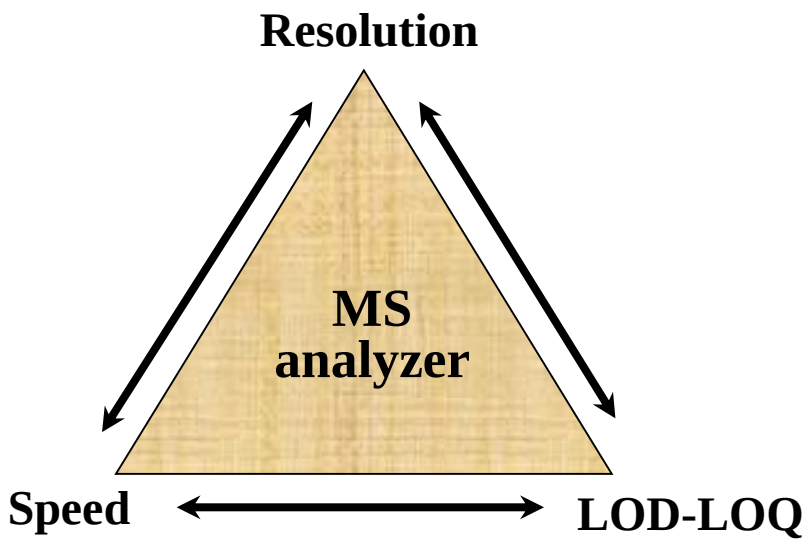
Methods of ions analysis and detection in MS

Ion analysis (*m/z*)	Ion detection
range	LOD-LOQ
resolution	dynamic range
accuracy	stability in time
speed	lifetime / durability



Methods of ions analysis in MS

- **ion analysis is realized using a mass analyzer (alternatively called mass filter or mass separator)**
- **mass analyzer = part of mass spectrometer, which distinguishes ions according to their *m/z* value**
- **parameters of mass analyzers:**
  - **a) range of analyzed *m/z* values**
  - **b) scan speed, switching of scan modes**
  - **c) resolution power (resolution) of *m/z* values**
  - **d) mass accuracy**

Parameters of MS analyzers

- **range of analyzed *m/z* values:**

  a) lower limit: from technical ‘0‘ or from a higher value

  b) upper limit: up to a defined maximum value
  (for multiply charged ions higher M)

- **scan speed and the ability to switch between different modes:**

  a) number of scans per second:
  < 1 → low speed
  1 - 10 → medium speed
  10 - 500 → high speed

  b) measurement modes: full scan, segment scan, SIM, SRM, MRM

  c) display modes:

  - TIC (total ion current) → total ion current (including noise) for the selected measurement mode

  - RIC/EIC (reconstructed/extracted ion chromatogram) → record for the selected *m/z* value

  - BPC (base peak chromatogram) → record for basic (most intensive) *m/z* values in spectrum at each point of the chromatogram

Parameters of MS analyzers

- **resolving power – RP (mass analyzer or spectrometer):**
- **two different definitions – depends on the type of mass analyzer**
- **a measure of the mass analyzer's ability to distinguish close *m/z* values – i.e. what the smallest difference can be recorded; relative data related to *m/z* values**

1. definition for two ions:

$RP = m_2 / (m_2 - m_1)$; $z_1, z_2 = 1$

- peaks m_1 and m_2 have 10% overlap at the same height

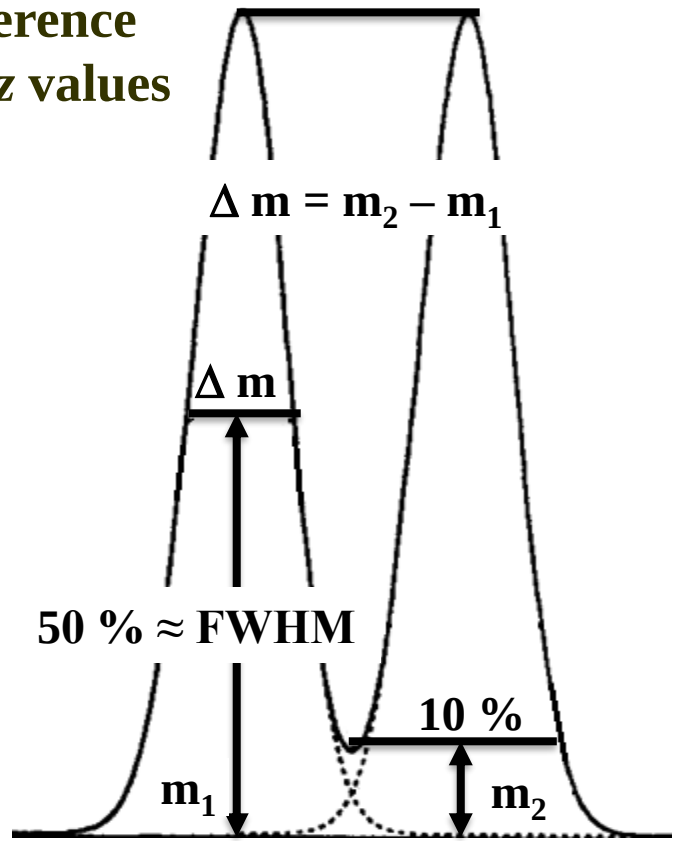
dimensionless

2. definition for one ion (preferred):

$RP = m_1 / \Delta m$ (alt. $t / 2 \Delta t$ - TOF)

- FWHM (full width at half maximum) for the corresponding *m/z*

dimensionless



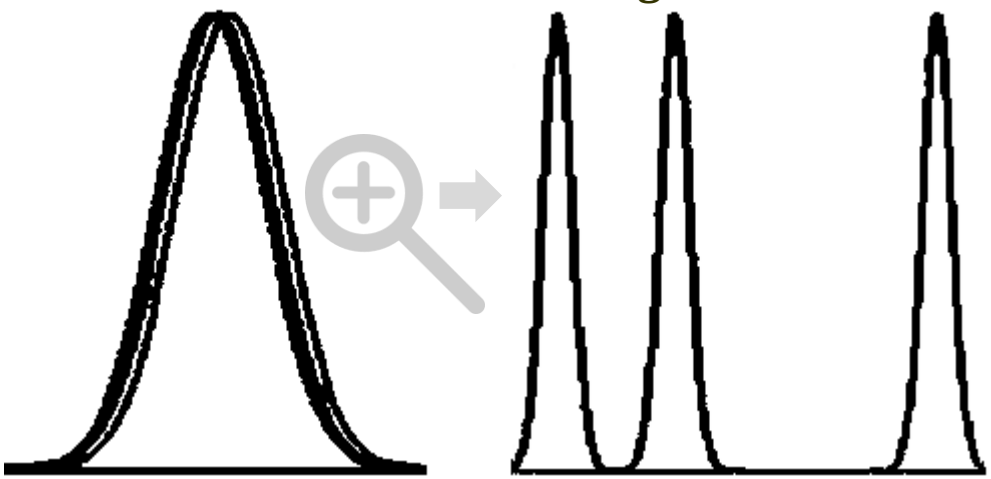
Parameters of MS analyzers

- **resolution - R = 1/RP (mass analyzer or spectrometer):**
- **two different definitions – depends on the type of mass analyzer**
- **a measure of the mass analyzer's ability to distinguish close m/z values – i.e. what the smallest difference can be recorded; relative data related to *m/z* values**

$R = (m_2 - m_1) / m_1 = \Delta m / m_1$

- expressed in ppm for the corresponding *m / z*

Low resolution **High resolution**



As the resolution increases, the number of compounds corresponding to the determined *m/z* value decreases.

So the probability of identification increases.

Parameters of MS analyzers

- **mass accuracy:**
- **a measure of agreement between measured (experimental) and calculated (exact / theoretical) *m/z***
- **a measure of the ability of mass analyzer to determine the correct *m/z***

Relative measure in ppm - depends on *m/z* value:

$$ppm = 10^6 . (m/z_{EXP} - m/z_{CAL}) / m/z_{CAL}$$

Parameters of MS analyzers

Examples of relationships between parameters and *m/z* values

1. Resolving power (RP) = 50000

(often given as a resolution FWHM 50000)

- for *m/z* = 1000 ions distinguished with difference ±0,01 (1000/50000 = 0,02)

- for *m/z* = 100 ions distinguished with difference ±0,001 (100/50000 = 0,002)

2. Resolution (R) for RP 50000 is 20 ppm (i.e. $1/50000 = 20.10^{-6}$)

3. Mass accuracy

a) ppm = 10^6. (266,16315 – 266,16304) / 266,16304 = + 0,41 ppm
b) ppm = 10^6. (266,16187 – 266,16304) / 266,16304 = - 4,40 ppm
c) ppm = 10^6. (266,17087 – 266,16304) / 266,16304 = + 29,4 ppm

Methods of ions analysis in MS

Principle of mass analyzer

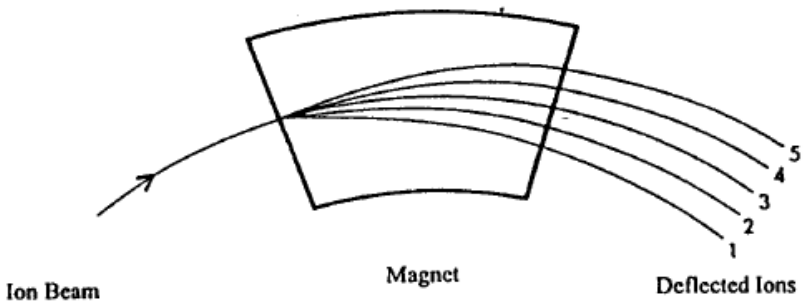
- ion analysis is realized at low pressure (< 10^{-4} Pa)
- mass analyzer determines *m/z* value
- multistage mass analysis - combination of several mass analyzers

Physical principles of ion analysis

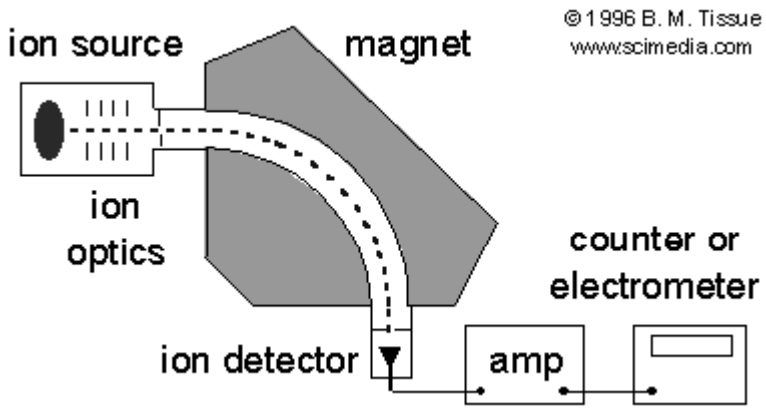
- curved flight path of ions in a magnetic or electric field
  - magnetic or electrostatic analyzer
- various stability of ion oscillations in two- or three-dimensional
  - combination of DC and high frequency AC voltage
  - quadrupole or ion trap - Q, IT
- different time of flight of ions - time of flight analyzer - TOF
- different frequency of harmonic oscillations - Orbitrap
- different energy absorption during cycloidal motion of ions in a combined magnetic and electric field - ionic cyclotron resonance - ICR

Principles of mass analyzers

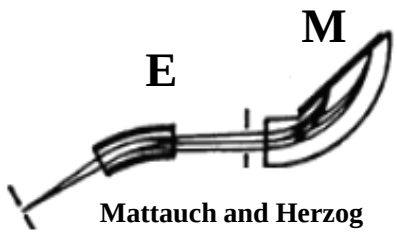
Magnetic sector



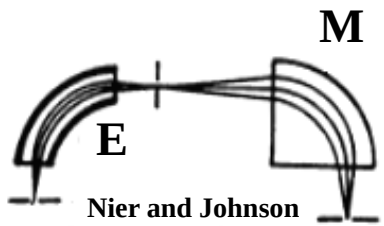
$$(m/z)_1 < (m/z)_2 < \ldots < (m/z)_5$$



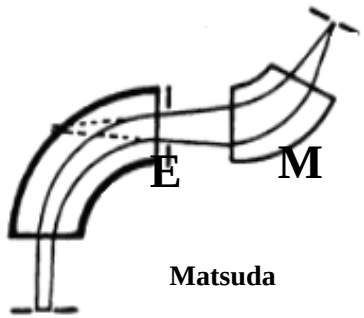
Double focusing: electrostatic (E) and magnetic (M)



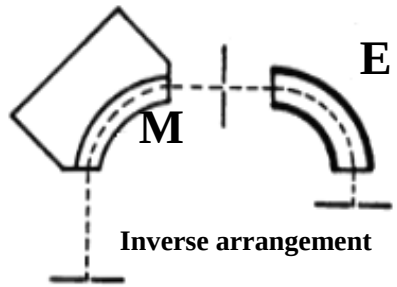
Mattauch and Herzog



Nier and Johnson



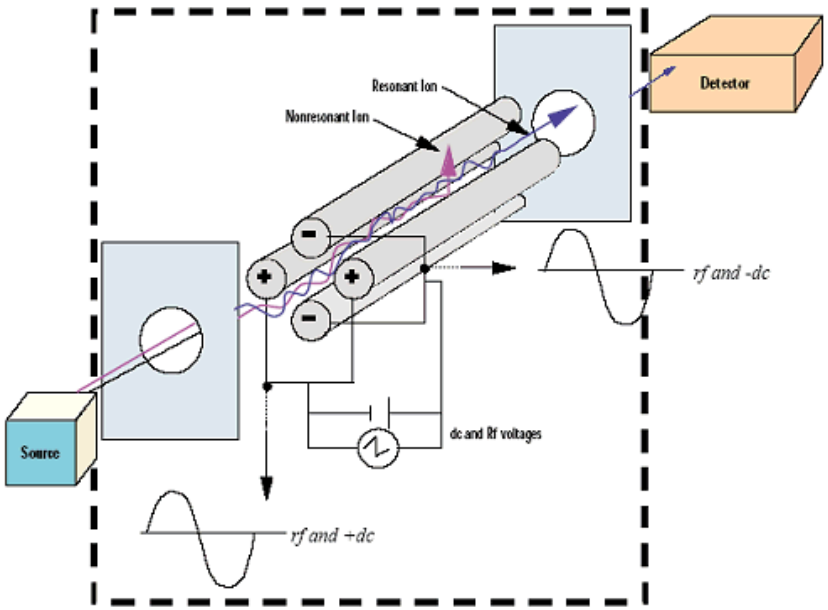
Matsuda



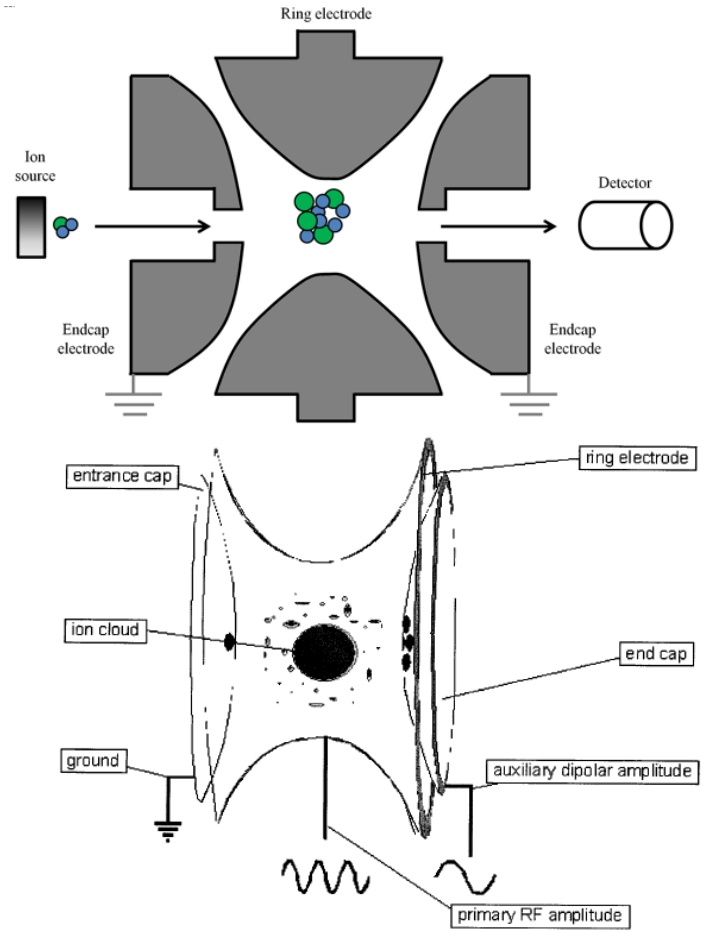
Inverse arrangement

Principles of mass analyzers

Quadrupole: a) straight (Q)



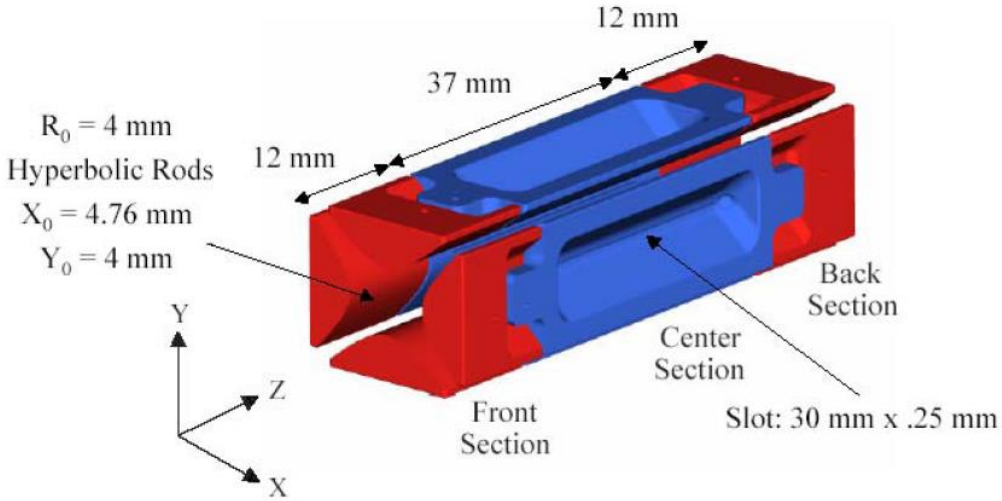
b) spherical - 3D trap (IT)

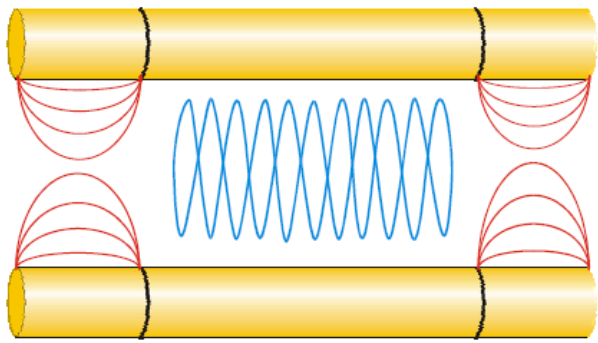


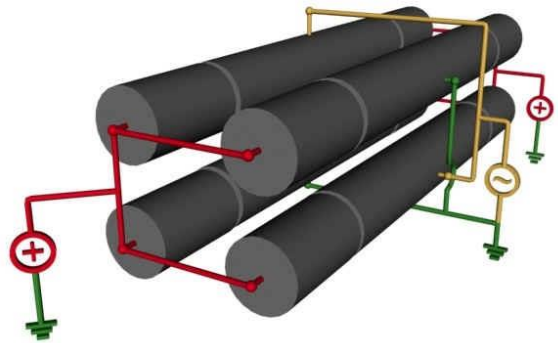
FIGURES: Agilent Technologies nad Thermo

Principles of mass analyzers

Quadrupole: linear ion trap (segmented quadrupole) 2D trap (IT)



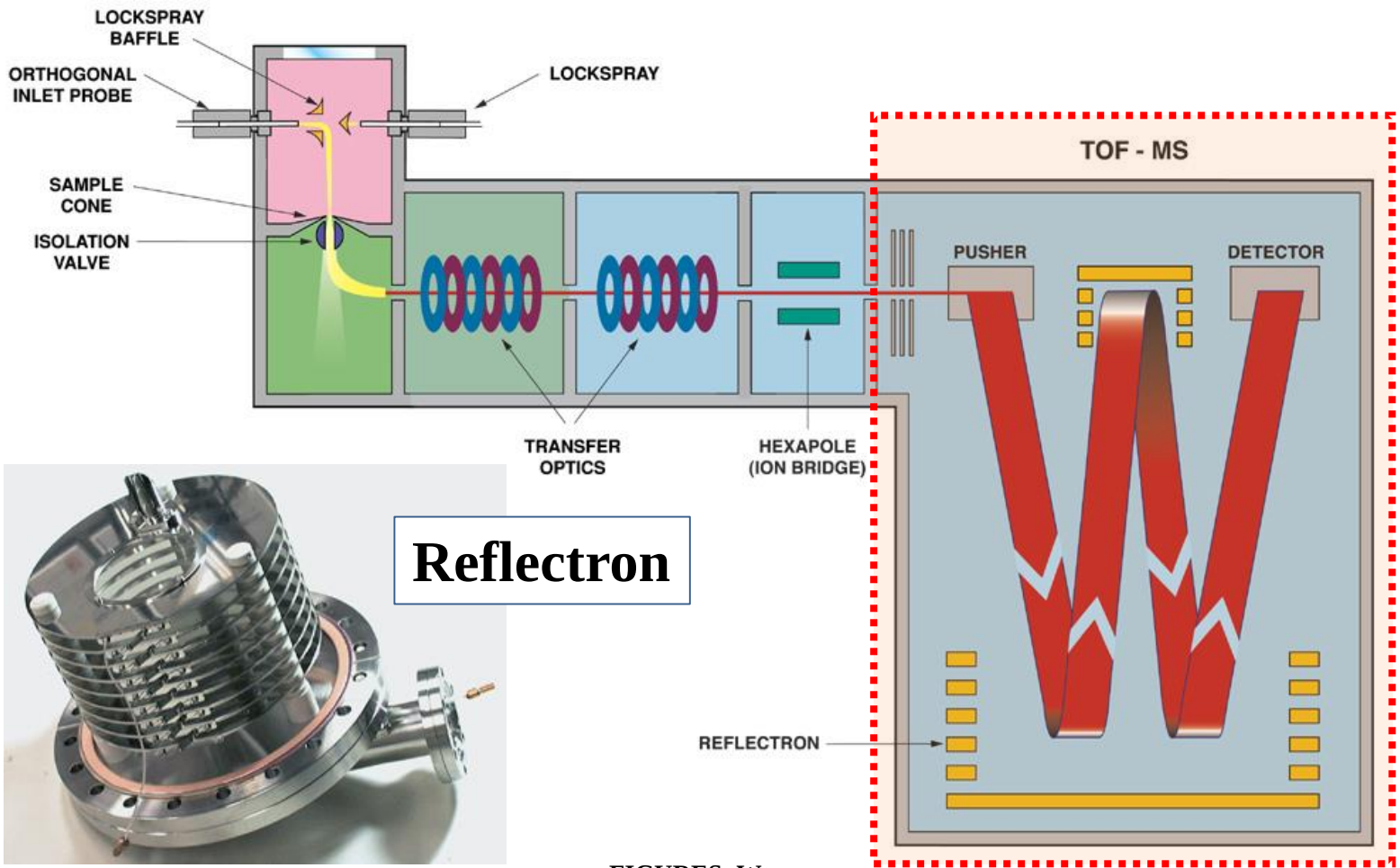




FIGURES: AB Sciex

Principles of mass analyzers

Time Of Flight (TOF)

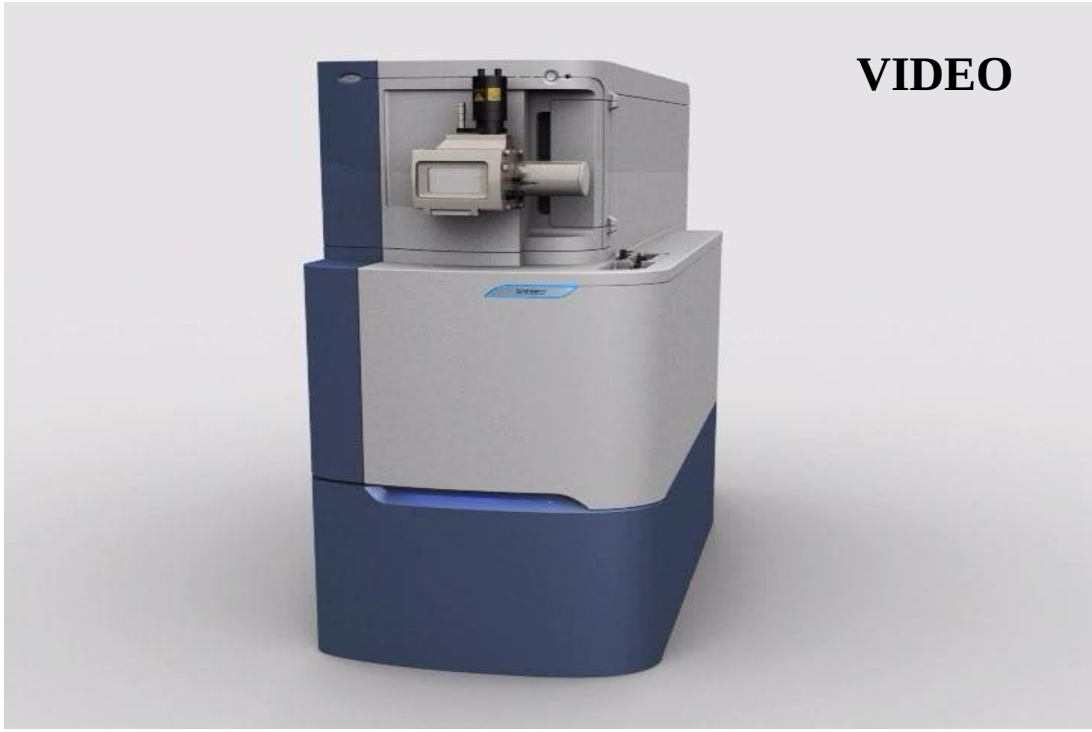


Reflectron

FIGURES: Waters

Principles of mass analyzers

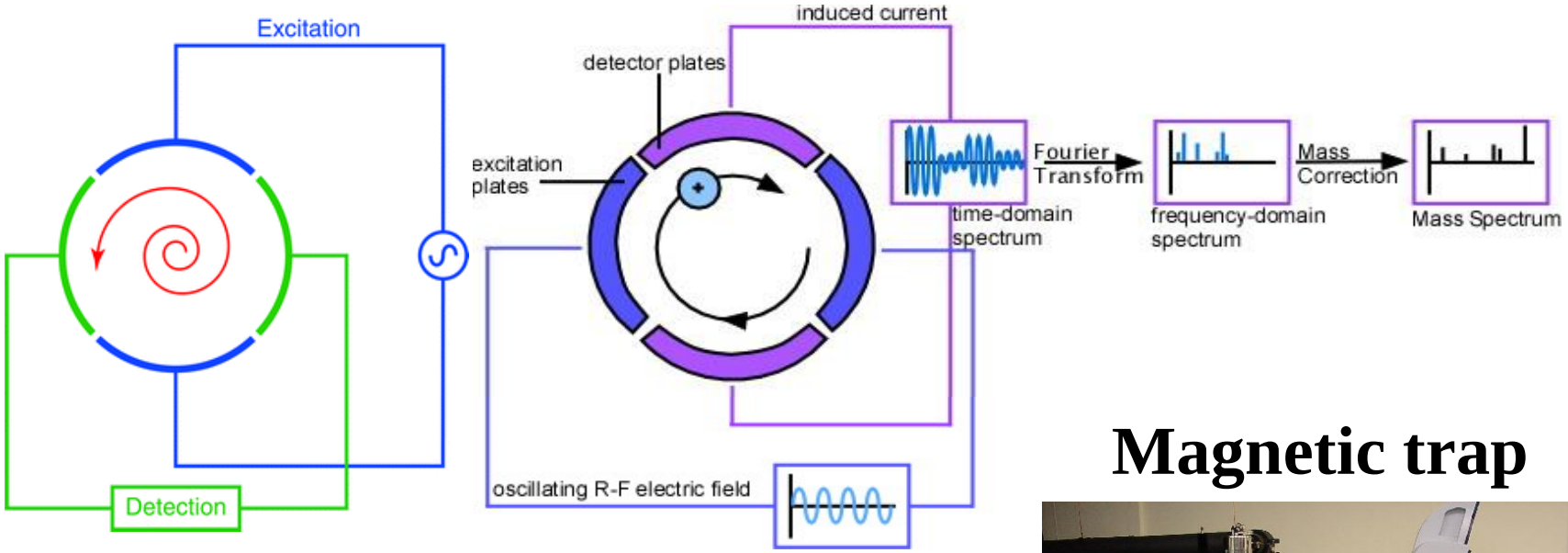
Time Of Flight (TOF)



Ion Mobility (travelling wave)
- TOF MS (with reflectron)

Principles of mass analyzers

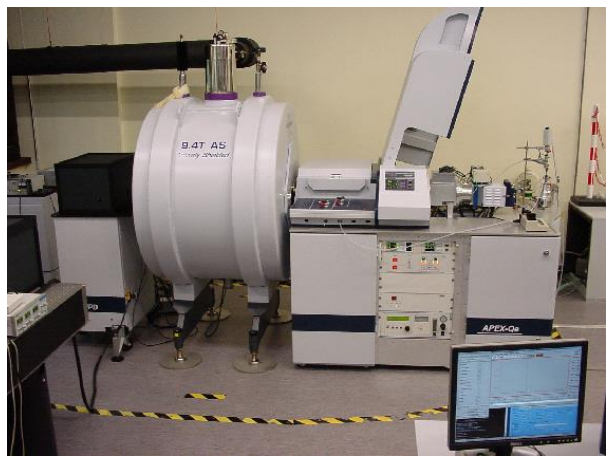
Fourier Transform Ion Cyclotron (FT-ICR)



Mark P. Barrow, William I. Burkitt and Peter J. Derrick
Analyst, 2005, 130, 18-28

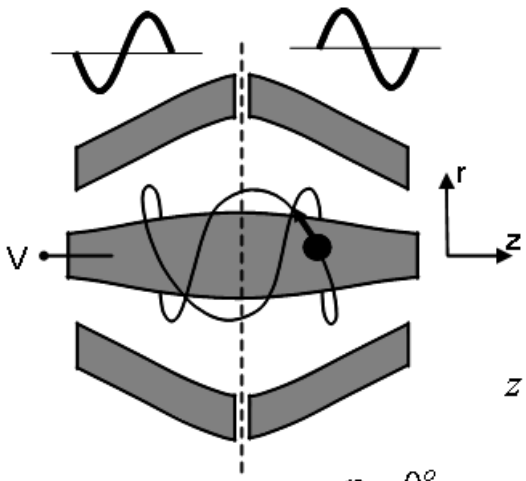
Nicole James
© Dunnivant & Ginsbach, 2008

Magnetic trap



Principles of mass analyzers

Electrostatic orbital trap - ORBITRAP



Undamped harmonic oscillator

(normal operation) $m\ddot{z} + kz = 0$

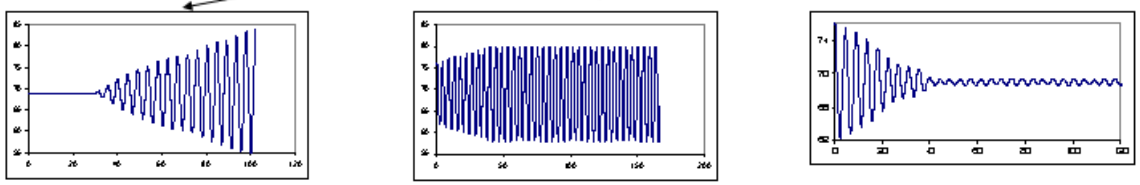
Forced, undamped harmonic oscillator

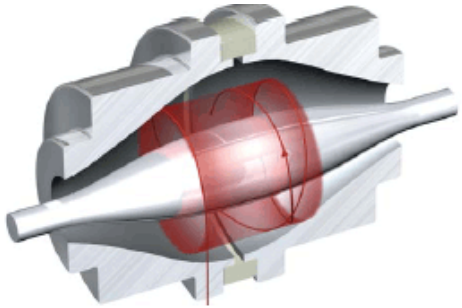
at resonance $\omega_{AC} = \omega_o$

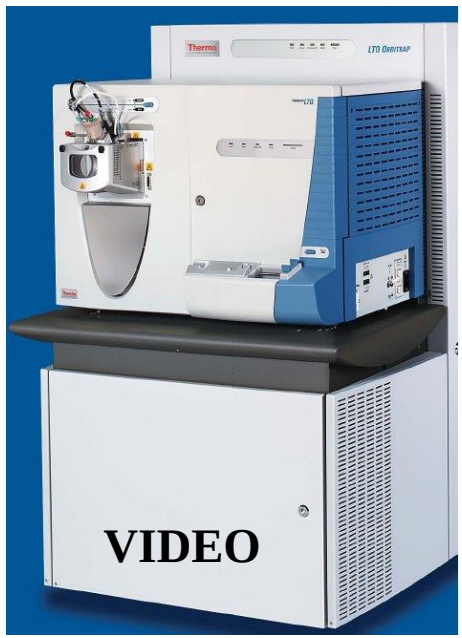
$$m\ddot{z} + kz = F_o \sin(\omega_o t)$$

$$z \approx z_o \cos(\omega_o t) + \frac{F_o}{2m\omega_o} \cos(\omega_o t - \varphi)$$

$\varphi = 0°$ $\varphi = 90°$ $\varphi = 180°$



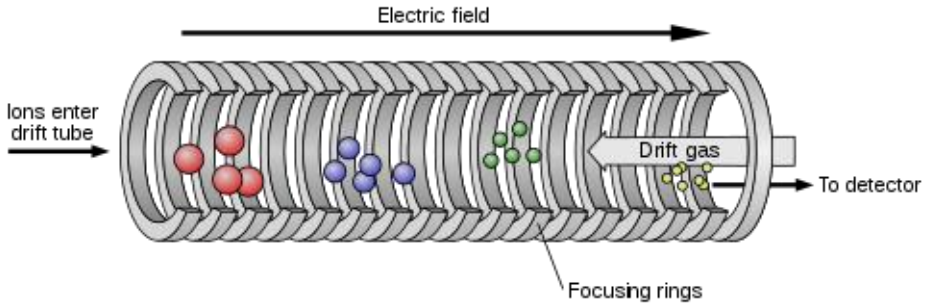




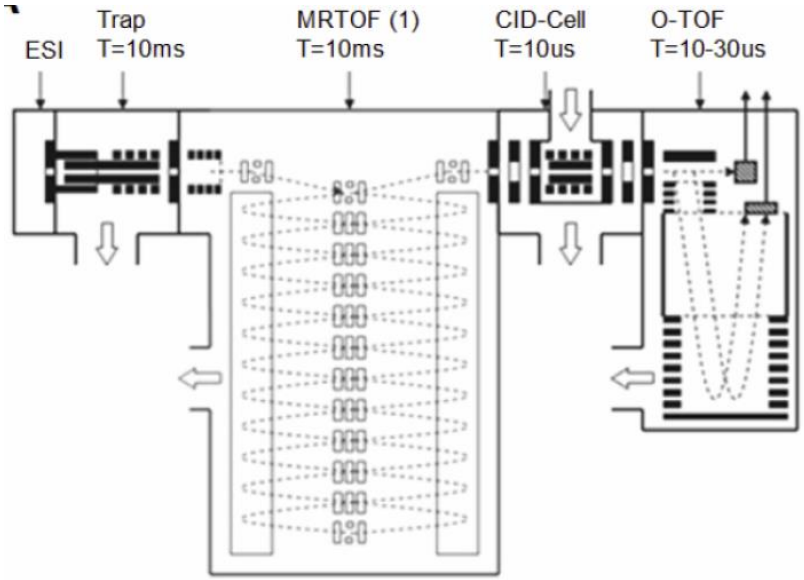
FIGURES: Thermo

Principles of additional MS parts

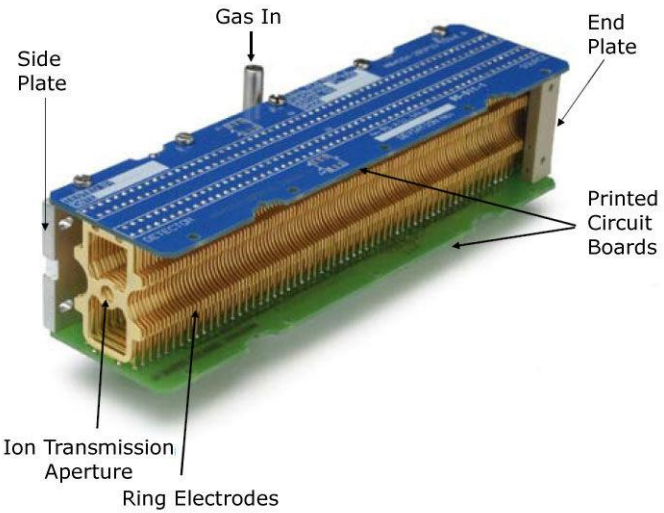
Ion mobility



Multi-reflective TOF



Traveling wave



FIGURES: Agilent Technologies, LECO, Waters,

Comparison of parameters of mass analyzers*

ANALYZER	Max. RP FWHM	Accuracy *ppm*	Range *m/z*	Scan speed	Price
Magnetic sector	10^5	< 5	10^4	low	high
Q	10^3	≈ 1000	10^3	medium	low
IT	10^3	≈ 1000	10^4	medium	medium
TOF	10^4	< 5	10^4	very high	medium
Orbitrap	10^5	< 3	10^3	high	high
FT-ICR	10^6	< 1	10^4	low	very high

* All parameters vary depending on technical progress and experimental settings

Realization of multistage (multiple) mass analysis

- **multistage or multiple mass analysis**
  → MS/MS = MS^2 = tandem MS; MS/MS/MS = MS^3

Principle: in the first stage we select primary (parent/precursor) ions, which break down in collision cell to secondary (daughter/ product/fragment) ions, which are analyzed in the second stage. It can be followed by process repetition for MS^3 realization etc.

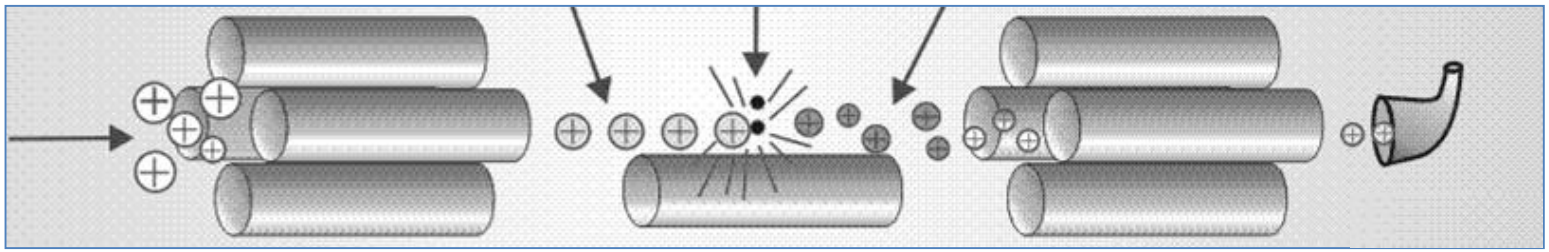
Technical realization:

***a) in space* – serial combination of the same or different mass analyzers (QqQ, Q-TOF) (chaining of experiments in space)**

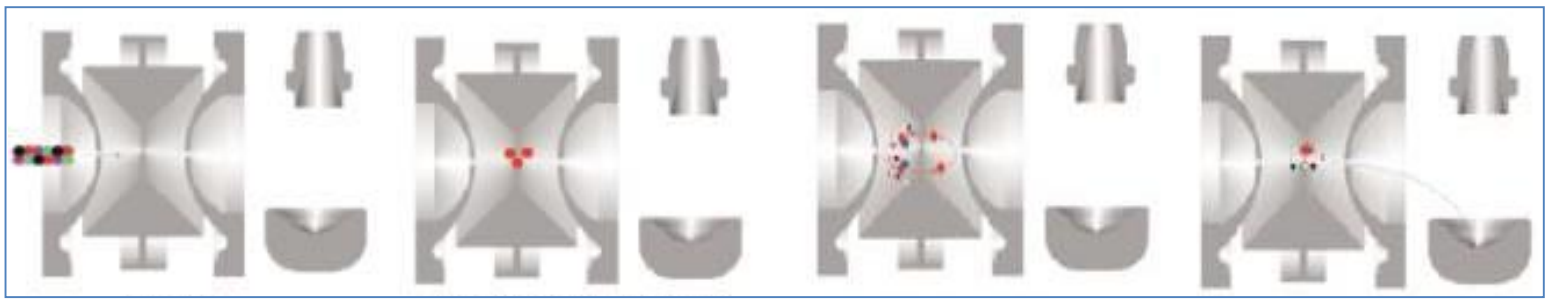
***b) in time* – takes place in one mass analyzer by timed parameter changes (IT) (chaining experiments in time)**

Realization of multistage (multiple) mass analysis

a) MS^2 in space

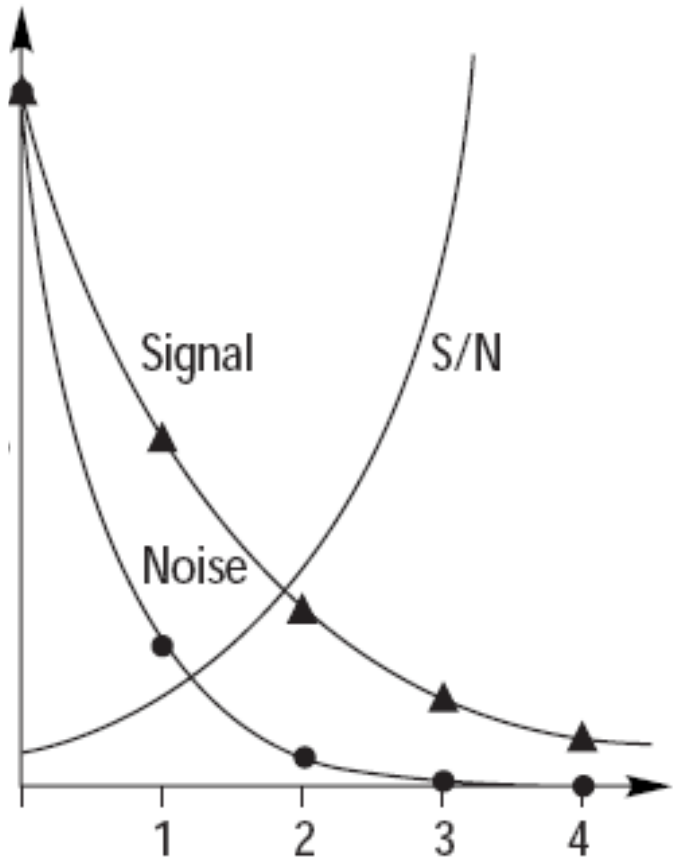


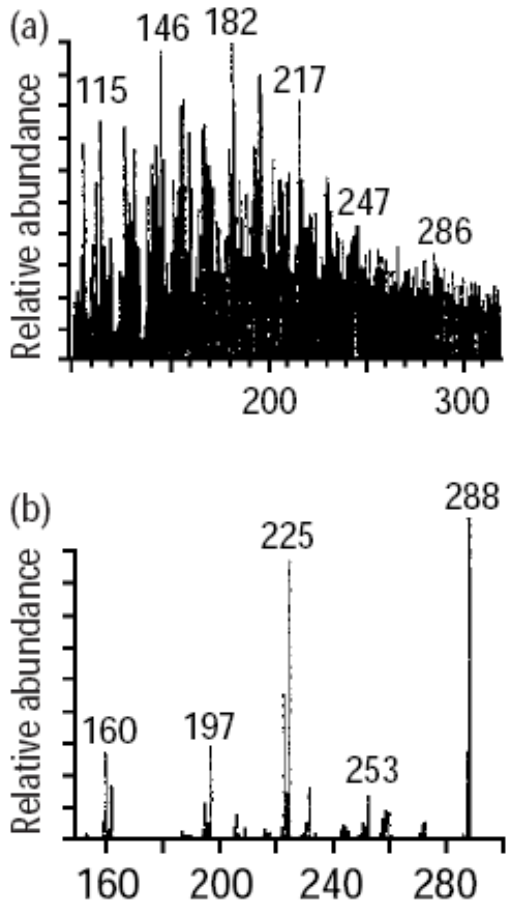
b) MS^2 in time



Realization of multistage (multiple) mass analysis

Noise reduction with number of MS analyzes → S / N increase



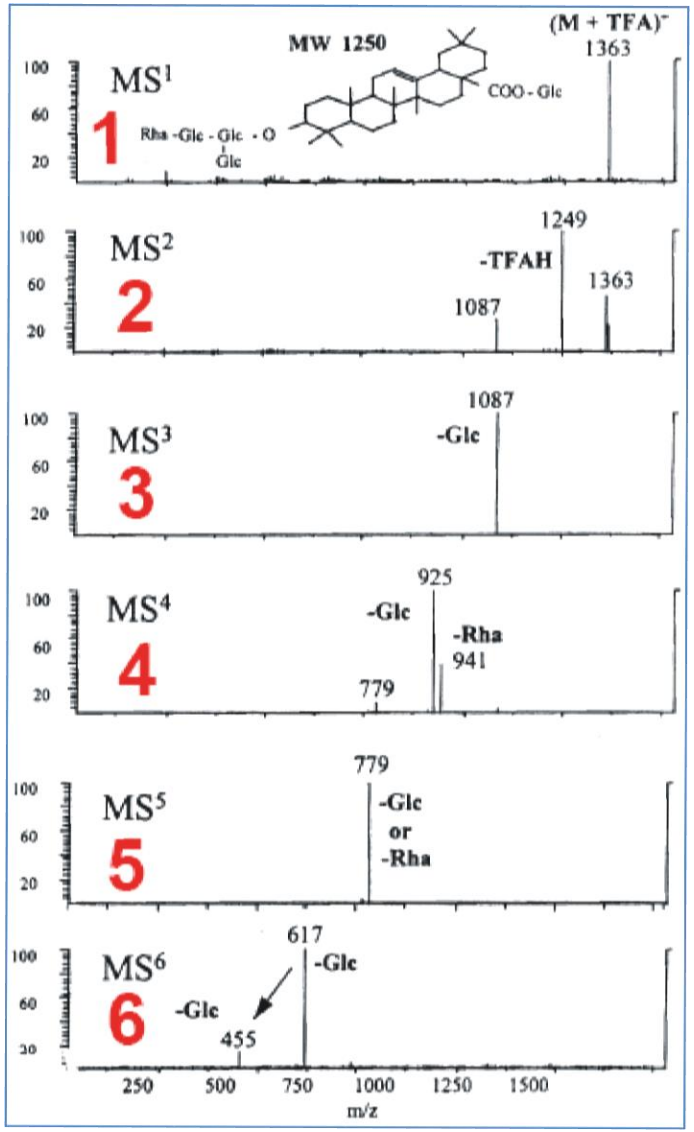


MS¹

MS²

Realization of multistage (multiple) mass analysis

Gradual fragmentation in ion trap

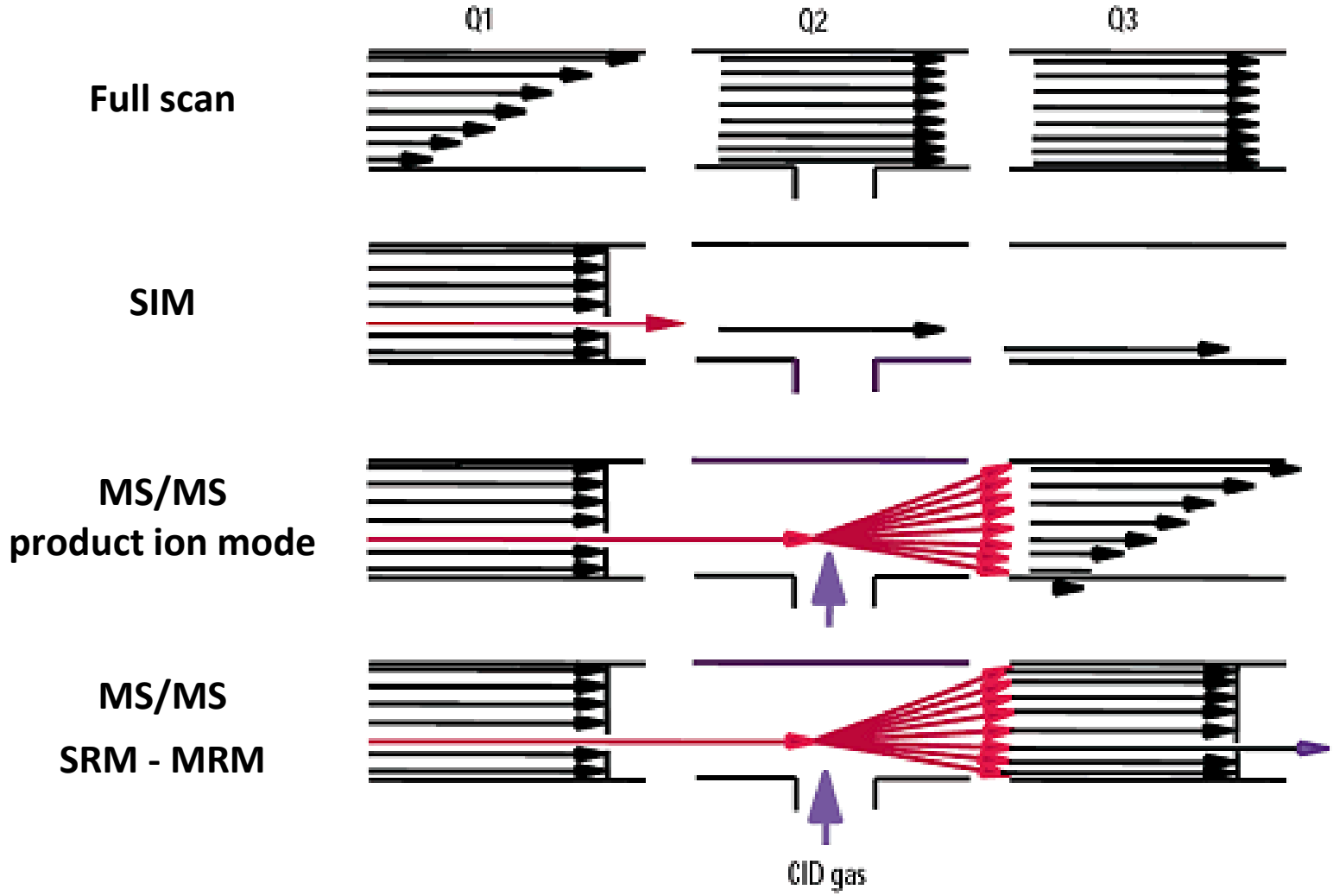


MS¹

MS⁶

Realization of multistage (multiple) mass analysis

Available measurement modes when using tandem MS



Ion detection in MS

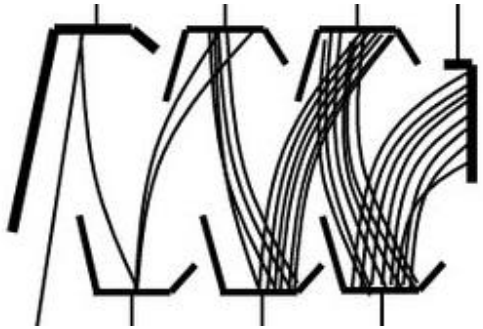
Ion detector in MS records numbers of ions, which pass through the mass analyzer

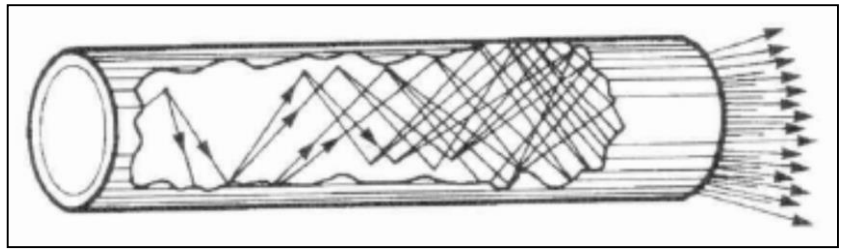
- the incident ion induces electron(s) whose current is amplified by impacts on another surface of electron multiplier (HED - high energy dynodes)

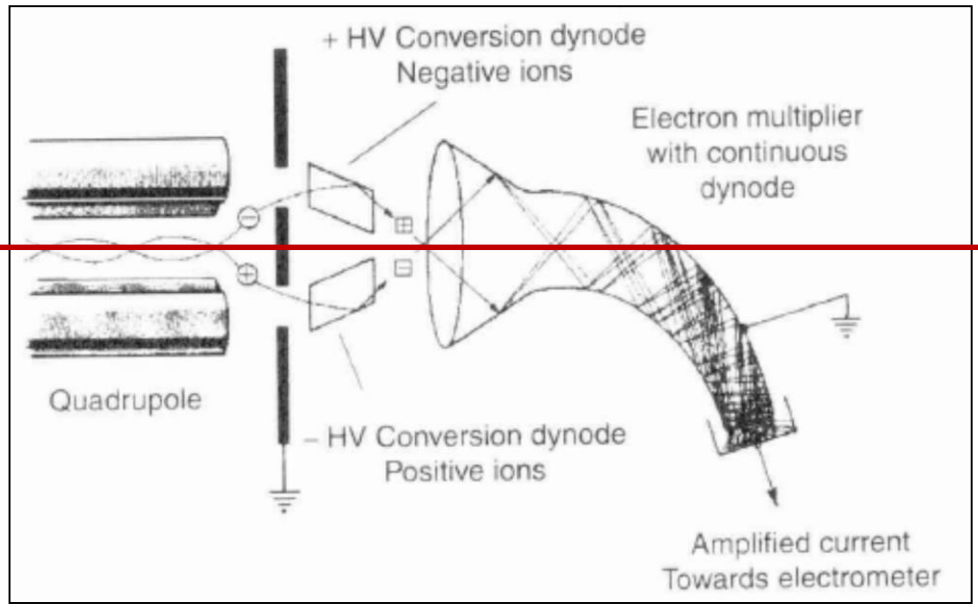
  a) plate dynodes
  b) continuous dynodes - tubes (straight, curved)
  c) parallel dynodes - microchannel plate

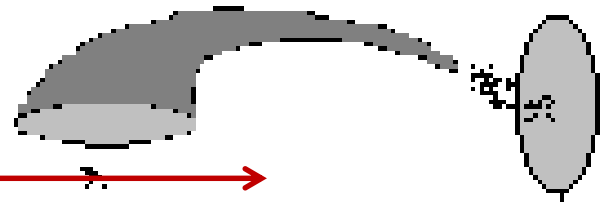
Parameters: amplification, lifetime, detection of [+] ions, detection of unwanted fragments

Ion detection in MS









Ion detection in MS