Quadrupole and Ion Trap Mass Analysers and an introduction to Resolution

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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

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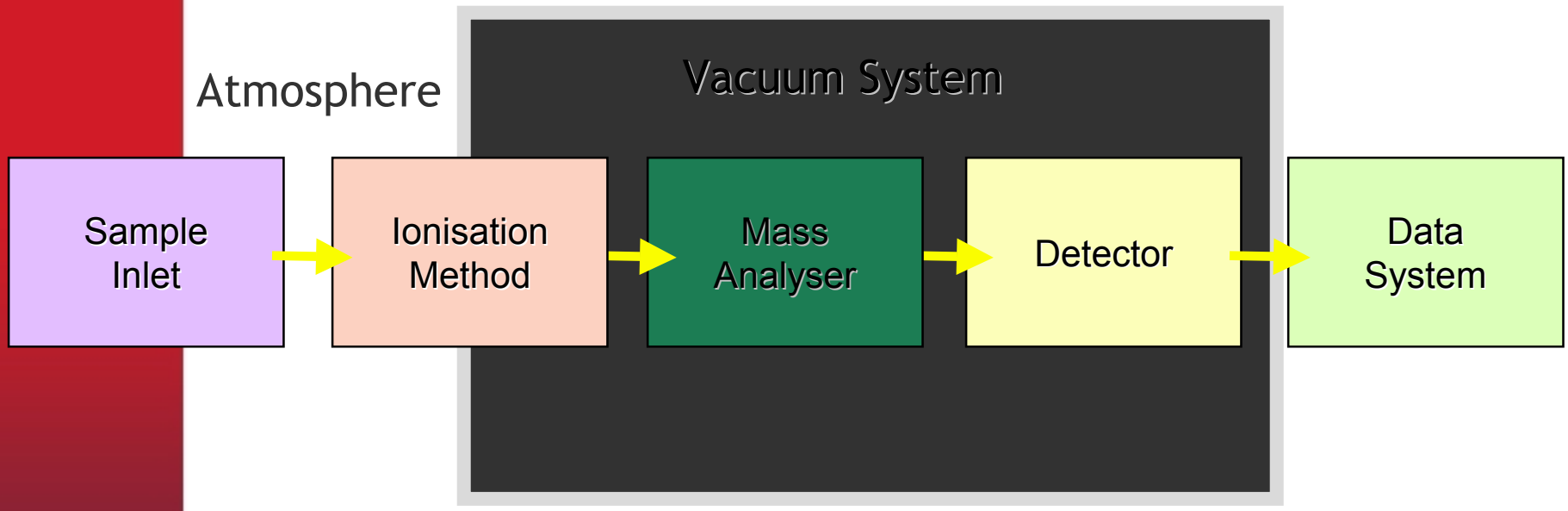
Components of a Mass Spectrometer



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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

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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

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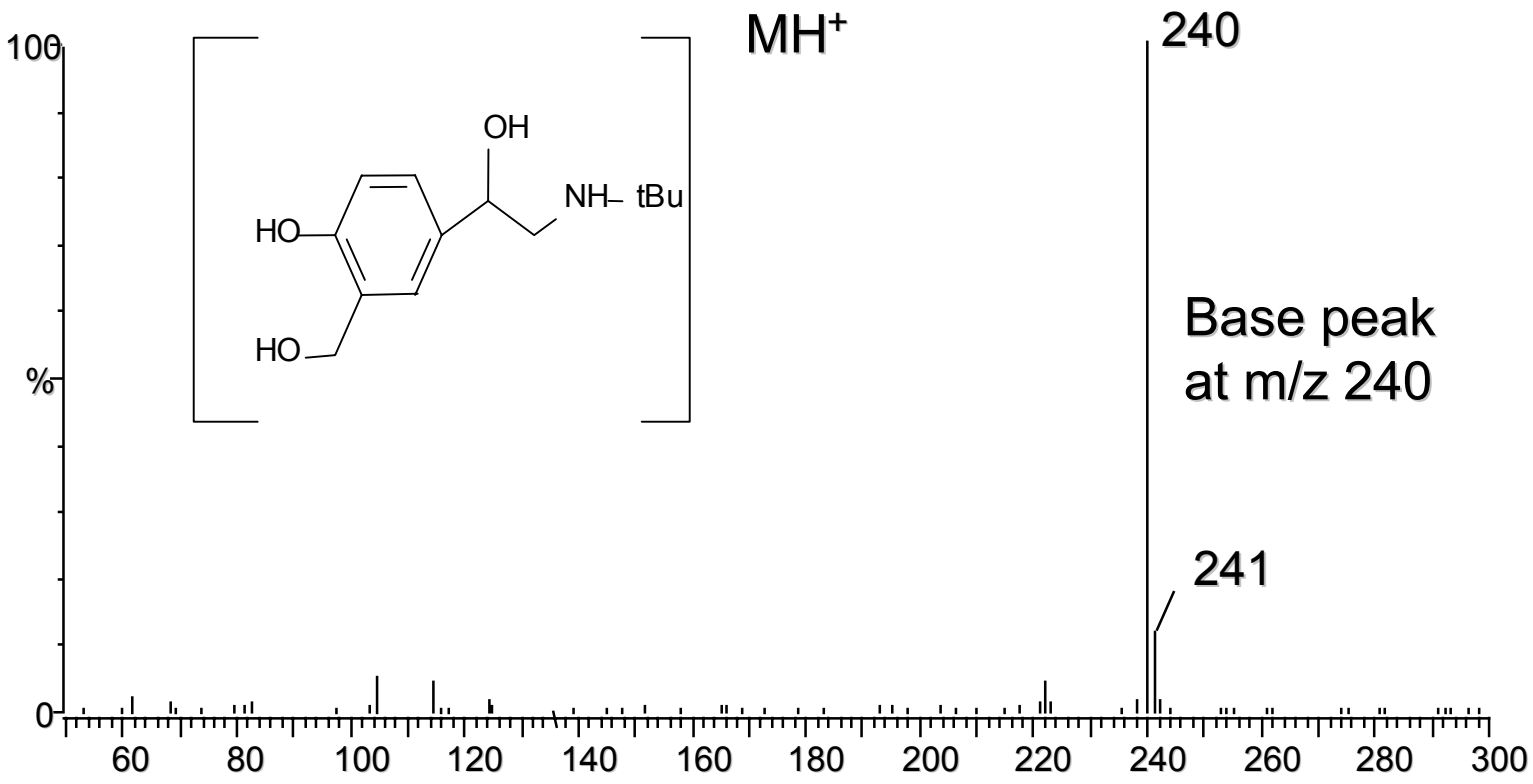
What does a mass spectrum look like ?

- Electrospray mass spectrum of salbutamol



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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

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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

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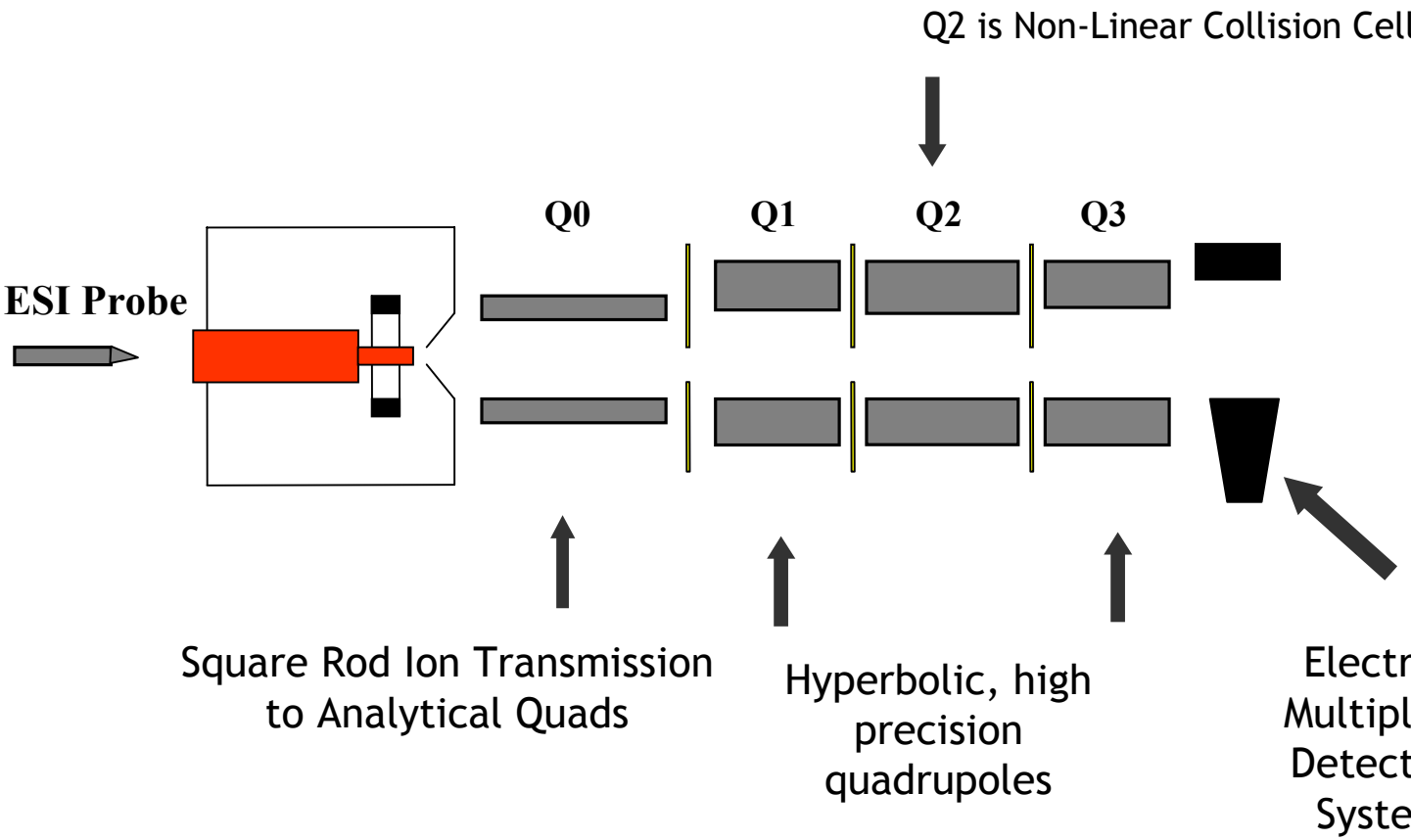
A Triple Stage Quadrupole Mass Analyzer

Finnigan TSQ



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Hyperbolic Quadrupoles

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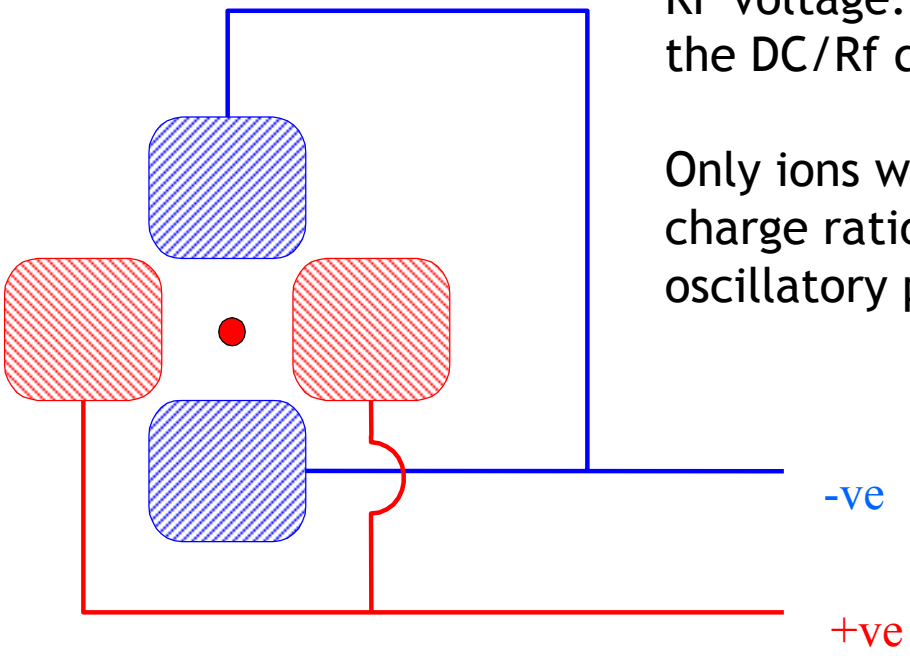
How does the quadrupole work ?

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.

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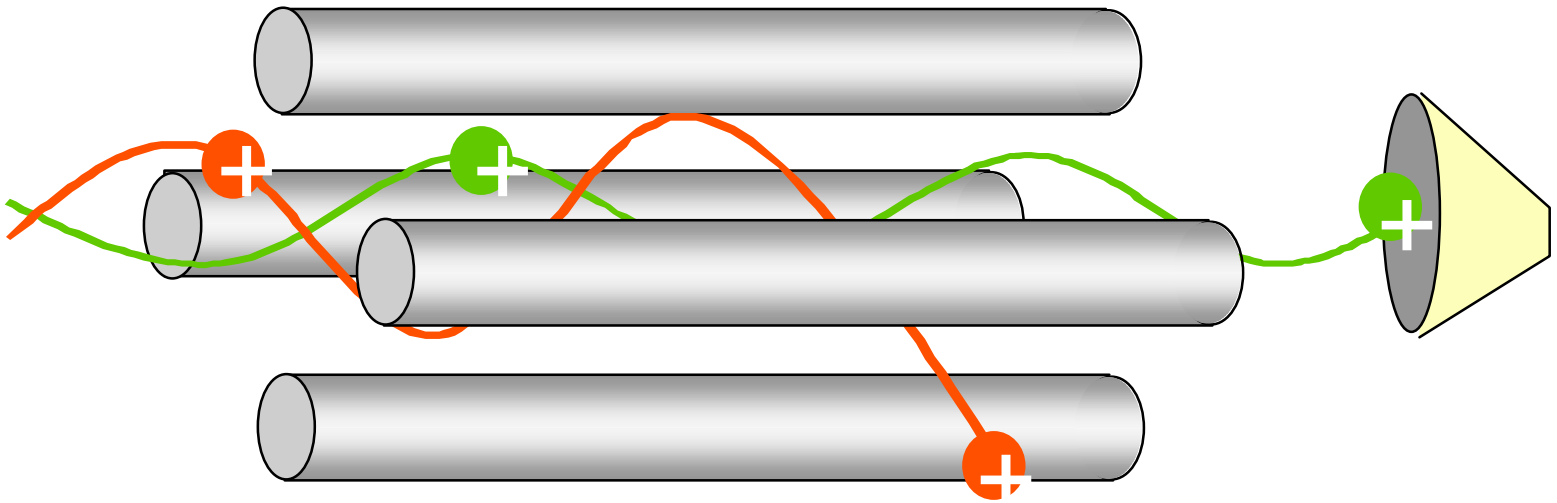
Quadrupole Mass Analyser



The ● ion is transmitted along the quadrupole in a stable trajectory Rf field. The ● ion does not have a stable trajectory and is ejected from the quadrupole.

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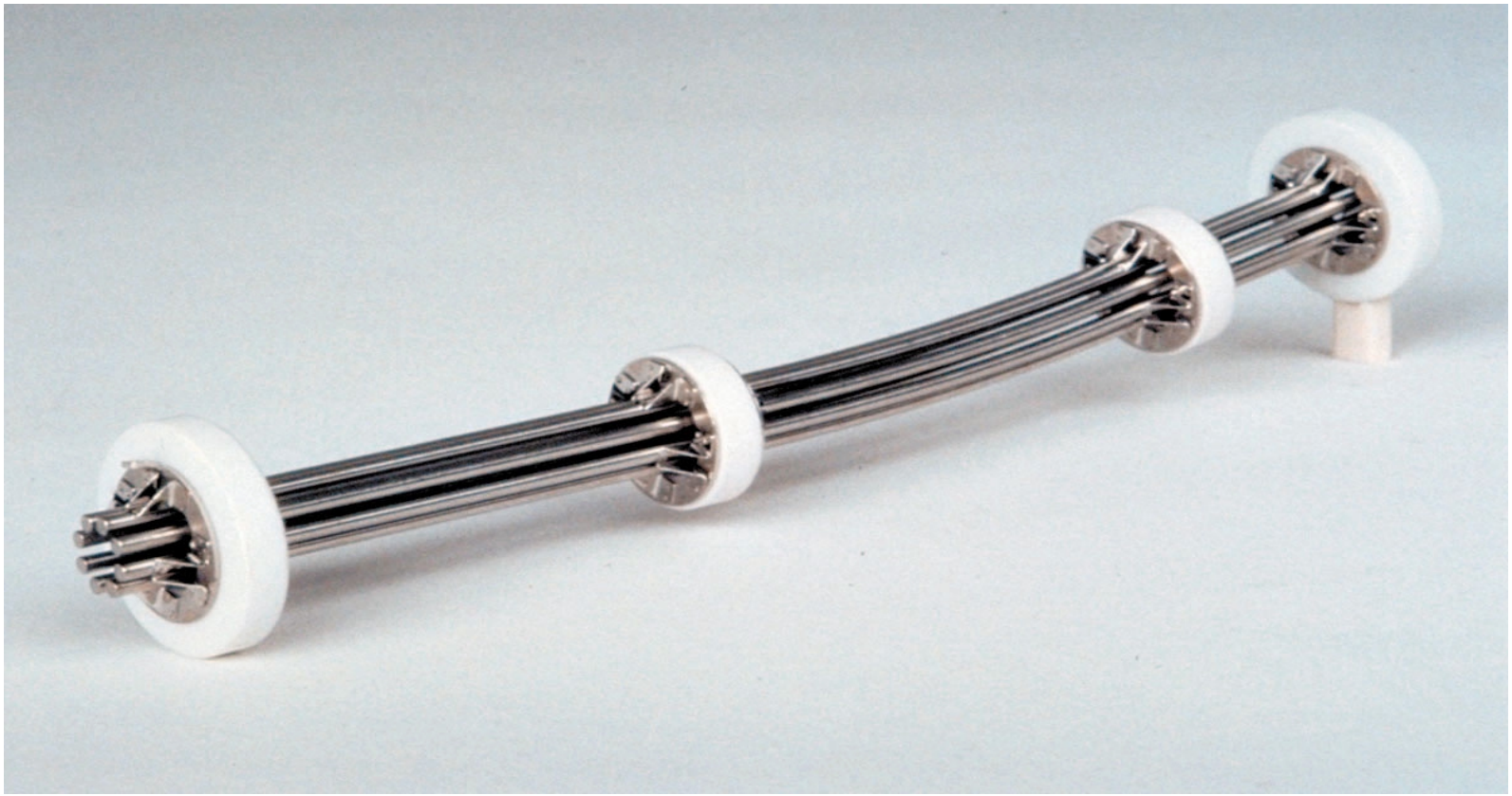
Non-linear collision cell in the TSQ

A non-linear Q2 ensures that neutral species are ejected from the mass analyser pathway



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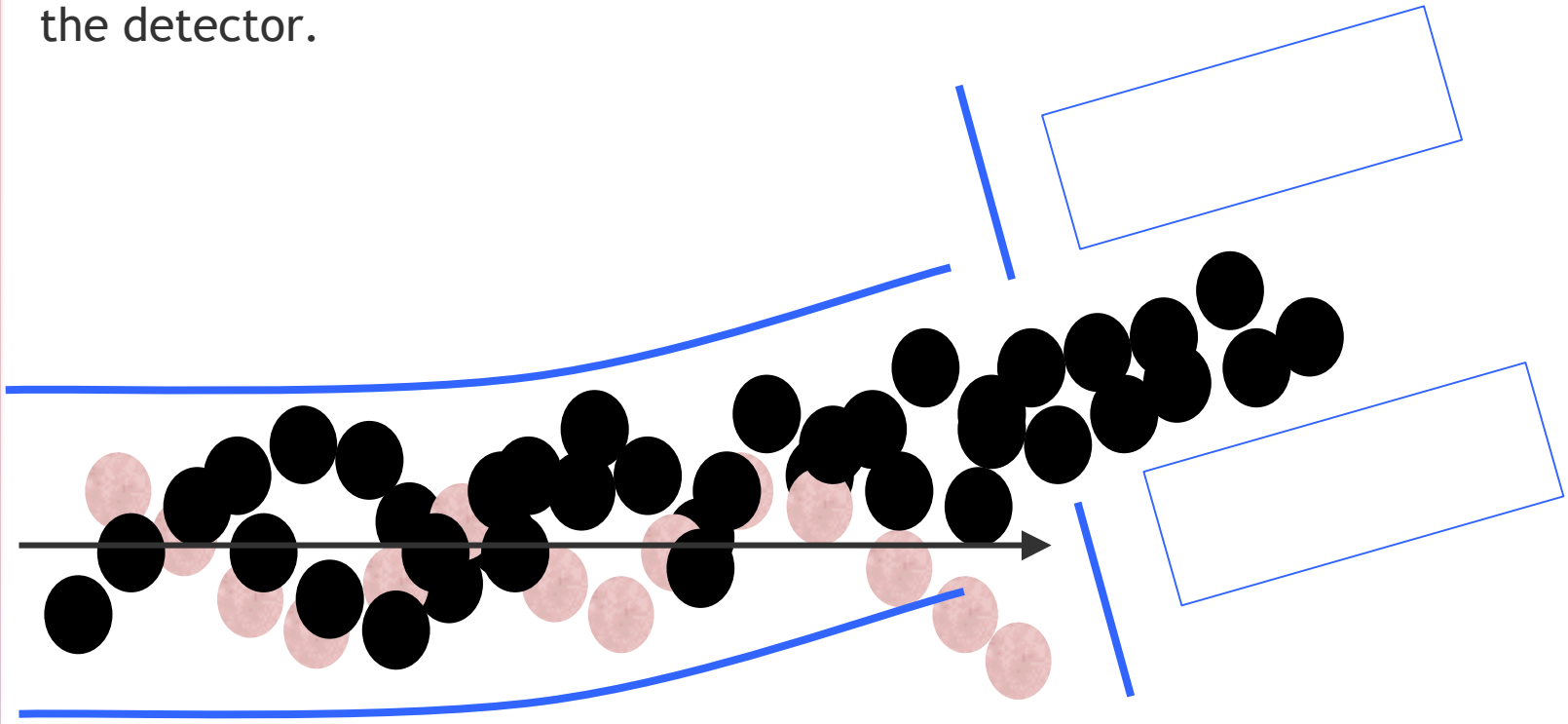
Non-linear collision cell in TSQ

Non-linear collision cell removes the line of sight to the detector for neutral species - reducing the noise at the detector.



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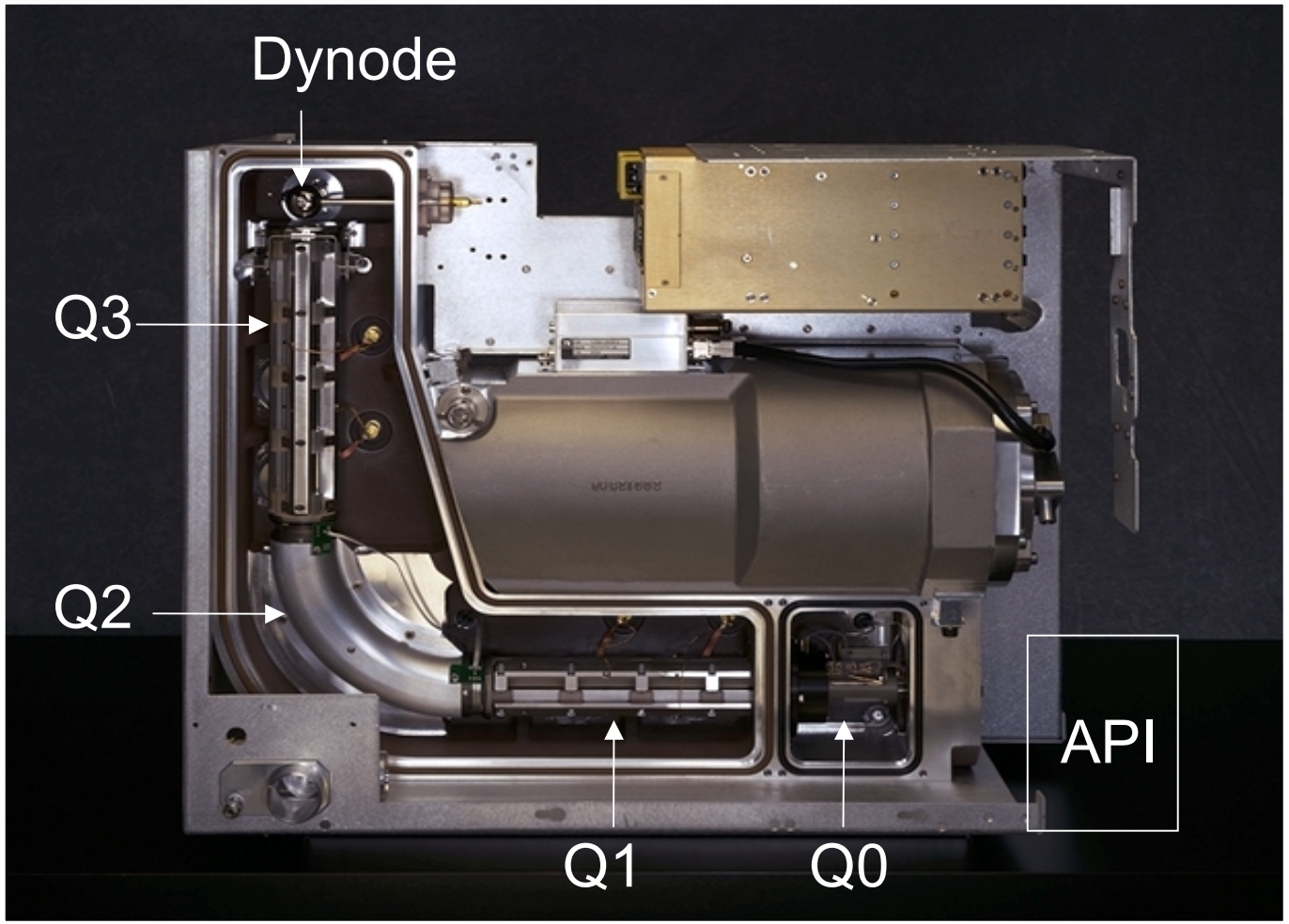
A 90 Degree Square Q2 in the TSQ Quantum



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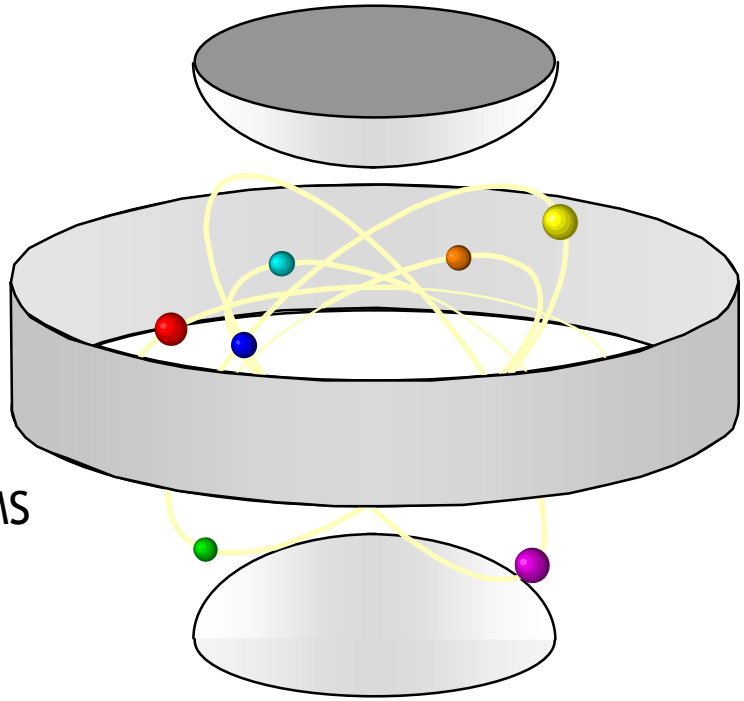
Ion Trap

- 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



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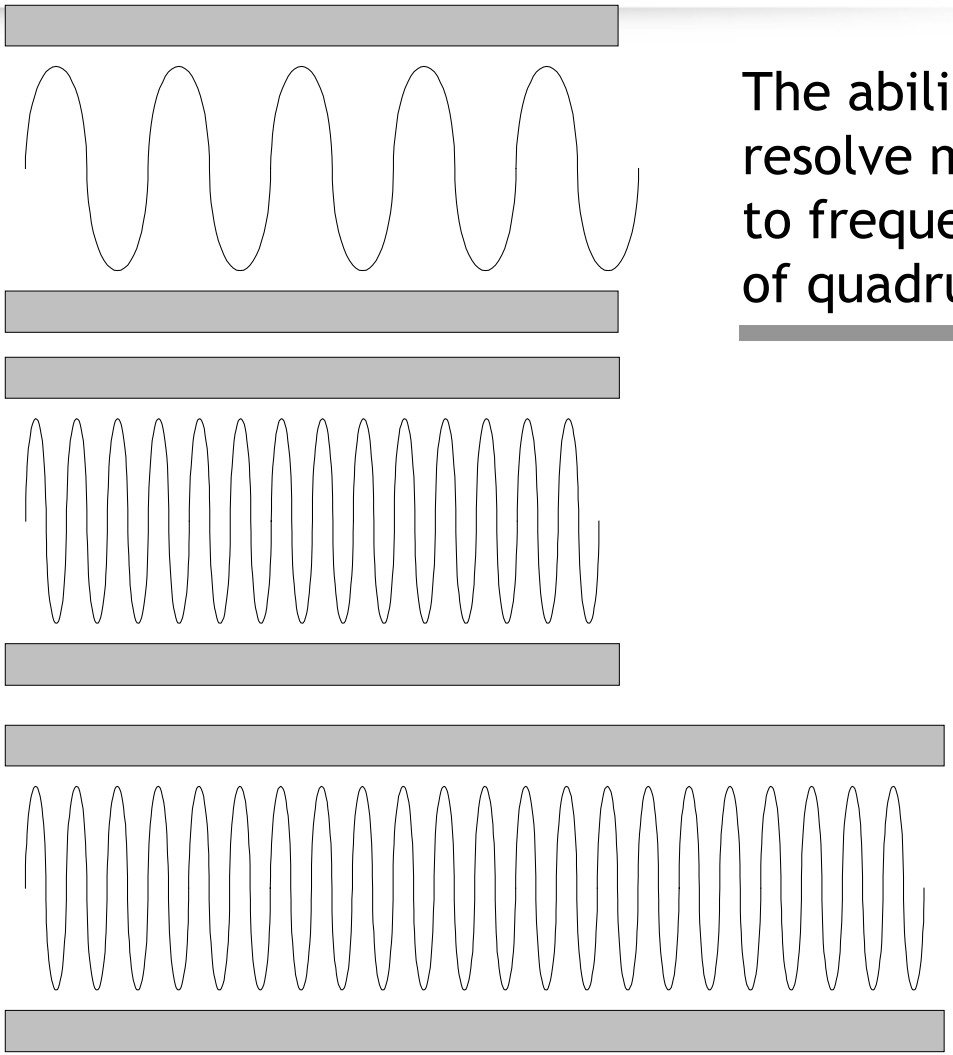
Resolving Power of a quadrupole



The ability of a quadrupole to resolve masses is proportional to frequency of AC and length of quadrupole

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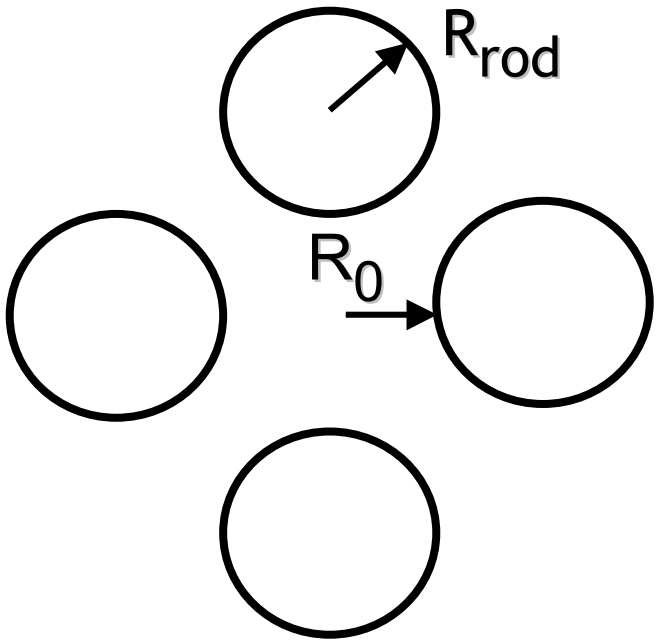
Resolving power of round rods

Round rods can only approximate the field generated by hyperbolic rods - most ideal when $R_{rod}/R_0 = 1.16$



R_{rod} = Radius of rod

R_0 = Position of rod relative to axis of instrument

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Resolving power of round rods

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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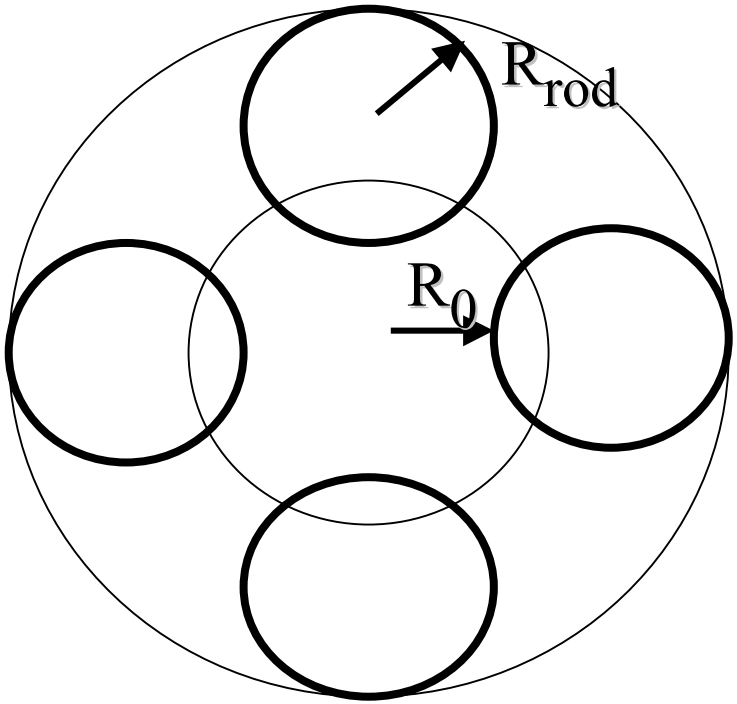
Manufacture of round rods

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.



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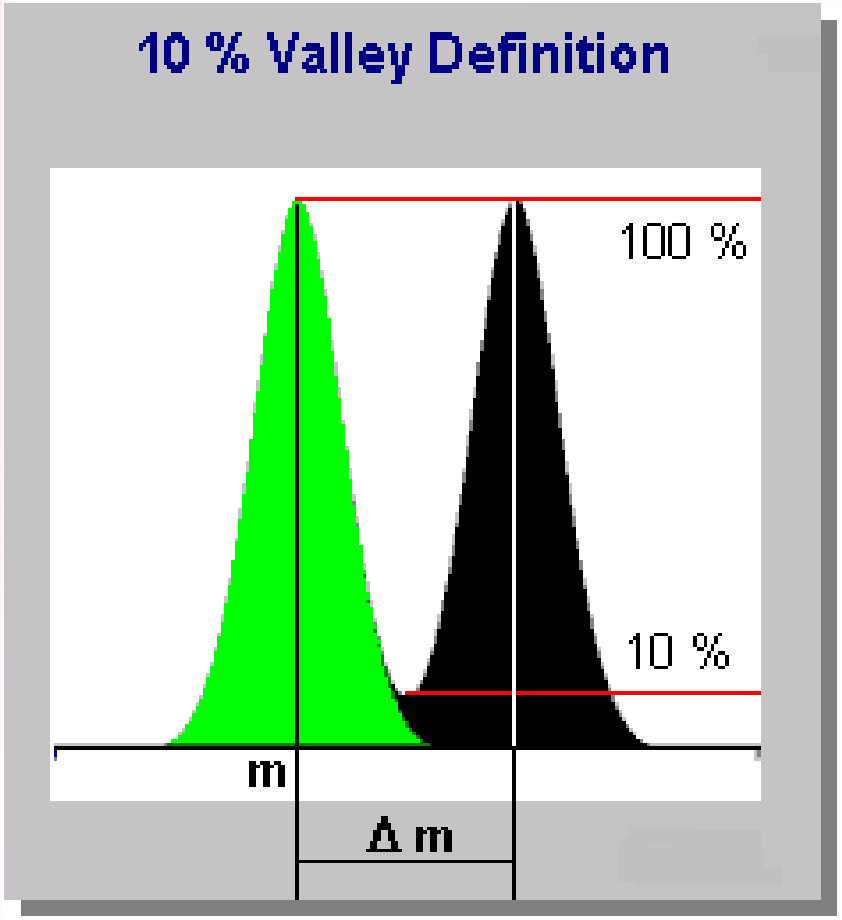
Resolution Basics



Magnetic Sector Instruments

Constant Resolution with mass

10% Valley Definition

Resolution = m / Δ m

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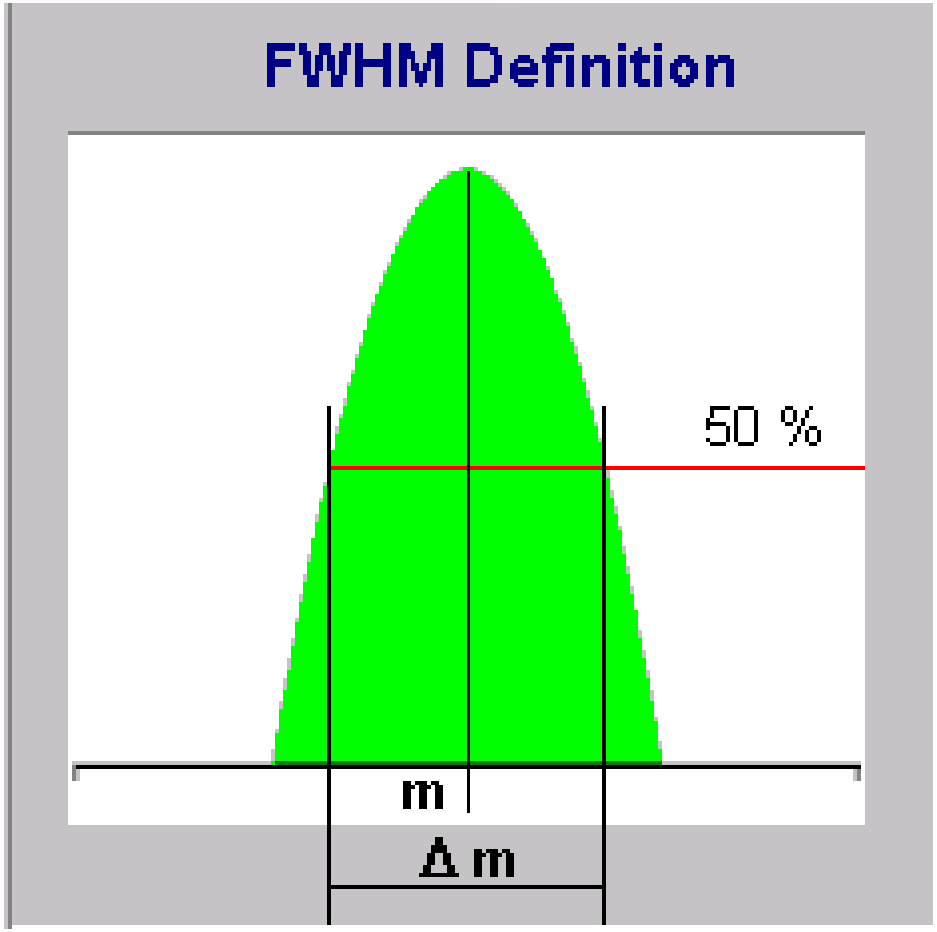
Resolution Basics



Quadrupoles

Ion traps

and TOF's

Constant peak widths

Variable Resolution

FWHM Definition

Resolution = m / Δ m

m/z 500/1, R = 500

m/z 500/0.1, R = 5000

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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:	R= 1000	R= 5000
Compound mass1: 372.351 Da Compound mass2: 372.421 Da	OVERLAPPING	SEPARATION

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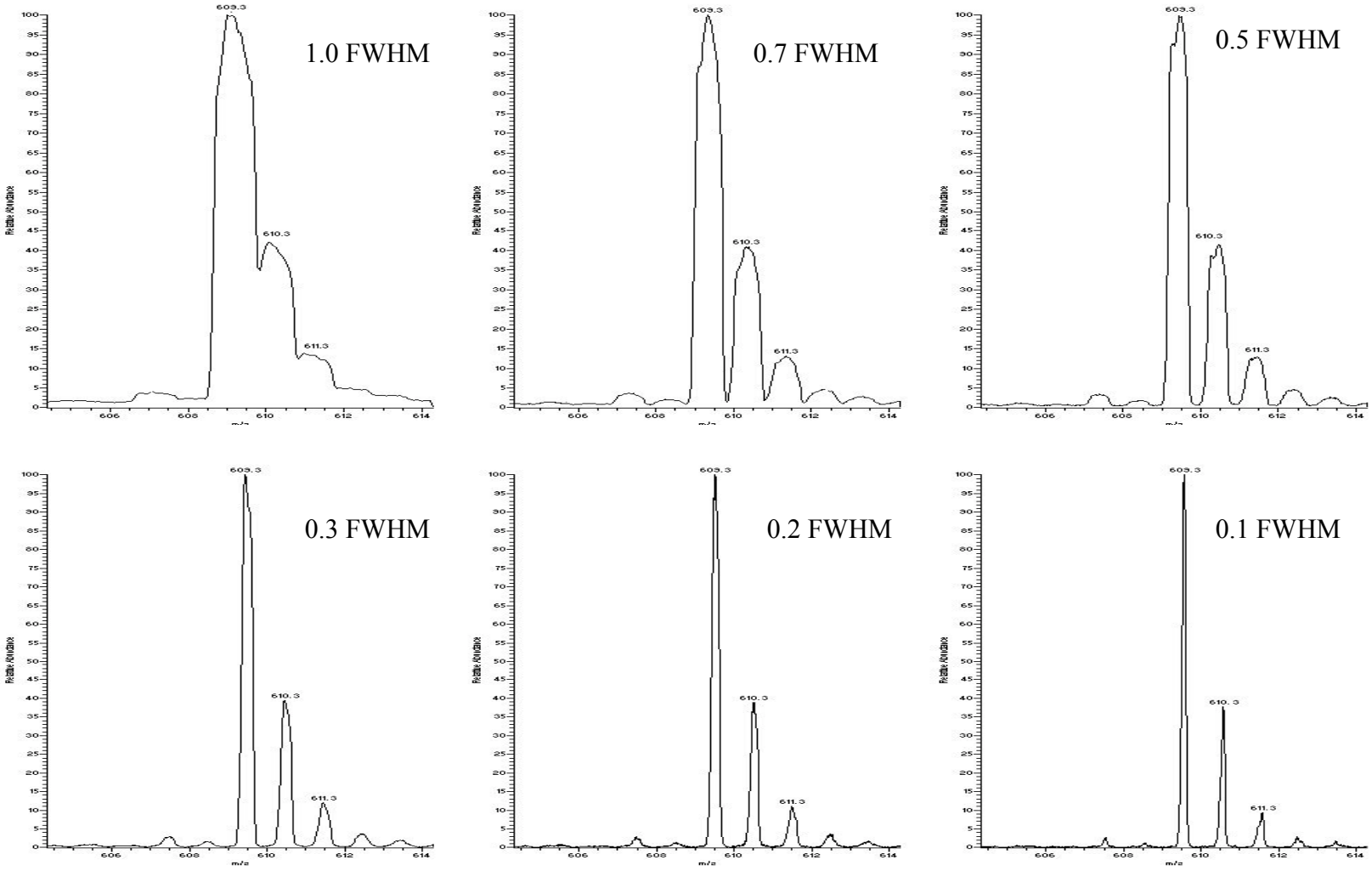
Effect of changing resolution on peak shape



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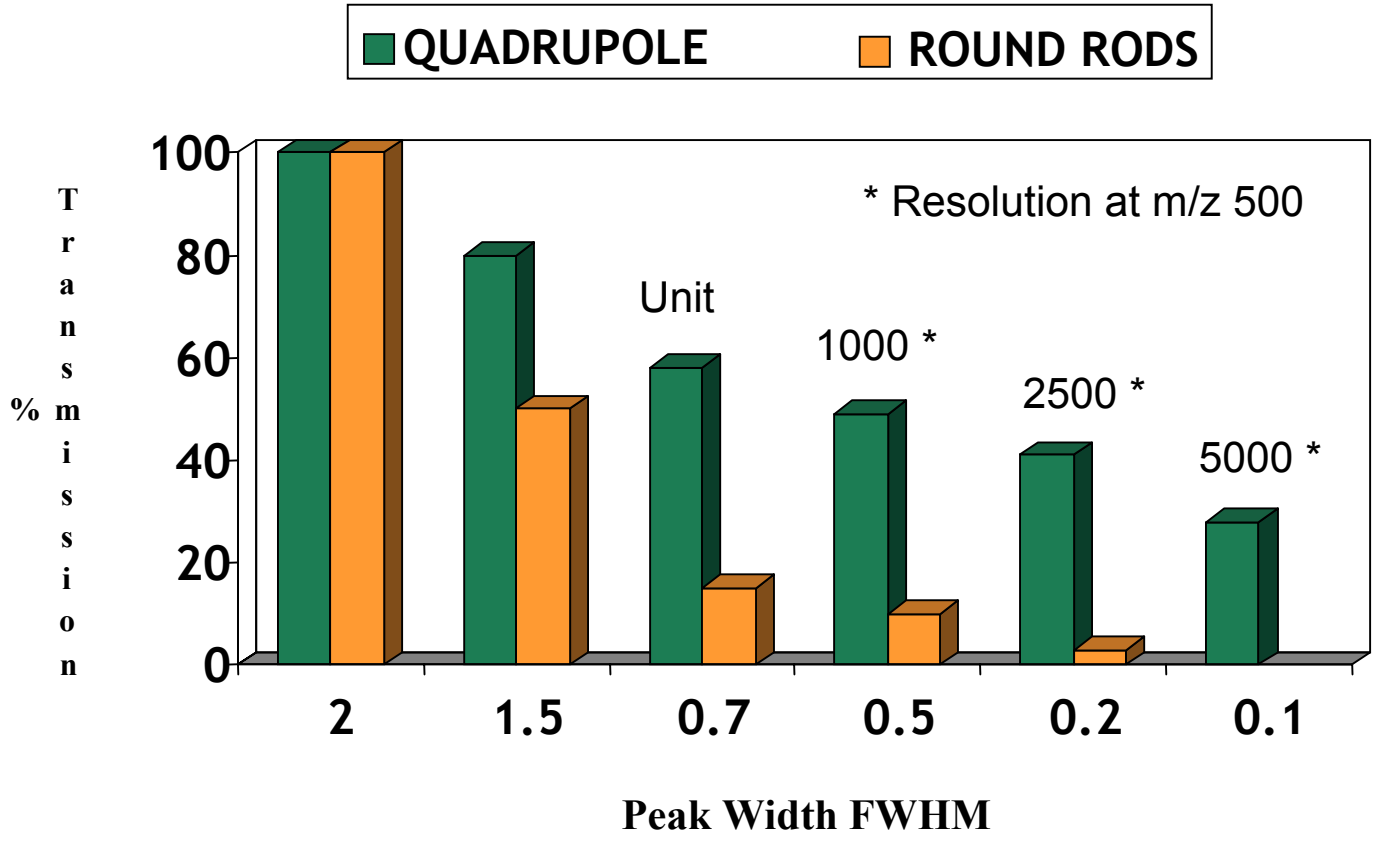
Effect of Peak Width On Transmission



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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

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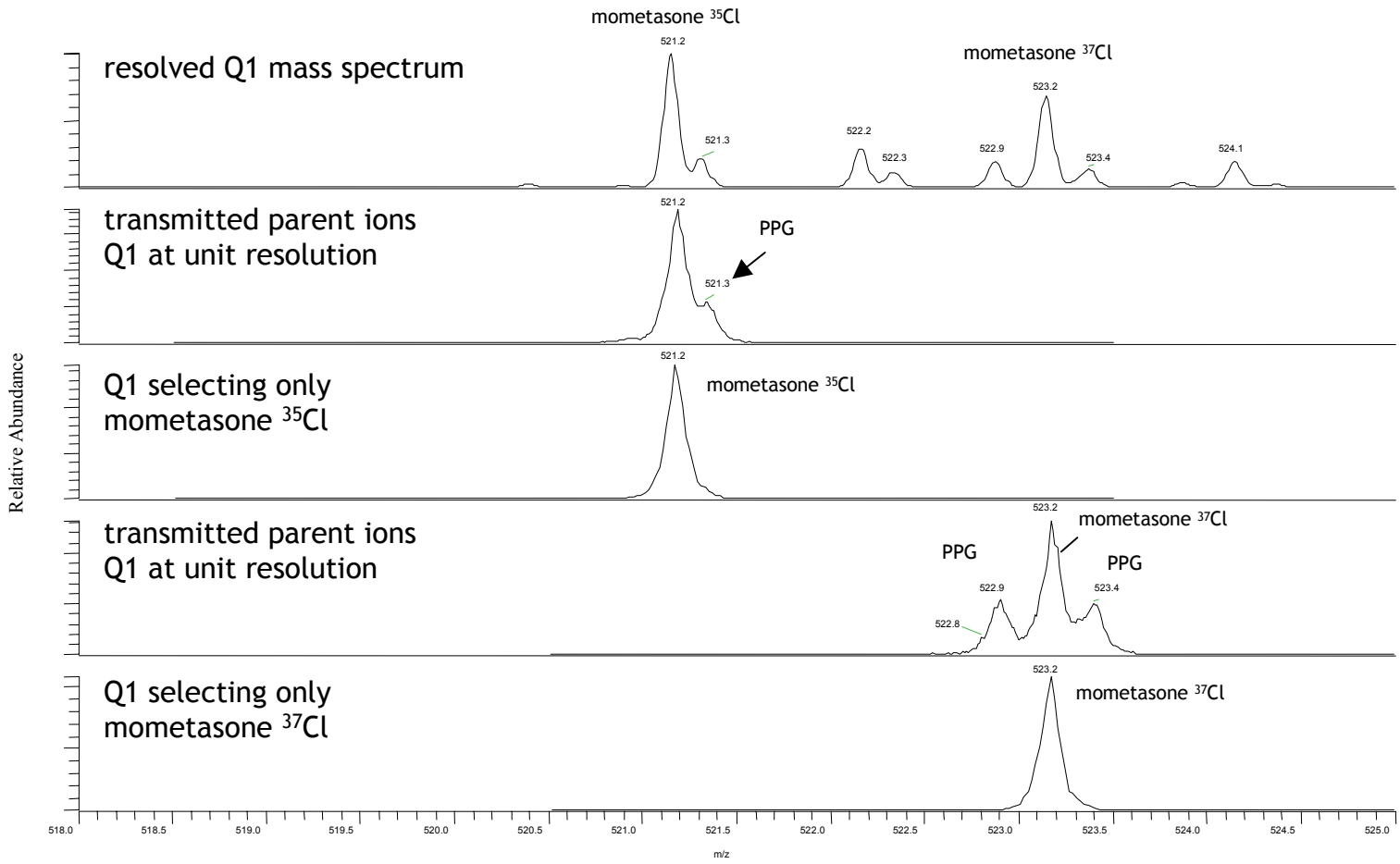
Mometasone resolution in the presence of PPGs

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



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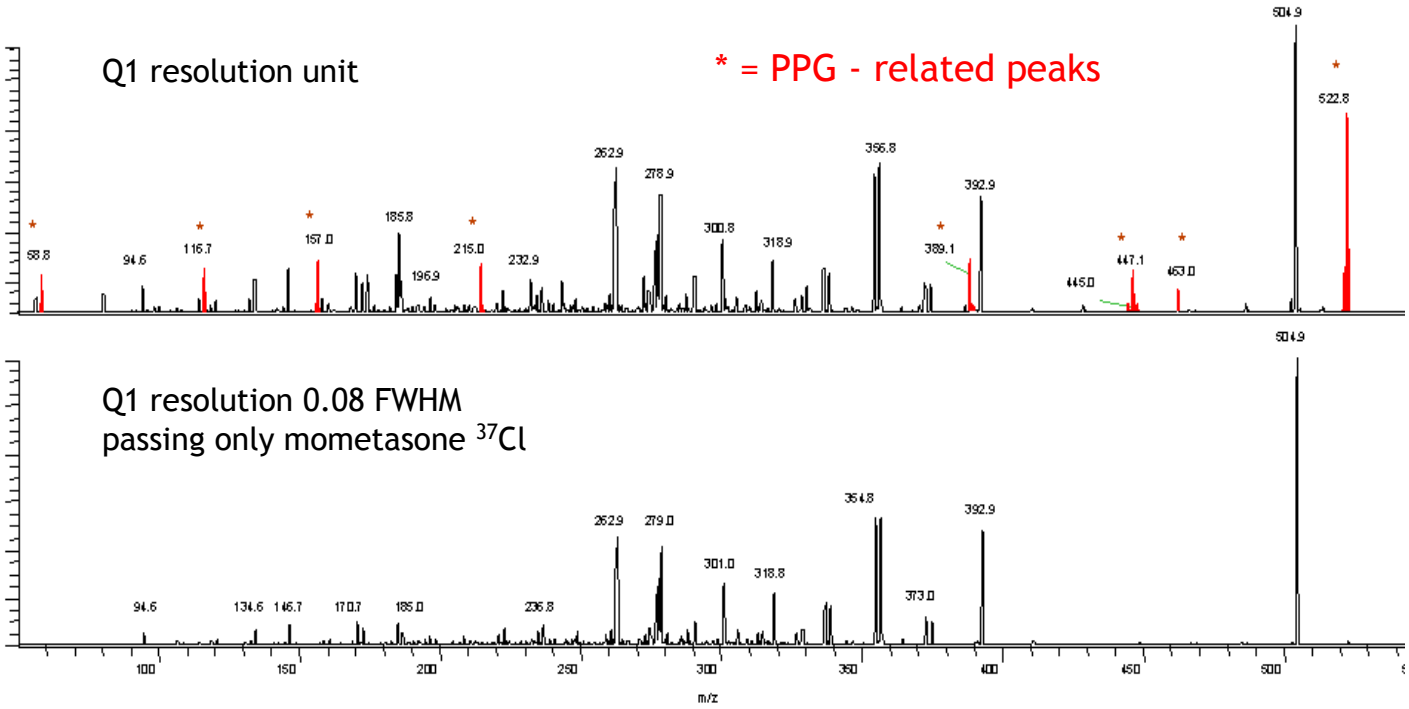
Mometasone resolution in the presence of PPGs

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.

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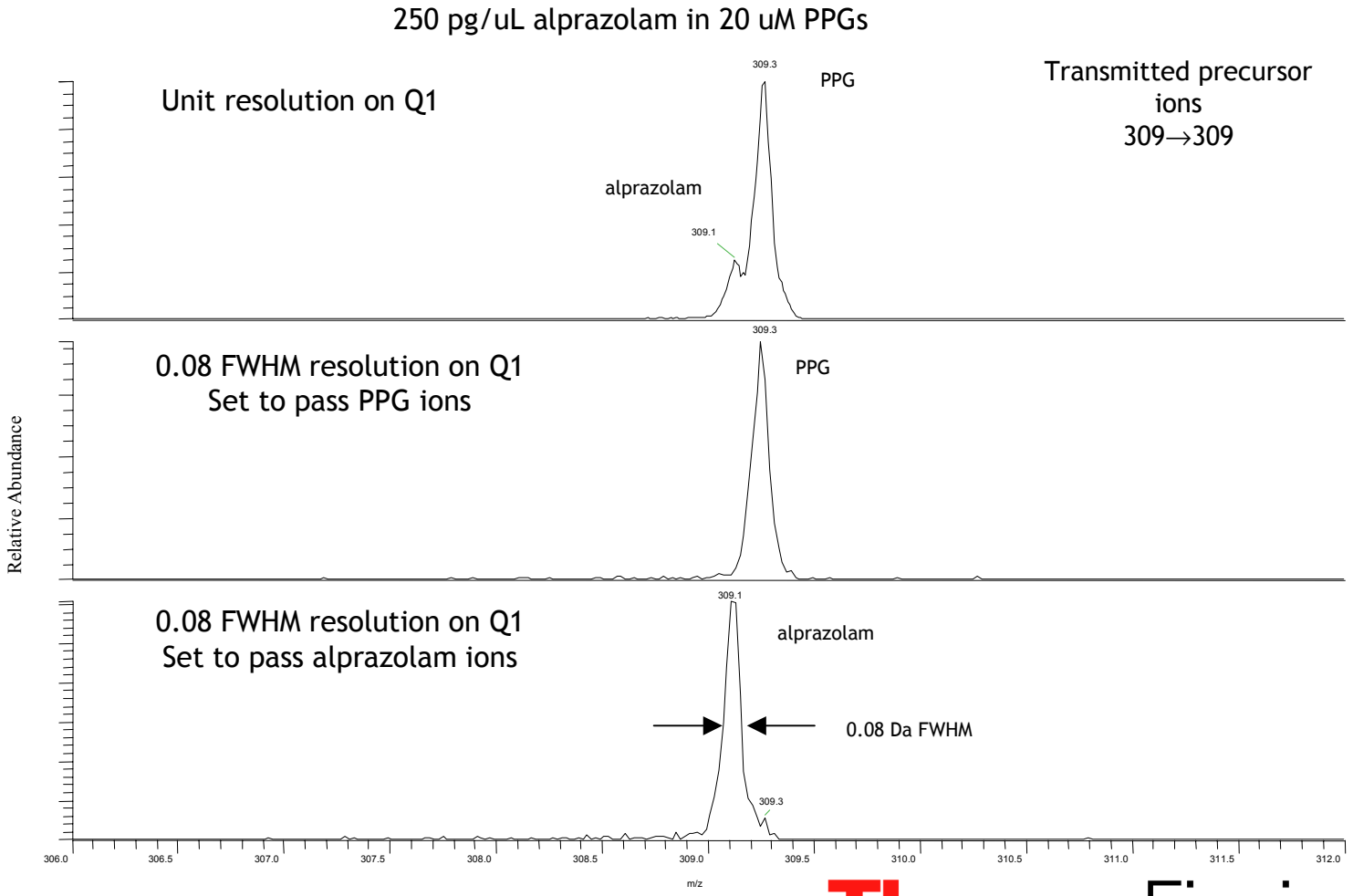
Alprazolam resolution in the presence of PPGs

(alprazolam $[M+H]^+$ = 309.0907, PPG (n=5) $[M+H]^+$ = 309.2277)



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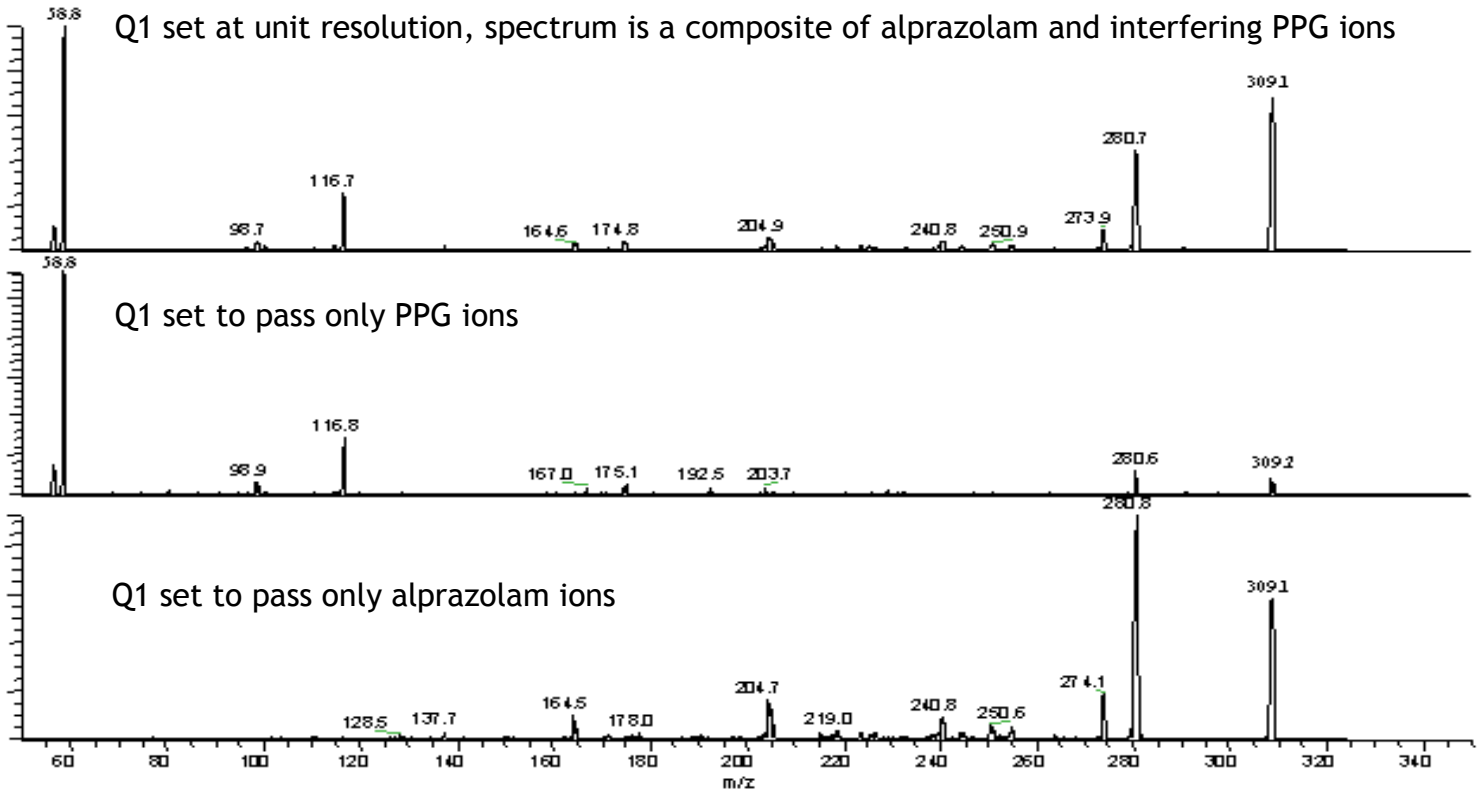
Alprazolam resolution in the presence of PPGs

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.

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Comparison of Quads and Traps

Ion Traps	Quadrupoles
Mass Separation in time	Mass Separation in space
High sensitivity Full Scan	Lower sensitivity Full Scan
Lower sensitivity SRM	High sensitivity SIM and SRM
Offer mutiple stages of MS^n	No mutiple stages of MS
Offers higher resolution	Lower resolution
	Parent and neutral loss scans

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