Quadrupole and Ion Trap Mass Analysers and an introduction to Resolution
A simple definition of a Mass Spectrometer

A Mass Spectrometer is an analytical instrument that can separate charged molecules according to their mass-to-charge ratio.

The mass spectrometer can answer the questions “what is in the sample” (qualitative structural information) and “how much is present” (quantitative determination) for a very wide range of samples at high sensitivity.
Components of a Mass Spectrometer

Atmosphere

Vacuum System

Sample Inlet → Ionisation Method → Mass Analyser → Detector → Data System
How are mass spectra produced?

- Ions are produced in the source and are transferred into the mass analyser.

- They are separated according to their mass/charge ratio in the mass analyser (e.g. Quadrupole, Ion Trap).

- Ions of the various m/z values exit the analyser and are ‘counted’ by the detector.
What is a Mass Spectrum?

- A mass spectrum is the relative abundance of ions of different m/z produced in an ion source.
  - a “chemical fingerprint”

- It contains:
  - Molecular weight information (generally)
  - Structural Information (mostly)
  - Quantitative information
What does a mass spectrum look like?

Electrospray mass spectrum of salbutamol

Base peak at m/z 240
What information do you need from the analysis?

- Low or High Mass range
- Average or Monoisotopic mass (empirical)
- Accurate Mass
- Quantitation - precision, accuracy, selectivity
- Identification
- Structural Information
- Isotope Ratios
Mass Analyzers

Types of Mass Spectrometer

- Magnetic Sector
- Quadrupole
- Ion Trap
- Time-of-flight
- Hybrid- Sector/trap, Quad/TOF etc

Mass Spectrometers separate ions according to their mass-to-charge (m/z) ratios
A Triple Stage Quadrupole Mass Analyzer

Finnigan TSQ

ESI Probe

Square Rod Ion Transmission to Analytical Quads

Hyperbolic, high precision quadrupoles

Q2 is Non-Linear Collision Cell

Electron Multiplier, Detection System
Hyperbolic Quadrupoles
How does the quadrupole work?

The quadrupole consists of four parallel rods. The opposing rods have the same polarity whilst adjacent rods have opposite polarity.

Each rod is applied with a DC and an RF voltage. Ions are scanned by varying the DC/Rf quadrupole voltages.

Only ions with the selected mass to charge ratio will have the correct oscillatory pathway in the Rf field.
Quadrupole Mass Analyser

The green ion is transmitted along the quadrupole in a stable trajectory Rf field. The red ion does not have a stable trajectory and is ejected from the quadrupole.
Non-linear collision cell in the TSQ

A non-linear Q2 ensures that neutral species are ejected from the mass analyser pathway.
Non-linear collision cell removes the line of sight to the detector for neutral species - reducing the noise at the detector.
A 90 Degree Square Q2 in the TSQ Quantum

Dynode

Q3

Q2

Q1

Q0

API

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Ion Trap

- Consists of ring electrode and two end caps
- Principle very similar to quadrupole
- Ions stored by RF & DC fields
- Scanning field can eject ions of specific m/z
- Advantages
  - MS/MS/MS.....
  - High sensitivity full scan MS/MS
The ability of a quadrupole to resolve masses is proportional to frequency of AC and length of quadrupole.
Resolving power of round rods

Round rods can only approximate the field generated by hyperbolic rods - most ideal when \( \frac{R_{rod}}{R_0} = 1.16 \)

- \( R_{rod} \) = Radius of rod
- \( R_0 \) = Position of rod relative to axis of instrument
Manufacturing rods such that $R_{rod}/R_0 = 1.16$ over the full length of quadrupole is non-trivial. Variability would assure that one $M^+$ is selected at one position and another where the ratio is different - loss of specificity and sensitivity.

Thermal expansion coefficients must be very low - expansion / contraction within the length of the rod changes $R_{rod}/R_0$.

Hyperbolic rods give excellent transmission across the full range of resolution - providing optimal analytical specificity. Compare sensitivity at unit resolution versus open resolution. At tighter resolution round rods systems tend to lose a greater proportion of ions through variation in $R_{rod}/R_0$. 

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Round rods manufacture typically requires several steps - first, machine rods. Second, machine ‘holder’ by drilling four holes into a cylinder. Third, machine ‘dropout’ to create ion path. Insert rods. Error in $R_{rod}/R_0$ grows by number of processes.
Resolution Basics

Resolution = \( \frac{m}{\Delta m} \)

Magnetic Sector Instruments
Constant Resolution with mass
10% Valley Definition

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Resolution Basics

Quadrupoles
Ion traps
and TOF’s

Constant peak widths
Variable Resolution

FWHM Definition

Resolution Basics

Resolution = \frac{m}{\Delta m}

m/z 500/1, R = 500
m/z 500/0.1, R = 5000
What is the advantage of using high resolution mass spectrometry?

The advantage of high resolution measurement is to eliminate chemical background of the same nominal mass but different accurate mass and, therefore to increase the signal to noise ratio and the sensitivity respectively.

Better selectivity is obtained by applying high resolution in case of isobaric compounds, i.e. two compounds of same nominal mass but different accurate mass. With low resolution only a combined Spectral result is obtained under Product ion conditions. With high resolution separate detection and therefore separate isolation and MS/MS spectra are obtained.

Example:

\[
\begin{align*}
\text{Compound mass1: } & 372.351 \text{ Da} & \text{R= 1000} \\
\text{Compound mass2: } & 372.421 \text{ Da} & \text{R= 5000}
\end{align*}
\]

\[
\begin{align*}
\text{OVERLAPPING} & \quad \text{SEPARATION}
\end{align*}
\]
Effect of changing resolution on peak shape

- 1.0 FWHM
- 0.7 FWHM
- 0.5 FWHM
- 0.3 FWHM
- 0.2 FWHM
- 0.1 FWHM
Effect of Peak Width On Transmission

[Bar chart showing the effect of peak width FWHM on transmission for QUADRUPOLE and ROUND RODS. The x-axis represents peak width FWHM (2, 1.5, 0.7, 0.5, 0.2, 0.1) and the y-axis represents transmission (%). The chart includes a note: * Resolution at m/z 500.]
Resolving Target Compounds in the Presence of Interferences

- Examples: Mometasone and Alprazolam were spiked into PPG
- >5000 (FWHM) parent ion resolution allows mass selection of these compounds differing by less than 0.2 Da from PPG
- Increasing the resolution to exclude the PPG interference increases the selectivity and specificity for the quantitative assay
Mometasone resolution in the presence of PPGs

(Mometasone [M+H]^+ = 521.2, PPG (n=8) [M+Na]^+ = 521.3)

resolved Q1 mass spectrum

transmitted parent ions
Q1 at unit resolution

Q1 selecting only
mometasone ^{35}\text{Cl}

transmitted parent ions
Q1 at unit resolution

Q1 selecting only
mometasone ^{37}\text{Cl}
Mometasone resolution in the presence of PPGs
product ion spectra of $^{37}$Cl mometasone at various precursor ion resolutions

The increased resolution on product ion scan of $^{37}$Cl mometasone can selectively exclude PPG interferents with an actual mass difference of less than 0.2 Da.
Alprazolam resolution in the presence of PPGs
(alprazolam [M+H]^+ = 309.0907, PPG (n=5) [M+H]^+ = 309.2277)

250 pg/μL alprazolam in 20 μM PPGs

Unit resolution on Q1

Transmitted precursor ions 309→309

0.08 FWHM resolution on Q1
Set to pass PPG ions

0.08 FWHM resolution on Q1
Set to pass alprazolam ions
Alprazolam resolution in the presence of PPGs

Product ion spectra at various precursor ion resolutions

The increased resolution on product ion scan of alprazolam can selectively exclude PPG interferents with an actual mass difference of less than 0.2 Da.
## Comparison of Quads and Traps

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