Mass Analyzers 1:  
Time-of-flight

CU- Boulder  
CHEM-5181  
Mass Spectrometry & Chromatography

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Business Items

• Next week: Paul will teach on interpretation
• Leapfrogging HW4, due on Tue 23-Sep-2014
  – Function to calculate resolution from quad and TOF spectra
  – Simulation of a linear TOFMS
    • We will build on this one later, important to get it right
    • I will grade all of the HWs for this one
  – Make good use of office hours, don’t leave it till the 22\textsuperscript{nd} or you will do poorly
Types of Mass Analyzers

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

**MALDI Time-of-Flight MS: HW4**

Principle of a linear TOF instrument tuned to analyze positive ions produced by focusing a laser beam on the sample.
Time-of-Flight Mass Spectrometry

Bipolar TOF voltage scheme

Relative Intensity

\[ m/z \propto t^{1/2} \]

Animation courtesy of Deborah Gross Carleton College
ESI o-TOFMS Animation from Agilent:
https://www.youtube.com/watch?v=iF21xzaY07w

For purposes of calibration, instrument parameters (Voltage and Distance) can be bundled into a constant.

Fortunate --- Exact measurement of distance and voltage would be tedious, if not impossible.

Recall that these equations are an ideal system. Groups modify calibration fit in order to accommodate non-idealities.
Resolution

For any m/z in a time-of-flight mass spectrum, the recorded peak will be the sum of signals corresponding to multiple, independent, ion arrival events.

Each ion arrival will be recorded at a unique TOF, as determined by expression on previous slide.

TOF, which is the center of the peak in the mass spectrum, will be an average of all individual ion arrival TOFs.

The width of TOF, Δt, will depend on the distribution of the individual ion arrival TOFs (and other factors ...)

\[ R = \frac{m}{\Delta m} = \frac{TOF'}{2\Delta t} \]

Clicker Q: Why is there a 2 in the denominator on the RHS?

A. Because of the relationship between kinetic and potential energy
B. Because of the calibration equation between m/z and time
C. Because of the drift-free region in the TOF
D. Because of delayed extraction
E. I don’t know

Clicker Q

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 an initial chamber pressure of 9e-6 mbar.

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 1e-5 mbar 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) I don’t know
Clicker Q: Ions A and B have the same m/z, and are at rest when the field is set up. Will the different initial positions of A and B result in different values for the recorded TOF (linear TOF)?

A. Yes
B. No
C. Sometimes yes and sometimes no
D. It depends on their relative initial kinetic energies
D. I don’t know

TOF = total recorded flight time of an ion

\[ TOF = t_o + t_a + t_D + t_d \]

- \( t_o \): Ion formation time after \( T_0 \) of TOF measurement
- \( t_a \): Time in acceleration region, which depends on initial position and initial energy
- \( t_D \): Time in drift region, which depends on initial position and initial energy (velocity)
- \( t_d \): Response time of detector

Improving Resolution

- TOFMS was first commercialized in 1950s
  - Bendix corporation
- Early instruments had low resolution
  - Speed of electronics
  - Energy distribution
- Recent “Renaissance ….”
  - Amazing improvements in electronics
  - Design “tricks” (e.g. reflectrons, DE)

Reflectron consists of a series of electrodes, forming a linear field in direction opposite of initial acceleration.

Ions are slowed by this field, eventually turning around and accelerating back in direction of detector.

Penetration depth depends on $U_s$, which is function of $U_0$ and acceleration field, $E$.

Reflectron voltages are tuned to create a space focus at the plane of the detector.

From: http://www.chemistry.wustl.edu/~msf/damon/reflectrons.html
Delay between ionization and extraction events.

At ionization: \( U = U_0 \) (Initial Energy of Ion)
At exit of extraction: \( U = U_0 + E_{ext}xq \)
At beginning of drift: \( U = U_0 + E_{ext}xq + (V_1 - V_2)q \)

Tune source voltages and/or delay to compensate for \( \Delta U_0 \) and create space focus at detector. Mass dependent.

Comparison of DE vs Reflectron

- In Delayed Extraction, we give ions different \( U \) to achieve same TOF.
- In Reflectron, ions possess different \( U \). We force them to travel different \( D \) to achieve same same TOF.
Precursor Ion Selection w/ Gate

Figure 2.42
TOF spectrometer fitted with a deflection electrode for precursor ion selection. The instrument can be operated in either the linear or the reflectron mode. The selection resolution is about 250, which for example gives a 4 Th window at m/z 1000.

MS/MS by TOF/TOF

Figure 2.45
Schematic representation of a tandem mass spectrometer comprising two RTOF analysers and, in between, a collision cell.
An Inherent Dilemma

TOFMS is an ideal detector for pulsed ionization methods. If ionization event is synchronized with time zero, high duty cycle is achieved.

Because of pulsing, ions are wasted when TOFMS is applied to a continuous source & increased efficiency comes at the expense of mass range and mass resolution. Still, figures of merit and cost make the technique desirable.

Laser Desorption: Static, solid sample probed with a pulsed laser.

ESI: Sample is continuously flowing towards the mass analyzer.

Performance Trade-offs: On Axis

Gating Function

Sampling Time

Drift Time

$Duty\ Cycle \approx \frac{Sampling\ Time}{Sampling\ Time + Drift\ Time}$

$\Delta t$ proportional to sampling time

Mass Range proportional to drift time
Orthogonal Extraction

Ions are extraction in a direction orthogonal to source trajectory.
Extraction event is still rapid ($\Delta t$), but extraction volume is determined by length of gate region.

oTOFMS

- Able to reduce average initial energy in ToF direction to 0 (resolution and accuracy).
- Independent control of beam energy and drift energy, allows maximum duty cycle.
- Want tightly collimated beam in extraction region.

Euler Method

- Example of a numerical method: solve problems approximately when analytical solution doesn’t exist
  - To calculate trajectories of ions in mass specs, we need to solve the equations of motion:

\[
F = ma = qE = q \frac{\Delta V}{\Delta x}
\]

\[
a = \frac{dv}{dt}
\]

\[
a = \frac{\Delta V}{\Delta t} = \frac{V_{t+1} - V_t}{\Delta t}
\]

Euler Method II

\[
V_{t+1} = V_t + a\Delta t
\]

- Exercise in class: solve for position
- Write strategy to do TOF problem with Euler method