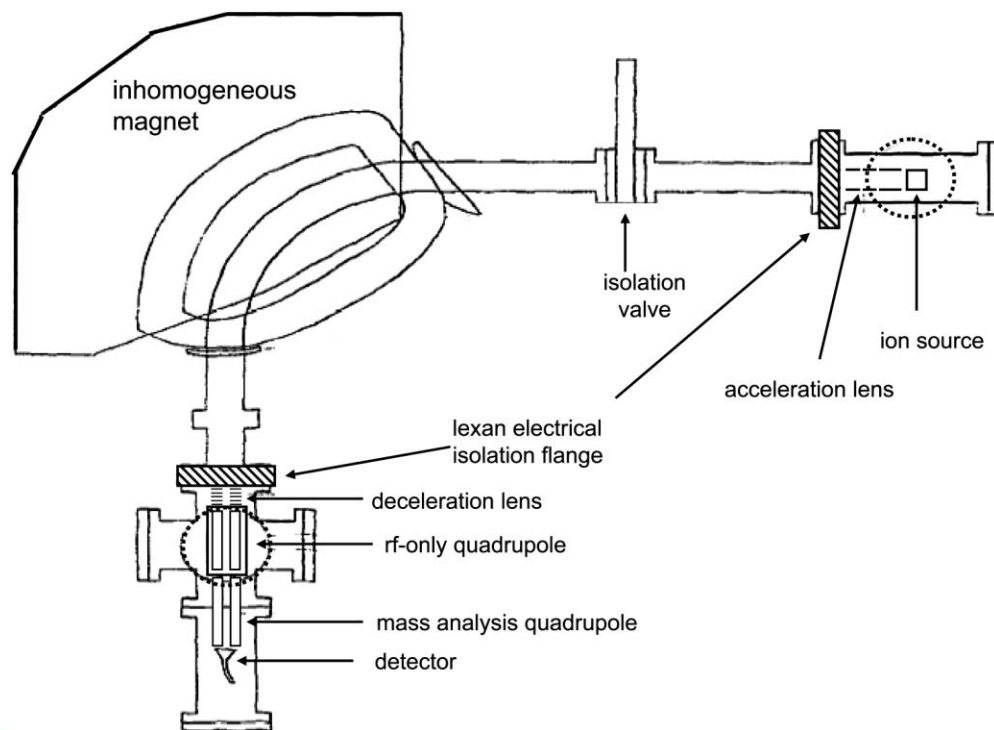
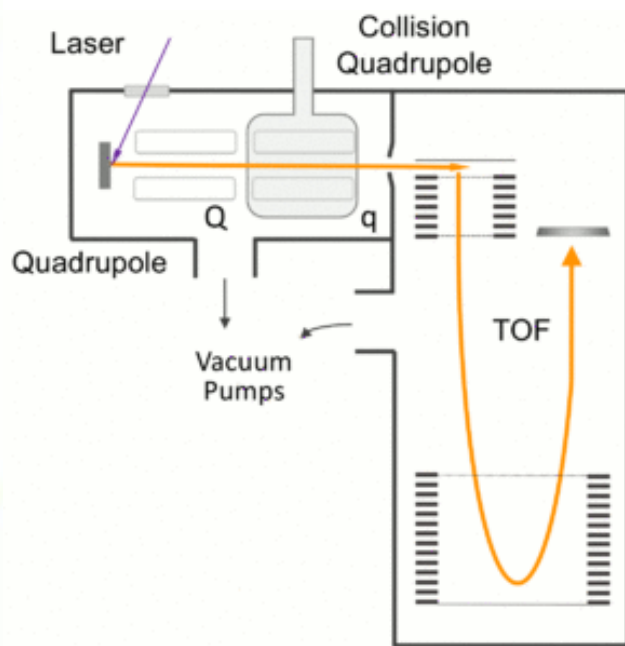
Both sets of rods may be controlled to allow the transmission of ions of a single m/z ratio or a range of m/z values to give the desired analytical information.

Mass Spectrometry (MS)

The Hybrid Mass Spectrometer

When a quadrupole of a triple quadrupole is replaced by another mass analyzer, the instrument is termed a hybrid.

There are many variations.

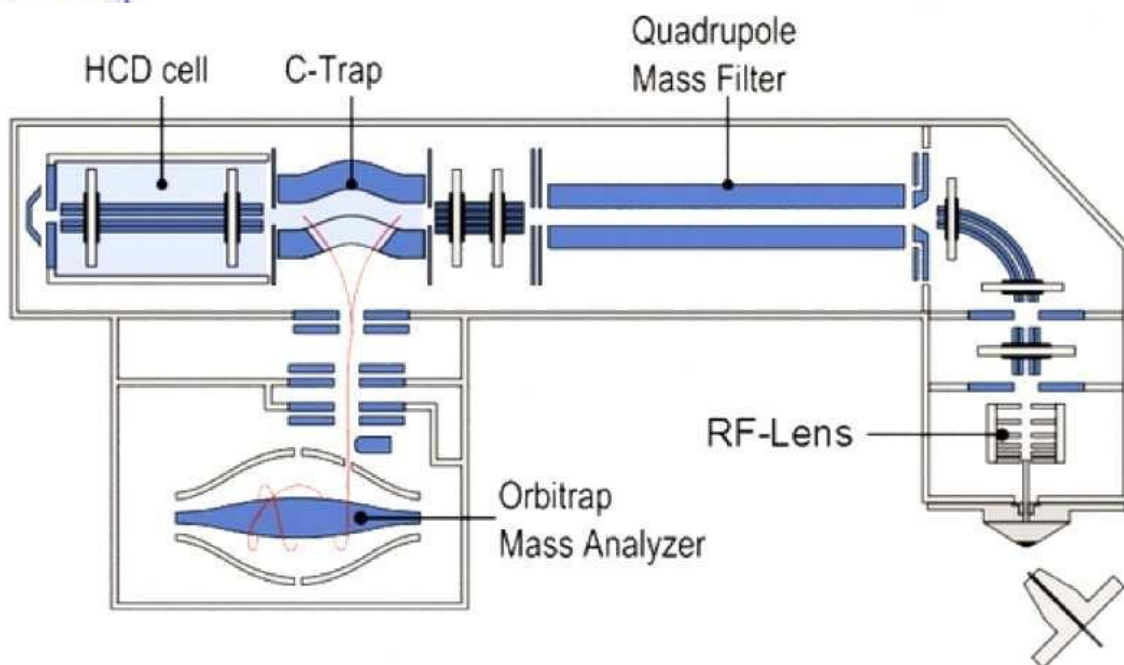
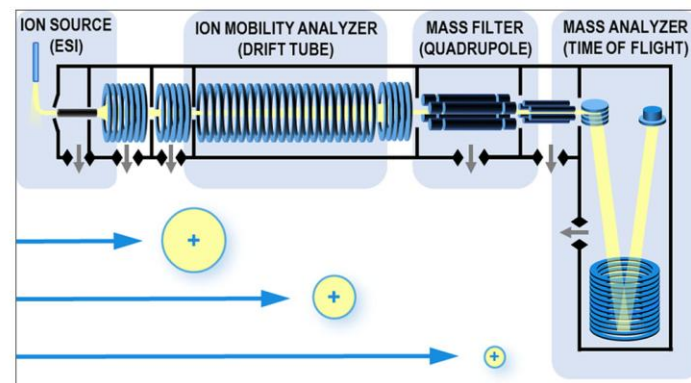


Mass Spectrometry (MS)

The Hybrid Mass Spectrometer

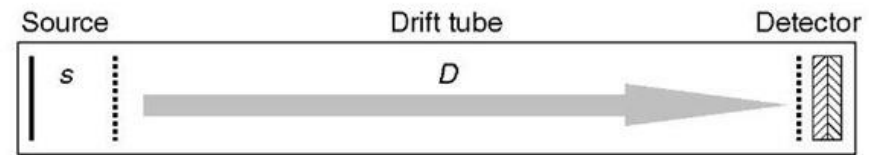
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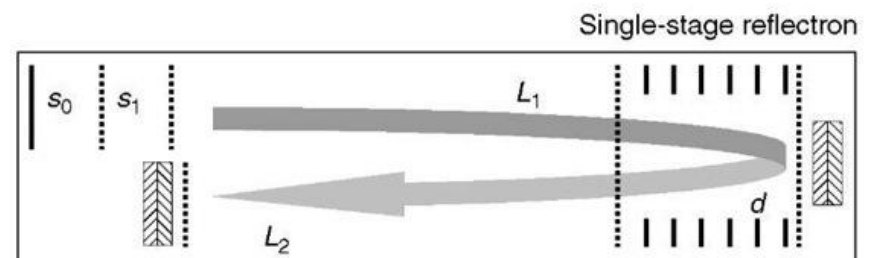


Mass Spectrometry (MS)

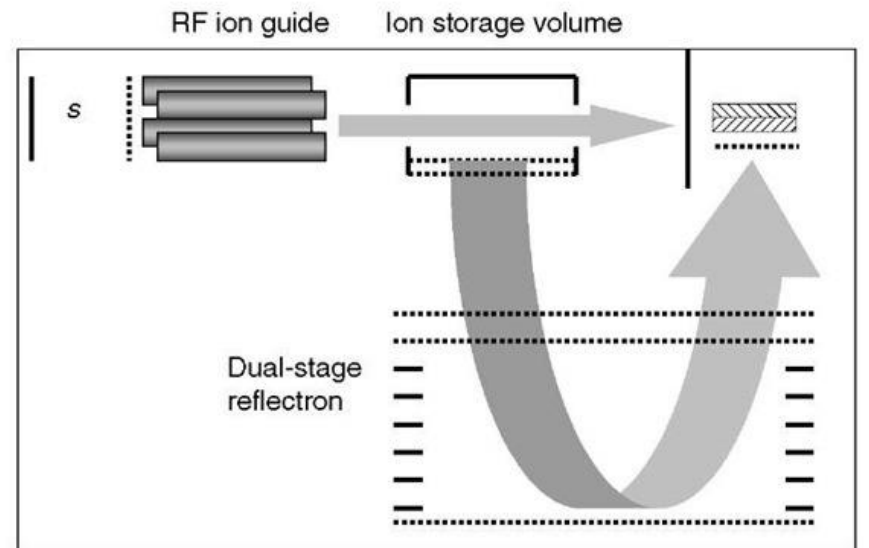
Basic configurations of time-of-flight mass spectrometers: (a) a simple linear TOF mass analyzer with a single-stage ionization source, (b) a reflectron TOF mass analyzer with a dual-stage ion extraction source, and (c) an orthogonal acceleration mass analyzer with a quadrupole ion guide and a dual-stage reflectron



(a)



(b)



(c)

Mass Spectrometry (MS)

Instrumentation can be simple to very complex.

Hopefully, you now have the tools to continue your knowledge of instrumental design, theory, and use.

Never stop learning. Always be curious.

Keep exploring all the different scientific instruments that are out there – and maybe invent a few of your own 😊

Assignment

- Read Chapter 11
- HW 18 Chapter 11: 2, 4, 5, 7
- HW 18 Due 04/27/26

- Read Chapter 20
- HW 19 Chapter 20: 1-5, 7-11, 17
- HW 19 Due 04/29/26

- Test 4 - Lectures 24-31 Monday April 27th

- Final – ACS Exam Wednesday May 6th 7:30 am to 9:30 am
(Note early start time)

Mass Spectrometry (MS)

Instrumentation

Transducers

Photographic plates – used with spark source instruments

Scintillation-type (produces flashes of light detected by PMT)

Mass Spectrometry (MS)

Instrumentation

Pumps

Mass Specs operates in a vacuum.

Pumps - Rough pumps

Takes pressure down to $\sim 10^{-2}$ torr

Mass Spectrometry (MS)

Instrumentation

Pumps - Oil Diffusion Pump

Diffusion pump oil is boiled and vapor rises and condenses on chamber wall.

The first downward flow of oil vapor collides with gas from MS and compresses it in bottom of chamber.

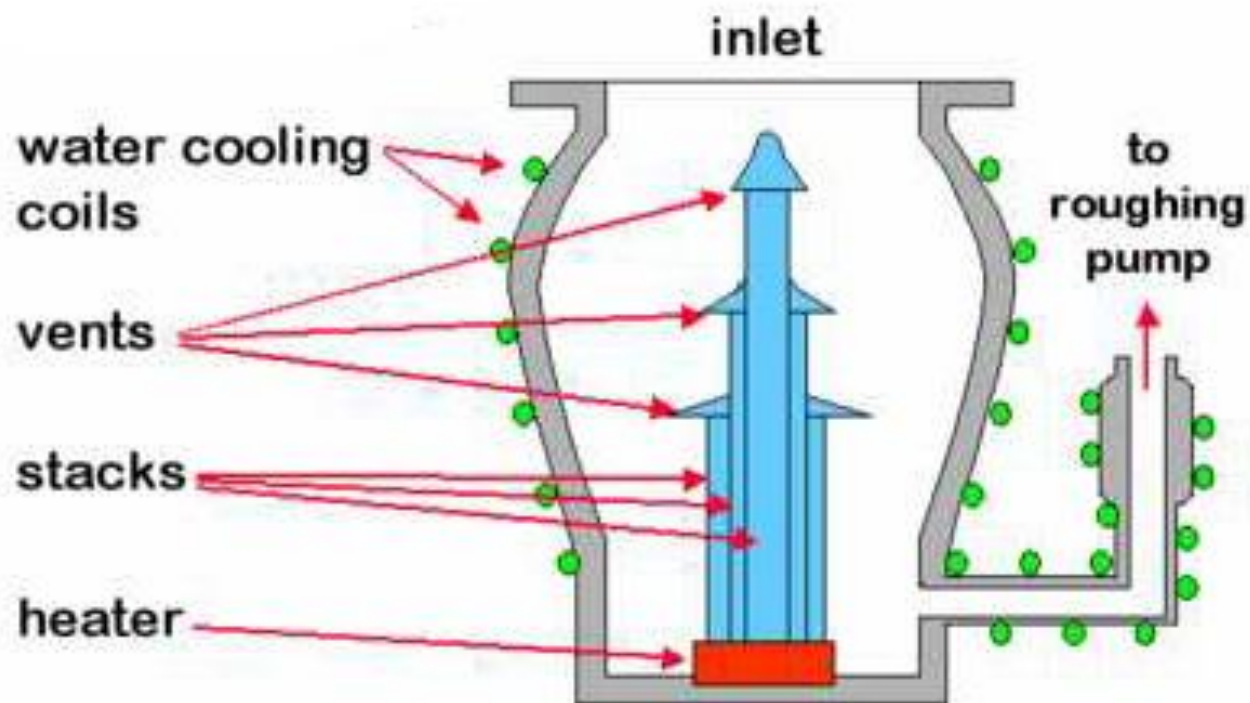
Rough pump removes gases from bottom.

Inexpensive – but if rough pump fails oil vapor can contaminate MS.

Mass Spectrometry (MS)

Instrumentation

Pumps - Oil Diffusion Pump



Mass Spectrometry (MS)

Instrumentation

Pumps - Turbo Pump

Composed of a set of fans similar to a jet engine.

Alternate sets of blades rotate while others are stationary.

Blades turn at speeds over 20,000 revolutions per minute.

Molecules collide with the blades and are deflected downward and removed by rough pump.

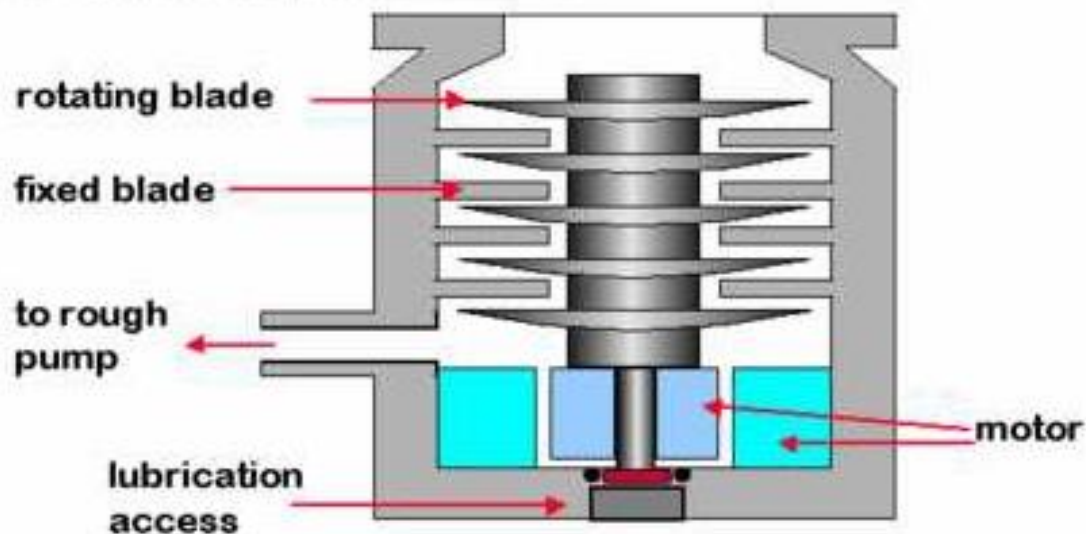
Advantage – quick startup and shutdown.

Disadvantage – expensive.

Mass Spectrometry (MS)

Instrumentation

Pumps - Turbo Pump



Mass Spectrometry (MS)

Instrumentation

Pumps – Cryo Pump

Work by condensing or adsorbing gas molecules on a cold surface. Typically cooled to below $-150\text{ }^{\circ}\text{C}$. To get to ultra-high vacuum need a cryo pump after the turbo pump. Turbo pumps get to low vacuum quickly, cryo pumps keep it there.

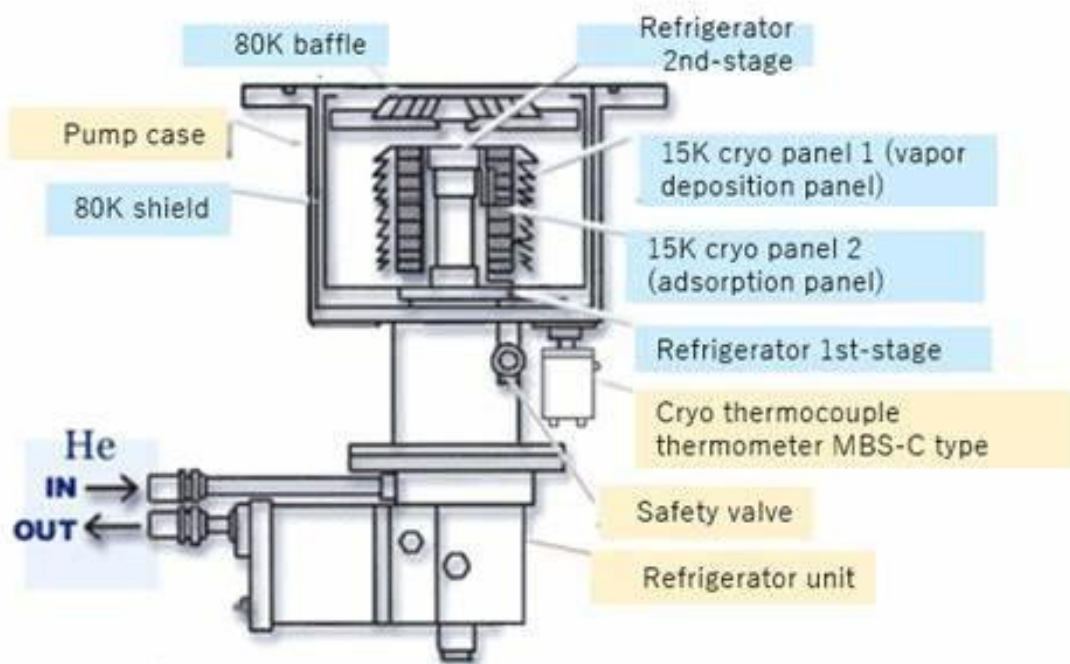
Advantage – minimal maintenance.

Disadvantage – more expensive, do need to be regenerated periodically, refill with He daily.

Mass Spectrometry (MS)

Instrumentation

Pumps - Cryo Pump



Mass Spectrometry (MS)

TABLE 20-5 Applications of Molecular Mass Spectrometry

1. Elucidation of the structure of organic and biological molecules
2. Determination of the molecular weight of peptides, proteins, and oligonucleotides
3. Identification of components in thin-layer and paper chromatograms
4. Determination of amino acid sequences in sample of polypeptides and proteins
5. Detection and identification of species separated by chromatography and capillary electrophoresis
6. Identification of drugs of abuse and metabolites of drugs of abuse in blood, urine, and saliva
7. Monitoring gases in patient's breath during surgery
8. Testing for the presence of drugs in blood in thoroughbred racing horses and in Olympic athletes
9. Dating archaeological specimens
10. Analyses of aerosol particles
11. Determination of pesticide residues in food
12. Monitoring volatile organic species in water supplies

Mass Spectrometry (MS)

Tandem Mass Spectrometry (MS–MS)

The two analyzers (MS-MS) can be separated by a collision cell (can be another MS) into which an inert gas (e.g. argon, xenon) is admitted to collide with the selected sample ions and bring about their fragmentation.

Tandem MS have the ability to perform multiple steps on a single sample.

The MS selects a specific ion, fragment the ion, and generate another mass spec – able to repeat the cycle several times.

Mass Spectrometry (MS)

Tandem Mass Spectrometry (MS–MS)

The two stages of mass spectrometry are related in specific ways in order to provide the desired analytical information.

There are a large number of different collision-induced dissociation MS–MS experiments that can be carried out but the four most widely used are

- (i) the product-ion scan,
- (ii) the precursor-ion scan,
- (iii) the constant-neutral-loss scan, and
- (iv) selected decomposition monitoring.