Components of a Mass Spectrometer

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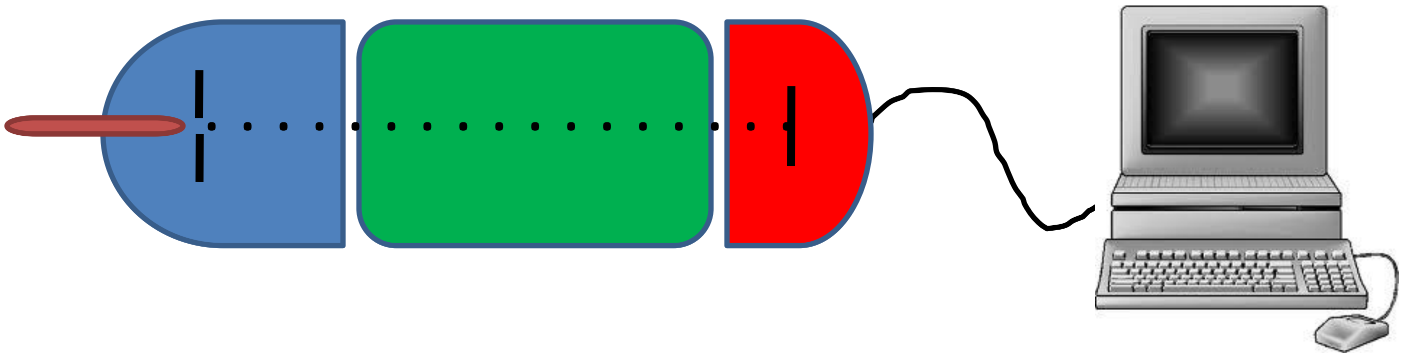
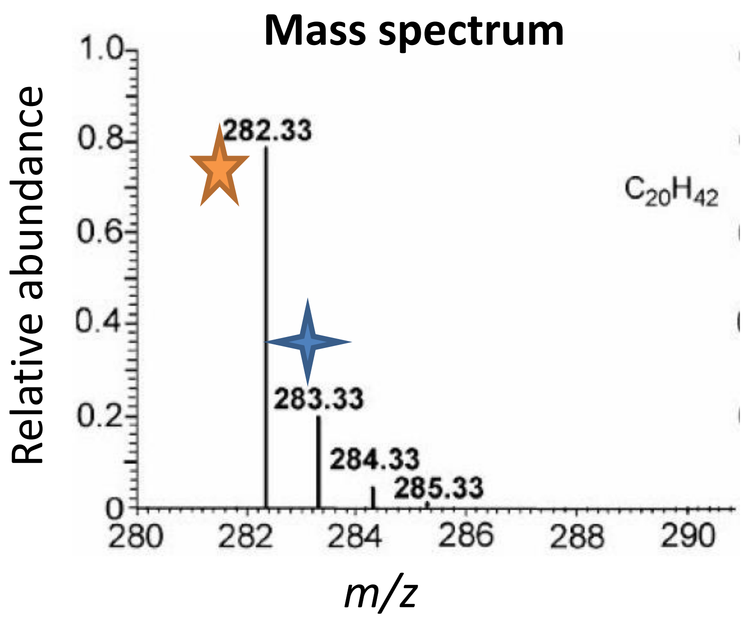
Mass spectrometer

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





m/z – mass to charge ratio

Base peak

Isotopic peak

Molecular ion

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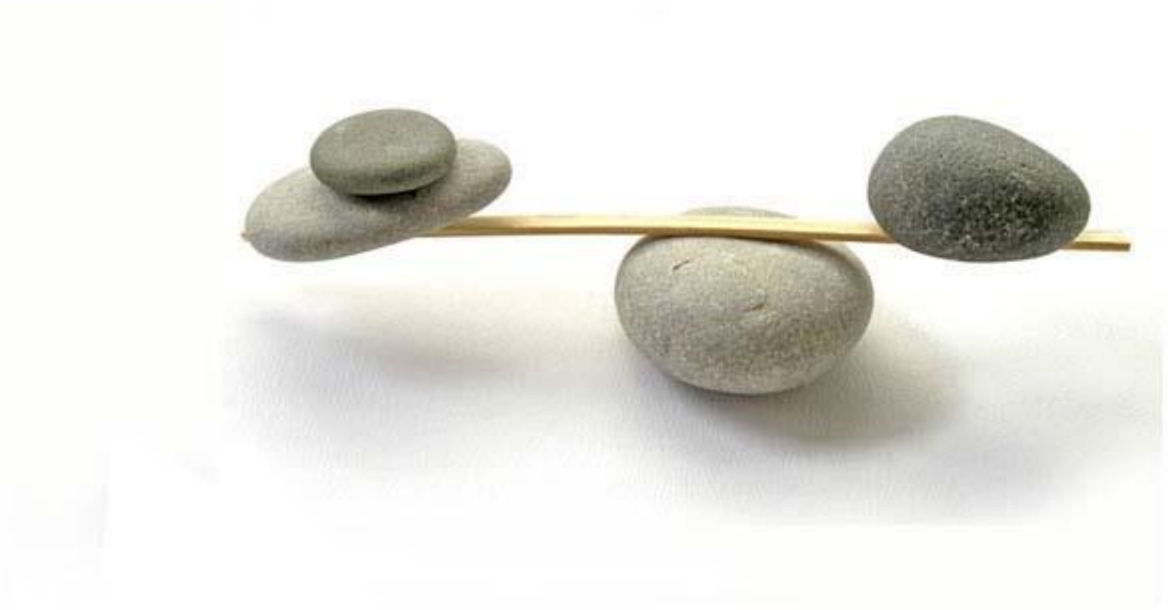
Mass



Mass unit $1\ u = 1\ Da = 1.660\ 540 \times 10^{-27}\ kg.$

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 (6×10^{23} atoms or molecules) of a molecule/compound (i.e. isotope-averaged atomic mass for the constituent elements)

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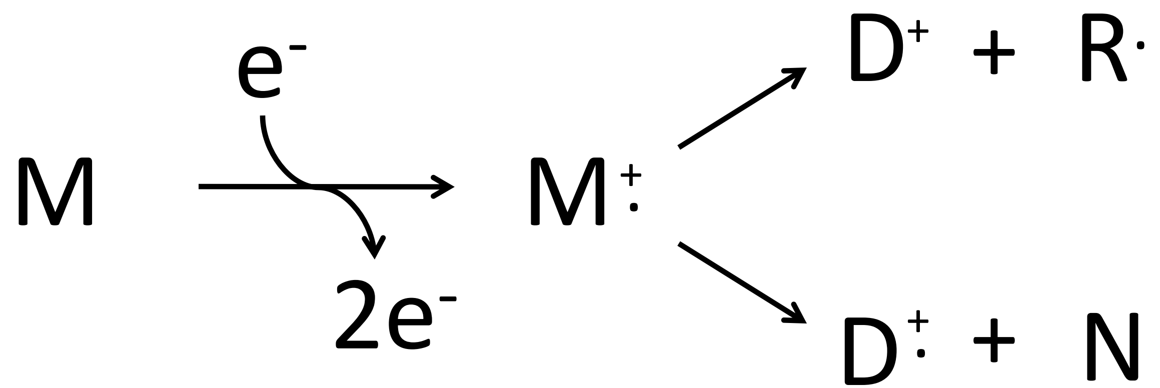
MS principle



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

Only charged species are detected in MS

e.g. $[M+nH]^{n+}$; $[M-nH]^{n-}$; $[M+Na]^+$

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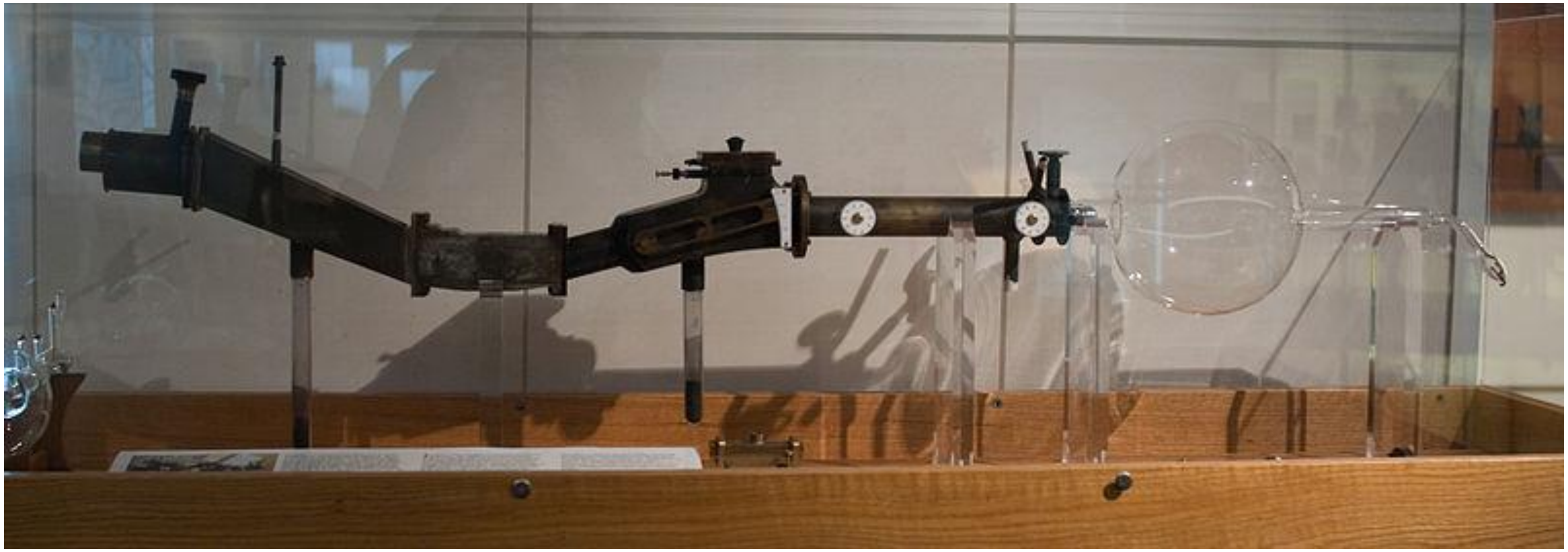
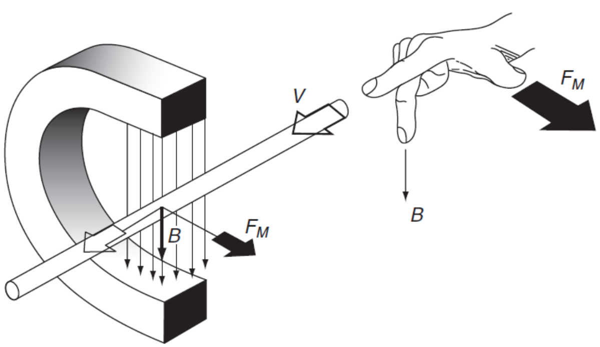
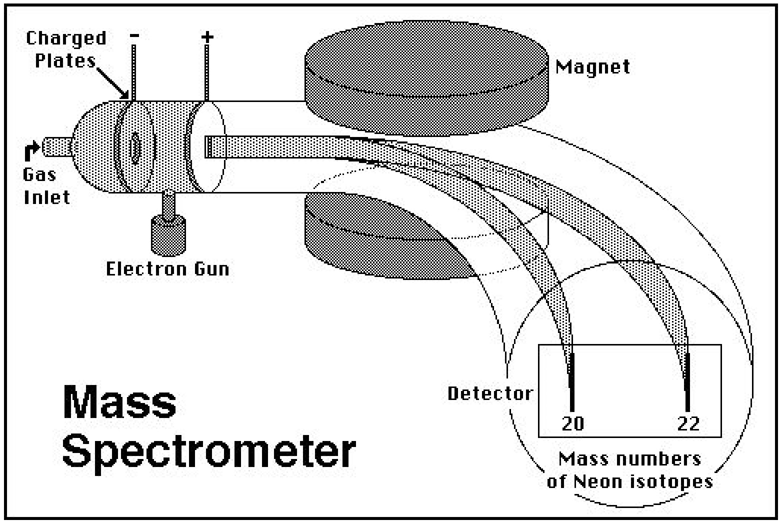
JJ Thamson's 3rd Parabola Mass Spectrograph







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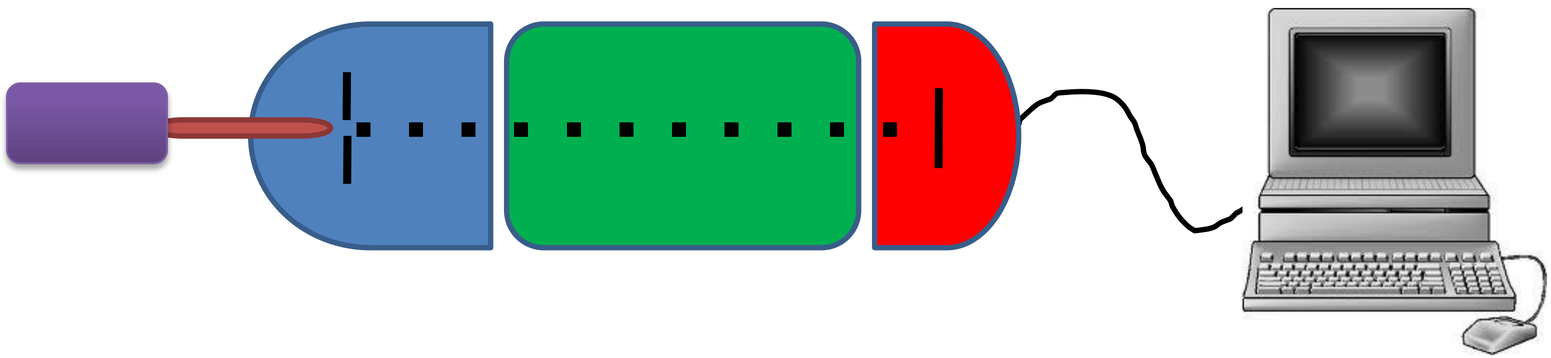
Components of a Mass Spectrometer



Sample Inlet	Ion Source	Analyzer	Detector	Data collector and processor
HPLC	Electron Ionization (EI)	Sector	Photoplate	
GC	Chemical (CI)	Quadrupole	Faraday cup	
Syringe	APCI	TOF	Electron multipliers (MCP)	
Plate	APPI	Orbitrap	Solid-State	
Capillary	Electrospray (ESI)	FTICR	Image current	
	Fast Atom Bombardment (FAB)			
	MALDI			

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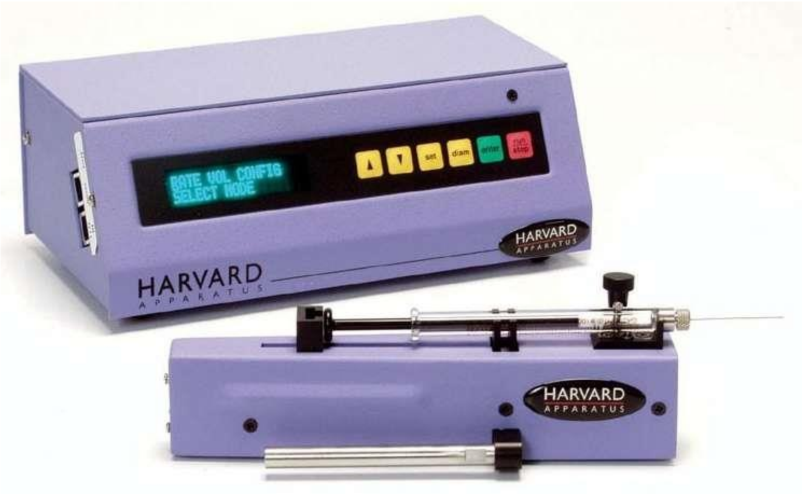
Sample Inlet

HPLC
GC
Syringe
Plate
Capillary



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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)

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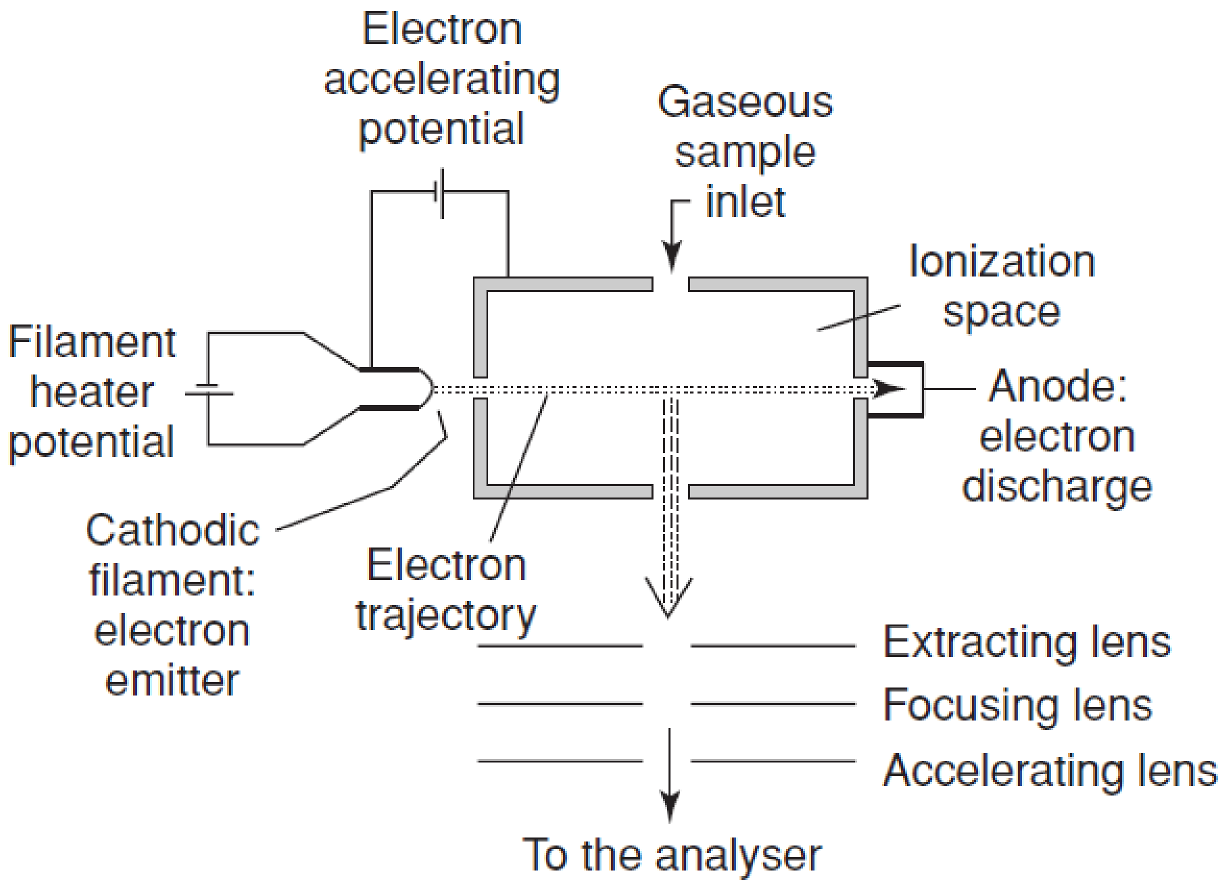
Electron impact ionization (EI)



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

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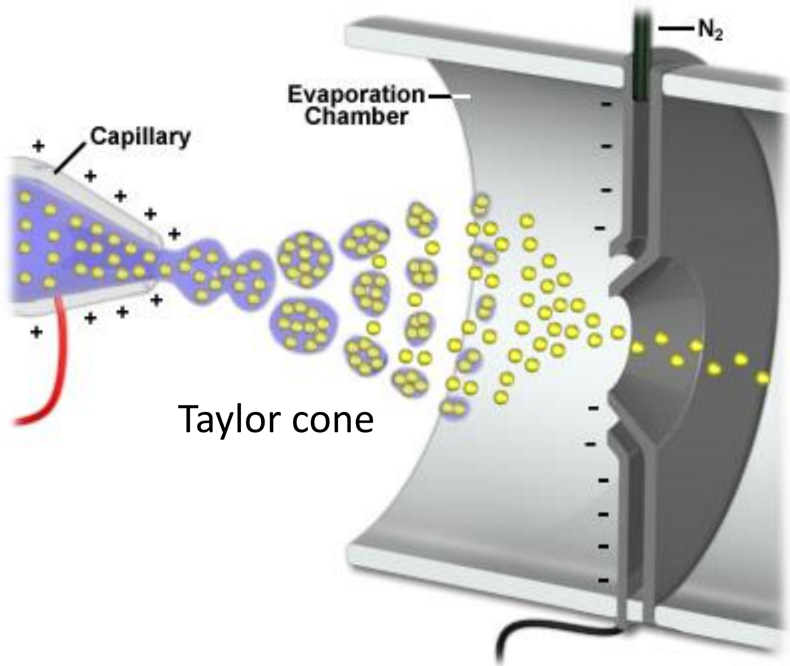
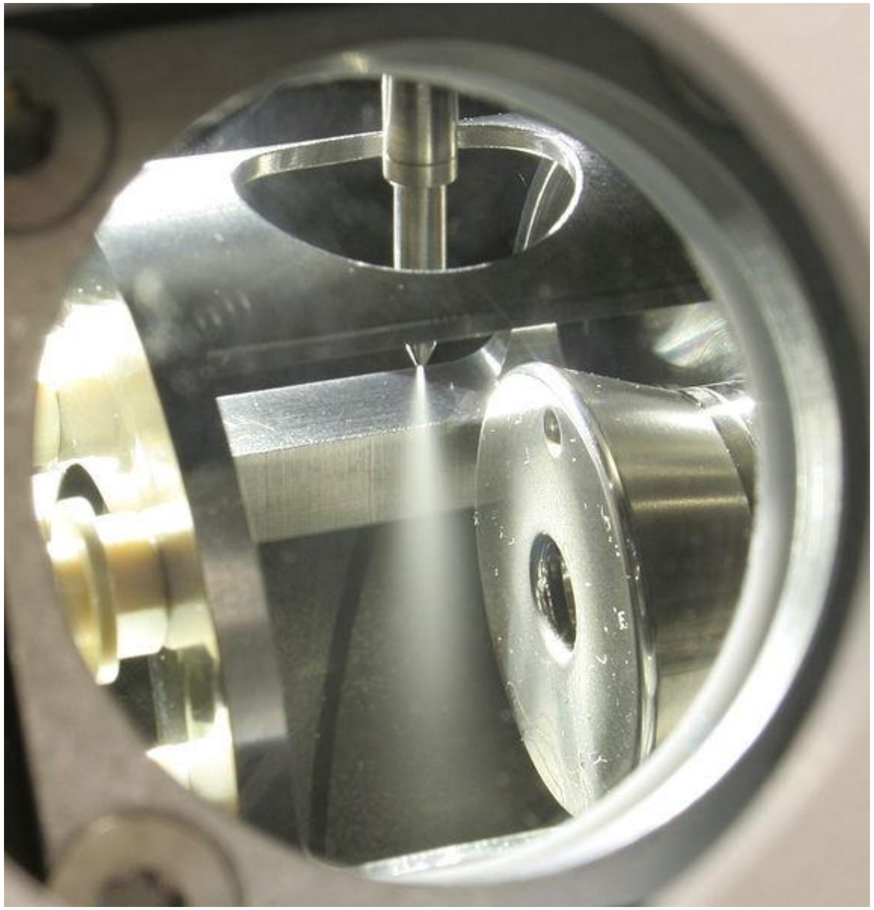
Electrospray ionization





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

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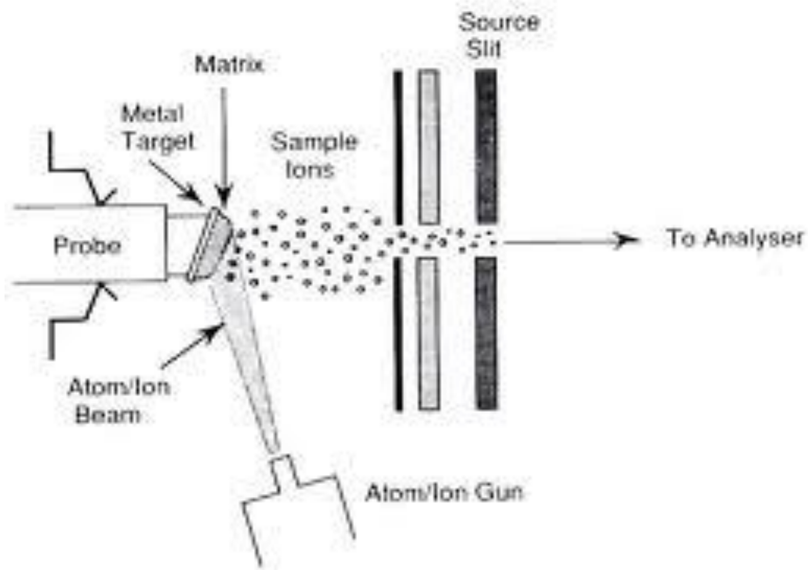
Very soft ionization – less fragmentation, non-covalent complex

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

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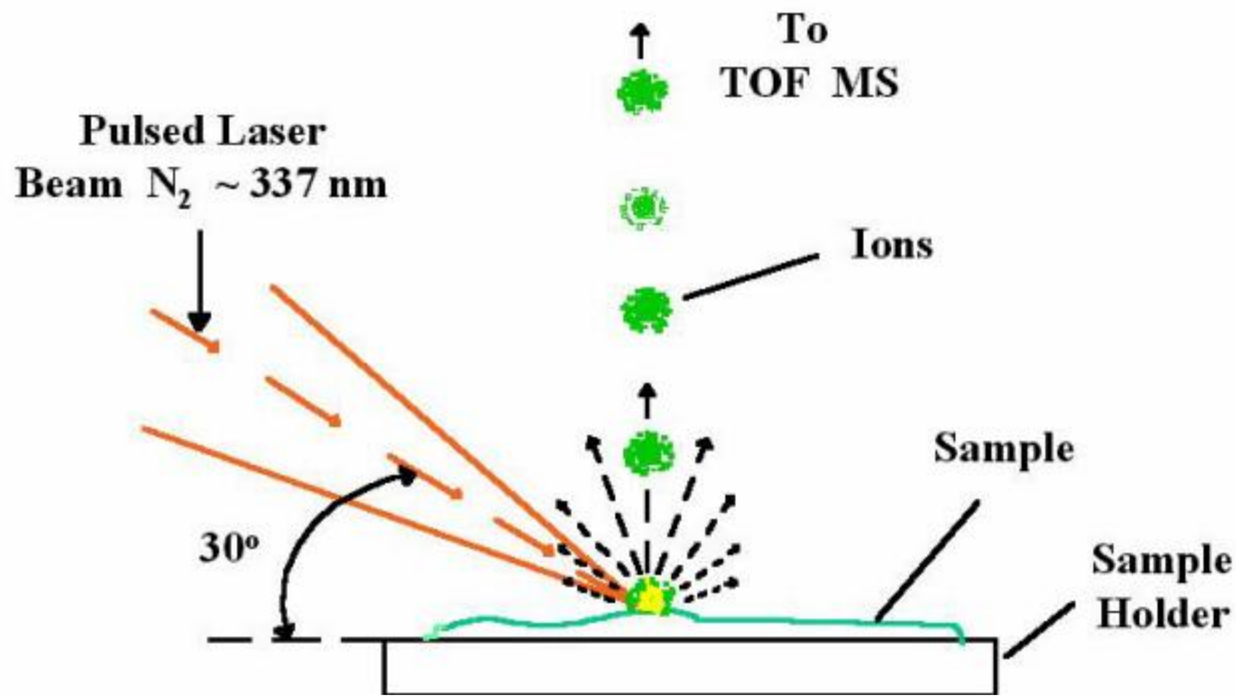
Matrix Assisted Laser Desorption Ionization (MALDI)



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)

Very soft ionization – good ion source for biomolecules

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Analyzers

A mass analyzer is a device that can separate atoms and molecules according to their mass

Sector
Quadrupole
TOF
Orbitrap
FTICR

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 [u (m)S^{-1}]
3) the transmission = No. of ion reaching the ions/No. of ions entering mass analyzer
4) the mass accuracy
5) the resolution

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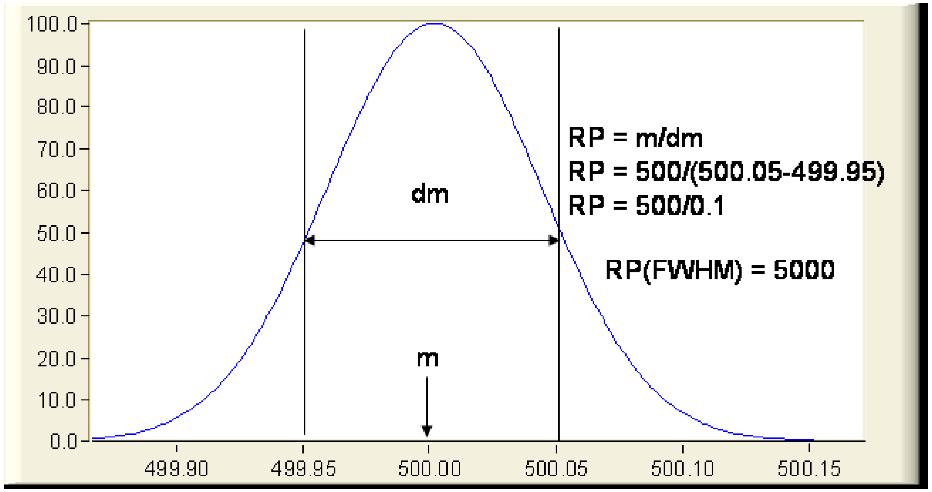
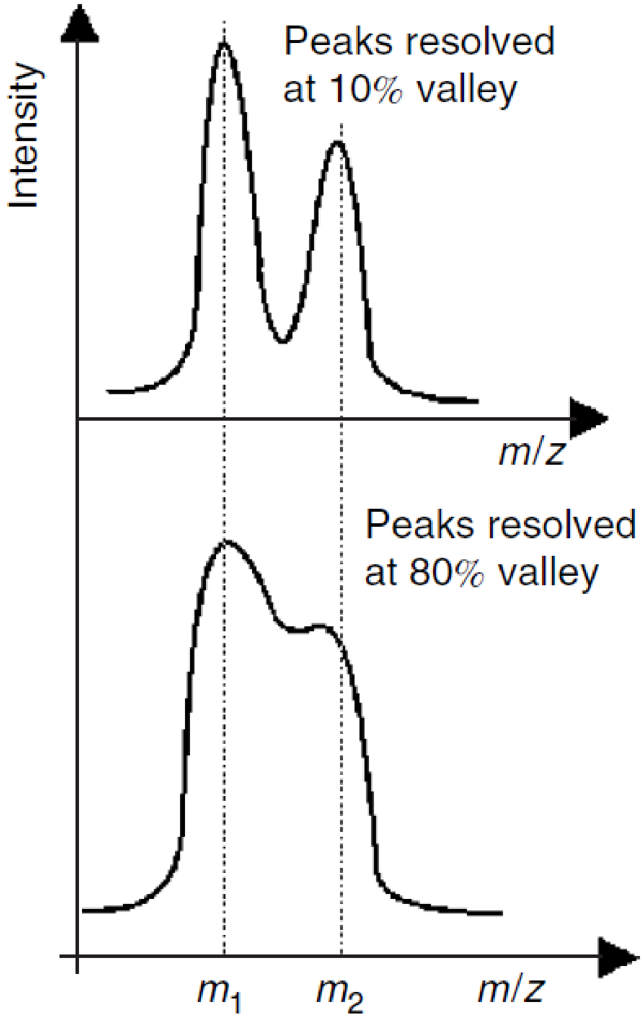
Resolution and Mass accuracy

Resolution = FWHM = $\delta m/m$





Mass accuracy = theoretical *m/z* vs measured *m/z* (ppm)

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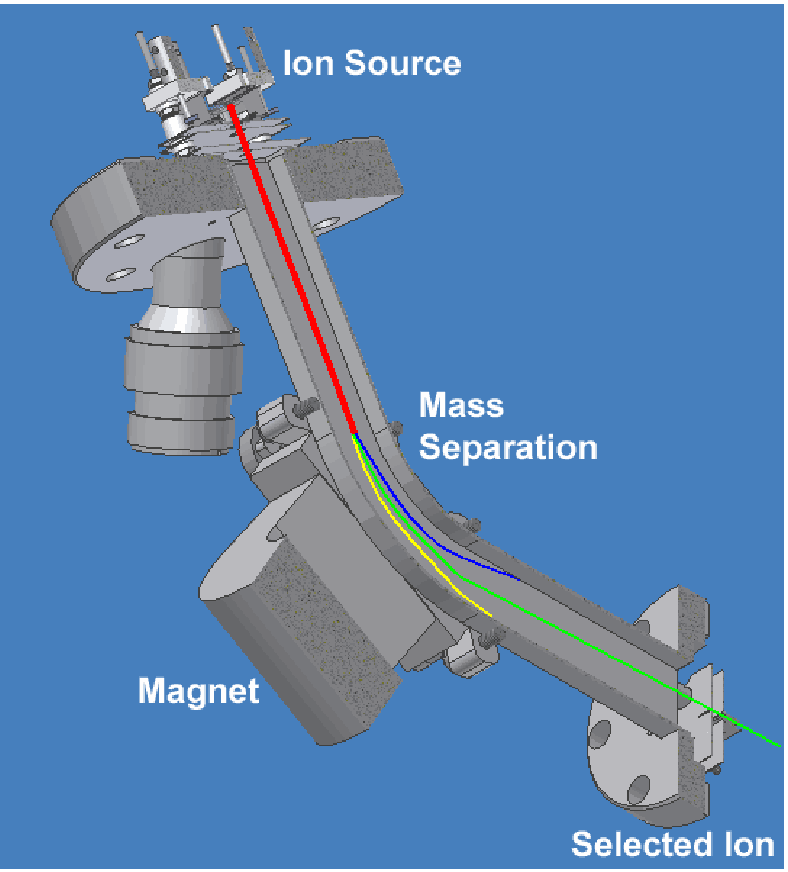
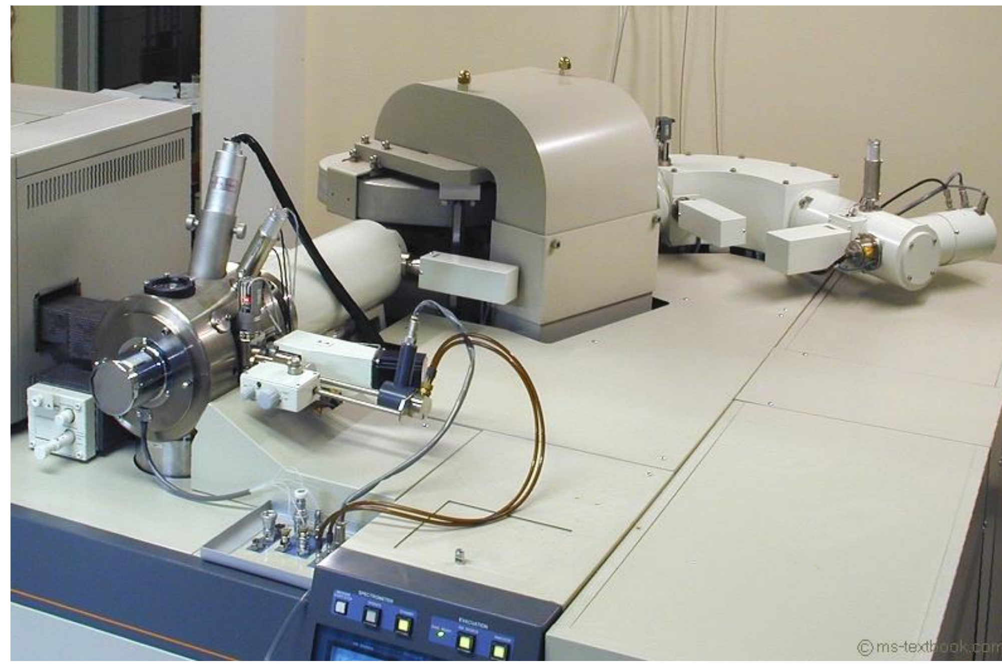
Sector analyzer





m/z = $B^2r^2/2V$

$$\mathbf{F} = q(\mathbf{E} + \mathbf{v} \times \mathbf{B}),$$

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Sector analyzer

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

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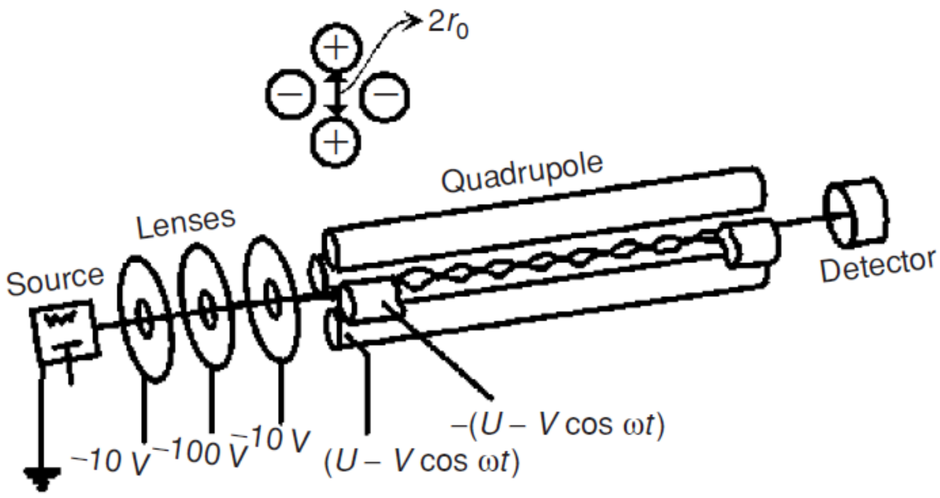
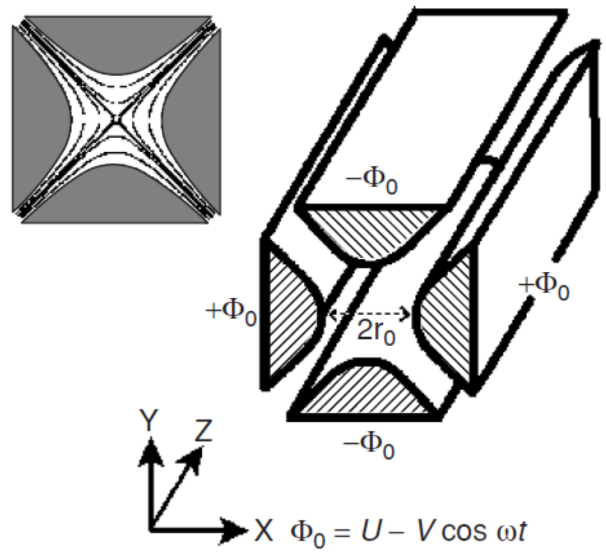
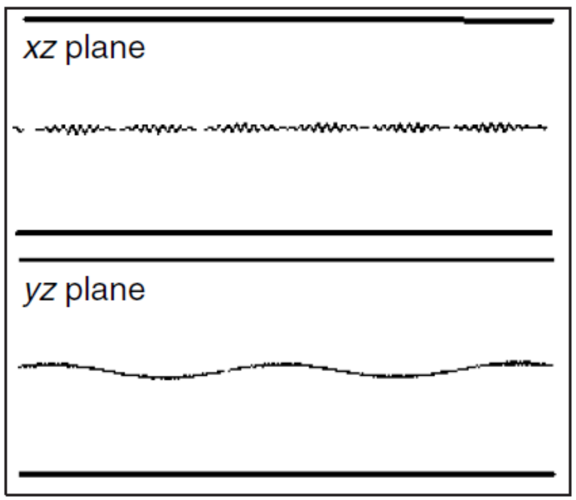
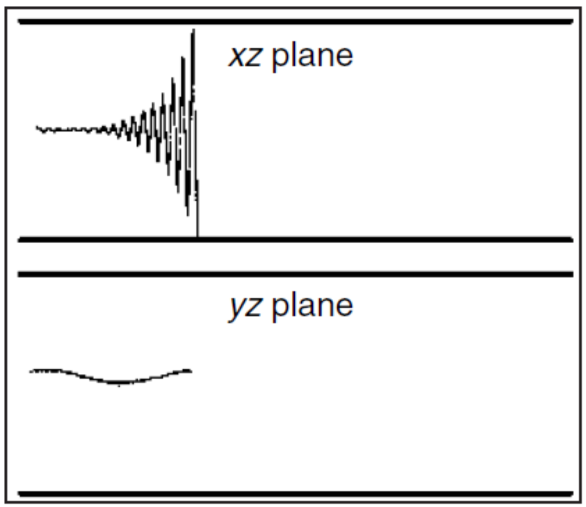
Quadrupole analyzer







Stable along both *x* and *y*



Stable along *y*, unstable along *x*

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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.

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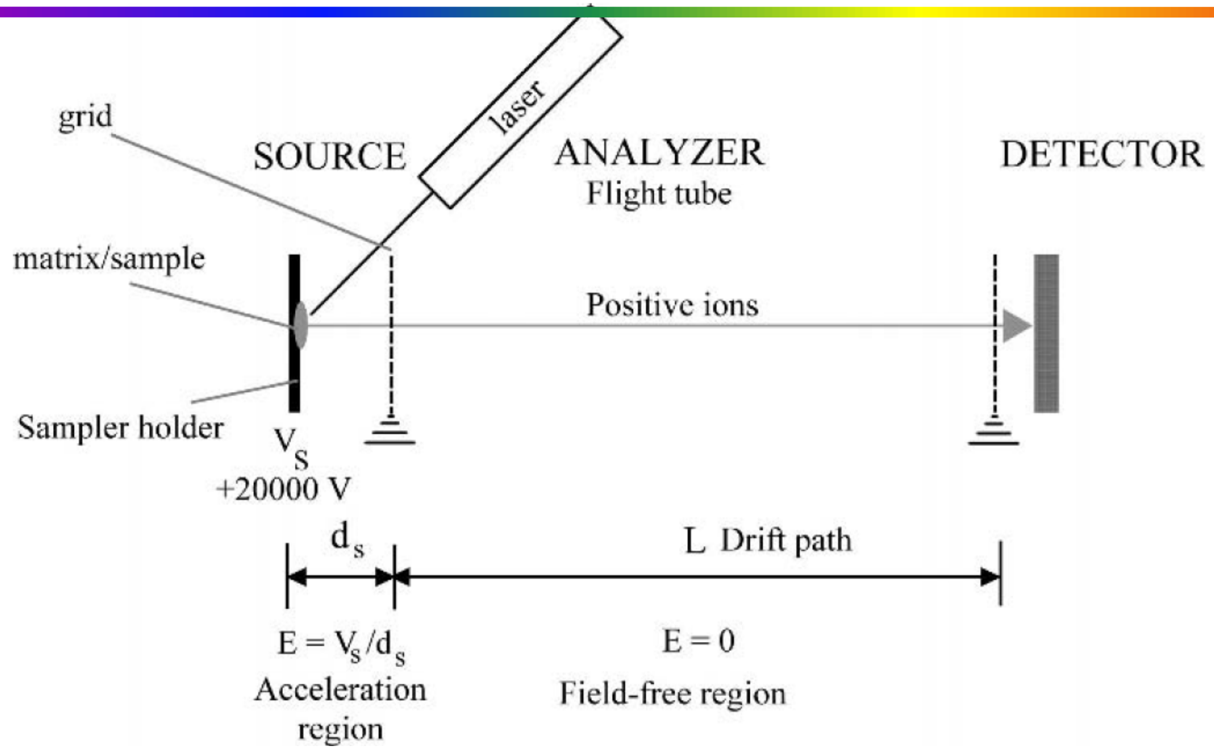
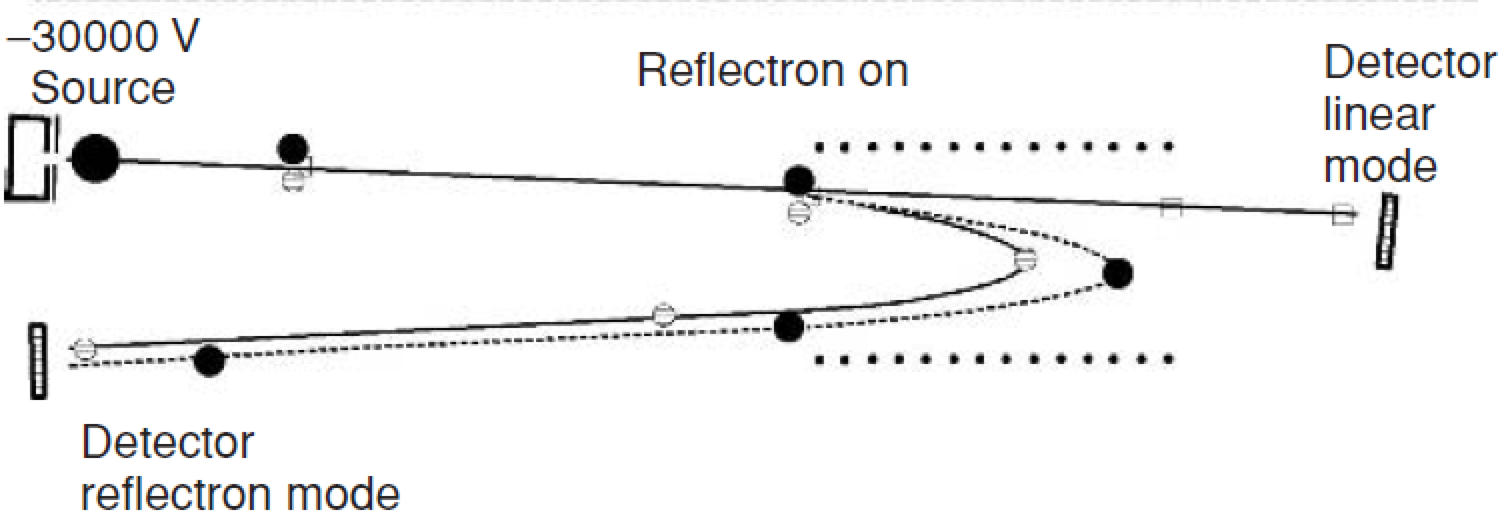
Time-of-flight (TOF) analyzer



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



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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

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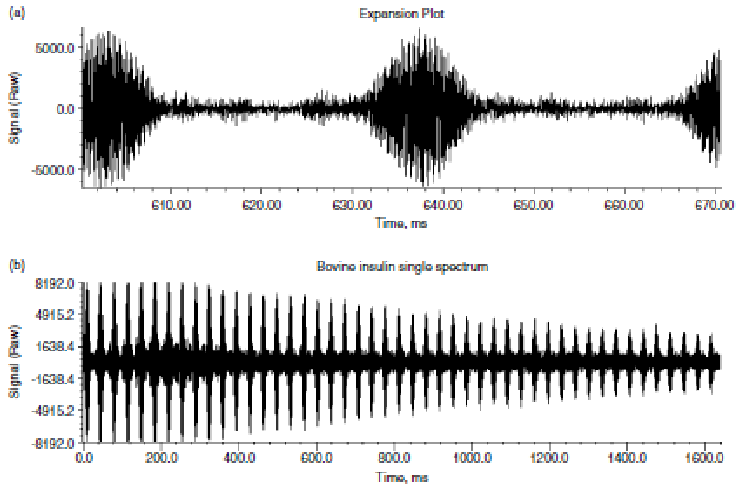
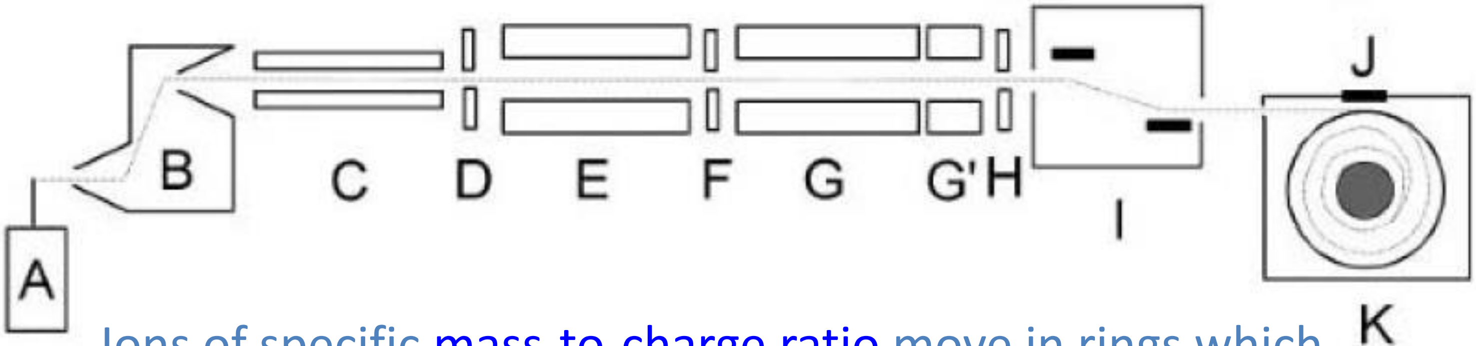
Orbitrap analyzer

$$\omega = \sqrt{(q/m)k}$$





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*).

Hu et. al. J. Mass Spectrom. 2005; 40: 430–443

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Comparison of various analyzers

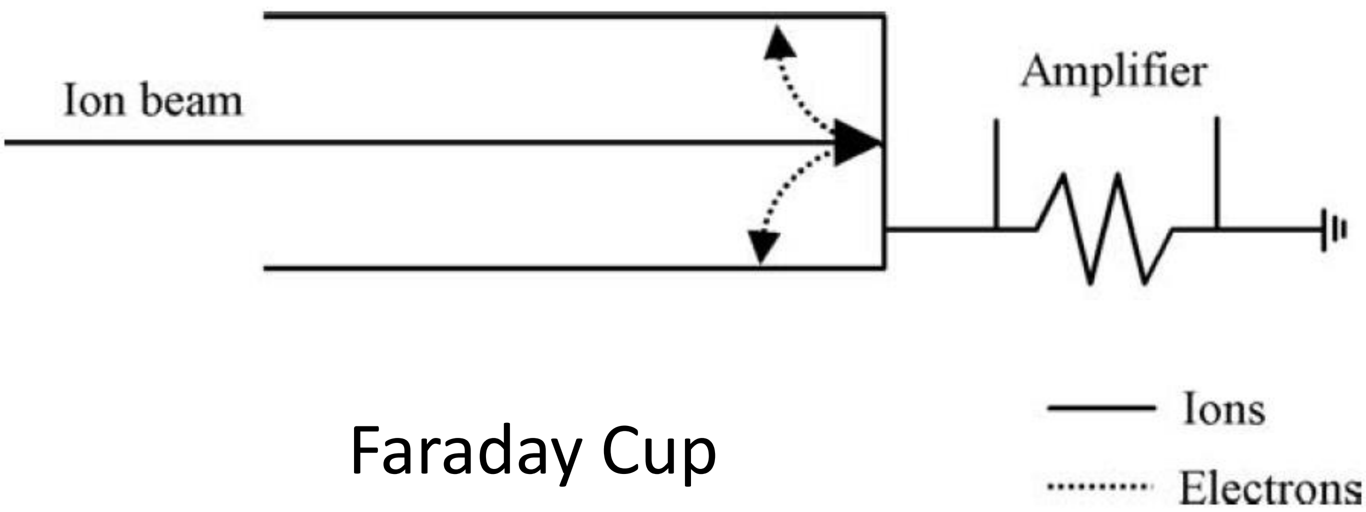
Table 2.2 Comparison of mass analysers.

	Quadrupole	Ion trap	TOF	TOF reflectron	Magnetic	FTICR	Orbitrap
Mass limit	4000 Th	6000 Th	>1 000 000 Th	10 000 Th	20 000 Th	30 000 Th	50 000 Th
Resolution FWHM (m/z 1000)	2000	4000	5000	20 000	100 000	500 000	100 000
Accuracy	100 ppm	100 ppm	200 ppm	10 ppm	<10 ppm	<5 ppm	<5 ppm
Ion sampling	Continuous	Pulsed	Pulsed	Pulsed	Continuous	Pulsed	Pulsed
Pressure	10^{-5} Torr	10^{-3} Torr	10^{-6} Torr	10^{-6} Torr	10^{-6} Torr	10^{-10} Torr	10^{-10} Torr
	Triple quadrupoles	—	—	PSD or TOF/TOF	Consecutive sectors	—	—
Tandem mass spectrometry	MS/MS fragments precursors neutral loss	MS^n fragments	—	MS/MS fragments	MS/MS fragments precursors neutral loss	MS^n fragments	—
	Low-energy collision	Low-energy collision	—	Low- or high-energy collision	High-energy collision	Low-energy collision	—

Detectors

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)



Faraday Cup

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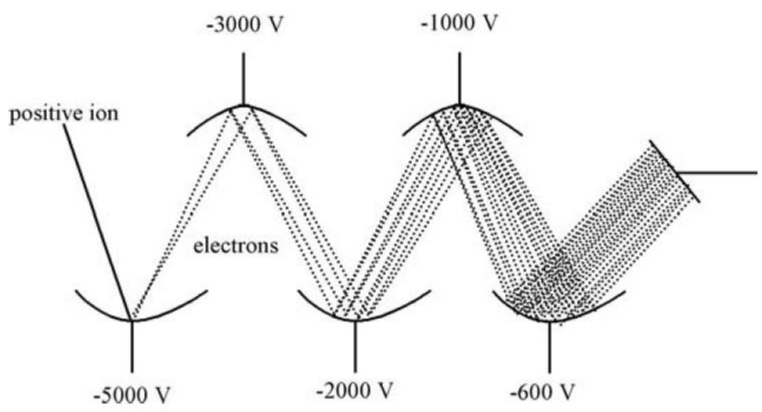
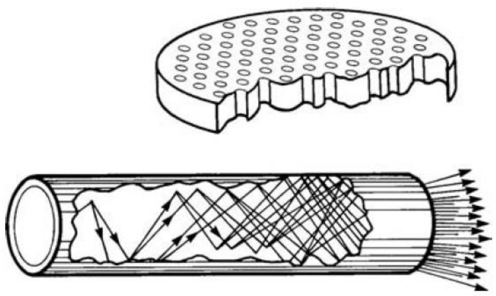
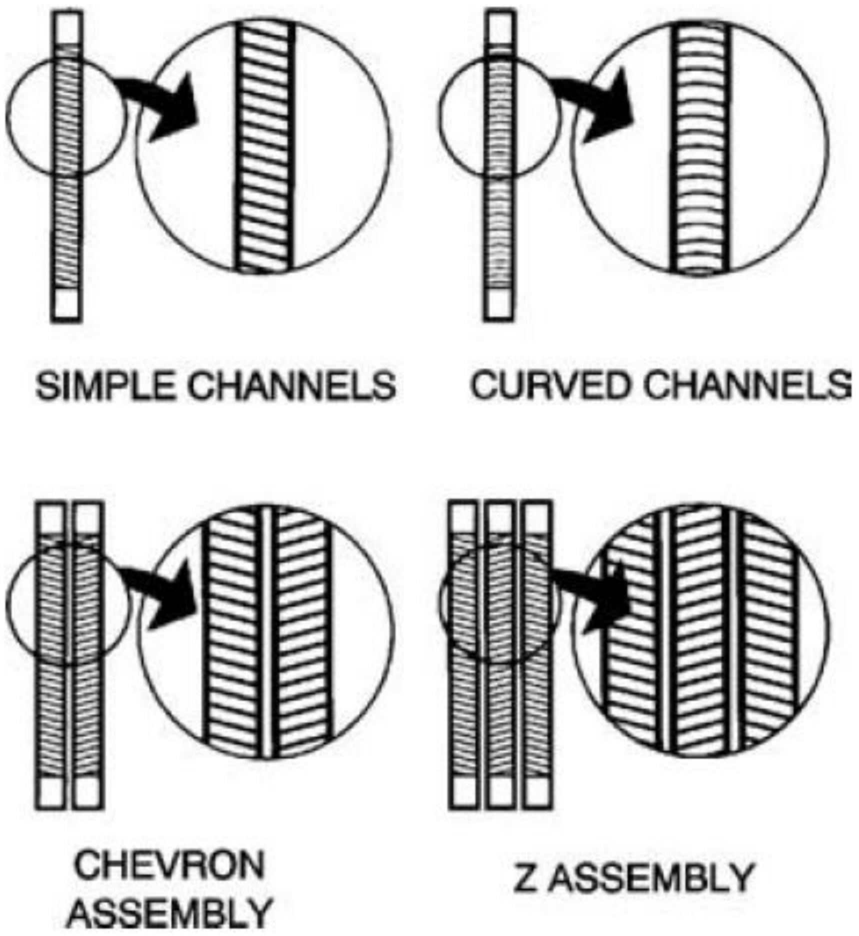
Electron multipliers (MCP)







MCP

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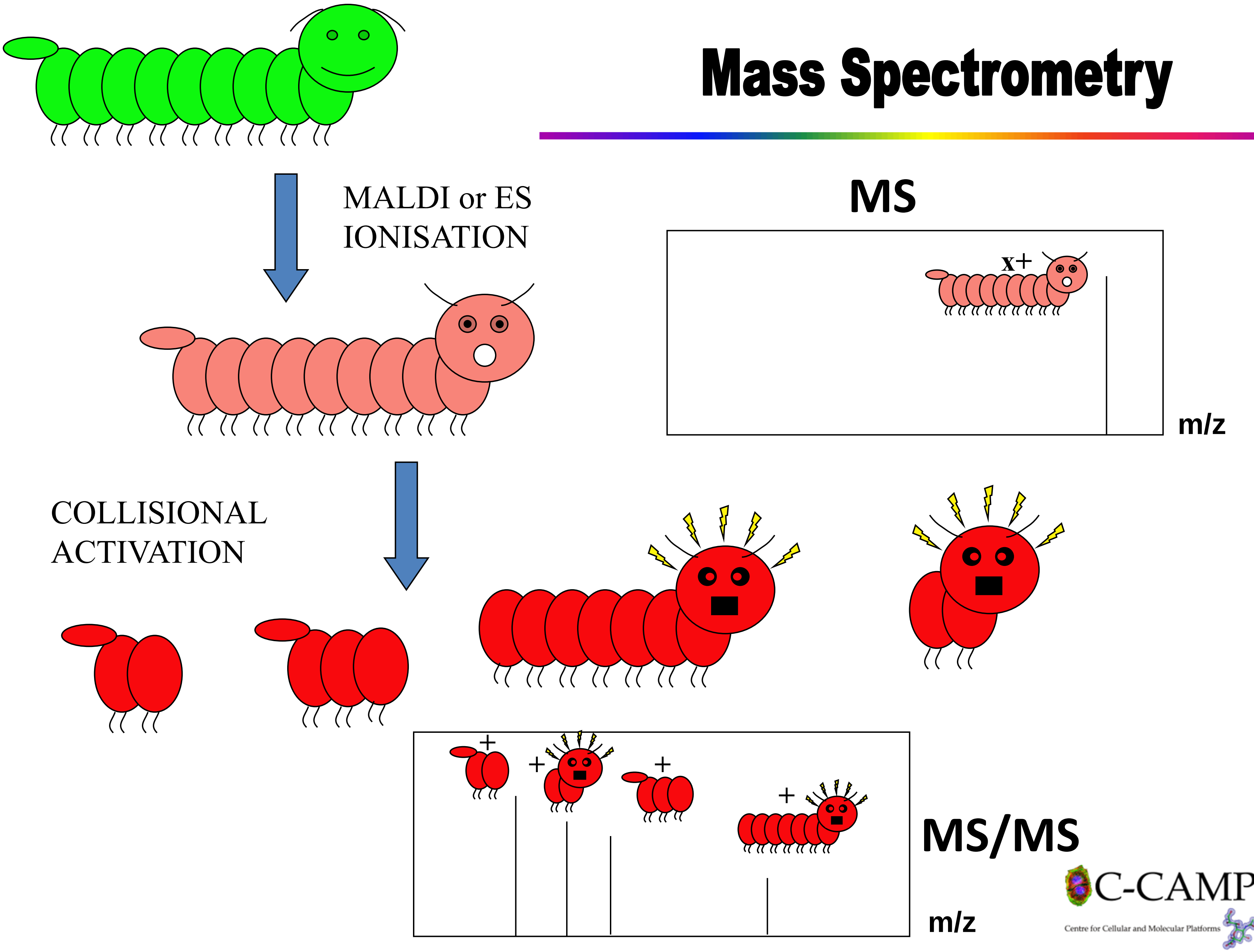
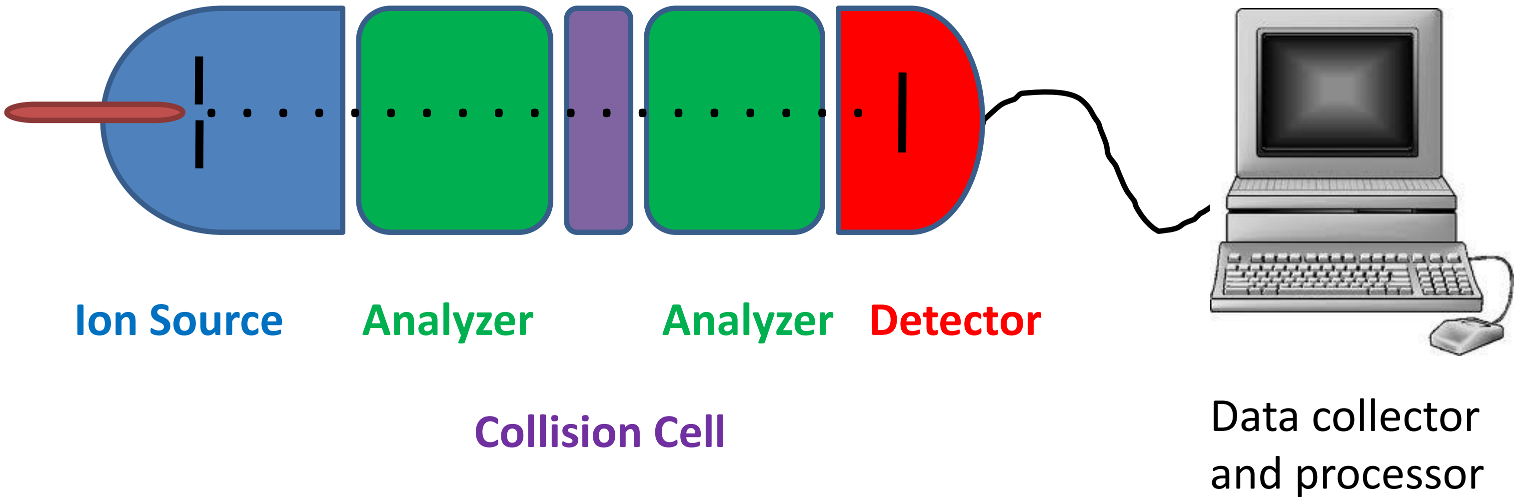
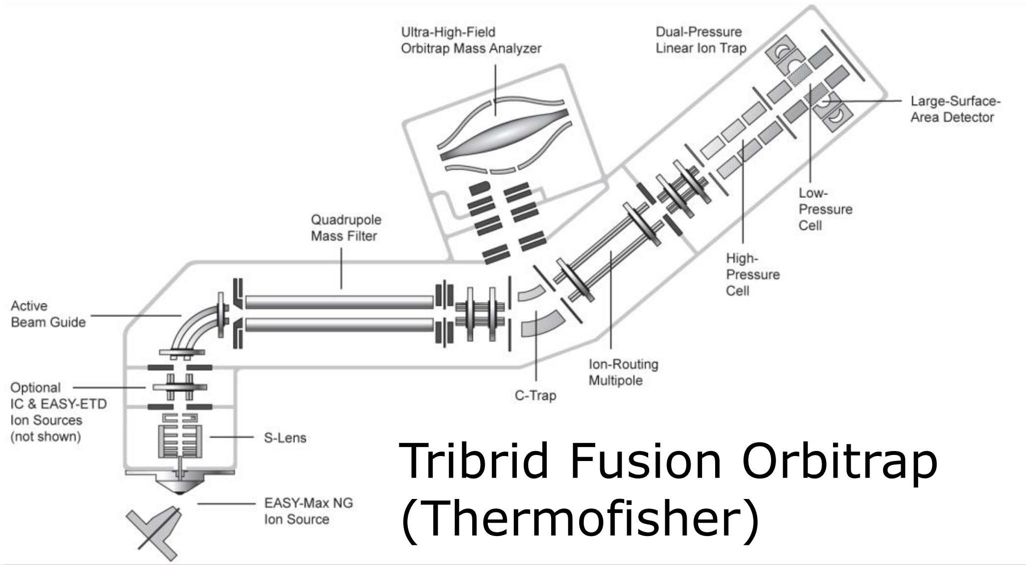
Mass Spectrometry



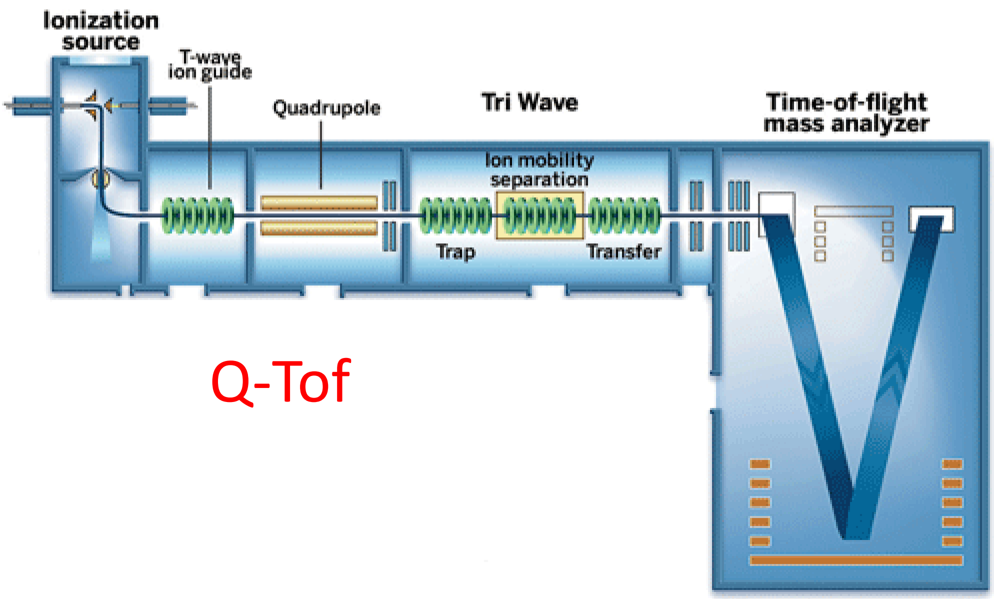
Tandem MS (MS^n)



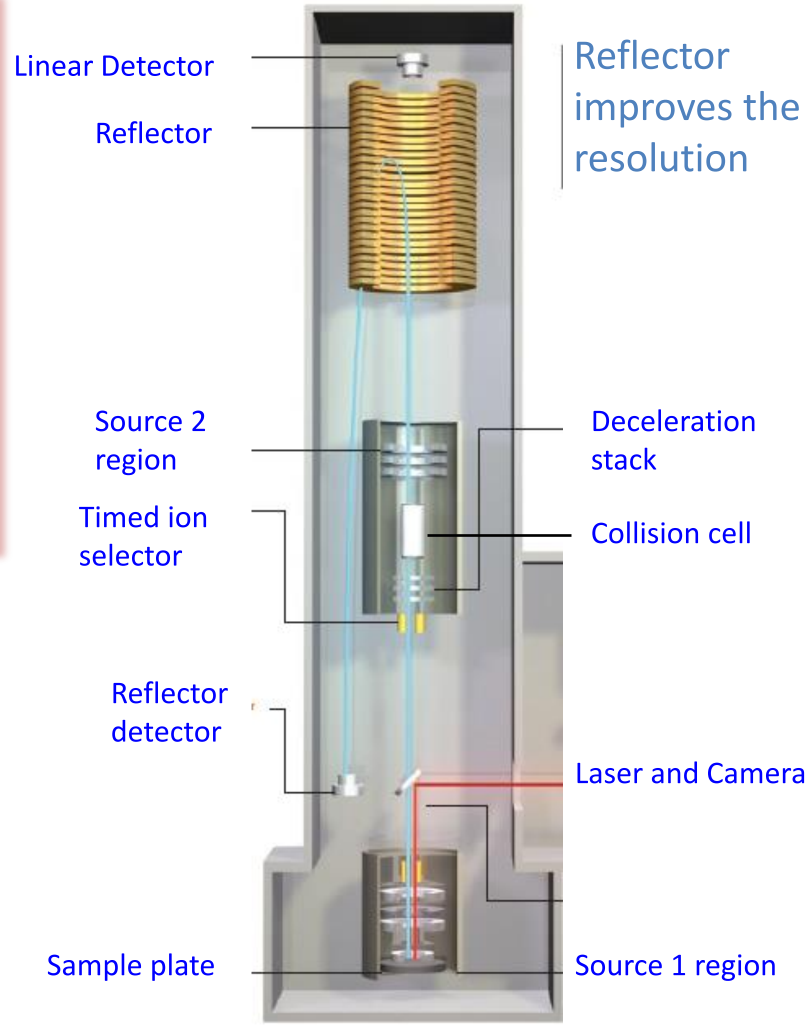
Hybrid Tandem MS Instruments



Tribrid Fusion Orbitrap (Thermofisher)



Q-Tof



Applied Biosystems, USA

MALDI-TOF/TOF

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References

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

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