Mass Analyzers

Ion Trap, FTICR, Orbitrap

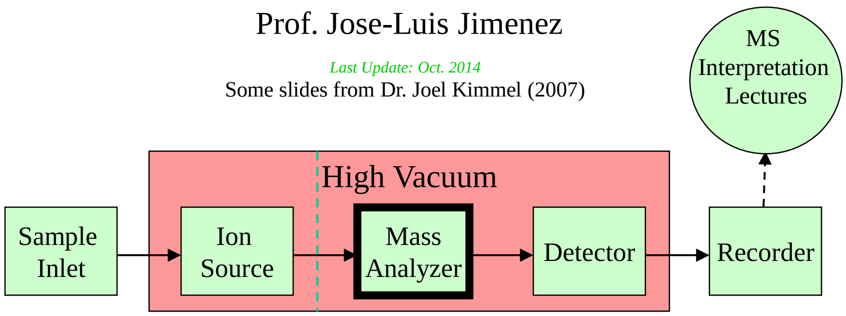
CU- Boulder

CHEM 5181: Mass Spectrometry & Chromatography

Prof. Jose-Luis Jimenez

Last Update: Oct. 2014

Some slides from Dr. Joel Kimmel (2007)



Business Items

- Questions or comments?
- Labview
  - Megan C is done

Review Clicker Q on Quadrupoles

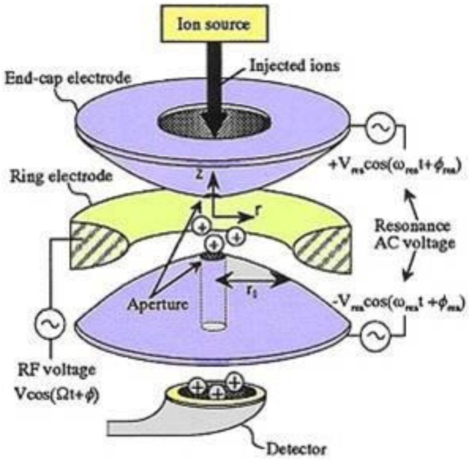
To operate a quadrupole in a scanning mode, where individual m/z values are transmitted one after the other (e.g., m/z = 100; 101; 102 …)

A. U is held constant, while V is scanned
B. V is held constant, while U is scanned
C. U is held constant, while V and ω are scanned
D. U and V are both changed
B. A or B

Types of Mass Analyzers

- Time-of-flight (TOF)
- Quadrupoles
- **Ion traps**
- **Ultrahigh resolution**
  - **Orbitrap**
  - **Ion-Cyclotron Resonance (ICR)**
- Sector
  - Magnetic
  - Electric
- **Hybrids** & specialized

Quadrupole Ion Traps



Ring electrode (r)

End cap electrodes (z)

Fundamental RF: Fixed frequency (1.1 MHz) variable voltage (up to 7 kV) applied to Ring Electrode

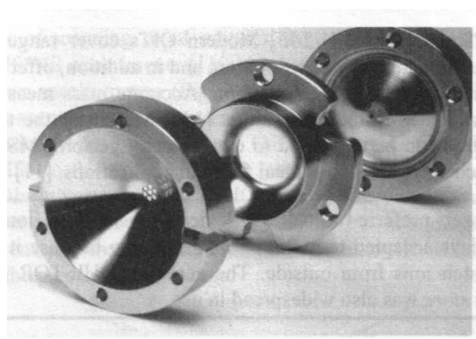
DC: An optional DC voltage may be applied to the ring electrode, which will affect the stability of ion trajectories

Resonance AC: Fixed frequency voltage applied to end caps for resonant ejection or fragmentation

Note that ions enter and exit along z axis

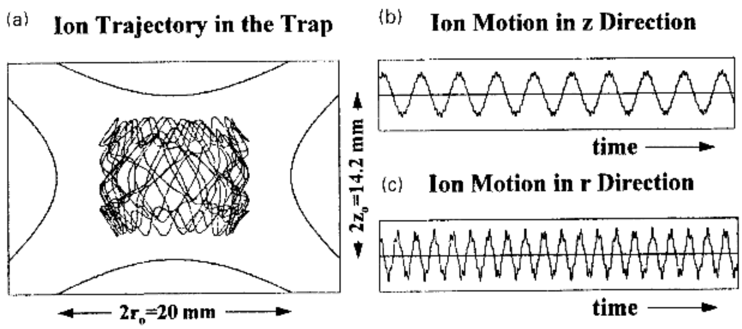
Pressure (1 mTorr) dampens extra kinetic energy and E of repulsion

3D Ion Trap Pictures



Hand-held dimensions

Ion Motion Inside an Ion Trap



From Lambert

•RF fields induce oscillations in r and z directions

•A "trapped" ion is stable along both axes

"Space Charge" Effects

- Trapping lots of ions in a small volume
  - Ions repel each other
  - Good performance based on ions responding to external E field (as in quad simulation). If the E field from other ions is significant, the performance is distorted
    - "Space charge", i.e. E field due to charges in 3D space, not only surfaces of our mass analyzer
  - Also a consideration in design of some ion sources, and other traps
- Ion energy is dampened by collisions with He neutrals. It would be worse under vacuum.
- SC limits the total number of ions ➔ sensitivity

Quadrupole vs Quad. Ion Trap

Quadrupole

- RF fields yield m/z band of stability
- **2D** Manipulation of trajectory
- Detect those ions that are selectively **transmitted** with stable trajectories
- Continuous analysis

Quad. Ion Trap

- RF fields yield m/z band of stability
- **3D** Manipulation of trajectory
- Detect those ions that are **selectively ejected** due to destabilized trajectory
- Pulsed analysis

Stability Diagram for an Ion Trap

From Watson

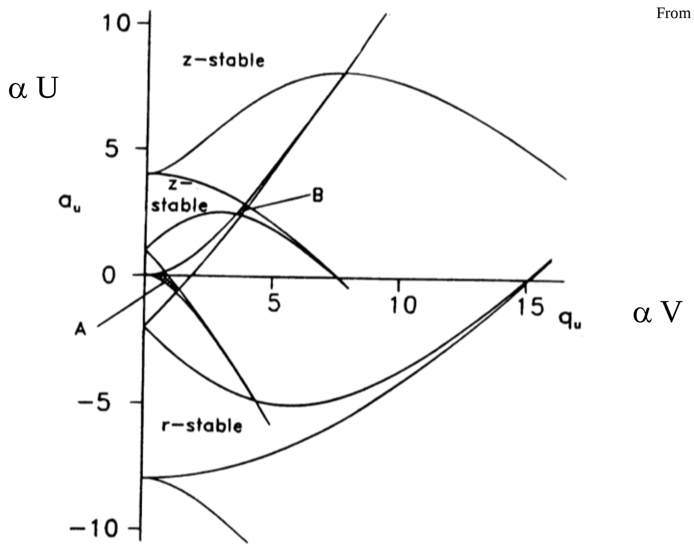
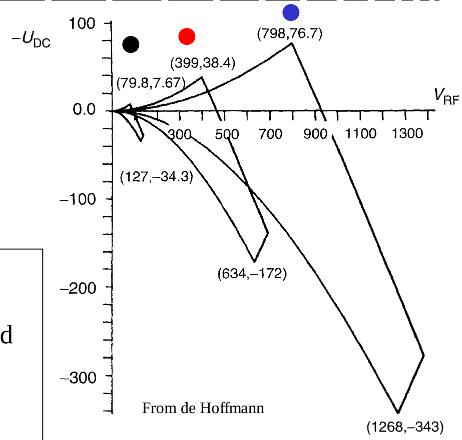


FIG. 4.12. Comprehensive stability diagram of *a-q* space for the ion trap

m/z Dependent Stability

$$q_z = \frac{8ezV}{m(r_o^2 + 2z_o^2)(2\pi\upsilon)^2}$$



Stability boundary at q_z = 0.908

Stability diagrams for m/z = **10**, **50**, and **100** in V(RF) - U(DC) space.

Note that, like quadrupole, broadest range of m/z stability at U=0

Increasing V will destabilize low m/z ions. That is, high m/z stable to higher V.

Clicker Q: if U = 0, can we eject *m/z* 100 while keeping *m/z* 50?
(A) Yes (B) No
(C) I don't know

Stability Diagram

Like a quadrupole mass spectrometer, ion stability described by variables related to RF and DC components.

For most operation, DC component is zero. And stability determined by q_z

$$q_z = \frac{8ezV}{m(r_o^2 + 2z_o^2)(2\pi\upsilon)^2}$$

q_z depends on mass, charge, dimensions, RF frequency, and RF amplitude (V)

Ions trapped with stable trajectory up to q_z of 0.908

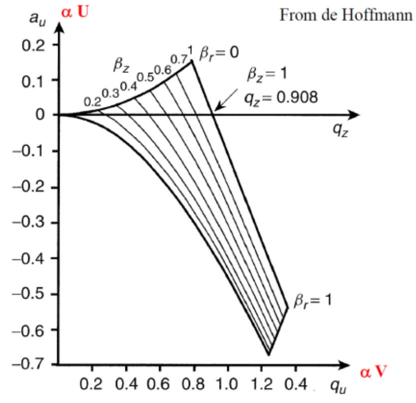


Figure 2.16
Typical stability diagram for a quadrupole ion trap. The value at $\beta_z = 1$ along the q_z axis is $q_z = 0.908$. At the upper apex, $a_z = 0.149998$ and $q_z = 0.780909$. (Data from Ref.12)

Clicker Question

True or False. Just like in a quadrupole, I can select only a given m/z value by adjusting U and V so that ions of that m/z (•) are just inside the apex the stability diagram.

A. Definitely True
B. Maybe
C. Probably Not
D. Definitely False
E. I don't know

From de Hoffmann

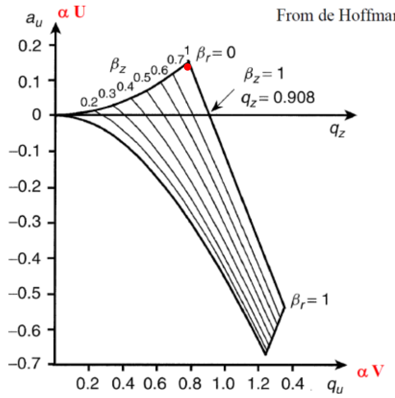


Figure 2.16
Typical stability diagram for a quadrupole ion trap. The value at $\beta_z = 1$ along the q_z axis is $q_z = 0.908$. At the upper apex, $a_z = 0.149998$ and $q_z = 0.780909$. (Data from Ref.12)

Ion Ejection at the Stability Limit

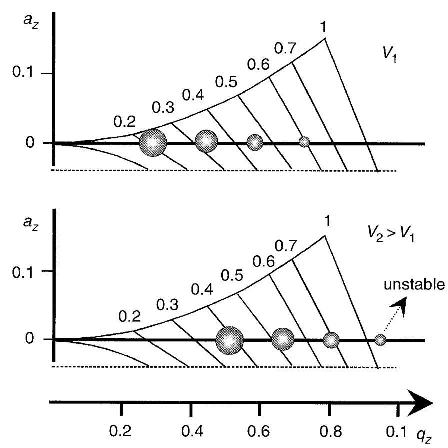


Figure 2.20
At a fixed value of the RF potential V applied to the ring electrode, heavier ions will have lower β_z values and thus lower secular frequencies. If V is increased, β_z values increase for all the ions, as do the secular frequencies. In the example given, the lightest ion now has a β_z value larger than unity and is thus expelled from the trap. The highest mass that can be analyzed depends on the limit V value that can be applied: around 7000–8000 V from zero to peak. For a trap having $r_0 = 1$ cm and operating at a ν frequency of 1.1 MHz, the highest detectable mass-to-charge ratio is about 650 Th

From Hoffmann

Clicker Question: Ion Traps

- In a 3D quadrupole ion trap, ions are detected by:
  A. Ejecting ions by suddenly stopping the DC voltage (U)
  B. Ejecting ions by suddenly stopping the RF voltage (V)
  C. Detecting the image current of the ions on the surfaces of the trap
  D. Ejecting ions by moving U, V to a region where those ions are unstable
  E. I don’t know

Secular Frequency

- Because of inertia, ions do not oscillate at the fundamental frequency applied to the trap, *v*
- Instead, ions oscillate at a **secular frequency, *f*, that is lower than *v***
- It is possible to calculate the value of f_z based on applied V
- Along the z axis, f_z is proportional to q_z (See text 2.2.2)
- If an RF voltage at frequency = f_z is applied to the end caps, ions with secular frequency f_z will come into **resonance** and the amplitude of its oscillation along z axis will increase
- If the increase is large enough, the ion will be ejected

Resonant Ejection

- f_z is proportional to q_z
- For fixed fundamental frequency, q_z of an ion is adjusted by varying V
- f_z applied to end caps creates a "hole" in the stability diagram at the q_z corresponding to ion oscillation frequency f_z
- Scan of V destabilizes ions of changing m/z

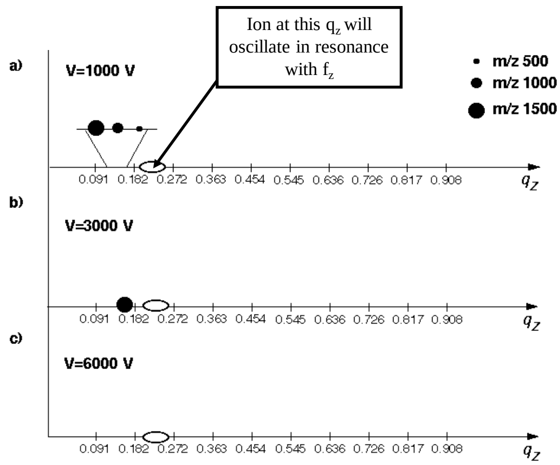


Figure from:
http://www.abrf.org/ABRFNews/1996/September1996/sep96iontrap.html

Resonant Ion Ejection

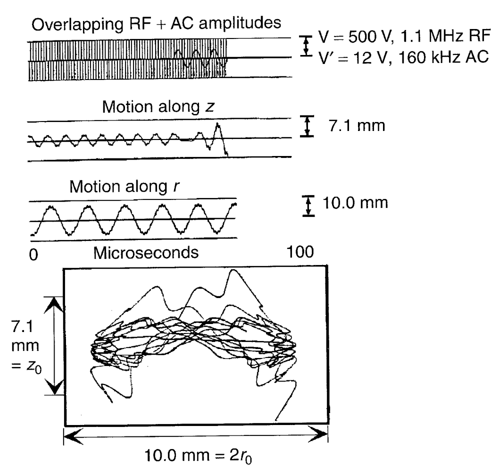
Example:

v = 1.1 MHz causes z oscillation with f_z= 160 kHz

Apply v' = 160 kHz to end caps

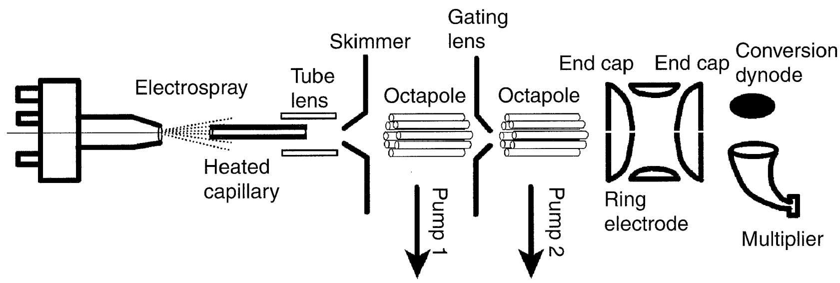
Energy transferred to ion through resonance causes destabilization along z

Resonant ejection allows selective detection of ions at q_z lower than 0.908



From de Hoffmann

Ion Trap Movies (linked on course page)



Ions from source are focused along z axis of trap by standard transfer optics

Continuous beam is **gated** into trap. Ionization period is set to maximize signal and minimize **space charge effects.**

Cell is filled with inert gas (e.g., He) at 1 mTorr to dampen kinetic energy of ions and contract trajectories toward center – improves resolution

Resonant Ejection Enables MS^N

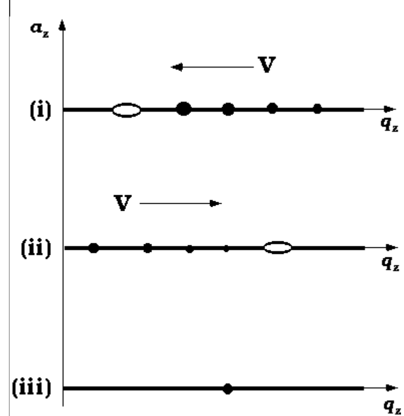
Forward and reverse scanning of V allows user to isolate single m/z value in trap

Isolated ions can be fragmented by collisions with background gas

- Excite ion with resonance
- Keep amplitude low enough to avoid ejection

The ability to repeat the isolation-and-fragmentation cycle allows MS^N analysis

(Demos)



Clicker Q

How many of the following are true?

(i) At any moment, an ion trap detects those *m/z* values that are "stable"

(ii) Ion traps typically have ~100% duty cycle when coupled to continuous ion sources

(iii) In the scanning mode we discussed, the largest *m/z* of an ion trap is limited by the minimum RF voltage that can be applied while still inducing stable trajectories

(iv) In the scanning mode that we discussed, increasing V yields detection of higher *m/z* ions

(a) 0 (b) 1 (c) 2 (d) 3 (e) 4

MS/MS with an Ion Trap

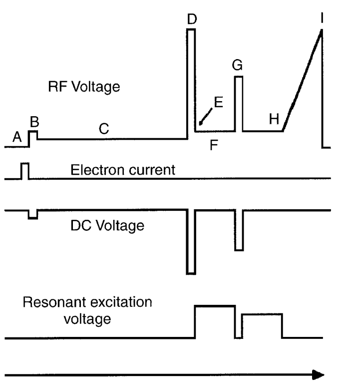


Figure 2.24
Computer-controlled sequence of operations used to carry out a typical MS/MS/MS experiment in an ion trap. (A) Electron impact ionization of the chemical ionization gas. (B) Correct tuning of *U* (DC voltage) and *V* (RF voltage) allows the selection of ions with a given *m/z* for chemical ionization. (C) Protonation of the analyte by the chosen ion for 200 ms. (D) The parent ion is selected. (E) Voltage *V* is increased in order to select a mass range to observe the fragments, while keeping the surviving precursors in the trap. (F) Resonant excitation is used to fragment the selected precursor ions. (G) One of the fragments is selected. (H) Resonant excitation is used to fragment this fragment. (I) Mass scanning to observe the second-generation fragments

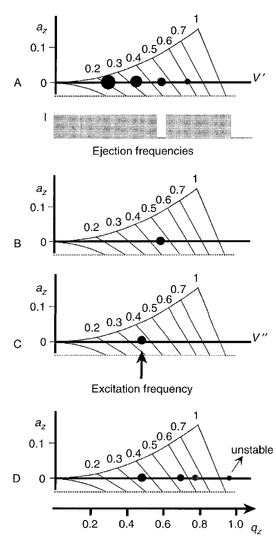
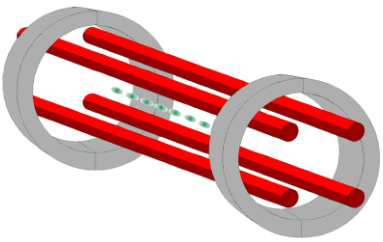


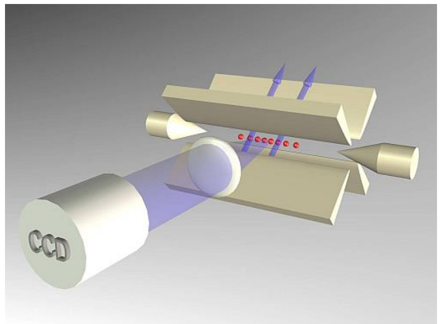
Figure 2.25
One possible sequence of events to produce an MS/MS spectrum. (A) Ions of one mass-to-charge ratio are selected by expelling all the others at their resonance frequency applied to the caps. (B) Only ions of the selected *m/z* are present in the trap. (C) Voltage *V* is adjusted so as to bring the ion in resonance with the excitation frequency applied to the caps. (D) Ions are analyzed by ejection at the stability limit

From Hoffmann

Linear Ion Trap

- Similar idea with new geometry:
  - RF-only quad with end electrodes
  - Ions can be trapped for several days

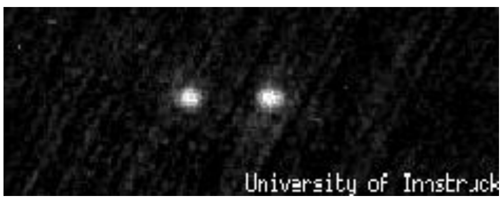




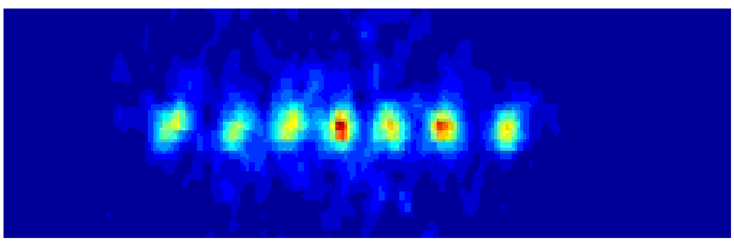
From http://heart-c704.uibk.ac.at/research/lintrap/

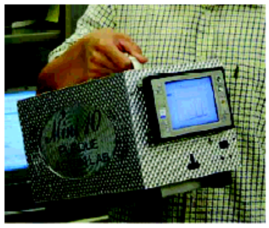
Linear Ion Trap II

- Picture of two ions in the trap



- Animation of the Trapping





A – Processor board
B – Vacuum Manifold
C – Turbo pump
D – Diaphragm pump
E – Lens power supply
F – Communication PCB
G – Filament control
H – Handheld computer

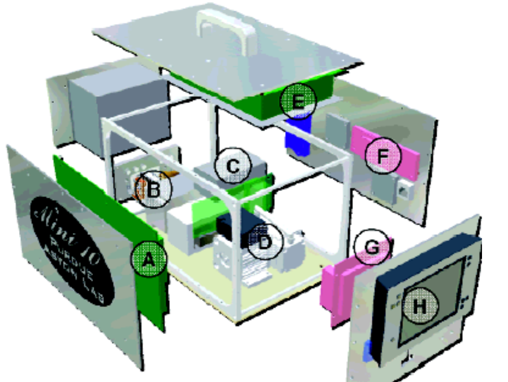


Figure 1. Mini 10 mass spectrometer and its components.

Anal. Chem. **2006**, *78*, 5994–6002

Handheld Rectilinear Ion Trap Mass Spectrometer

Liang Gao,† Qingyu Song,† Garth E. Patterson,‡ R. Graham Cooks,*,† and Zheng Ouyang*,†

Department of Chemistry, Purdue University, West Lafayette, Indiana 47907, and Griffin Analytical Technology, Inc., West Lafayette, West Lafayette, Indiana 47906

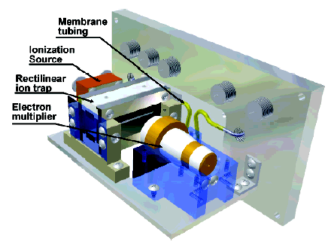
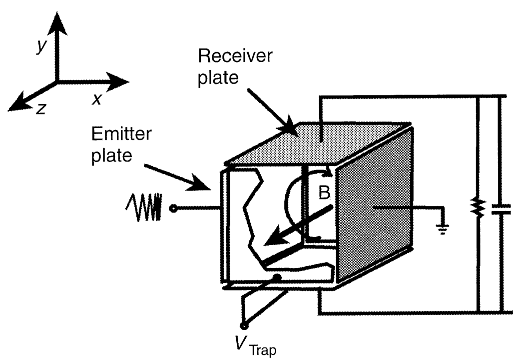


Figure 2. In-vacuum components, including rectilinear ion trap mass analyzer, ionization source, electron multiplier, and sample introduction system.

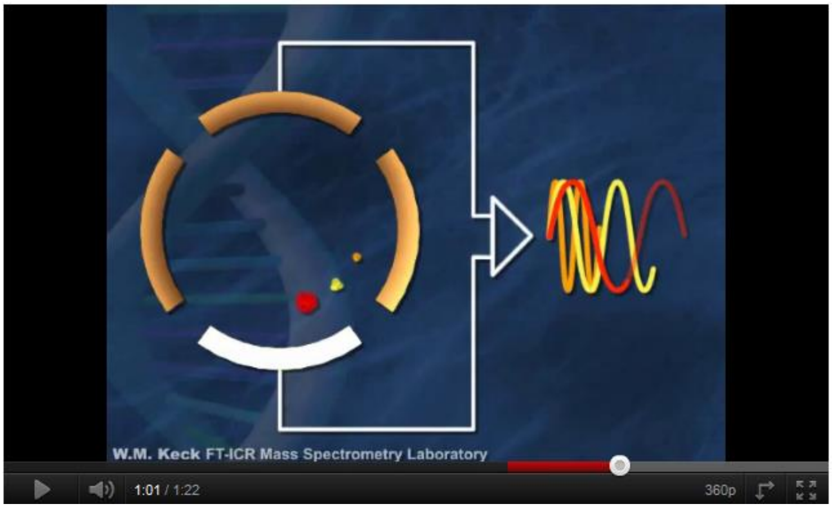
ICR Geometry, Excitation, & Ion Motion



From Hoffmann

Figure 2.50
Diagram of an ion cyclotron resonance instrument. The magnetic field is oriented along the *z*-axis. Ions are injected in the trap along the *z*-axis. They are trapped along this axis by a trapping voltage, typically 1 V, applied to the front and back plates. In the *x*,*y* plane, they rotate around the *z*-axis due to the cyclotronic motion and then go back along the *z*-axis between the electrostatic trapping plates. The sense of rotation indicated is for positive ions. Negative ions will orbit in the opposite direction

FTICR: Animation



http://www.youtube.com/watch?v=a5aLlm9q-Xc

FTMS: Time to Frequency Conversion

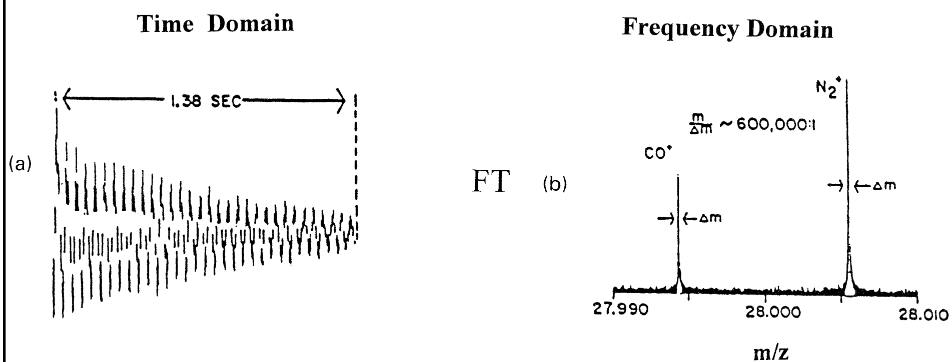


Figure 13-25 (a) Time domain signal (transient) recorded for a mixture of $CO^{+\cdot}$ and $N_2^{+\cdot}$ ions of nominal *m/z* 28 and (b) the corresponding frequency (mass) domain signal. (Courtesy of A.G. Marshall.)

From Lambert

- No traditional detector (multiplier, MCP)
- Detection of image currents induced by flying ions, measured over and over and over…

FTMS Extreme Resolution

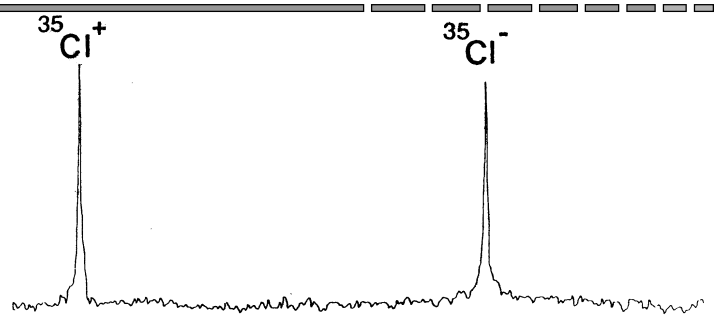


FIG. 4.22. Segment of mass spectrum in region of nominal mass 35 showing a resolution greater than ????????? (FWHM definition) when using FT-MS. The peaks represent the positive and negative ions of ^{35}Cl that have a difference in mass equivalent to the mass of two electrons. The spectrum was obtained using a FT-ICR mass spectrometer with a superconducting magnet (4.7 tesla); the instrument was switched from the positive-ion-detection mode to the negative-ion-detection mode during the scan between the two peaks (Courtesy of Spectrospin AG.)

Clicker: resolution is about:

(a) 10^3 (b) 10^6 (c) 10^7 (d) 10^8 (e) Don't know

From Watson

FT-ICR MS: Sensitivity & non-destructiveness

Clicker: mean free path?

(a) 10 m

(b) 1 km

(c) 100 km

(d) Can't be determined

(e) I don't know

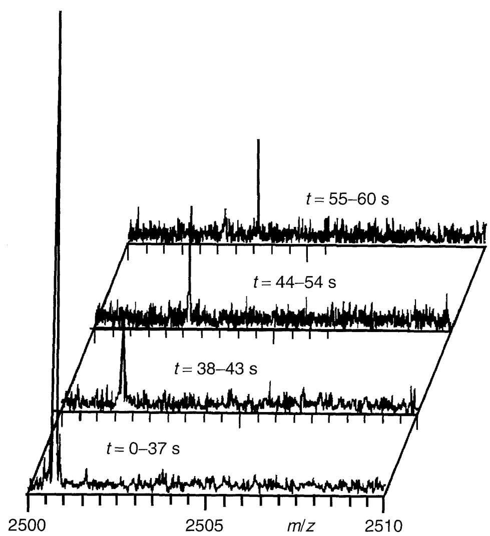


Figure 2.53
One multiply charged ion, produced in an electrospray source, is isolated in an ICR/FTMS cell. During this time it discharges by collision with a neutral gas in a quantified way, proving that it is indeed an isolated ion. From the observed masses, the number of charges can be determined, as explained for the electrospray source. (Reproduced from Ref. 47 with permission)

From Hoffmann

Clicker

How many of the following are true.

(i) An ion trap requires lower vacuum than an FTICR

(ii) Resolution in an ion trap depends critically on the precision of the power supplies used to set the voltage of the ring electrode

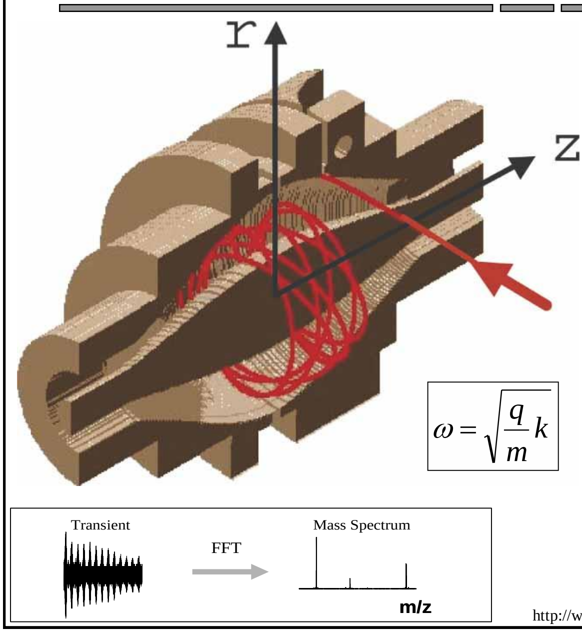
(iii) Resolution in an ion trap depends critically on the speed of the acquisition electronics

(iv) For the scanning mode we discussed, the duty cycle of an ion trap depends on the m/z range recorded

(a) 0 (b) 1 (c) 2 (d) 3 (e) 4

Perspective: The Orbitrap: a new mass spectrometer. Q. Hu, R.J. Noll, H. Li, A. Makarov, M. Hardman, R. Graham Cooks. *J. Mass Spec.*, 40(4): 430 – 443, 2005.

Orbitrap

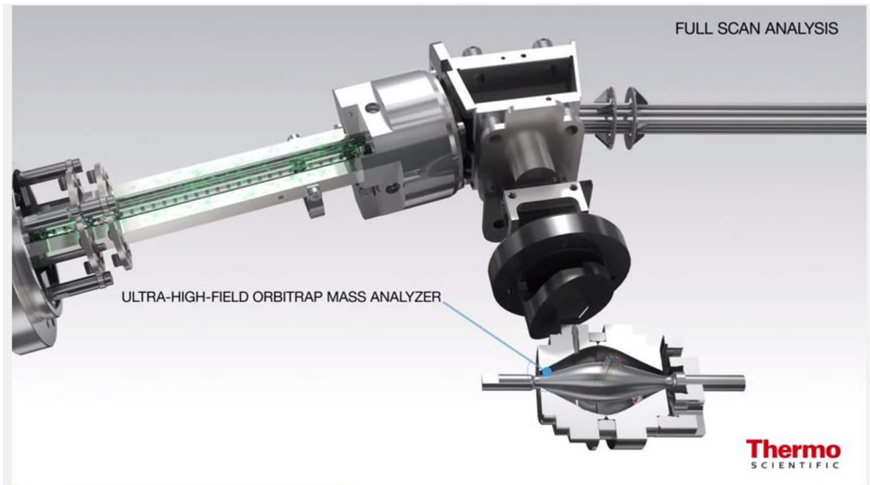


$$\omega = \sqrt{\frac{q}{m}k}$$

Cutaway view of the Orbitrap mass analyzer. Ions are injected into the Orbitrap at the point indicated by the red arrow. The ions are injected with a velocity perpendicular to the long axis of the Orbitrap (the *z*-axis). Injection at a point displaced from *z* = 0 gives the ions potential energy in the *z*-direction. Ion injection at this point on the *z*-potential is analogous to pulling back a pendulum bob and then releasing it to oscillate.

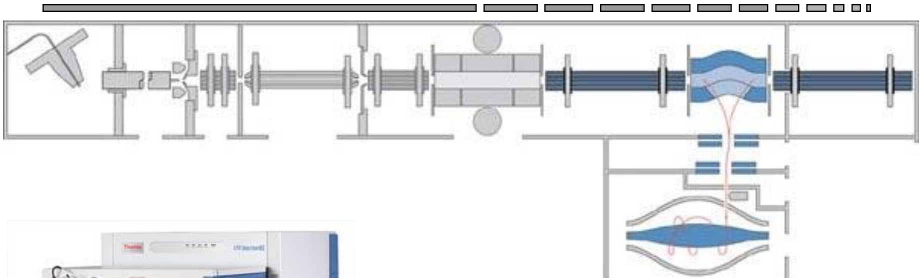
http://www.chem.purdue.edu/iii/Orbitrap%20Instrument.htm

Orbitrap Animations



http://www.youtube.com/watch?v=zJagpUbnv-Y

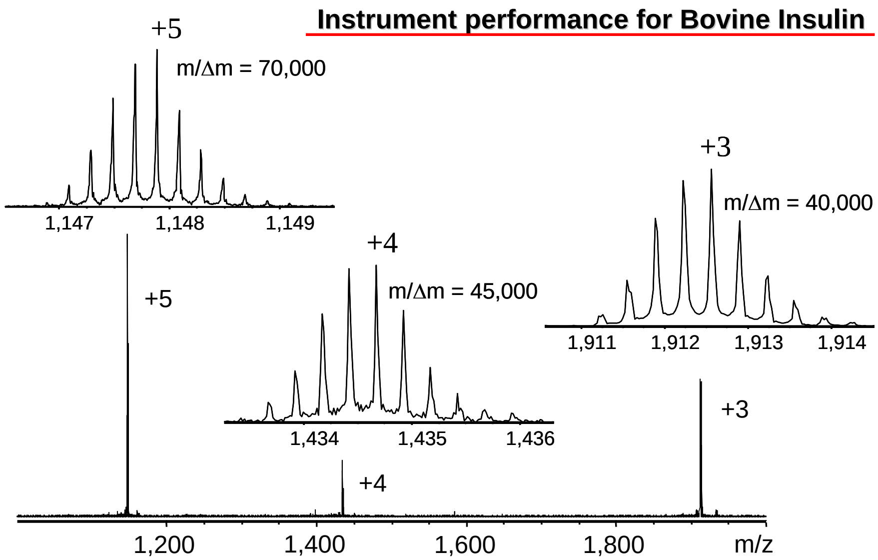
Orbitrap II



- C-Trap for injection
- Linear ion trap interface
- Orbitraps have a high mass accuracy (1-2 ppm), a high resolving power (up to 200,000) and a high dynamic range (around 5000)

http://www.thermo.com/com/cda/resources/resources_detail/1,,200176,00.html

Example Orbitrap Data



http://www.chem.purdue.edu/iii/Orbitrap%20Instrument.htm

Clicker Question: High-Resolution MS

- The use of ultrahigh resolution MS:
  A. Eliminates the need for chromatographic separation
  B. Reduces the need for chromatographic separation
  C. Does not reduce the need for chromatography
  D. I don't know
  E. All of the above

As Impressive as this is, even ultrahigh resolution often it is not enough on its own!

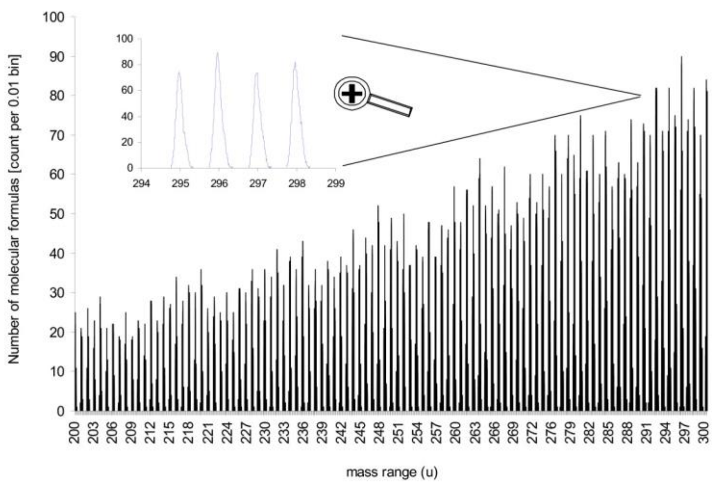


Figure 4: Trend pattern histogram for mathematical possible number of molecular formulae (C, H, N, S, O and P) for the mass range 200 u-300 u. A step size of 0.01 u was taken for counting the number of formulae.

Metabolomic database annotations via query of elemental compositions: Mass accuracy is insufficient even at less than 1 ppm. Tobias Kind and Oliver Fiehn. *BMC Bioinformatics* 2006, 7:234, doi:10.1186/1471-2105-7-234. http://www.biomedcentral.com/1471-2105/7/234

Hybrid Instruments

From Hoffmann

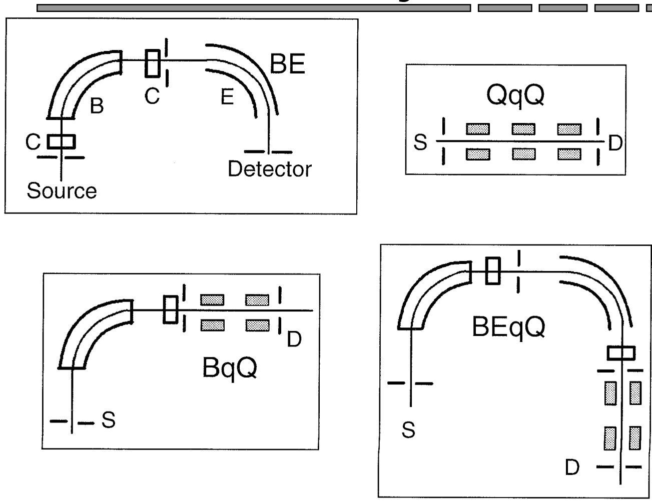
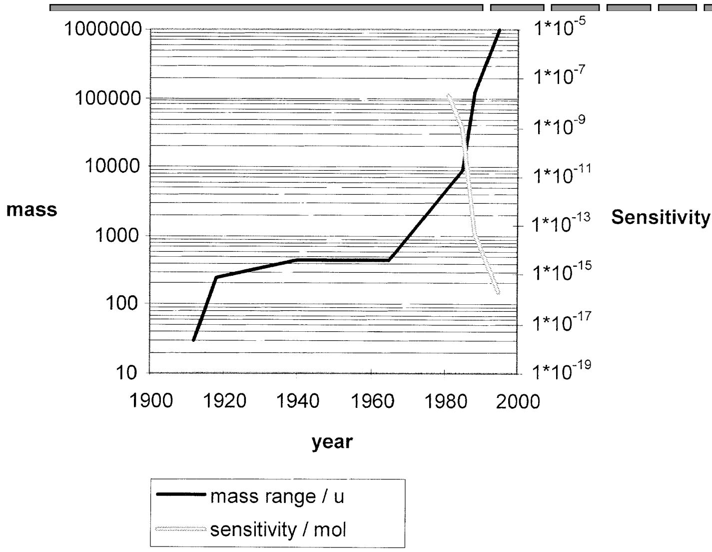


Figure 2.56
Common combinations of electric (E) and magnetic (B) *sectors, quadrupoles (Q) and collision cells (C)*

- Very common, combine the advantages of various analyzers

Progress of MS Analysis



From James (Ed.). "Proteome Research: Mass Spectrometry." Springer, 2000. (QP551 .P7558 2001 at CU Libraries)

Fig. 3.1. Progress of mass-spectrometric techniques with time, expressed as the two parameters "accessible mass range" and "analytical sensitivity"

Comparison of Mass Analyzers I

TABLE 13-17
Characteristics of Mass Analyzers

Method	*Quantity Measured*	*Mass Analysis Equation*	*Mass-to-Charge Range**	*Reso-lution*†*	*Mass Measure-ment Accuracy**	*Dynamic Range‡*	*Oper-ating Pressure (torr)*
Sector magnet	Momentum/charge	14–24	10^4	10^5	<5 ppm	10^7	10^{-6}
Time of flight	Flight time	14–27	10^6	10^3–10^4	0.1–0.01%	10^4	10^{-6}
Quadrupole ion trap	Frequency	14–32	10^4–10^5	10^3–10^4	0.1%	10^4	10^{-3}
Quadrupole	Filters for *m/z*	14–29	10^3–10^4	10^3	0.1%	10^5	10^{-5}
Cyclotron resonance	Frequency	14–35	10^5	10^6	<10 ppm	10^4	10^{-9}

* At 1000 Da/charge.
† Mass/peak width.
‡ Number of orders of magnitude of concentration over which response varies linearly.

From Lambert

Comparison of Mass Analyzers II

TABLE 2.1
General Comparison of Mass Analyzers

Mass analyzer	Typical mass range and resolution	Advantages	Disadvantages
Quadrupole	Range *m/z* 3000 Resolution 2000	Tolerant of high pressures Well-suited for electrospray Ease of switching between positive/negative ions Small size Relatively low cost	Mass range limited to about 3000 *m/z* Poor adaptability to MALDI
Ion trap	Range *m/z* 2000 Resolution 1500	Small size Medium resolution Simple design, low cost Well-suited for tandem mass spectrometry (MS^n, $n \leq 4$) Easy for positive/negative ions	Limited mass range of current commercial versions; however, progress is being made in their development
Magnetic sector	Range *m/z* 20,000 Resolution 10,000	Capable of high resolution Capable of exact mass Medium mass range Can be very reliable, manufacturer dependent	Not tolerant of high pressures Expensive Instrumentation is massive Relatively slow scanning
Time-of-flight (TOF)	Range *m/z* ∞ Resolution 350	Highest mass range Very fast scan speed Simple design, low cost Ease of adaptation to MALDI	Low resolution Difficulty of adaptation to electrospray
Time-of-flight reflectron	Range *m/z* ∞ Resolution 1500	Good resolution Very fast scan speed Simple design, low cost	Good resolving power has limited *m/z* range Lower sensitivity than TOF
Fourier transform–mass spectrometry (FT-MS)	Range *m/z* 10,000 Resolution 30,000	High resolution Well-suited for tandem mass spectrometry (MS^n, $n \leq 4$)	High vacuum ($<10^{-7}$ Torr) required Superconducting magnet required, expensive Instrumentation massive

G. Siuzdak. "Mass Spectrometry for Biotechnology." Academic Press, 1996. QP519.9.M3 S58 1996 at CU Libraries.

Comparison of Mass Analyzers III

Table 3.1. A comparison of different types of mass analyzer

Characteristic	Magnetic Sector	Quadrupole	QIT	TOF	FT-ICR
Mass range (Da)	15,000	4,000	100,000	Unlimited	$>10^6$
Resolution	200,000	Unit	30,000	15,000	$>10^6$
Dynamic range	+ + ++	+++	+ + +	+ + +	++
MS/MS	+ + ++	+ + +	+ + +	+ + +	++
LC (or CE)MS	+	+ + ++	+ + +	++	++
Cost	$$$$	$	$	$$	$$$$

C. Dass. "Principles and Practice of Biological Mass Spectrometry." Wiley Interscience, New York, 2001. QP519.9.M3 D33 2001 at CU Libraries.