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)

Sample Inlet → Ion Source → Mass Analyzer → Detector → Recorder

High Vacuum

MS Interpretation Lectures

Business Items

• Questions or comments?
• Labview
  – Megan C is done
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

- 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

\[ q_z = \frac{8eZV}{m(r_o^2 + 2z_o^2)(2\pi\nu)^2} \]

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 \( q_z \)

\[ q_z = \frac{8eZV}{m(r_o^2 + 2z_o^2)(2\pi\nu)^2} \]

\( q_z \) 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

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, $\alpha_z = 0.149998$ 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 $\beta_z$ values and thus lower secular frequencies. If $V$ is increased, $\beta_z$ values increase for all the ions, as do the secular frequencies. In the example given, the lightest ion now has a $\beta_z$ 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 $r_z = 1$ cm and operating at a $\nu$ frequency of 1.1 MHz, the highest detectable mass-to-charge ratio is about 650 Th.
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
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\textsuperscript{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\textsuperscript{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
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
ICR Geometry, Excitation, & Ion Motion

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

- 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 100 000 (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

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)
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


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.

Orbitrap Animations

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

Instrument performance for Bovine Insulin


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.


---

**Hybrid Instruments**

- 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

(QP551 .P7558 2001 at CU Libraries)

Comparison of Mass Analyzers I

<table>
<thead>
<tr>
<th>Method</th>
<th>Quantity Measured</th>
<th>Mass Analysis Equation</th>
<th>Mass-to-Charge Range*</th>
<th>Resolution**</th>
<th>Mass Measurement Accuracy*</th>
<th>Dynamic Range†</th>
<th>Operating Pressure (torr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sector magnet</td>
<td>Momentum/charge</td>
<td>14–24</td>
<td>10⁴</td>
<td>10²</td>
<td>&lt;5 ppm</td>
<td>10⁶</td>
<td>10⁻⁴</td>
</tr>
<tr>
<td>Time of flight</td>
<td>Flight time</td>
<td>14–27</td>
<td>10⁸</td>
<td>10⁻¹⁰⁻¹⁰⁴</td>
<td>0.1–0.01%</td>
<td>10⁶</td>
<td>10⁻⁶</td>
</tr>
<tr>
<td>Quadrupole ion trap</td>
<td>Frequency</td>
<td>14–32</td>
<td>10⁻¹⁰⁻¹⁰⁵</td>
<td>10⁻¹⁻¹⁰⁴</td>
<td>0.1%</td>
<td>10⁴</td>
<td>10⁻²</td>
</tr>
<tr>
<td>Quadrupole Cyclotron resonance</td>
<td>Filters for m/z</td>
<td>14–29</td>
<td>10⁻³⁻¹⁰⁴</td>
<td>10³</td>
<td>0.1%</td>
<td>10⁶</td>
<td>10⁻⁶</td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
<td>14–35</td>
<td>10⁵</td>
<td>10⁸</td>
<td>&lt;10 ppm</td>
<td>10⁸</td>
<td>10⁻⁹</td>
</tr>
</tbody>
</table>

* 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**

<table>
<thead>
<tr>
<th>Mass analyzer</th>
<th>Typical mass range and resolution</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quadrupole</td>
<td>Range m/z 3000 Resolution 2000</td>
<td>Tolerant of high pressures</td>
<td>Mass range limited to about 3000 m/z</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Well-suited for electrospray</td>
<td>Poor adaptability to MALDI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ease of switching between positive/negative ions</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Small size</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relatively low cost</td>
<td></td>
</tr>
<tr>
<td>Ion trap</td>
<td>Range m/z 2000 Resolution 1500</td>
<td>Small size</td>
<td>Limited mass range of current commercial versions; however, progress is being made in their development</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medium resolution</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Simple design, low cost</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Well-suited for tandem mass spectrometry (MS², n=4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Easy for positive/negative ions</td>
<td></td>
</tr>
<tr>
<td>Magnetic sector</td>
<td>Range m/z 20,000 Resolution 1500</td>
<td>Capable of high resolution</td>
<td>Not tolerant of high pressures</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Capable of exact mass</td>
<td>Instrumentation is massive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medium mass range</td>
<td>Relatively slow scanning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Can be very reliable, manufacturer dependent</td>
<td></td>
</tr>
<tr>
<td>Time-of-flight (TOF)</td>
<td>Range m/z= Resolution 350</td>
<td>Highest mass range</td>
<td>Low resolution</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Very fast scan speed</td>
<td>Difficulty of adaptation to electrospray</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Simple design, low cost</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ease of adaptation to MALDI</td>
<td></td>
</tr>
<tr>
<td>Time-of-flight reflectron</td>
<td>Range m/z= Resolution 1500</td>
<td>Good resolution</td>
<td>Good resolving power has limited m/z range</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Very fast scan speed</td>
<td>Lower sensitivity than TOF</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Simple design, low cost</td>
<td></td>
</tr>
<tr>
<td>Fourier transform-mass spectrometry (FT-MS)</td>
<td>Range m/z 10,000 Resolution 30,000</td>
<td>High resolution</td>
<td>High vacuum (&lt;10⁻⁵ Torr) required</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Well-suited for tandem mass spectrometry (MS², n=4)</td>
<td>Superconducting magnet required, expensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Instrumentation massive</td>
</tr>
</tbody>
</table>


### Comparison of Mass Analyzers III

**Table 3.1. A comparison of different types of mass analyzer**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Magnetic Sector</th>
<th>Quadrupole</th>
<th>QIT</th>
<th>TOF</th>
<th>FT-ICR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass range (Da)</td>
<td>15,000</td>
<td>4,000</td>
<td>100,000</td>
<td>Unlimited</td>
<td>&gt;10⁵</td>
</tr>
<tr>
<td>Resolution</td>
<td>200,000</td>
<td>Unit</td>
<td>30,000</td>
<td>15,000</td>
<td>&gt;10⁶</td>
</tr>
<tr>
<td>Dynamic range</td>
<td>+ + + +</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>MS/MS</td>
<td>+ + +</td>
<td>+ + +</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>LC (or CE)MS</td>
<td>+</td>
<td>+ + +</td>
<td>+++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Cost</td>
<td>$$$$</td>
<td>$</td>
<td>$</td>
<td>$</td>
<td>$$$$</td>
</tr>
</tbody>
</table>