Lecture 3

Mass Analyzers

Types of Mass Analyzers

Magnetic Sector
- double focusing sector

Quadrupole
- Single quadrupole mass filter
- Triple quadrupole (QQQ)

Ion trap (IT)
- 3D quadrupole ion trap (QIT)
- 2D linear ion trap (LIT)

Ion cyclotron resonance (ICR)

Orbitrap
- LIT – OT (LTQ-OT velos, 기초과학공동기기원)
- Q - OT (Q-Exactive)
- Q - OT - LIT (OT Fusion Tribrid)

Time-of-flight (TOF)
- TOF/TOF (MALDI-TOF-TOF-MS, 기초과학공동기기원)
- Q-TOF (Triple TOF, Nicem)

Beam-Type Mass Analyzers (continuous ion flow)

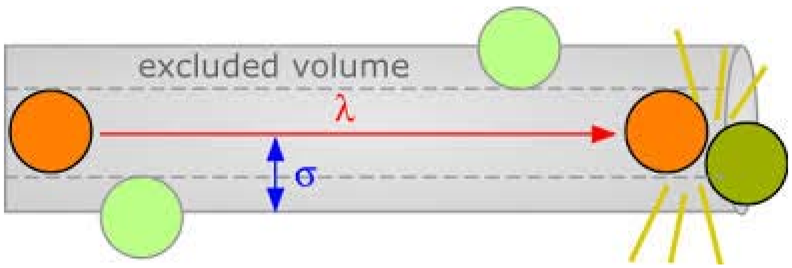
Ion-Trapping Mass Analyzers (pulsed ion flow)

Mass Analyzer & Vacuum

- **Mass analyzer**: An instrument that separates the gas-phase ions according to their *mass-to-charge ratio* (*m/z*) based on their characteristic behavior in electric and/or magnetic fields.

- **High vacuum** requirement of the mass analyzer: $10^{-4} - 10^{-7}$ Pa.
  - *Avoid collision* with molecules and other neutrals (radicals) or with other ions.
  - **Collision**: Deflect the ion's trajectory, result in collisional activation, or cause charge neutralization.

Mean free path & Vacuum



$$n_V = \frac{nN_A}{V} = \frac{nN_A}{\frac{nRT}{P}} = \frac{N_A P}{RT}$$

Mean free path

$$\lambda = \frac{RT}{\sqrt{2}\pi d^2 N_A P}$$

Vacuum range	Pressure in mbar	Molecules / cm3	Mean free path
Ambient pressure	1013	2.7×10^{19}	68 nm
Low vacuum	300 – 1	$10^{19} – 10^{16}$	0.1 – 100 μm
Medium vacuum	$1 – 10^{-3}$	$10^{16} – 10^{13}$	0.1 – 100 mm
High vacuum	$10^{-3} – 10^{-7}$	$10^{13} – 10^{9}$	10 cm – 1 km
Ultra high vacuum	$10^{-7} – 10^{-12}$	$10^{9} – 10^{4}$	1 km – 10^{5} km
Extremely high vacuum	$<10^{-12}$	$<10^{4}$	$>10^{5}$ km

Comparison of various types of mass analyzers

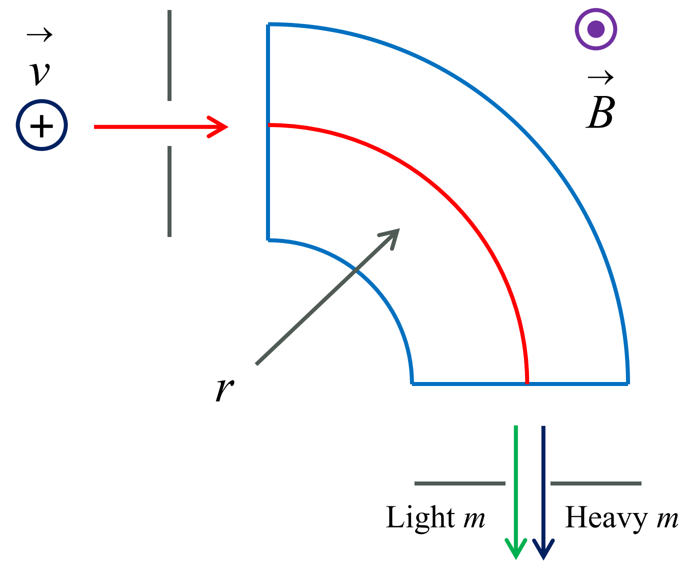
Feature	Magnetic	Qaudrupole	LIT	TOF	FT-ICR	Orbitrap
Mass range (Da)	20,000	4,000	4,000	Unlimited	$> 10^4$	$> 10^4$
Resolving power	10^5	2,000	10^3 - 10^4	20,000	$> 10^6$	5×10^5
Mass accuracy (ppm)	< 10	100	50-100	5-50	< 5	< 5
Speed (Hz)	0.1- 20	20	20	~30 (>100)	10^{-2} - 10	15
Dynamic range	10^9	10^7	10^5	10^6	10^5	10^6
Pressure (Torr)	10^{-6}	10^{-5}	10^{-3}	10^{-6}	10^{-10}	10^{-10}
Ion sampling	Continuous	Continuous	Pulsed	Pulsed	Pulsed	Pulsed
Cost	$$$$	$	$$	$$-$$$	$$$$	$$$

Magnetic sector analyzer
: Momentum analyzer

- **Working principle**: Ions are accelerated to high velocity through a **magnetic field** that is *perpendicular* to the direction of ion motion.
- **Ion trajectory**
  - Ion kinetic energy: $KE = zeV = \frac{1}{2}mv^2$
  - Forces: $F_M = Bzev$ & $F_c = \dfrac{mv^2}{r}$
  - Because $F_M = F_c$: $\boxed{\dfrac{m}{z} = \dfrac{B^2 r^2 e}{2V}}$ & $\boxed{r = \dfrac{mv}{Bze}}$

where B: magnetic field (T), v: velocity (m/s), V : the accelerating voltage

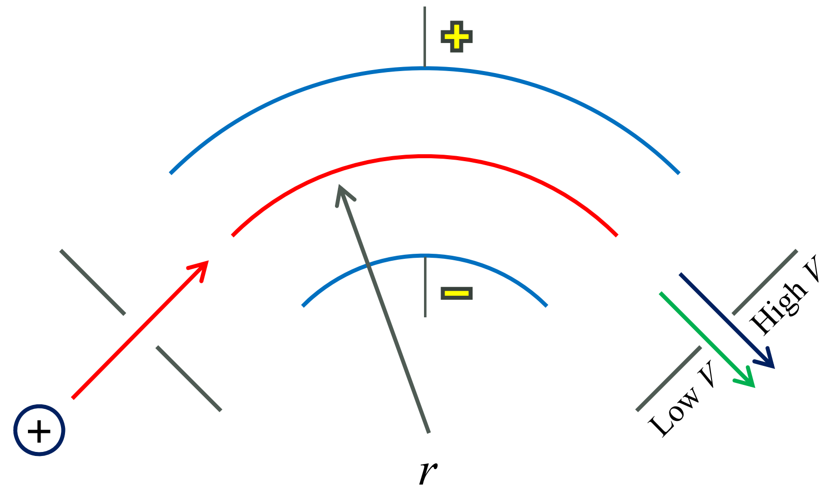
Scan m/z by varying **B** (not V)



Schematic of a magnetic sector analyzer.

Electrostatic analyzer (ESA)
: Kinetic energy filter

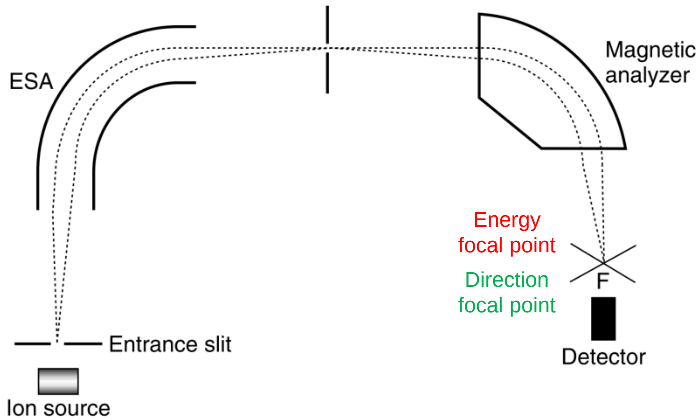
- **Instrumentation**: Consists of two parallel plates, one of which is held at a positive potential & the other at a negative potential of equal magnitude.
- **Working principle:** Ions that enter this radial electric field are forced to follow a *circular trajectory* & are dispersed according to their *KE*.
- **Ion trajectory**
  - Ion kinetic energy: $KE = zeV = \frac{1}{2}mv^2$
  - Forces: $F_E = zeE$ & $F_c = \frac{mv^2}{r}$
  - Because $F_E = F_c$: $\frac{m}{z} = \frac{reV}{v^2}$ & $r = \frac{2V}{E}$
  - *V* can be varied to bring ions of different *KE*.



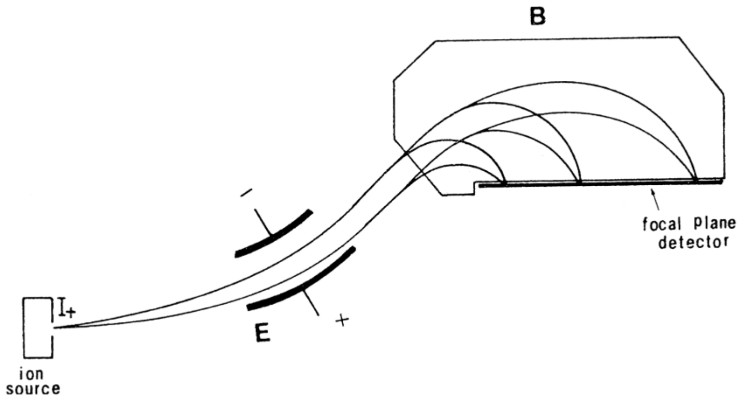
Schematic of ESA.

Double-focusing sector analyzer
: Achieve high resolution (~10^5)

- Ions of **equal *m/z*** but with *different kinetic energies* result in a spread-out beam.
  - **Solution**: Minimize *energy & directional differences* between ions of the same *m/z*.



Nier-Johnson design.



Mattauch-Herzog design.

C. Dass, *Fundamentals of Contemporary MS* **(2007)**

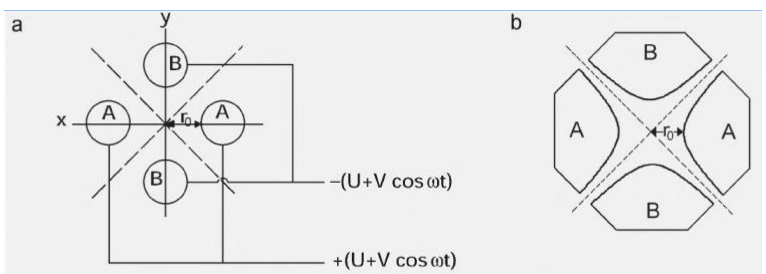
Characteristics of sector mass analyzer

Benefits	Limitations
Very high reproducibility	Not well-suited for pulsed ionization methods
Best quantitative performance of all mass analyzer	Usually larger & higher cost than other mass analyzers
High resolution, high sensitivity, & high dynamic range	
Very reproducible high-energy CID MS/MS	

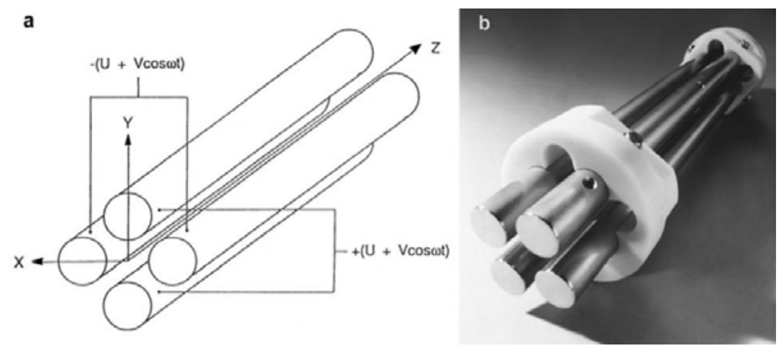
Applications	
All organic MS analysis methods	Quantitation
Accurate mass measurements	Isotope ratio measurements

Quadrupole mass filter (QMF)
: Compatible for chromatography

- **Instrumentation**
  - Four *parallel cylindrical* (originally *hyperbolic*) *metal rods.*
  - *Opposite rods* are connected electrically: One pair is attached to the positive side of a variable dc (***U***) source & the other pair to the negative terminal.
  - In addition, variable radio-frequency (RF) ac voltages (***V***), which are 180° out of phase, are applied to each pair of rods.



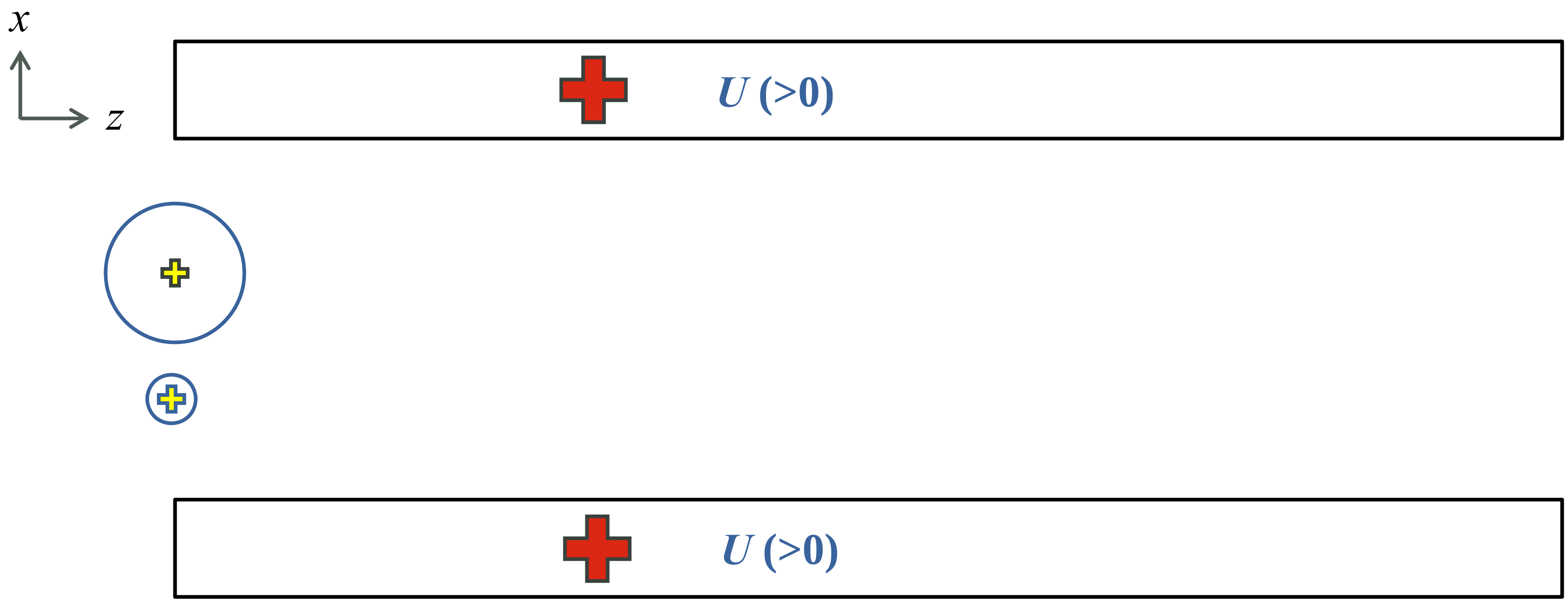
Cross section of a quadrupole for (a) cylindrical & (b) hyperbolic rods.



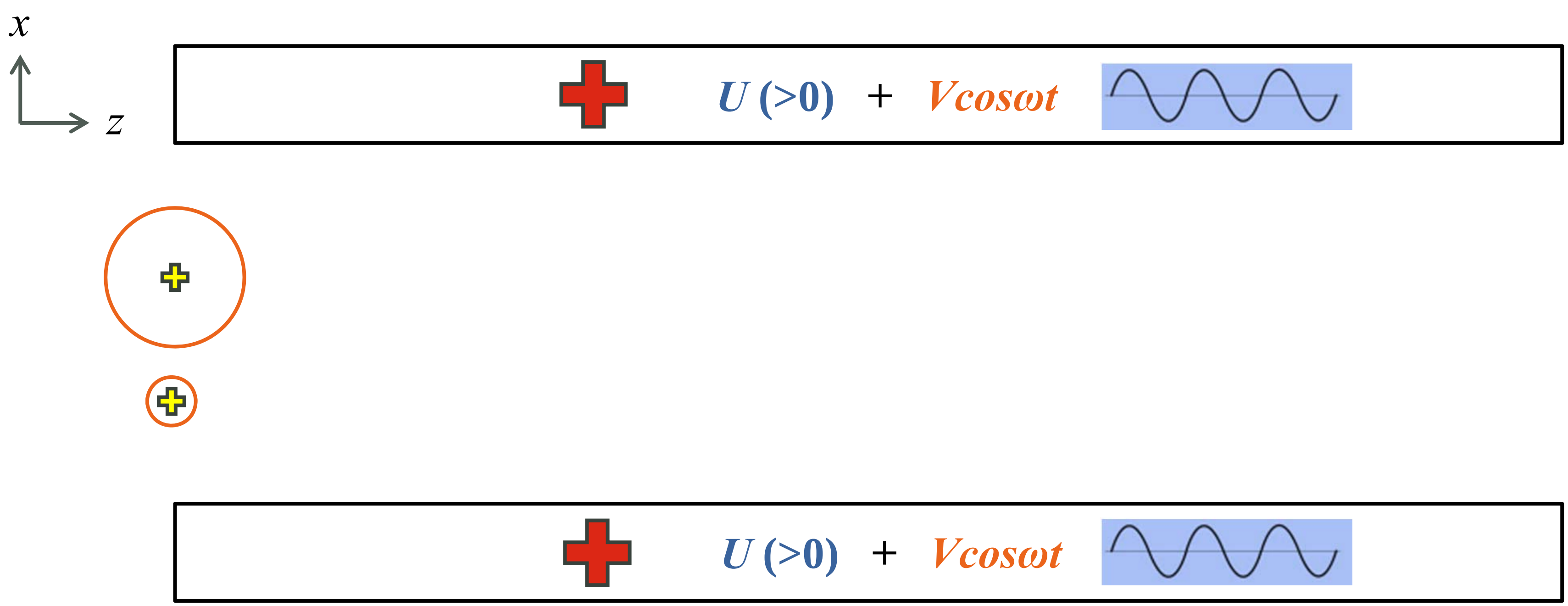
(a) Schematic & (b) photograph of qaudrupole mass analyzer.

J. H. Gross, *Mass Spectrometry* **(2011)**

How a QMF work?
The pair of rods in the *xz* plane: Only DC

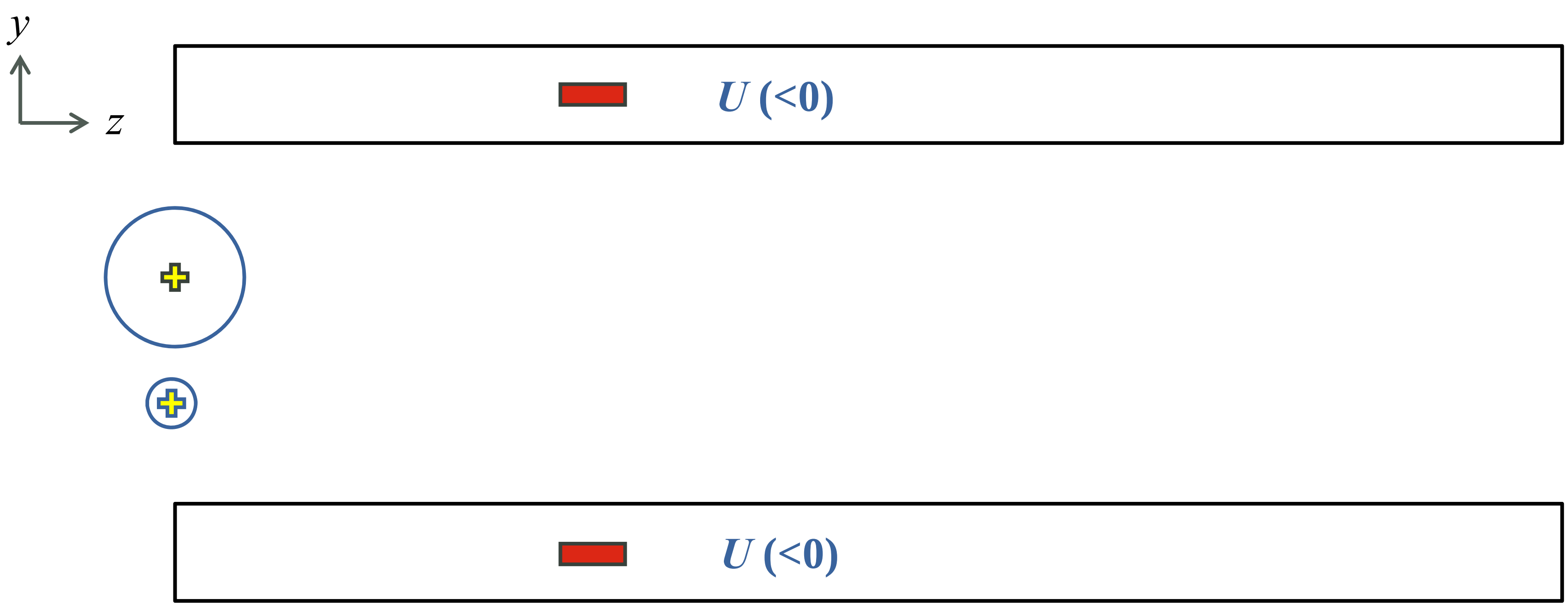


How a QMF work?
The pair of rods in the *xz* plane: DC + RF

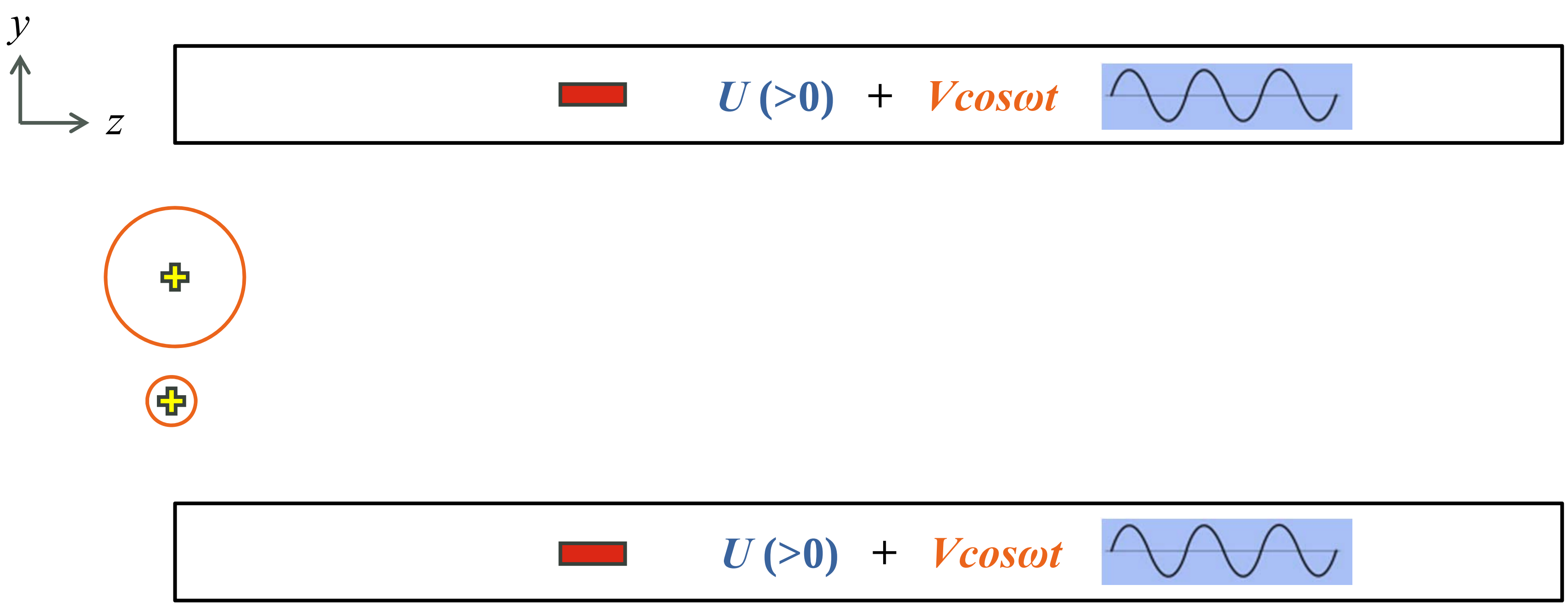


High-mass pass filter!

How a QMF work?
The pair of rods in the *yz* plane: Only DC

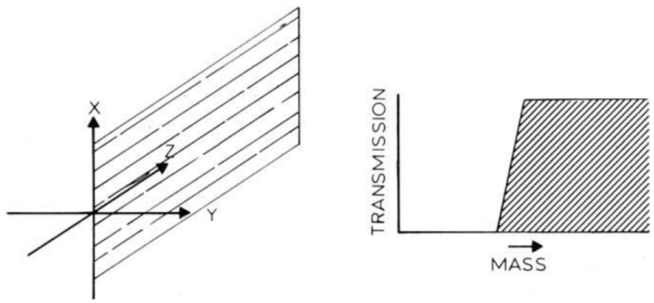


How a QMF work?
The pair of rods in the *yz* plane: DC + RF

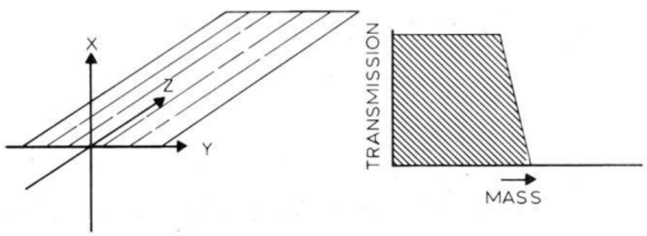


Low-mass pass filter!

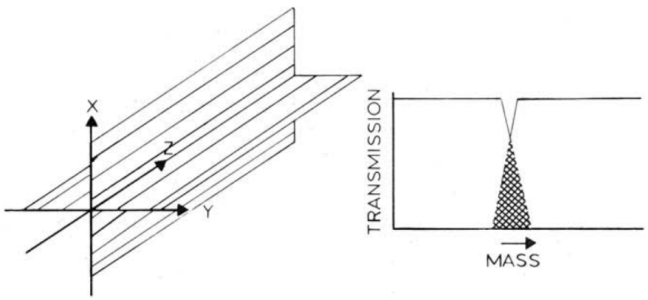
How a QMF work?
: A narrow-band filter



A high-mass pass filter in the *xz* plane.



A low-mass pass filter in the *yz* plane.



A narrow-band filter.

J. Chem. Edu. (1986) **63**, 617

Mathieu equation

- **Mathieu equation**: A quadratic equation describing the motion of an ion in the *x*- & *y*-directions.

$$\frac{d^2u}{d\xi^2} + (a_u - 2q_u \cos 2\xi)u = 0$$

  - *u*: The transverse displacement in the *x*- & *y*-directions from the center of the field.
  - ξ: Equal to $\omega t/2$.

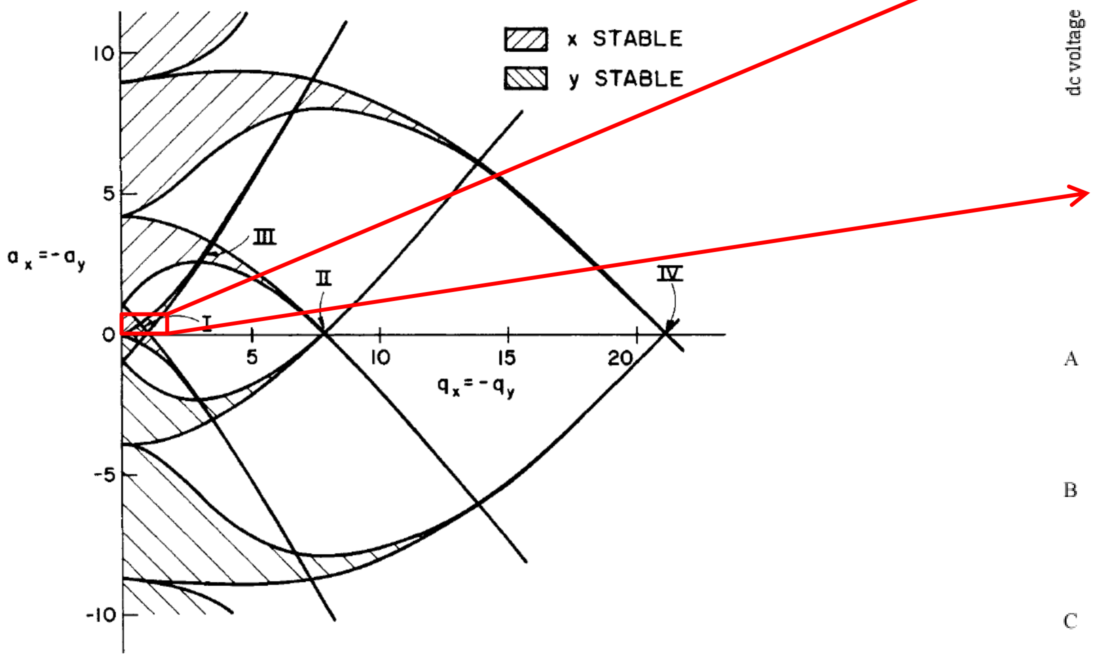
- **Solutions of the Mathieu equation** provides two dimensionless parameters *a* & *q*:

$$a_u = a_x = -a_y = \frac{8zeU}{m\omega^2 r_0^2}$$

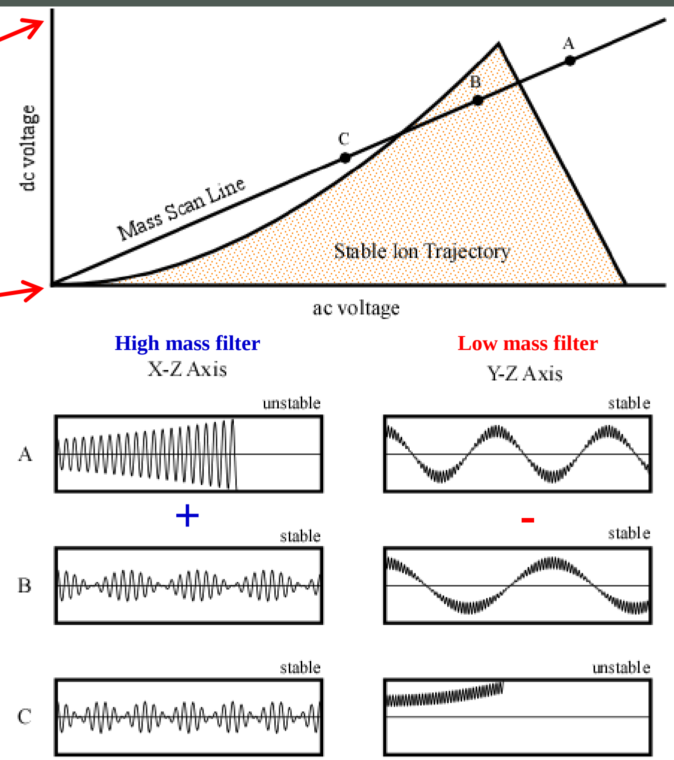
$$q_u = q_x = -q_y = \frac{4zeV}{m\omega^2 r_0^2}$$

Stability diagram for a QMF

- The *a*/*q* stability diagram



Mass Spectrom. Rev. (1986) **5**, 1

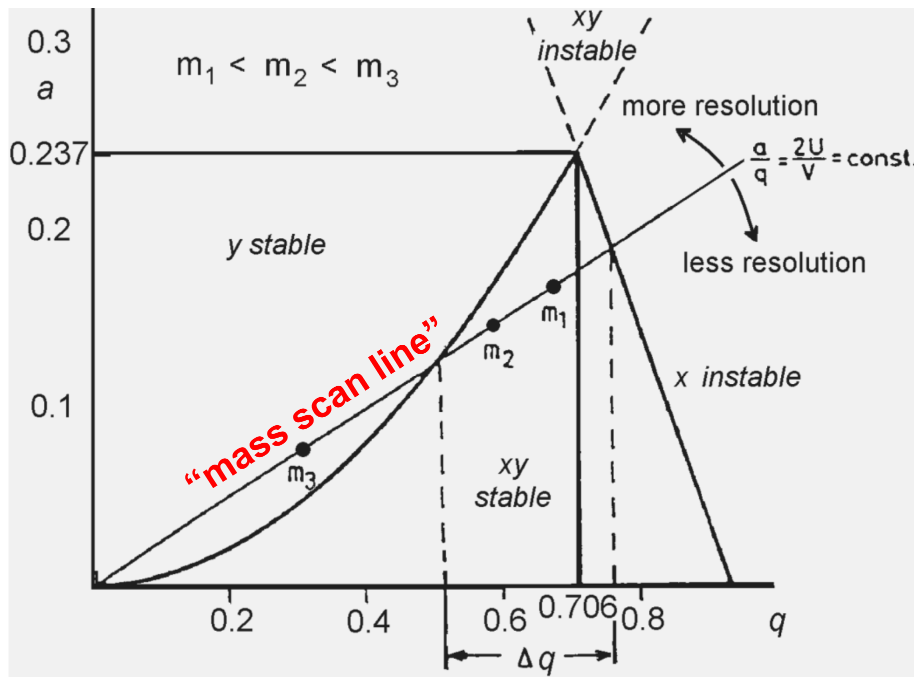


J. Chem. Edu. (1998) **75**, 1051

Obtain a mass spectrum with a QMF : Perform a constant *U*/*V* linked scan

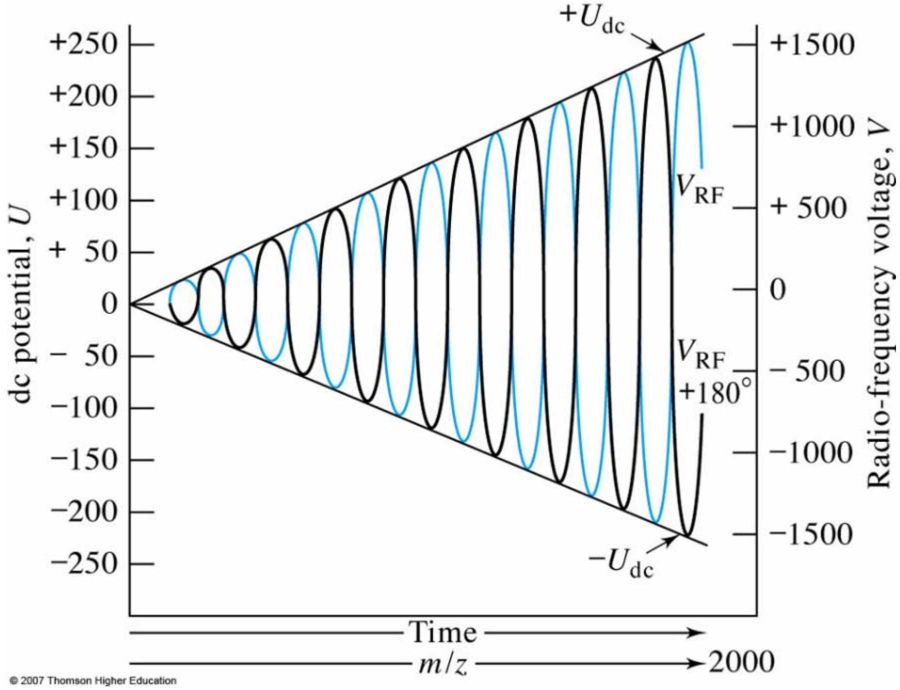
- **Mass scan line**: A line maintaining the *U*/*V* ratio *constant* while raising both *U* & *V* simultaneously.
  - A plot of *U* & *V* becomes a straight line, starting at the origin & with a slope of *U*/*V*.
  - Only ions above the line will pass through the quadrupole.
  - *Resolution* is controlled by the *slope* of the scan line (*i.e.*, *U*/*V*).

- **RF-only mode**: If ***U*** **= 0** (or *a* = 0), the quadrupole pass all ions above a certain mass → quadrupole ion guide



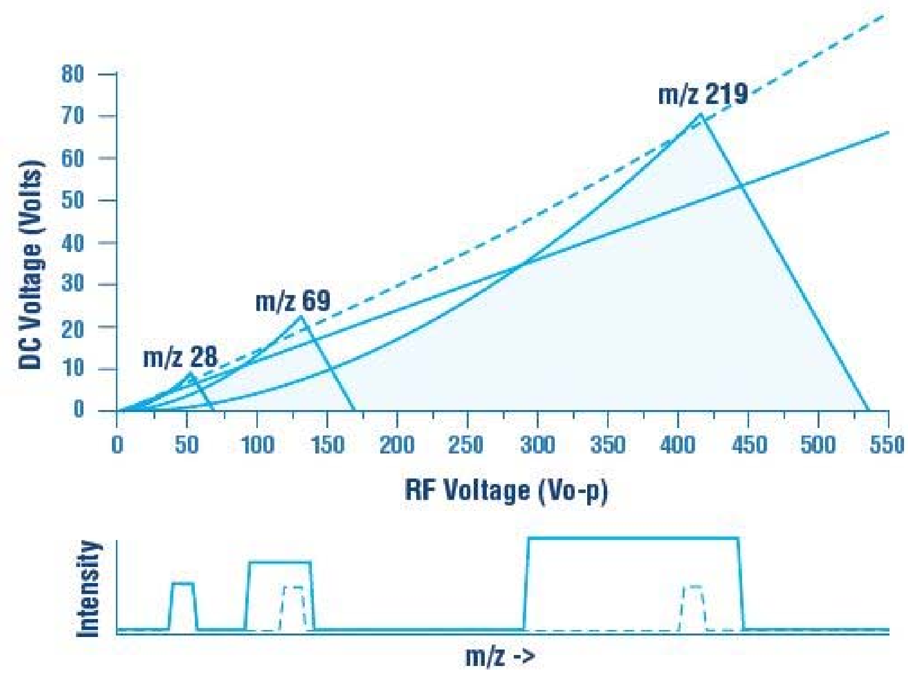
Rev. Mod. Phys. (1990) **62**, 531

Scanning a QMF
: Slope of the mass scan line vs. resolution



Voltage relationship during a mass scan with a quadupole analyzer.

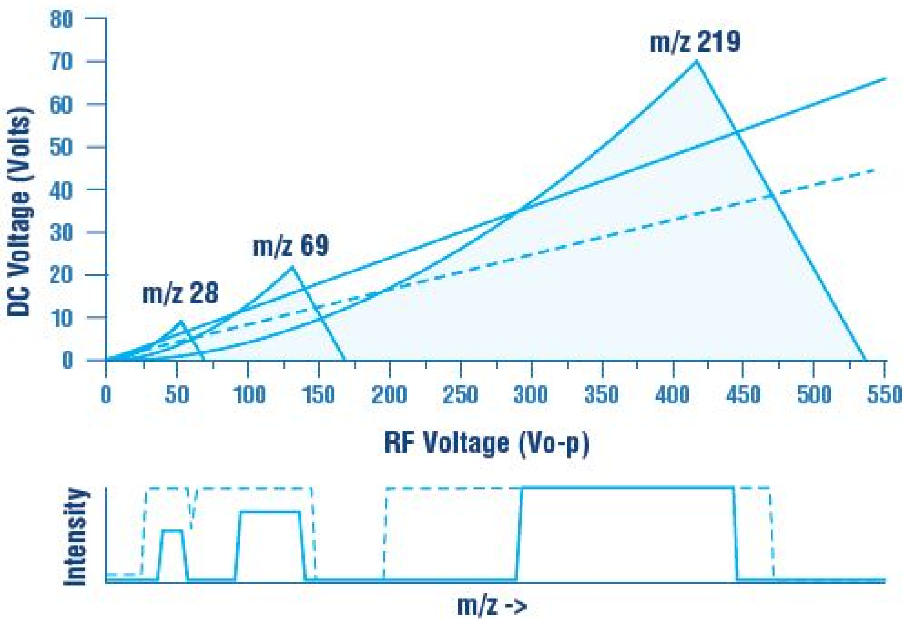
D. A. Skoog, et al., *Principles of Instrumental Analysis* **(2007)**

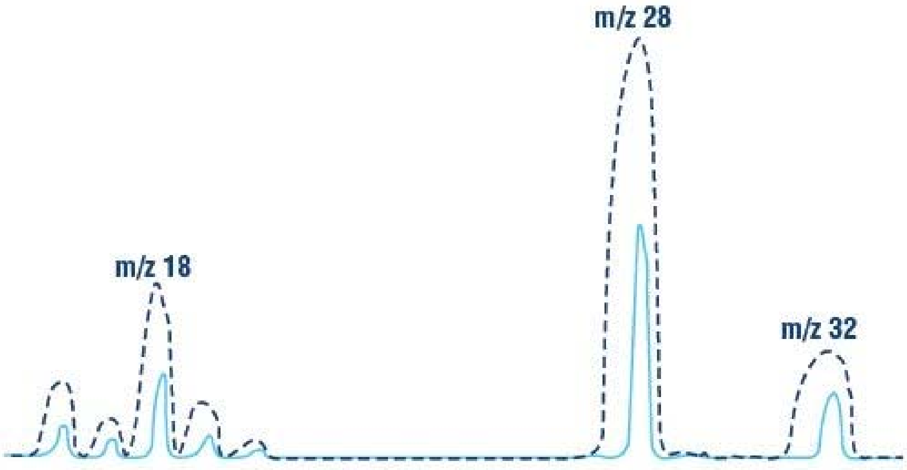


Relationship between the slope of the scan line & resolution.

http://www.azom.com/article.aspx?ArticleID=10996

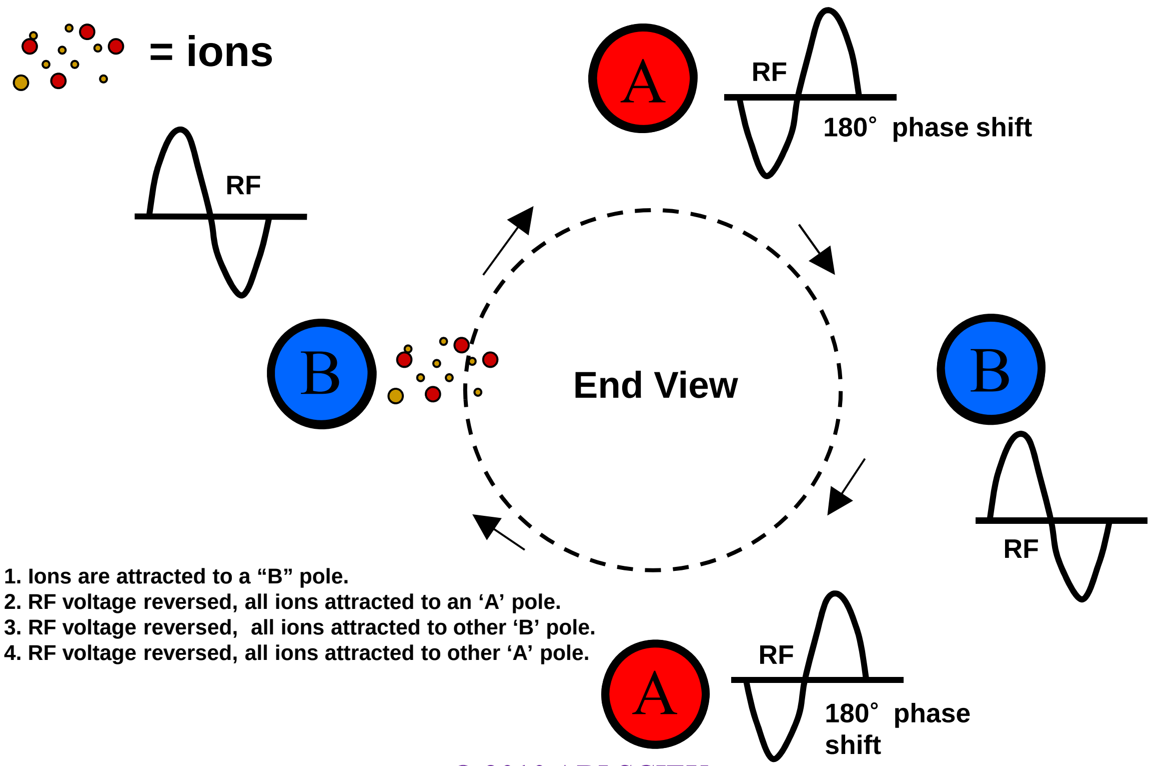
Scanning a QMF
: Slope of the mass scan line vs. resolution



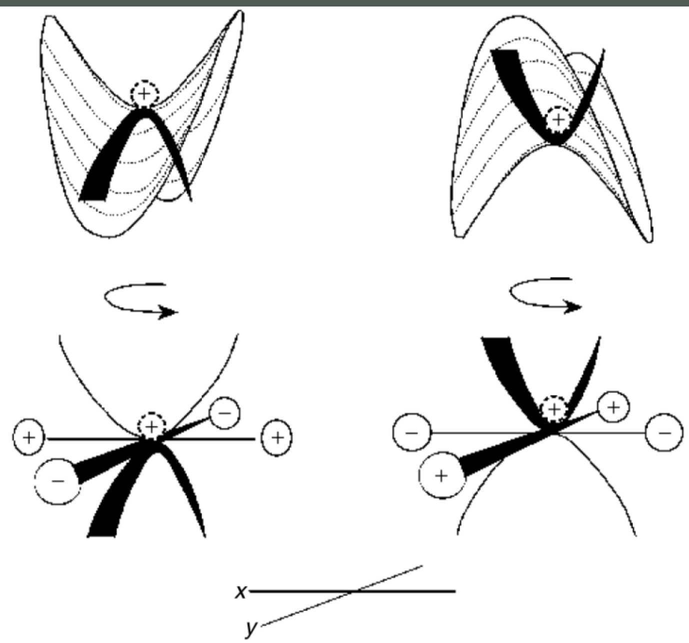


http://www.azom.com/article.aspx?ArticleID=10996

RF-only quadupole
: How RF focus ions?



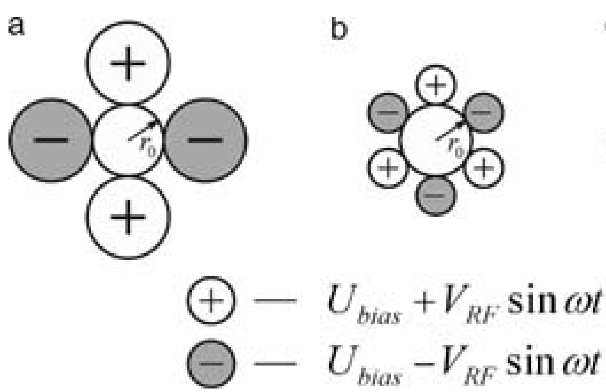
1. Ions are attracted to a "B" pole.
2. RF voltage reversed, all ions attracted to an 'A' pole.
3. RF voltage reversed, all ions attracted to other 'B' pole.
4. RF voltage reversed, all ions attracted to other 'A' pole.

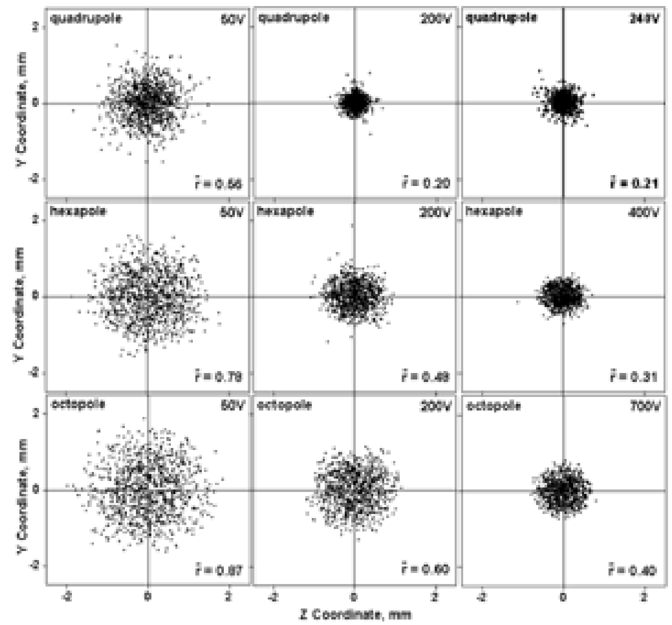


The potential energy of the positive ion
at the center of the rods of a quadrupole.

E. de Hoffmann, et. al., *Mass Spectrometry* **(2007)**

RF-only quadrupoles, hexapoles, & octupoles : Ion guides & collision cells

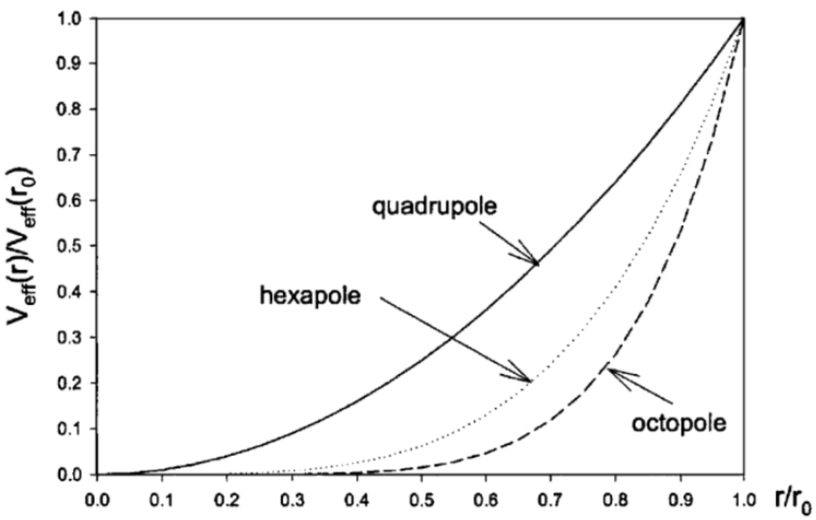




Rapid Commun. Mass Spectrom. 2008; 22: 3327–3333

RF-only quadrupoles, hexapoles, & octupoles
: Ion guides & collision cells

$$U_{eff}(r) = \frac{N^2}{4}\frac{(ze)^2}{m_i\Omega^2}\frac{V^2}{r_0^2}\left(\frac{r}{r_0}\right)^{2N-2}$$



Comparison of effective potentials for different multipoles.

Mass Spectrom. Rev. (2005) **24**, 1

Main characteristics of different multipoles.

Type	**Focusing power (mass filter for isolation)**	**Mass range for simultaneous transmission of ions (ion guide)**
Quadrupole	High	Narrow
Hexapole	↑	↓
Octupole	Low	Wide

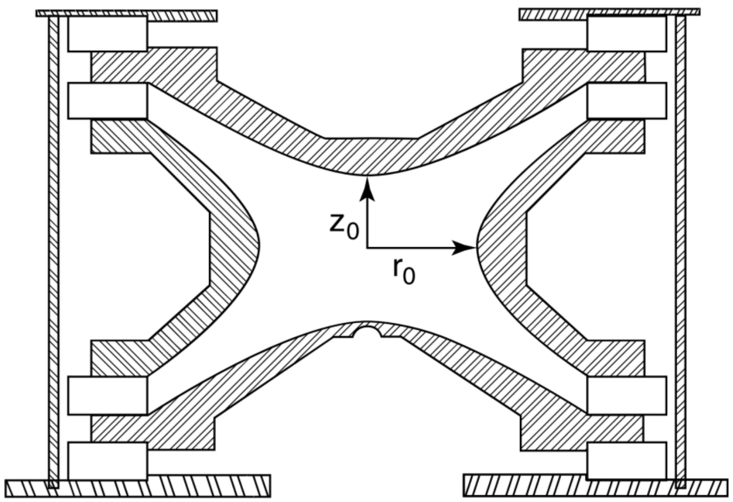
Characteristics of QMF

Benefits	Limitations
Good reproducibility	Limited resolution
Relatively small & low-cost systems	Peak heights are variable as a function of the mass (mass discrimination)
High efficient conversion of precursor to product in low-energy CID MS/MS spectra	Low energy CID MS/MS spectra strongly depends on collision energy, collision gas, pressure, & etc.

Applications	
Majority of benchtop GC/MS & LC/MS systems	Triple quadrupole MS/MS systems
Sector/quadrupole hybrid MS/MS systems	

3D-quadrupole Ion trap (QIT)
: Wolfgang Paul & Hans Dehmelt (Nobel Prize in 1989)

- **Instrumentation**: It consists of two hyperbolic end cap electrodes along with a ring electrode.

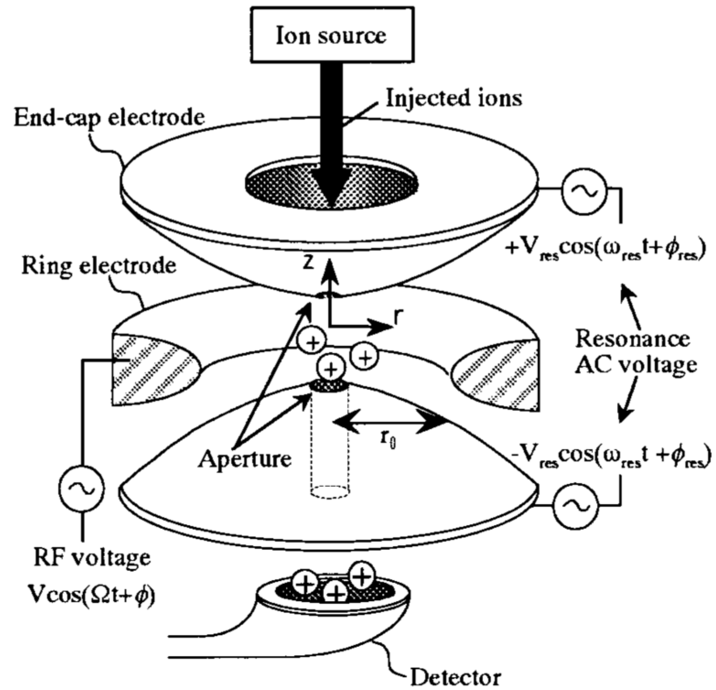


Schematic of a QIT.

R. E. March, et. al., *Quadrupole ion trap MS* **(2005)**

Working principle of QIT

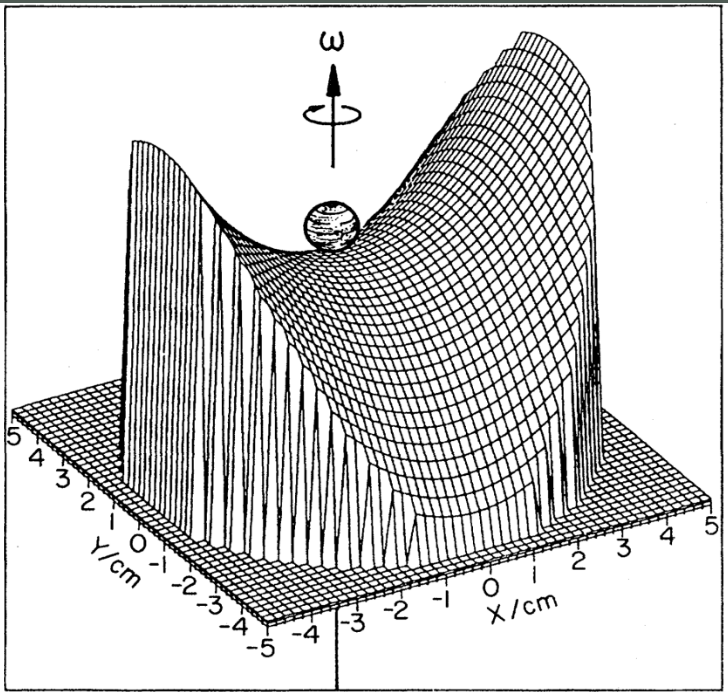
- **Trapped ions**: They can be formed *inside* the QIT or introduced from *outside* the ion trap.
- **Ion trapping**: A *constant frequency RF* voltage applied to the central ring electrode causes ions to *circulate* in stable & 3-dimensional orbits in the cavity.
- **Mass-selective ejection**: *Increasing the amplitude of the RF* voltage *destabilizes* the orbits of ions of one *m/z* value at a time, sending them flying out of the two end caps.
- **Ion detection**: Ions expelled through the lower end cap are detected by the detector.



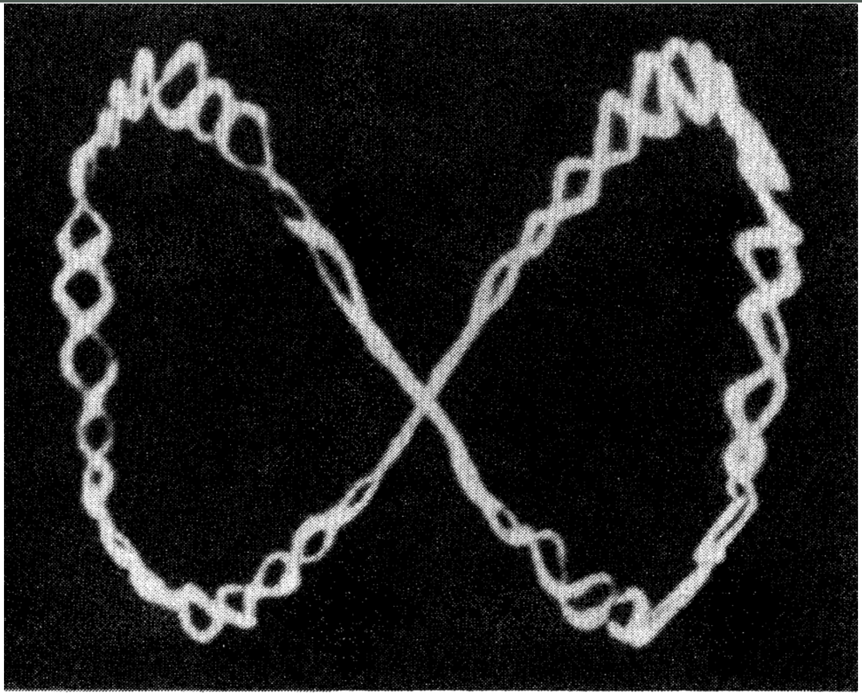
QIT with external ion source.

Rapid Commun. Mass Spectrom. (2000) **14**, 215

Visualization of ion motion in a QIT



Mechanical analog of a QIT.



Photograph of ion trajectories of charged aluminum particles in a QIT.

Rev. Mod. Phys. (1990) **62**, 531

Mathieu equation

- With the pair of end caps grounded, the **potential inside the trap** is given as

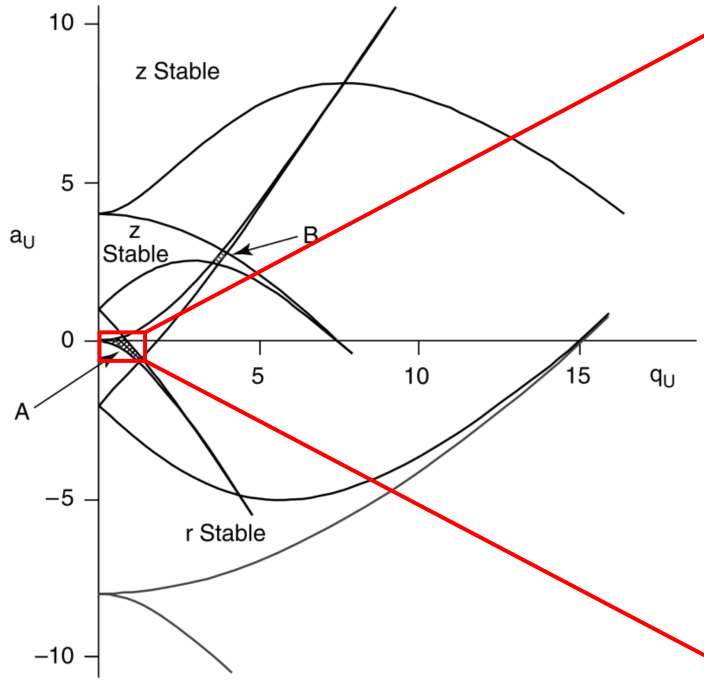
$$\Phi_0 = U + V\cos\Omega t$$

  - U: The amplitude of the dc potential applied to the ring electrode.
  - V : The amplitude of the ac potential applied to the ring electrode.
  - Ω: Equal to $2\pi f$ & f is the fundamental RF frequency of the trap (≈ 1 MHz).
- **Solutions of the Mathieu equation** provides two dimensionless parameters a & q:

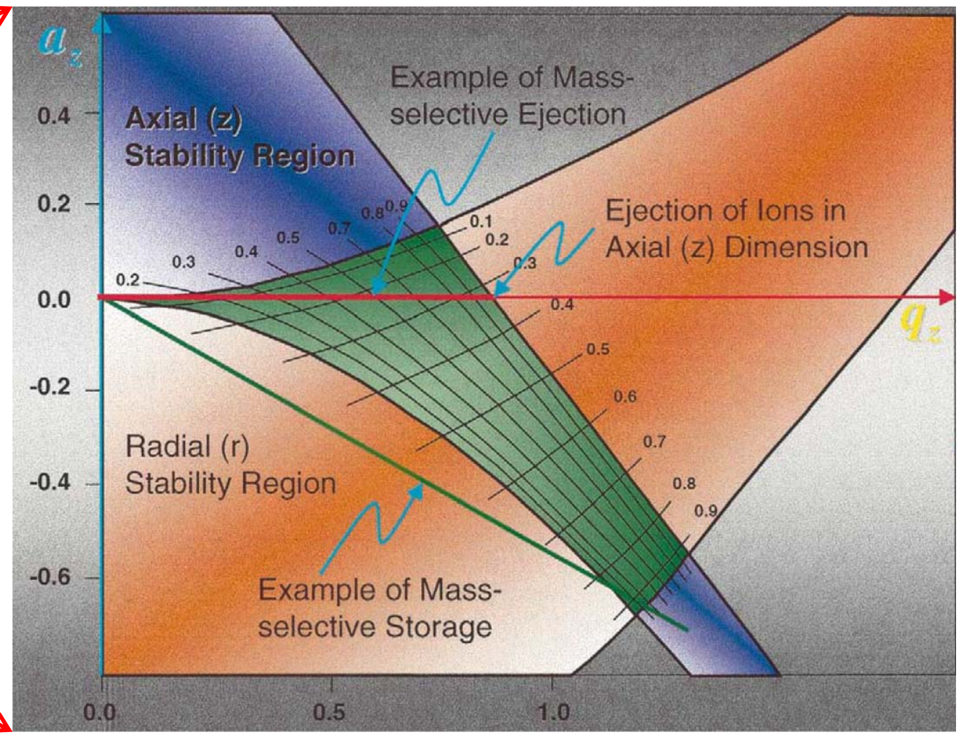
$$a_z = -2a_r = -\frac{16eU}{m\left(r_0^2 + 2z_0^2\right)\Omega^2}$$

$$q_z = -q_r = -\frac{8eV}{m\left(r_0^2 + 2z_0^2\right)\Omega^2}$$

Stability diagram for QIT



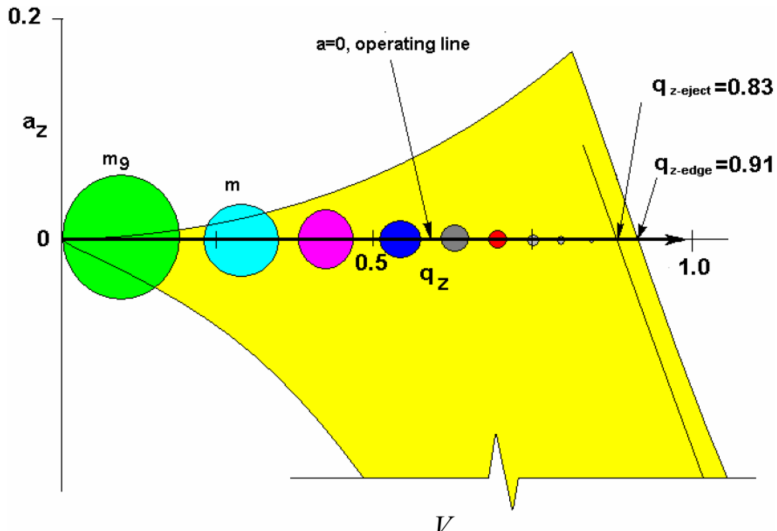
R. E. March, et. al., *Quadrupole ion trap MS* **(2005)**



J. Am. Soc. Mass Spectrom. (2002) **13**, 589

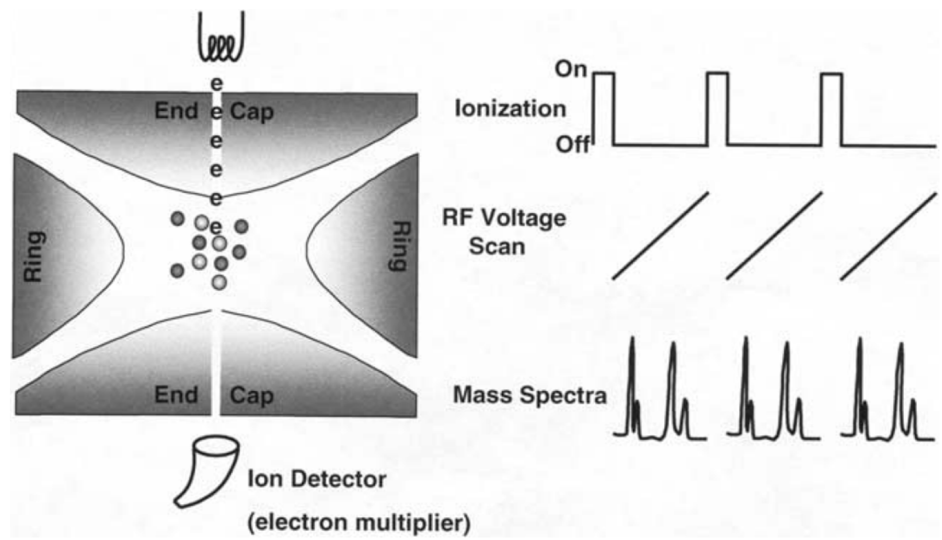
Mass-selective ejection in QIT

- With the pair of end caps grounded, an **RF-voltage (*V*) scan** is applied to the ring electrode: *Consecutive ejection* of ions in the order of their *m/z* values.



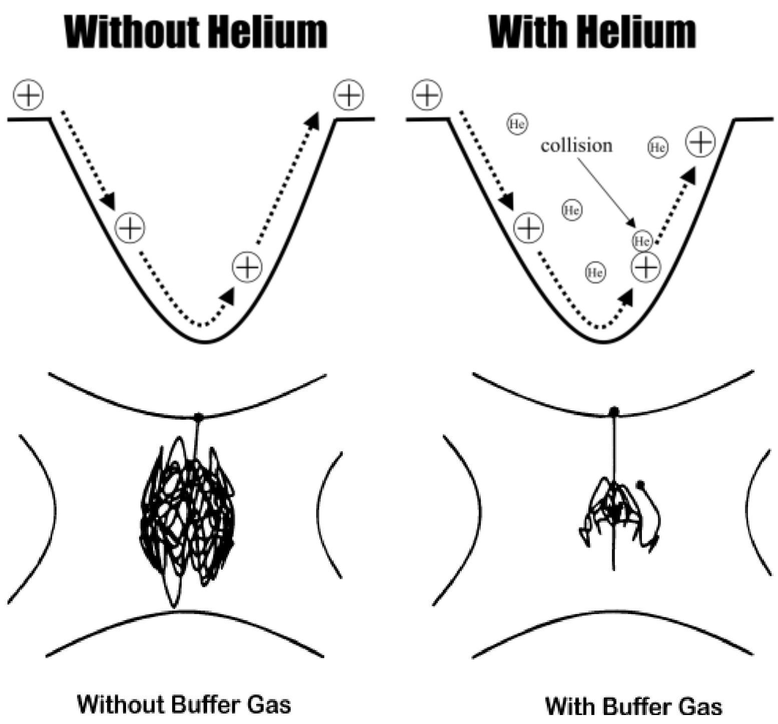
$$q_z = k\frac{V}{(m/e)}$$

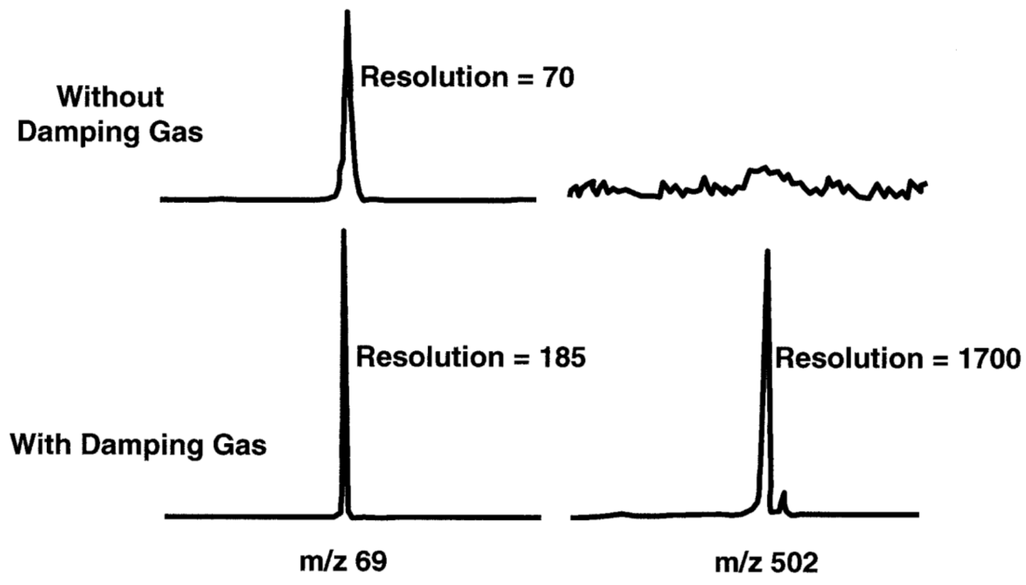
www.thermofisher.com



J. Am. Soc. Mass Spectrom. (2002) **13**, 589

Collision damping
: Helium as a **damping gas** in QIT





Int. J. Mass Spectrom. Ion Proc. (1984) **60**, 85

Characteristics of QIT

Benefits	Limitations
High sensitivity	Poor quantitation
Multi-stage MS (MS^n)	Very poor dynamic range
Compact size	Subject to space-charge effects & ion-molecule reactions
	Low mass cutoff in MS/MS spectra (i.e. 1/3 rule)
	Not easy to understand

Applications	
Benchtop GC/MS, LC/MS, & MS/MS systems	Target compound screening
Study ion chemistry	