

# Mass Analyzers II

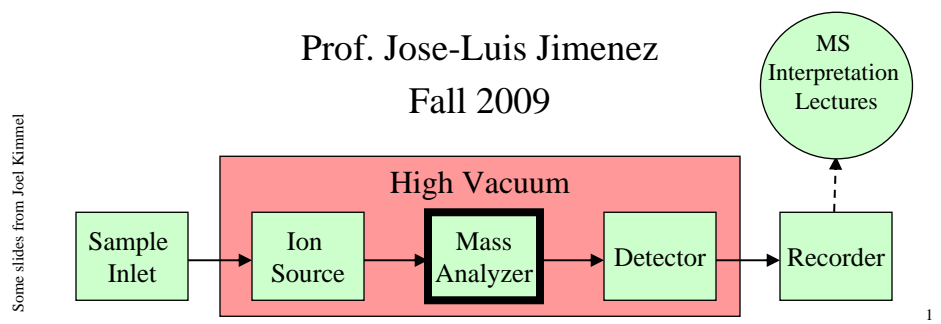
Sector, FTICR, Orbitrap

CU- Boulder

CHEM 5181: Mass Spectrometry & Chromatography

Prof. Jose-Luis Jimenez

Fall 2009



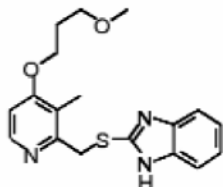
## Business Items

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- First Journal Skim due today
- Small change on lab times
- HW #4 due next Tue at start of class
  - No extensions, turn in what you have
  - Don't wait to start it, I expect some Igor hickups. Coding problems won't be a valid excuse for not completing the assignment.
  - Jose's office hours: today after class and Monday 1-2:30 pm
  - Don't expect that I'll reply to email questions sent Monday evening!

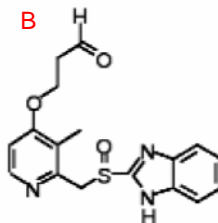
## Clicker Question on Mass Accuracy

A



$m/z = 344.1433$

B



$m/z = 344.1069$

Suppose you are attempting to separate these two compounds by LC-MS. The **first compound to appear** in your chromatogram has an intense peak at  $m/z = 344.1421$ . You know that your mass spectrometer has **mass accuracy greater than 7 ppm**.

What conclusion can you make?

- (A) Compound A is the first to come off of the column
- (B) Compound B is the first to come off of the column
- (C) You are measuring an average of the two compounds that contains mostly A
- (D) Nothing -- You do not have sufficient mass accuracy to determine which compound(s) you are measuring

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## Clicker Question in TOFMS

Q: **How many** of the following statements are **TRUE**

1. To increase the  $m/z$  range of a TOFMS, one must lengthen the drift axis
2. The magnitude of an ion's velocity is equal when entering and exiting a reflectron
3. A TOFMS can simultaneously measure positive and negative ions, but it cannot distinguish between ions having  $m/z$  of equal magnitude and opposite sign (e.g.,  $m/z = +100$  and  $m/z = -100$ )
4. Peak shapes in an averaged TOF mass spectrum are affected by differences in the initial positions of ions within the region where the accelerating potential is applied

A. 0      B. 1      C. 2      D. 3      E. 4

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## Clicker Question in TOFMS

A fact not discussed in class is that the resolution of a TOFMS can often be increased by lengthening the distance that ions drift ( $D$ ).

Suppose  $D$  is increased from 1 meter to 10 meters in a TOFMS having a chamber pressure of  $9\text{e-6 Torr}$ .

Should any change be made to the vacuum system to maintain TOFMS sensitivity (i.e., ion transmission)?

- (A) Yes. The pressure should be increased by a factor of 10; collisions help keep ions focused
- (B) No. Less than or equal to  $1\text{e-5 Torr}$  is ideal for TOFMS
- (C) Yes. The pressure should be decreased by a factor of 10 so that ions can drift the additional distance with low probability of collision
- (D) Yes. The pressure should be decreased by a factor of 100 so that ions can drift the additional distance with low probability of collision
- (E) No.  $9\text{e-6 Torr}$  is the lowest pressure that can be achieved in a mass spectrometer

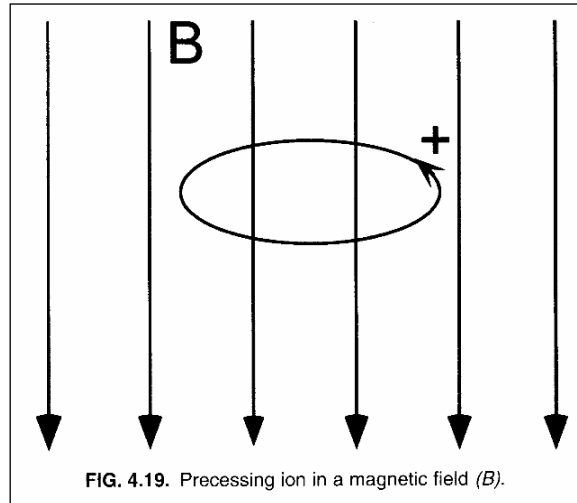
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## Types of Mass Analyzers

- Time-of-flight (TOF)
- **Sector**
  - **Magnetic**
  - **Electric**
- Quadrupoles
- Ion traps
- **Orbitrap**
- **Ion-Cyclotron Resonance (ICR)**
  - **Fourier Transform (FTMS)**
- Hybrids

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## An Ion in an Uniform Magnetic Field



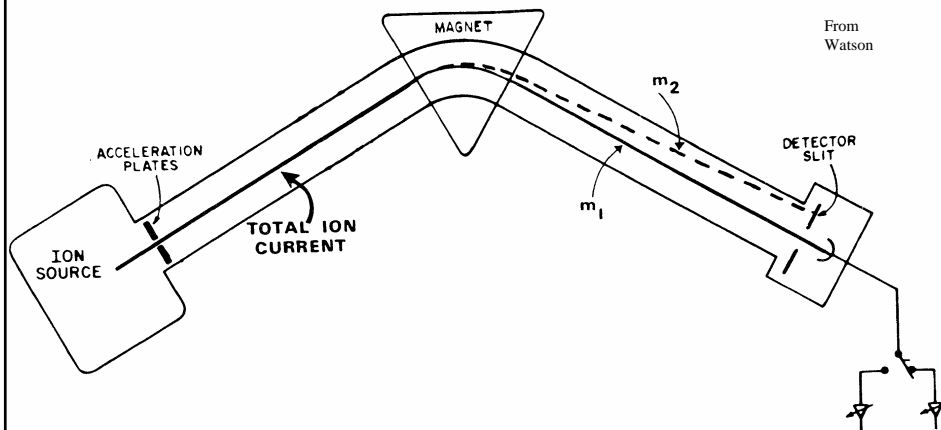
From  
Watson

FIG. 4.19. Precessing ion in a magnetic field ( $B$ ).

- Q: what determines the radius of rotation?

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## Magnetic Sector Analyzer



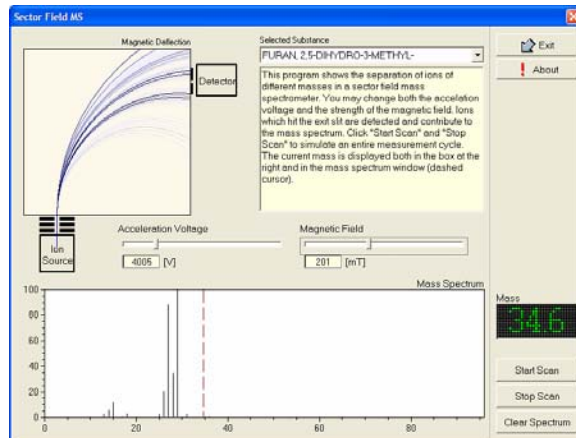
From  
Watson

FIG. 4.1. Schematic diagram of magnetic-sector mass spectrometer.

- Popular for certain applications, e.g. Prof. Jim White (ENVS) has 7 of these in East Campus for isotope ratio MS

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## Simulation of Magnetic Sector MS



- Clicker Q
- With  $V_s = 4000$  V and  $B = 200$  mT, we select  $m/z$  35.
- What  $m/z$  will we select if we double both  $V_s$  and  $B$ ?
  - $m/z$  35
  - $m/z$  17.5
  - $m/z$  70
  - $m/z$  350
  - All of the above

[http://www.vias.org/simulations/simsoft\\_ms\\_sectorfield.html](http://www.vias.org/simulations/simsoft_ms_sectorfield.html)

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## Magnetic Sector Analyzer

- Ion kinetic energy when leaving source:
- Action of the magnetic field:
- Trajectory of ion is determined by equilibration of magnetic force and centripetal acceleration:
- Ions with the same momentum ( $mv$ ) have the same  $R$ . This is a **momentum analyzer**.
- Taking into account the kinetic energy of the ions:

$$E_k = \frac{mv^2}{2} = qV_s$$

$$\vec{F}_M = q \vec{v} \times \vec{B}$$

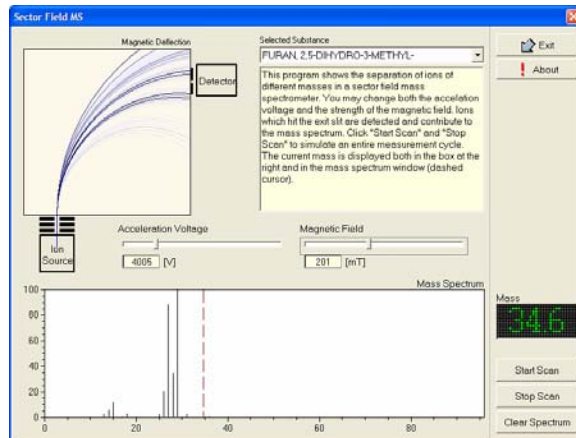
$$qvB = \frac{mv^2}{R} = m\omega^2 R$$

$$R = \frac{mv}{qB}$$

$$\frac{m}{q} = \frac{R^2 B^2}{2V_s}$$

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## Simulation of Magnetic Sector MS



- Clicker Q
- With  $V_s = 4000$  V and  $B = 200$  mT, we select  $m/z$  35.
- What  $m/z$  will we select if we double  $V_s$  and halve  $B$ ?
  - $m/z$  4
  - $m/z$  17.5
  - $m/z$  35
  - $m/z$  70
  - $m/z$  140

[http://www.vias.org/simulations/simsoft\\_ms\\_sectorfield.html](http://www.vias.org/simulations/simsoft_ms_sectorfield.html)

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## Magnetic Sector Analyzer Part II

- Fixed geometry instruments
  - If  $R$  is fixed by the geometry of the analyzer, for a given  $B$  only one  $m/z$  will reach the detector
  - Can be scanned by scanning  $B$  or  $V_s$
- Dispersive instruments
  - measure ions arriving with different  $R$
- Problem: ions with the same  $mE_k/q$  have same  $R$ :

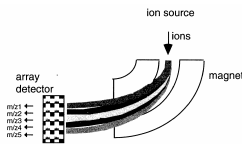


Figure 2.22 Illustration of the operation of an array detector

$$R = \frac{1}{B} \sqrt{\frac{2mE_k}{q}}$$

- Use electrostatic analyzer to narrow  $E_k$  range

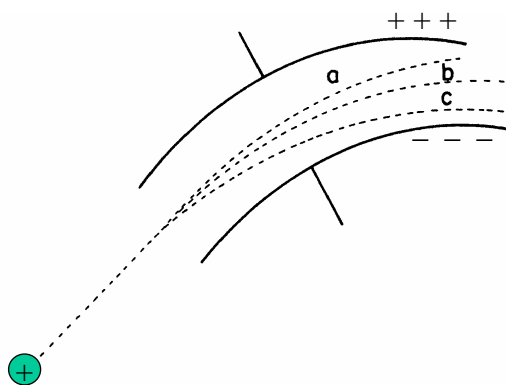
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## Clicker Question

- An ion source produces singly-charged ions of with an average energy of 5000 V and an energy dispersion of 100 eV. Can we use a magnetic-only analyzer with this source to separate ions at  $m/z$  200 with a resolution of 10000?
- A. Yes  
B. Marginally  
C. No  
D. I don't know

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## Electric Sector Analyzer



**Figure 3.3e** Flight paths of ions of different kinetic energies in an electrostatic analyser

From  
Barker  
44

## Electrostatic Analyzer

- Ion kinetic energy when leaving source:
- Action of the electric field:
- Trajectory of ion is determined by equilibration of electric force and centripetal acceleration:
- Ions with the same kinetic energy have the same R:
- So trajectory is independent of the mass, and this is really a **kinetic energy analyzer**

$$E_k = \frac{mv^2}{2} = qV_s$$

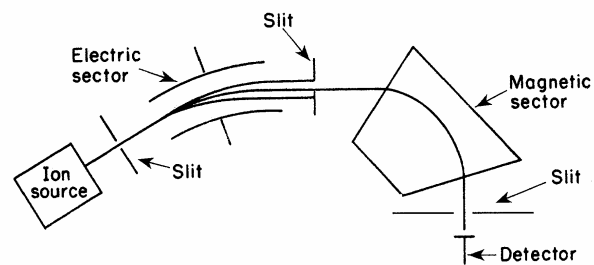
$$\vec{F}_E = q\vec{E}$$

$$qE = \frac{mv^2}{R} = m\omega^2 R$$

$$R = \frac{2E_k}{qE}$$

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## Double Focusing Mass Analyzer

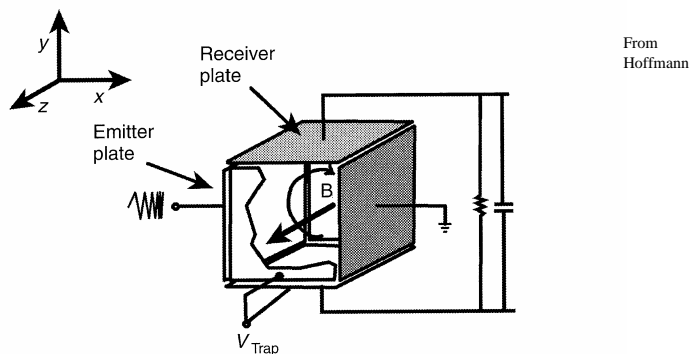


**Figure 3.3f** Schematic representation of a double-focusing mass spectrometer

- Electric analyzer passes a narrow range of  $E_k$
- So that magnetic analysis is really of  $m/q$

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## ICR Geometry, Excitation, & Ion Motion



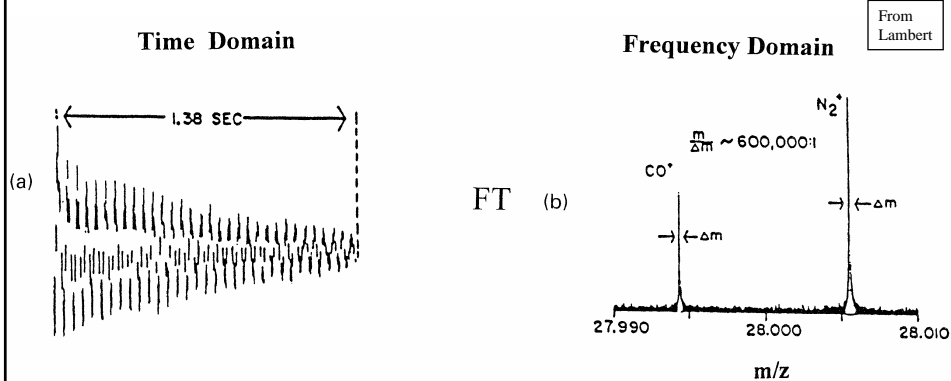
From Hoffmann

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

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## FTMS: Time to Frequency Conversion



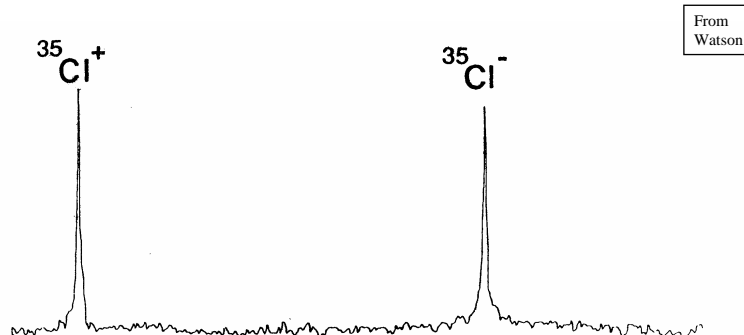
From Lambert

Figure 13-25 (a) Time domain signal (transient) recorded for a mixture of  $\text{CO}^+$  and  $\text{N}_2^+$  ions of nominal  $m/z$  28 and (b) the corresponding frequency (mass) domain signal. (Courtesy of A.G. Marshall.)

- No traditional detector (multiplier, MCP)

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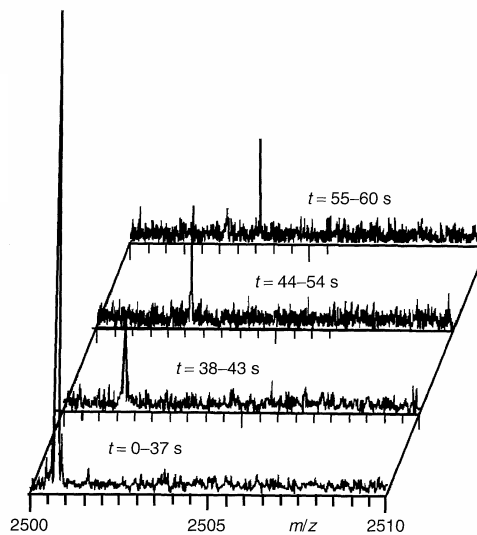
## FTMS Extreme Resolution



**FIG. 4.22.** Segment of mass spectrum in region of nominal mass 35 showing a resolution greater than 1,000,000 (FWHM definition) when using FT-MS. The peaks represent the positive and negative ions of  $^{35}\text{Cl}$  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.)

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## FT-ICR MS: Sensitivity & non- destructiveness



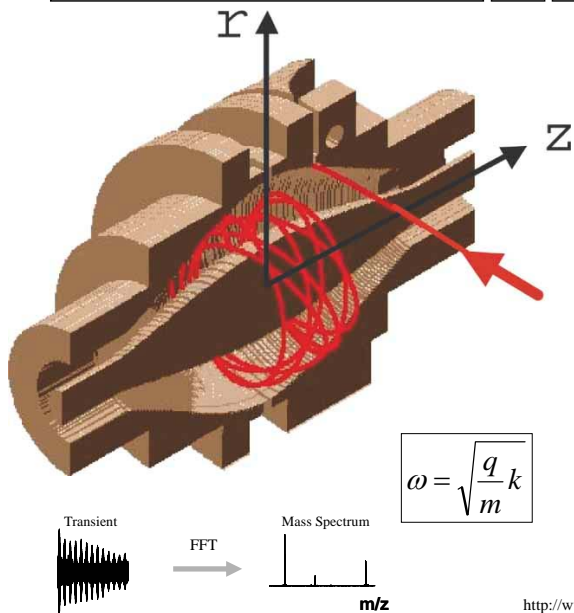
**Figure 2.53**

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

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

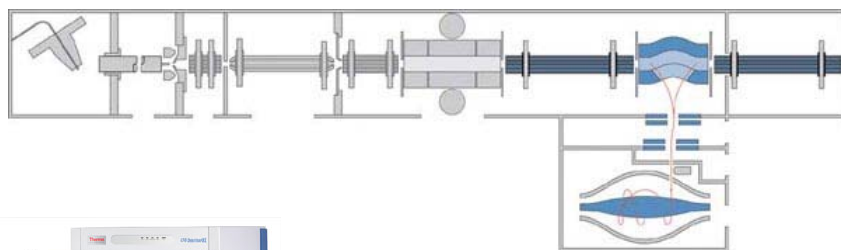


### Cutaway view of the Orbitrap mass analyzer.

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> 21

## Orbitrap II

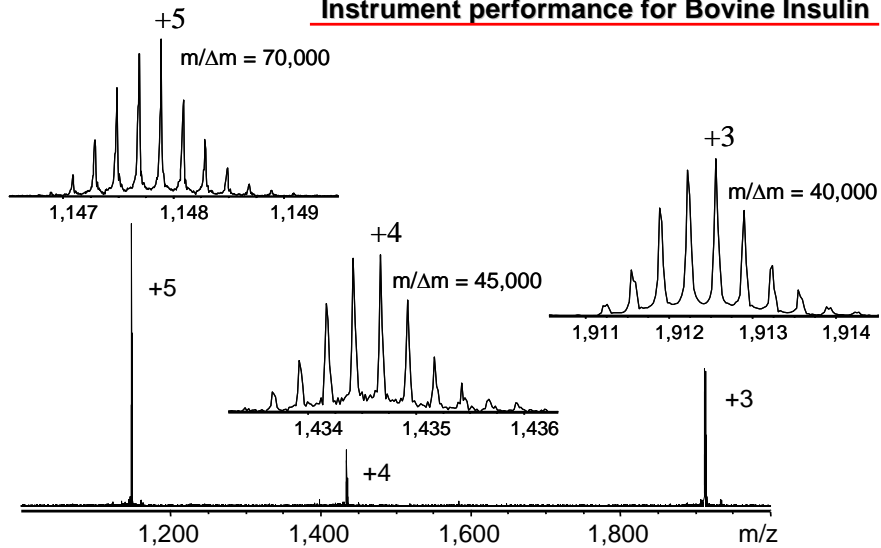


- C-Trap for injection
- Linear ion trap interface
- Orbitraps have a high mass accuracy (1-2 ppm), a high resolving power (up to 200,000) and a high dynamic range (around 5000)

[http://www.thermo.com/com/cda/resources/resources\\_detail/1,,200176,00.html](http://www.thermo.com/com/cda/resources/resources_detail/1,,200176,00.html)

## Example Orbitrap Data

### Instrument performance for Bovine Insulin

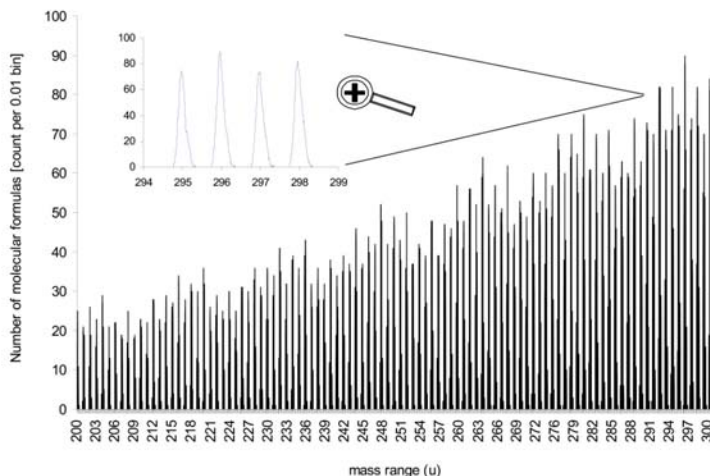


<http://www.chem.purdue.edu/iii/Orbitrap%20Instrument.htm>

## Clicker Question: High-Resolution MS

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

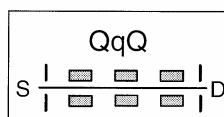
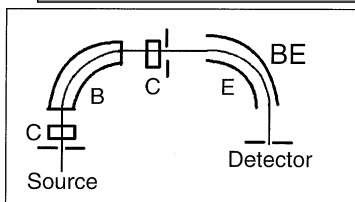
As Impressive as this is, often it is not enough  
on its own!



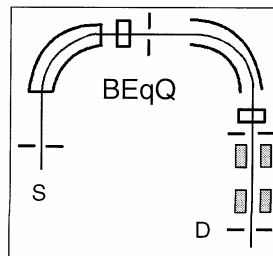
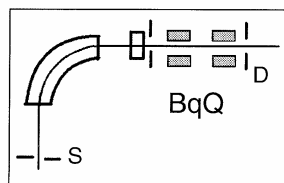
**Figure 4: Trend pattern histogram for mathematical possible number of molecular formulae (C, H, N, S, O and P) for the mass range 200 u-300 u. A step size of 0.01 u was taken for counting the number of formulae.**

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



• Very common, combine the advantages of various analyzers

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

## Progress of MS Analysis

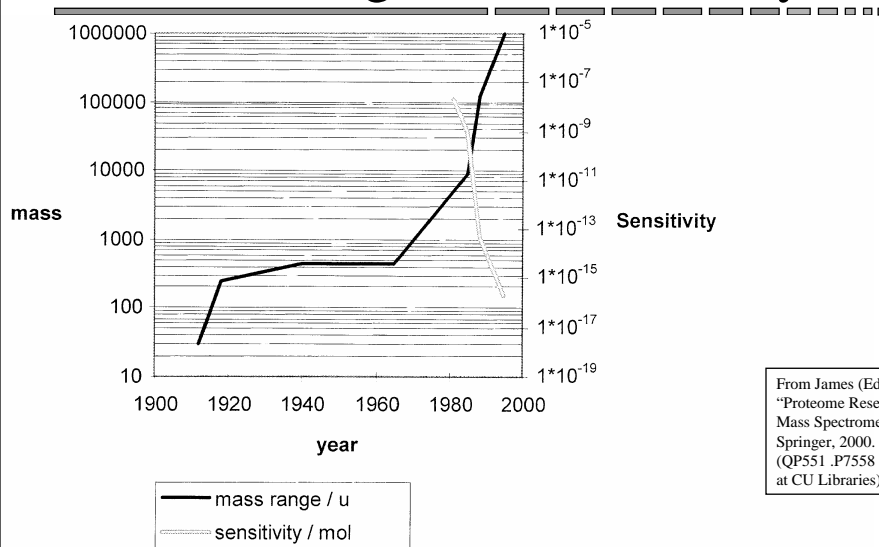


Fig. 3.1. Progress of mass-spectrometric techniques with time, expressed as the two parameters "accessible mass range" and "analytical sensitivity"

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## Comparison of Mass Analyzers I

From Lambert

TABLE 13-17  
Characteristics of Mass Analyzers

Method	Quantity Measured	Mass Analysis Equation	Mass-to-Charge Range*	Resolution**†	Mass Measurement Accuracy*	Dynamic Range‡	Operating 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.

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## 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 $m/z$ $\infty$ 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 $m/z$ $\infty$ 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. 29

## 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.