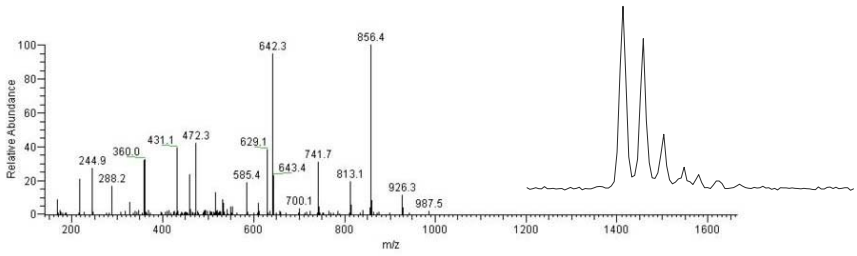
Mass Spectrometry

What is Mass Spectrometry?

- Mass Spectrometry (MS):
  The generation of gaseous ions from a sample, separation of these ions by mass-to-charge ratio, and measurement of relative abundance
- Mass-to-Charge: *m*/*z*
  - Mass in Unified Atomic Mass Units: *u* (Dalton [Da])
  - The “amu” is now officially frowned upon
- Molecular Ion: $M^{\bullet+1}$
  - Results from loss of single electron (*m*/*z* = *m*)
- Resolving Power: m/Δm
- Resolution: Δm at a given m, defined in ppm

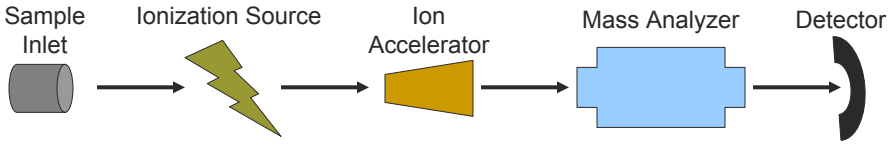
The Output

- Called Mass Spectrum
- Peak height is proportional to ion abundance
- Peak clusters result from isotope effects
  - Cluster distribution should follow isotope abundance



The Anatomy of a Mass-Spec

- Sample Inlet: Introduce analyte
- Ionization Source: Generate charged mol.
- Ion Accelerator
- Mass Analyzer: Mass/charge separation
- Detector



Ionization Sources

- Electron Ionization
- Chemical Ionization
- Atmospheric Pressure Chemical Ionization
- Electrospray Ionization
- Desorption Ionization
  - Laser Desorption
  - Matrix-Assisted Laser Desorption
  - Fast Atom Bombardment

Ion Acceleration

- Newly formed ions are accelerated into vacuum by high voltage application
  - Most protein applications, voltage is negative
  - For specialized work, voltage is positive
- Kinetic Energy (KE) imparted by voltage
  - KE is constant for all +1 charges in same voltage
  - Translational KE = $1/2mv^2$
  - So…Small *m*, Big *v* & Big *m*, Small *v*

$$v = (2zV / m)^{½}$$

Mass Analyzers

- Magnetic Sector
- Time-of-Flight
- Quadrupole (Octapole)
- Ion Trap
  - Quadrupole Ion Trap
  - Fourier Transform Ion-Cyclotron Resonance
- Orbit Trap

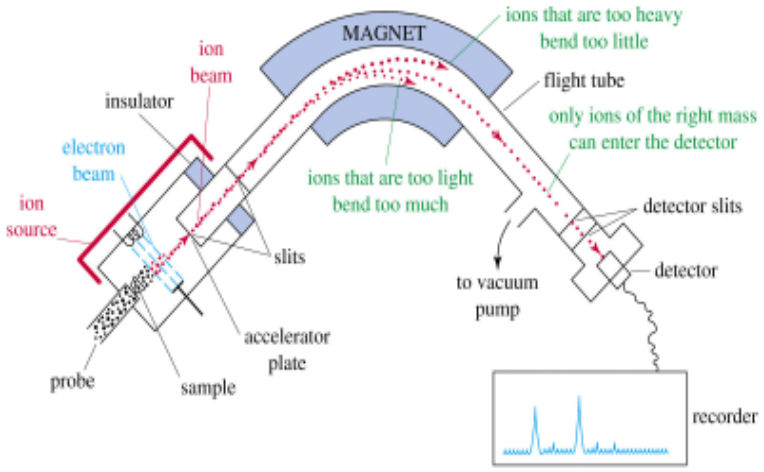
Sector Mass Analyzer

- Single-Focus MS: One *m*/*z* at a time
- Ions are accelerated into a curved path through a homogenous magnetic field (*B*)
- Magnet attractive force: Bzv
- Centrifugal force on ion: mv^2/r
- To avoid annihilation on tube wall: $Bzv=mv^2/r$

$$\boldsymbol{m/z = B^2r^2 / 2V}$$

- By scanning '*B*' the entire spectrum of *m*/*z* is obtained sequentially

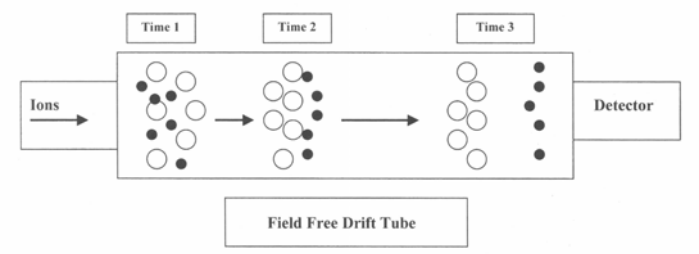
Sector MS: Schematic



Time-Of-Flight Mass Analyzer

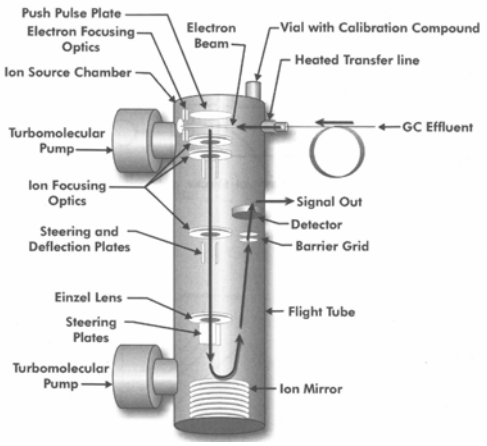
- Uses a pulse of ion mixtures, not steady stream
- Ions accelerated into *drift tube* by a pulsed electric field called the *ion-extraction field*
- Drift Tube is usually 1-2 m long, under vacuum
- Ions traverse the drift tube at different speeds

$$(L / t) = v = (2zV / m)^{1/2}$$



TOF: Reflectron/Ion Mirror

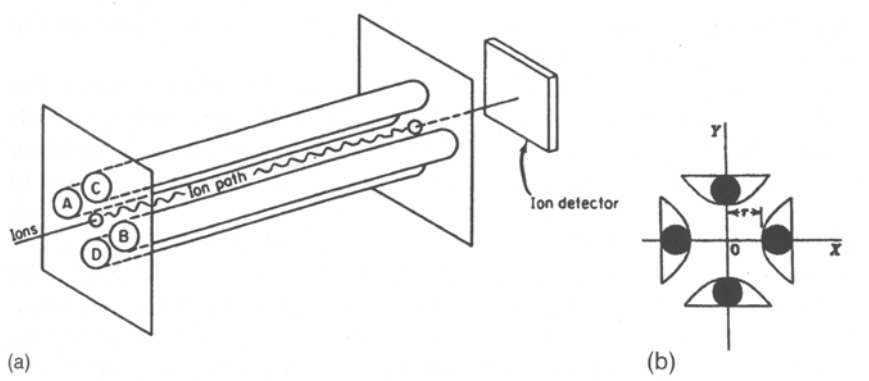
- Heterogeneity in starting position/velocity of ions reduces resolution
- Set of charged plates that reverses travel direction
  - Faster ions penetrate farther
  - Slower ions penetrate less
  - All ions of same *m/z* are accelerated the same
  - Net effect focuses signal and increases resolution



Quadrupole Mass Analyzer

- Electric, not magnetic field separates ions
- Two pairs of rods, connected to both a DC and RF voltage
- Oscillating RF voltages are 180° out of phase
- Ions are subjected to complex forces
  - Forward motion is not affected by fields
  - Sum of forces generates 'corkscrew' forward path
- Only specific *m/z* ratio is allowed to pass
- Scanning RF frequency, scan *m/z* ratios

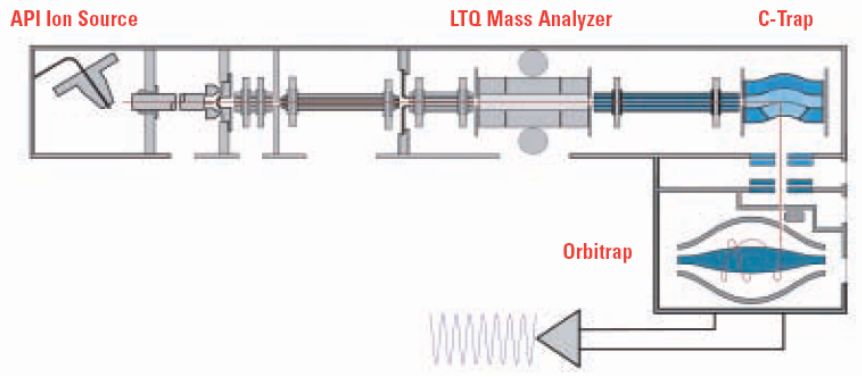
Quadrupole Schematic



Ion Trap Mass Analyzer

- Electric/magnetic fields trap, store, eject ions
- Requires an in-line quadrupole to act as mass pre-filter
- Contains a single ring electrode and a top and bottom cap electrode
- Varying RF frequency will vary the *m/z* ratios that are trapped
- Additional fragmentation can be performed on ions stored in the ion trap

Orbit Trap Mass Analyzer



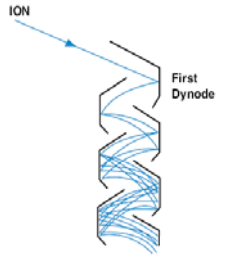
Detectors

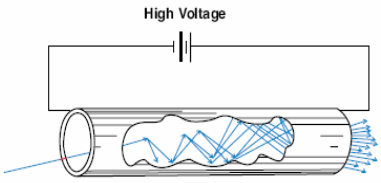
- Electron Multipliers (EM)
  - Discrete-Dynode EM
  - Continuous-Dynode EM
- Faraday Cup
- Microchannel Plate (Array Detector)

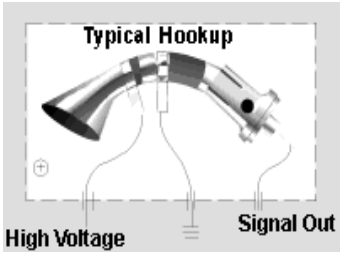
Electron Multiplier

- Most common detector
- Similar to Photomultiplier Tube or PMT
- Reactive surface that emits electrons when struck by high velocity particle
- Multiple surfaces are used in sequence, amplifying the initial response
- Degree of amplification is called the "*gain*"
- Signal is proportional to impact energy, incidence angle, and particle type

Electron Multiplier Diagrams





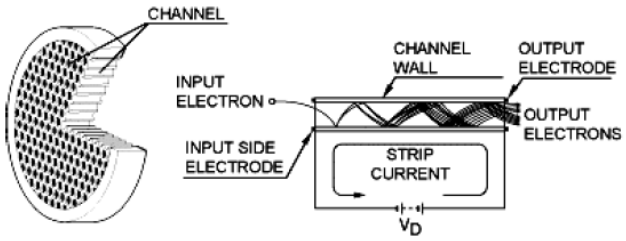


Faraday Cup

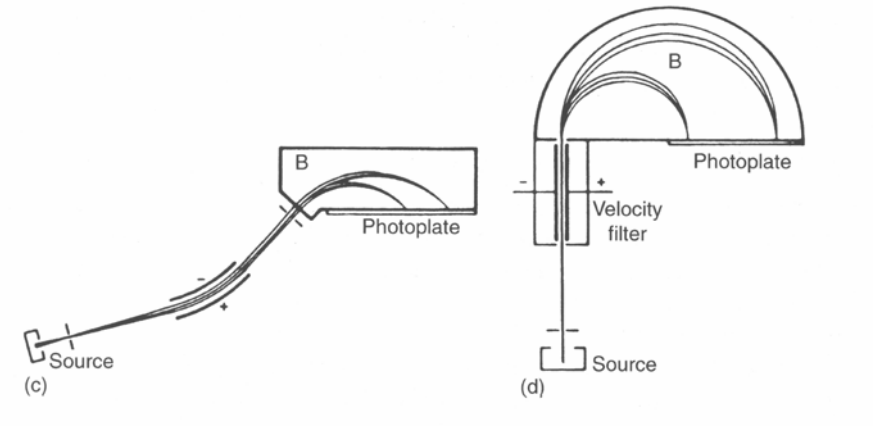
- Least expensive detector
- Metal or Carbon cup
- Captured ions transfer charge to cup
- Current generated is directly proportional to number of ions and number of charges/ion
  - No mass discrimination
  - Low sensitivity
- Faraday cups can be used to calibrate other MS detectors

Microchannel Plate Detectors

- Spatially resolved array of EM channels
- Not used as frequently, yet
- Allows '3-D' analysis of data
  - Intensity
  - Time
  - Space



Sector MS Using MCP



Undergraduate Instrumental Analysis, 6th ed. Robinson, Skelly-Frame, & Frame. 2005.