Clicker Quiz I:
an ion with \( m/z = m \) has charge equal:

(a) 1 Coulombs
(b) \( m \) Coulombs
(c) \( 1.6022 \times 10^{-19} \) Coulombs
(d) \( e \) Coulombs
(e) I don’t know
Clicker Quiz II:
The first mass spectrometer was built by:

(a) A. Einstein
(b) F. McLafferty
(c) J. Thompson
(d) E. Goldstein
(e) I don’t know

Clicker Quiz III:
Ions in an electric sector MS have a trajectory that depends on:

(a) Their speed
(b) Their kinetic energy
(c) Their potential energy
(d) Their acceleration
(e) I don’t know
Clicker Question:
an ion with $m/z = m$ has charge equal:

(a) 1 Coulombs  
(b) m Coulombs  
(c) $1.6022 \times 10^{-19}$ Coulombs  
(d) $e$ Coulombs  
(e) I don’t know

A mass spectrometer determines the mass-to-charge ratio ($m/z$) of gas-phase ions by subjecting them to known electric or magnetic fields under vacuum and analyzing their resultant motion.
The mass-to-charge ratio is often referred to as $m/z$ and is typically considered to be unitless:

$m$: the mass number = atomic mass/u  
$e$: the charge number = Q/e  

The Thompson has been proposed as a unit for $m/z$, but is only sometimes used.

Historically, most ions in MS had $z = 1$, which is likely the cause for the confusion in units. But, due to new ionization techniques, this is no longer true.
Signal Intensity

Depending on the type of mass spectrometer, ions may be detected by direct impact with a detector or by monitoring of an induced current image.

**Recorded signal can be measured in:**

- Counts per unit time (Digital)
- Voltage per unit time (Analog)
- Power (Frequency domain)

To a first approximation, relative signal intensity reflects relative ion abundance.

---

A short history of MS

**Early stages of MS:** Precise determination of atomic masses and isotope abundances.

**Last 60 years:** Shift towards analytical applications involving molecules of greater complexity.

**Last 20 years:** Explosion of biological applications.

- 1897: JJ Thompson discovers electron and determines its m/z
- 1912: JJ Thompson constructs first mass spectrometer
- 1918: Dempster develops electron ionization source
- 1942: First commercial instrument for organic analysis
- 1956: First GC-MS
- 1974: First HPLC-MS
- 1987: MALDI demonstrated; 1988 ESI Demonstrated; shared Nobel Prize in 2002

See extended history in introduction of De Hoffmann.
Ion Motion in Electrostatic Fields

- Electrical force on an ion:

\[ \overrightarrow{F_E} = q\overrightarrow{E} \]

Clicker Q: Would ions of the same m/z originating at X and Y (with zero velocity) be arrive at the negative surface at the same time?
A. Yes
B. X will arrive before Y
C. Y will arrive before X
D. I don’t know
E. I still need a coffee

Mass Analyzer Resolving Power

Figure 1: Mass accuracy determination and the FWHM method for determining resolution for a mass spectrometer measured at a given ion.

<table>
<thead>
<tr>
<th>Mass peak width ((\Delta m_{50%}))</th>
<th>Full width of mass spectral peak at half-maximum peak height</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass resolution / Resolving Power ((m / \Delta m_{50%}))</td>
<td>Quantifies ability to isolated single mass spectral peak</td>
</tr>
<tr>
<td>Mass accuracy</td>
<td>Mass accuracy is the difference between measured and actual mass</td>
</tr>
</tbody>
</table>

Figure from: M. P. Balogh, LC-GC Europe, 17(3), 152–159 (2004)
Calculate resolution and accuracy

Argon
Atomic Weight (Da): 39.948

<table>
<thead>
<tr>
<th>Atomic mass (m/u)</th>
<th>Abundance</th>
</tr>
</thead>
<tbody>
<tr>
<td>35.96754552</td>
<td>0.33%</td>
</tr>
<tr>
<td>37.9627325</td>
<td>0.06%</td>
</tr>
<tr>
<td>39.9623837</td>
<td>99.6%</td>
</tr>
</tbody>
</table>

Clicker Q: A mass spectrometer with a resolution of 5000 should be capable of resolving isotopic peaks (e.g. $^{12}$CH$_4$ vs $^{13}$CH$_4$) for singly charged species with $m/z$:

(a) Of any value  
(b) Less than $m/z$ 5000  
(c) Greater than $m/z$ 5000  
(d) It depends on the type of mass spectrometer  
(e) I don’t know
Intro to MS, Resolution / Accuracy, Sector Mass Spectrometers, and Ion Optics II

CU- Boulder
CHEM-5181
Mass Spectrometry & Chromatography
Prof. Jose-Luis Jimenez

Some slides adapted from 2007 lecture by Dr. Joel Kimmel, CU-Boulder

Business Items

• Pls erase board, lower screen, turn on projector, clean up front of room when you come in. Thanks in advance!
• Help sessions on Mon & Wed late afternoon will continue, instead of previously announced office hours
  – If you can’t make it to those, just make an appointment w/ me separately
• Remember that Ingrid is available for Igor help on M-Thu, 1-2 pm, Ekeley M170
• Pseudo-code or algorithm first!
  – Don’t build the walls before designing the house!
  – When I ask for the algorithm, having actual code will be a mistake
Clicker Quiz I: The difference between the two plots below is:

(a) The spectrometers have different resolution
(b) The resolution is calculated with a different definition
(c) With a more expensive instrument, the resolution improves
(d) The average is closer to the peak top on the left plot
(e) I don’t know

Clicker Quiz II: FT-ICR MS:

(a) Is great for GC-MS but not LC-MS
(b) Can work with LC-MS but not GC-MS
(c) It doesn’t work well with LC or GC because the signal is too weak
(d) It doesn’t work well with LC or GC because the time to take data is too short
(e) I don’t know
Very very useful for checking your calculations!

$m/z$ 100, 1 keV
$\Rightarrow v \approx 150$ mm $\mu$s$^{-1}$

**Mass Analyzer Resolution II**

- Question: what is the resolution (FWHM definition) in both cases
  - if $m_1 = 50$ Da?
  - If $m_1 = 2500$ Da?

$(m_2 = m_1 + 1$ amu $)$

---

FORCES ON CHARGED PARTICLES IN ELECTROMAGNETIC FIELDS

An ion of mass $m$ and charge $q$, that has been accelerated by a potential difference $U$ to a kinetic energy $K = qU$, moves with the velocity $v = \sqrt{2K/m}$ as long as this velocity is small as compared to the velocity of light $c \approx 299,792,458$ mm $\mu$s$^{-1}$. For numerical calculations it is advantageous to introduce dimensionless quantities $\bar{K}, \bar{m}, \bar{v}$ and $\bar{q}$ with $\bar{K} = \bar{K}$ eV, $\bar{m} = m u$, $\bar{v} = \bar{v}$ mm $\mu$s$^{-1}$ and $\bar{q} = \bar{q}e$, where $-e$ is the charge of an electron. Here $u$ stands for the mass of 1/12 of one $^{12}$C atom. With these quantities, one finds the velocity $\bar{v}$ of an ion of $\bar{K}$ eV energy and $\bar{m}$ mass units $u$ as

$$v \approx 9.8226967\sqrt{\frac{2K}{m}}$$

in mm $\mu$s$^{-1}$. To derive Eqn (1) use was made of the fact that the energy equivalent of one mass unit $m_u c^2$ is 931,493,700 eV, which leads to the numerical value of $299,792,458/\sqrt{31493,700} \approx 9.8226967$. 

---

Diagram showing the concepts of peak resolution and valley
What Resolution do we really need?

- What resolution is really needed to distinguish these two overlapping ions, *if we know that only these two ions are present*?
  
  A. \( \chi = 0.4 \)
  
  B. \( \chi = 0.8 \)
  
  C. \( \chi = 1.2 \)
  
  D. \( \chi = 1.6 \)
  
  E. \( \chi = 2.0 \)

\[ \chi = \text{peak separation} / \text{HWHM} \]
Clicker Q: Which of the following pairs requires the greatest mass resolving power to distinguish:

(A) Ar$^+$ from Ar$^{2+}$
(B) CO$^+$ from N$_2^+$
(C) CH$_3^+$ from CDH$_2^+$
(D) I don’t know
(E) I need a coffee

Info:
Ar = 39.9623837 u, C = 12 u, O = 15.9949 u, N = 14.003 u, H = 1.007 u, and D = 2.0141 u

MS Oscilloscope

http://www.vias.org/simulations/simusoft_msscope.html
Types of Mass Analyzers

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

**Electric Sector Analyzer**

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

From Barker
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

\[
E_k = \frac{mv^2}{2} = qV_s
\]
\[
\vec{F}_E = q \vec{E}
\]
\[
qE = \frac{mv^2}{R} = m\omega^2 R
\]
\[
R = \frac{2E_k}{qE}
\]

An Ion in an Uniform Magnetic Field

- Clicker Q: what determines the radius of rotation?
  
  (A) B only
  (B) Initial position of ion
  (C) Initial velocity of ion
  (D) mass of the ion
  (E) All of the above
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:

\[ E_k = \frac{mv^2}{2} = qV_s \]

\[ \vec{F}_M = q \vec{v} \times \vec{B} \]

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

\[ R = \frac{mv}{qB} \]

\[ \frac{m}{q} = \frac{R^2B^2}{2V_s} \]
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 $B$?
  A. $m/z$ 35
  B. $m/z$ 17.5
  C. $m/z$ 70
  D. $m/z$ 350
  E. All of the above

http://www.vias.org/simulations/simusoft_ms_sectorfield.html
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 $mv$ or $mE_k$ have same $R$:
  \[ R = \frac{1}{B} \sqrt{\frac{2mE_k}{q}} \]
  
  • Use electrostatic analyzer to narrow $E_k$ range

---

Double Focusing Mass Analyzer

From Barker

**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 $m/z$
Introduction to MS, Resolution / Accuracy, Sector Mass Spectrometers, and Ion Optics III

CU- Boulder
CHEM-5181
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Some slides adapted from 2007 lecture by Dr. Joel Kimmel, CU-Boulder

Business Items

• People are making great progress in programming!
  – Mistakes: mainly logic errors, made hard to find by ‘suboptimal’ organization and confusing function, variable, and wave naming
  – Also often make assumptions that are more complex than they need to be, or insist on using advanced features instead of easier ones
  – More advanced folks: please use moderation with advanced features, they can confuse the beginners

• Office Hrs / Help sessions on Mon & Wed late afternoon will continue, instead of previously announced office hours
  – Will start @ 4:30 pm and go for at least 1 hr, longer if there is interest and I am available
  – If you can’t make it to those, just make an appointment w/ me separately

• I always want a separate algorithm separately!
  – When I ask for the algorithm, having actual code will be a mistake
    • Do it as comments, then make a copy and write the code in between the comments
Business Items II

- Option of pasting Igor-formatted code as an image (thx Katie)
  - [https://piazza.com/class/hiy250ehses10?cid=52](https://piazza.com/class/hiy250ehses10?cid=52)
  - Easier to see, can’t copy the code though

- Online resources
  - Main Wiki page & Piazza
  - Point out reading for next time

- HW: Only code for HW 5.3 due on Thu (due to Rainer's exam)
  - I will review ALL submitted code and grade on following conventions
    - Will update conventions later today, will post in Piazza when done
  - Finish all of HW5 by Tue 1-Oct

- Changes to the course (per Piazza post yesterday)
  - Current system with reading / quiz / limited lectures is not optimal
  - We will try an alternative system (partially suggested by a student)
    - Assign reading
    - Ask the equivalent of clicker questions online, to be answered before class, only participation counts
    - Short lecture at the start of class
    - Graded clicker questions at the start of the next lecture?
    - Comments? Other alternatives?

The less scary Clicker Quiz Ever!

- The youtube video presenter of the bisection method was:
  A. Chinese, Korean, or Japanese
  B. Hispanic
  C. French
  D. Indian or South Asian
  E. I don’t know
**Ion Optics**

- Typically static electric fields, much like a sector MS
- Used in ion sources
  - Neutrals don’t feel electric or magnetic fields
  - Once molecules are ionized, they immediately feel the forces
  - Ion optics use electric fields to steer ions into mass spectrometer w/ right properties (e.g. limited energy dispersion)
- Also used in other parts of the MS
- Sometimes “active optics” such as quadrupoles

---

**Example of an EI Ion Source**

- **Clicker Q: a + ion**
  - A. Will go faster thru the base plate than thru the quad
  - B. Will go slower thru the base plate than thru the quad
  - C. Will have the same velocity in both cases
  - D. It doesn’t have enough energy to enter the quad
  - E. I don’t know

(From Balzers QMA 410 Manual (Ion source of the Aerosol Mass Spectrometer))
Ion Optics Simulation

- Fully deterministic, can be realistically simulated
- But quality of your ion beam (width, angle, energy) matters a lot

If you ever get serious, use SIMION http://www.simion.com/

http://www.vias.org/simulations/simusoft_ionoptics.html

An Einzel Lens

Figure 3. A ‘retarding Einzel lens’ built from three concentric tubular electrodes held at different potentials. The main effect of the Einzel lens shown is that the ion velocity is drastically decreased in the first half of the lens and then drastically increased again in the second half. The decelerating and accelerating forces are illustrated by small black arrows which indicate the directions of the forces on positively charged ions. These forces have small components perpendicular to the optical axis, the z-axis. In the first and the last section of the Einzel lens, these forces are defocusing and drive the ions away from the optical axis, while in the middle region these forces drive the ions toward the optical axis and thus are focusing. The overall effect of these forces is indicated by the hollow arrows. Since these forces toward and away from the optical axis are of comparable magnitude, they are most effective in the middle region where the ions are slow and consequently spend most of their time. For this reason the lens shown is overall focusing. Note here also that the potential of the middle electrode must be close to the potential of the ion source if the lens is to be effective.