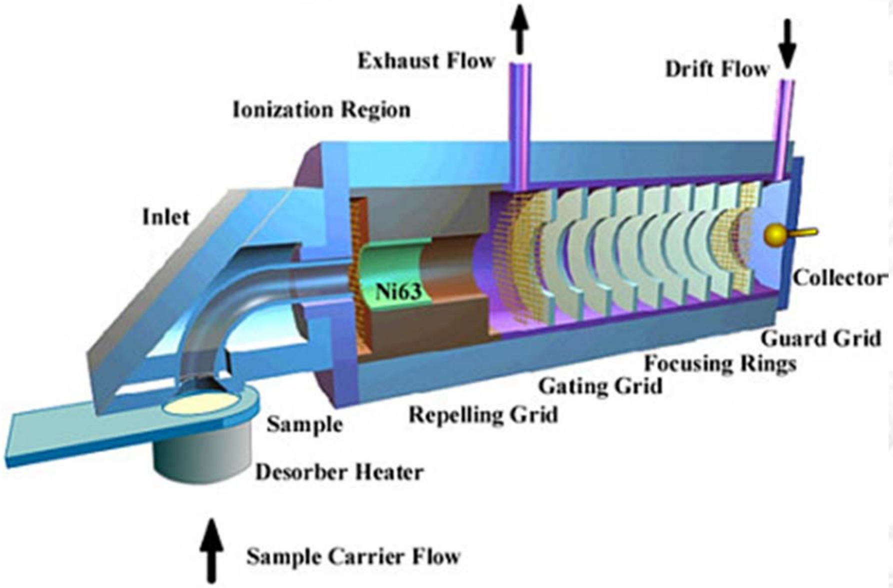
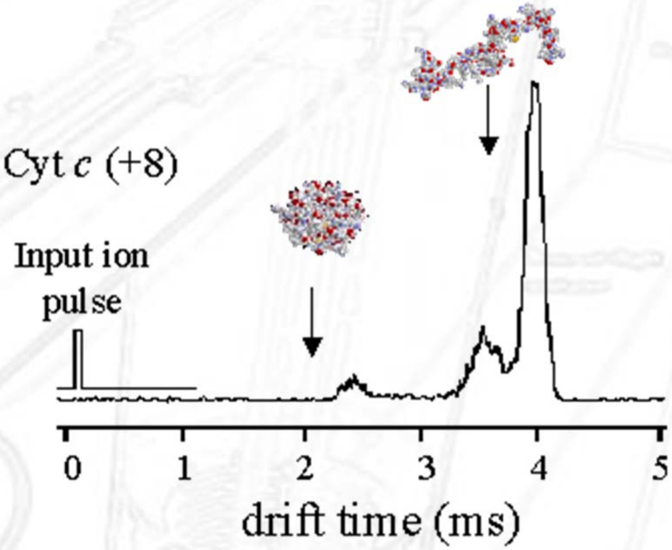
Week 8: Detectors, Small Molecule Applications

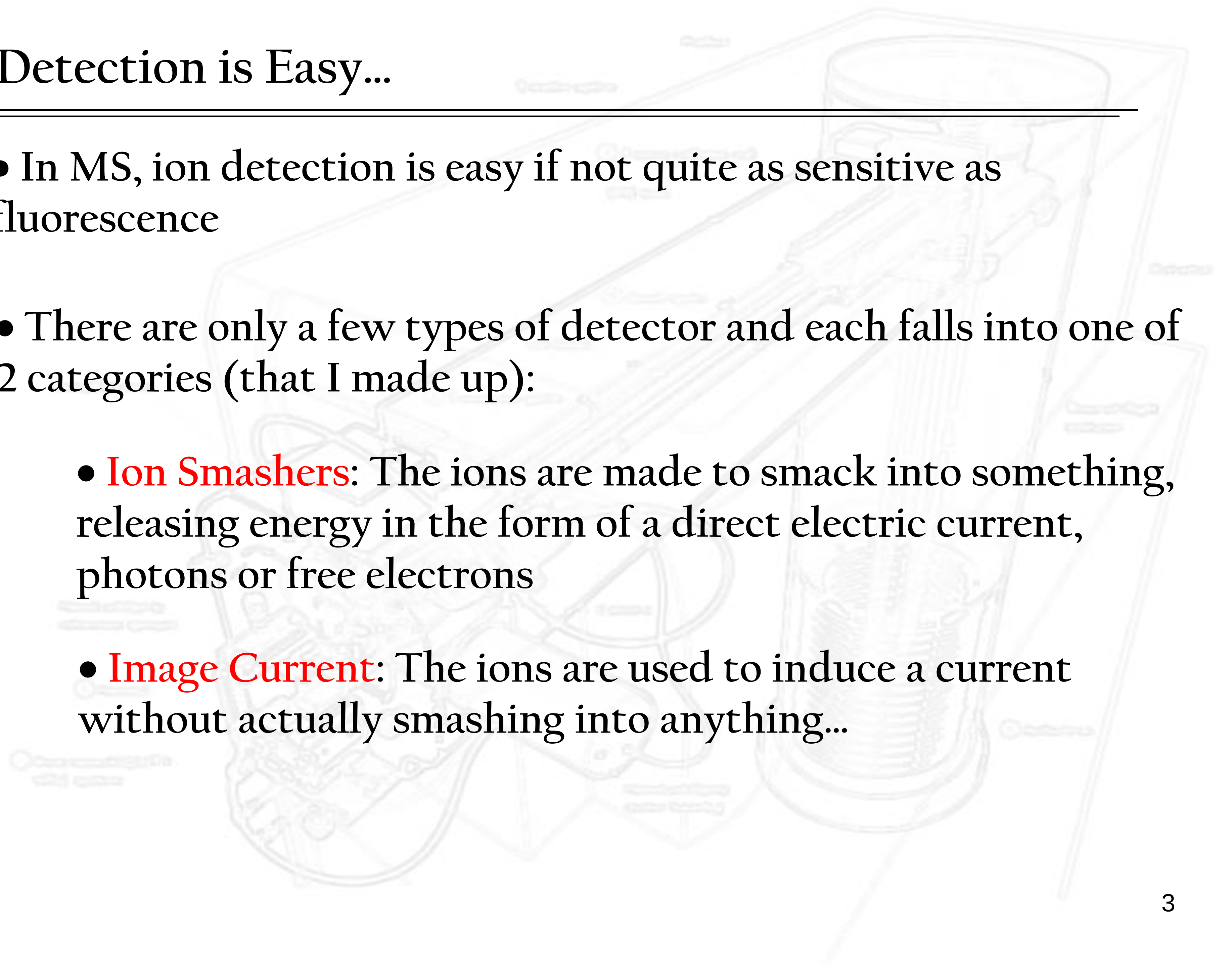
Last Time…

- Ion Mobility





Detection is Easy…



- In MS, ion detection is easy if not quite as sensitive as fluorescence

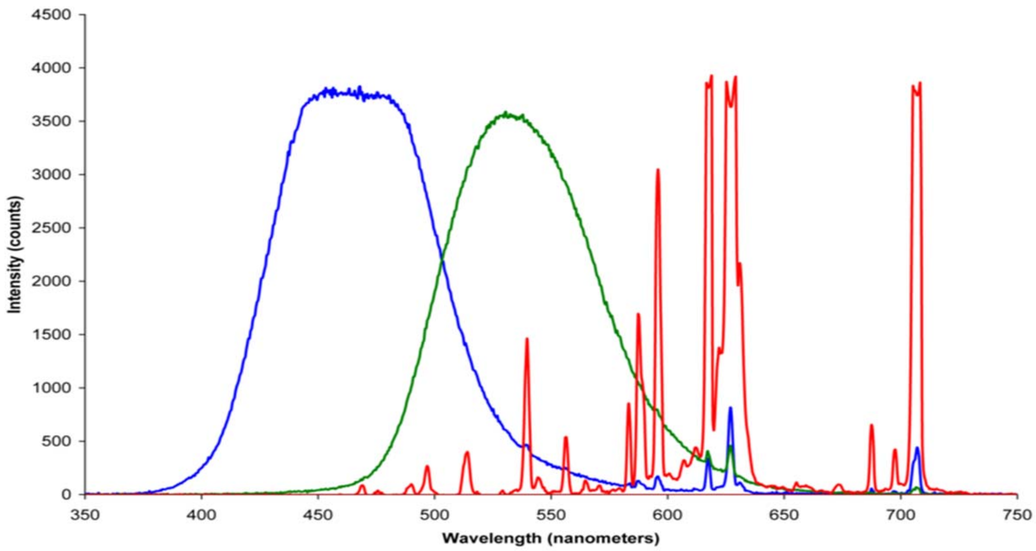
- There are only a few types of detector and each falls into one of 2 categories (that I made up):

    - Ion Smashers: The ions are made to smack into something, releasing energy in the form of a direct electric current, photons or free electrons

    - Image Current: The ions are used to induce a current without actually smashing into anything…

The First Detector: Phosphorescent Goop

- As you may recall, the first detectors for MS instruments (or at least cathode ray tubes) used phosphorescent goop on the inside of the vacuum tube to measure deflection.

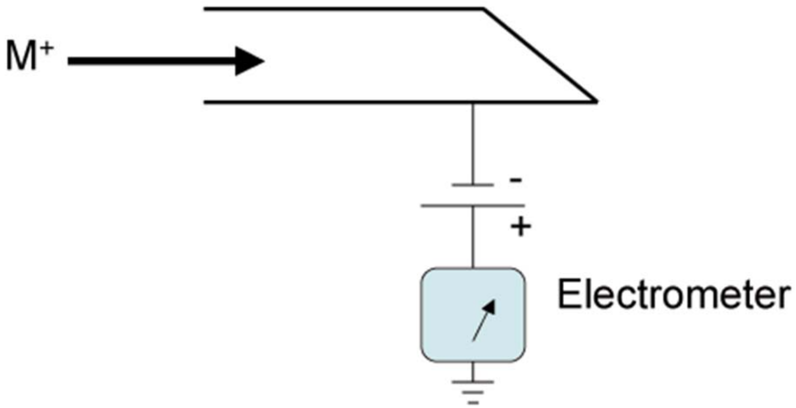


- Emission spectra of the phosphorescent goop on the inside of your grandpa's TV.

- Very shortly thereafter (*i.e.* the parabola era), the method of detection was the photographic plate, which were made with silver iodide on a copper backing.

The Second Detector: Faraday Cups

- A Faraday cup is simply a cup-shaped electrode charged oppositely from the particle you want to detect



- Neutralization of positively charged ions (for example) induces a current in the cup in order to maintain the potential.

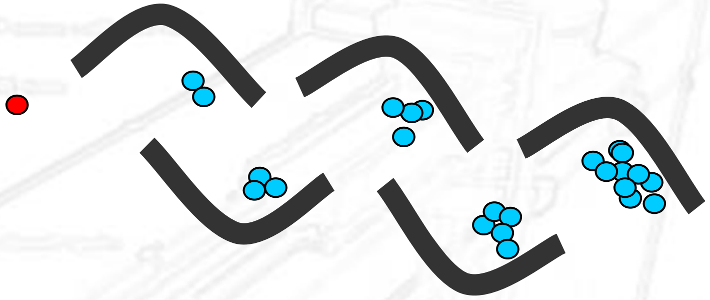
- Errors can occur due to the liberation of secondary electrons on impact. To avoid this, use low ‘resting potential’.

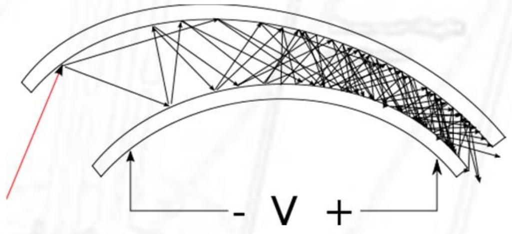
First Real Detector: The Secondary Electron Multiplier

- The Secondary Electron Multiplier (SEM) is used today, usually in triple quad instruments.
- They consist of a series of dynodes, which are increasingly positively charged.
- The ion collides with the first dynode and produces a small number of secondary electrons (2 – 3)
- Those electrons have a higher energy collision with the next dynode releasing more electrons, which collide with the next dynode etc.
- The result is that an ‘avalanche’ of electrons is generated for every ion impact, which produces an easily measurable current.

Chanel Electron Multipliers...

- If you use a seminconductor material, you can create a continuous voltage gradient down a curved tube. This is called a Chanel Electron Multiplier (CEM)

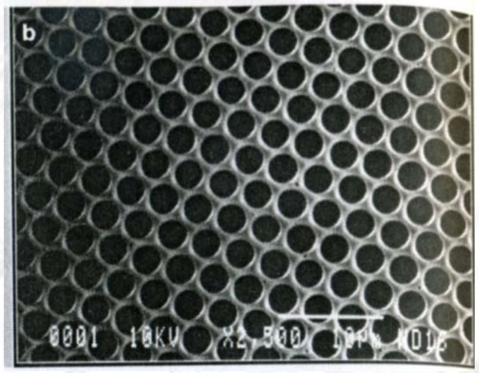




- So the main advantage of a CEM is that they are very sensitive 👍
- The main disadvantage is that the dynodes discharge substantially with every avalanche, so CEMs have a ‘refractory period’ of a few μs after each detection event in which they cannot detect an ion. This explains why they are useless for TOF measurements, where arrival times are tens of ns apart.

Multi Chanel Plates (MCPs)...

- For TOF-MS we need to regenerate our dynodes faster than is physically possible. The solution is to use an array of tiny CEMs, called an MCP:

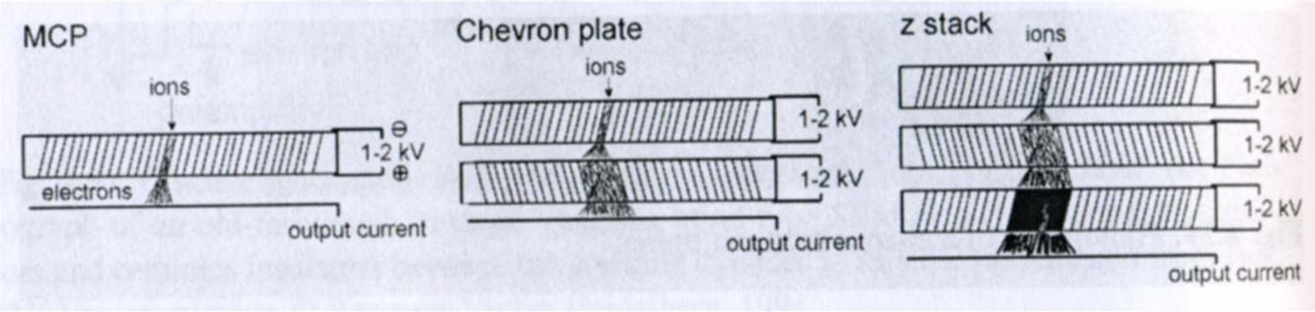


- The plate is formed from a semiconductor with a high negative potential applied to one face. Because it is a semiconductor, this potential drops off with distance from the charged face, just like in a CEM

Sensitivity and MCPs...

- Each chanel within the MCP is a pretty poor CEM

- One way to improve sensitivity is to stack the plates, so that electron avalanches from one plate activate a bunch of avalanches on the next etc.

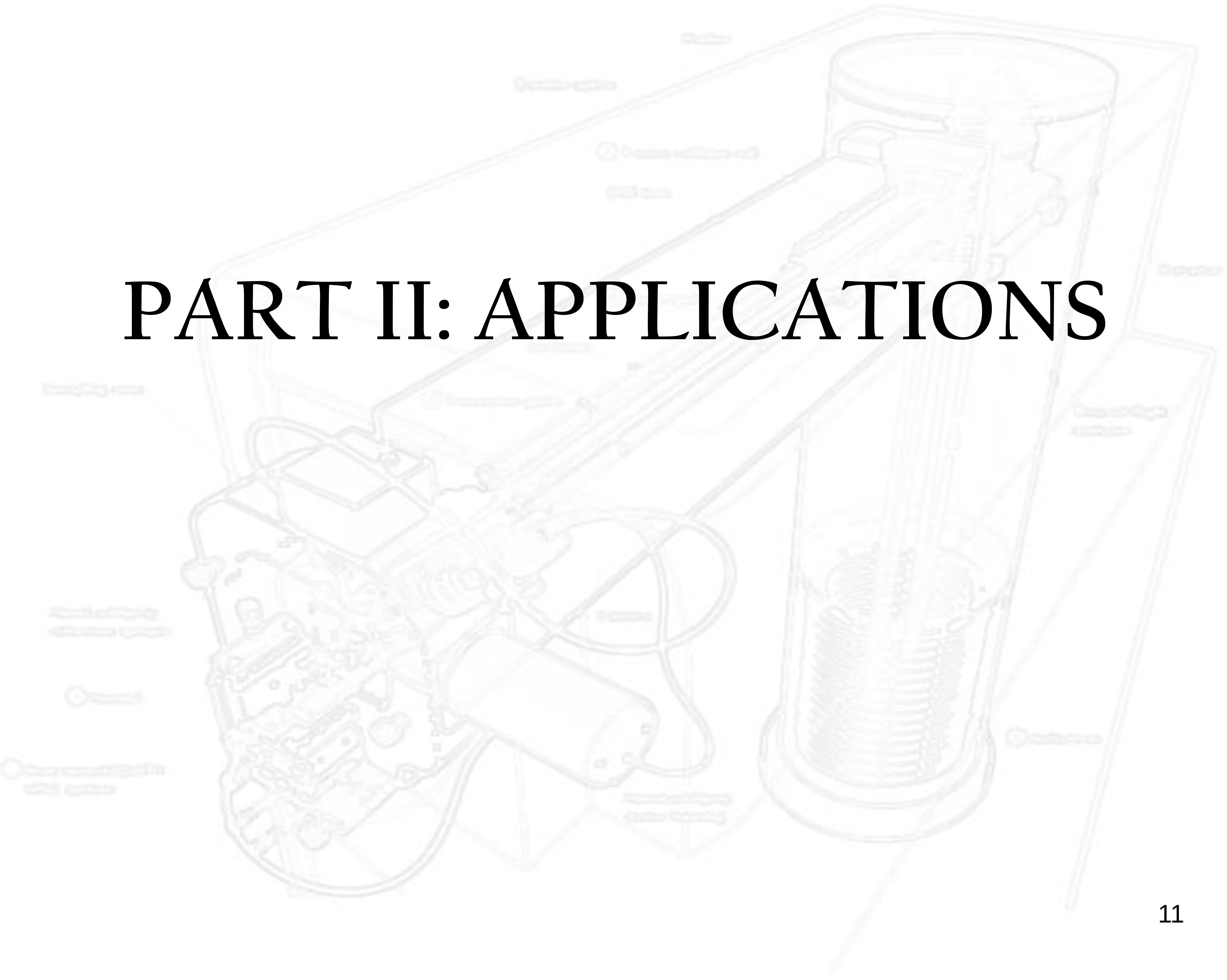


- Interesting to note that MCPs are equally capable of providing spatially resolved detection of ions...

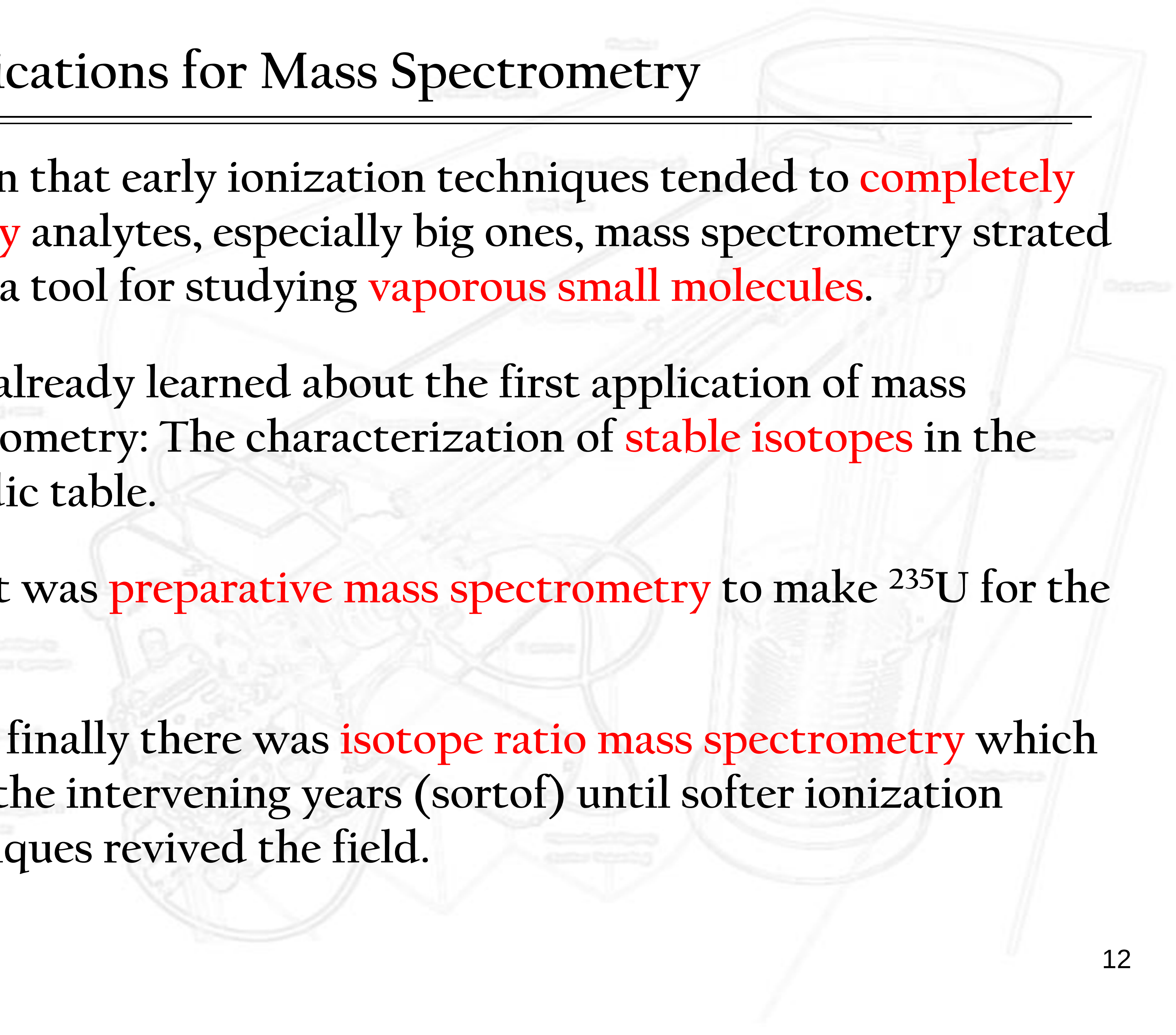
Comparing Detectors

Name	Gain (Sensitivity)	Duty Cycle	Linear Dynamic Range	m/z artifacts
Faraday Cup	None (use amplifier)	Bad; slow response time	Linear over 100% of measurable range	NO!
CEM	$10^6 + 10^6$ (amplifier)	Bad; μs refractory period	Good; linear over 5 orders of magnitude or so	Yes! More sensitive to higher energy (low m/z)
MCP	$10^3 + 10^6$ (amplifier)	Very good; less than 1 ns refractory period overall	Not great; linear over 3 – 4 orders of magnitude	Yes!! Much more sensitive to low m/z.

PART II: APPLICATIONS



Applications for Mass Spectrometry



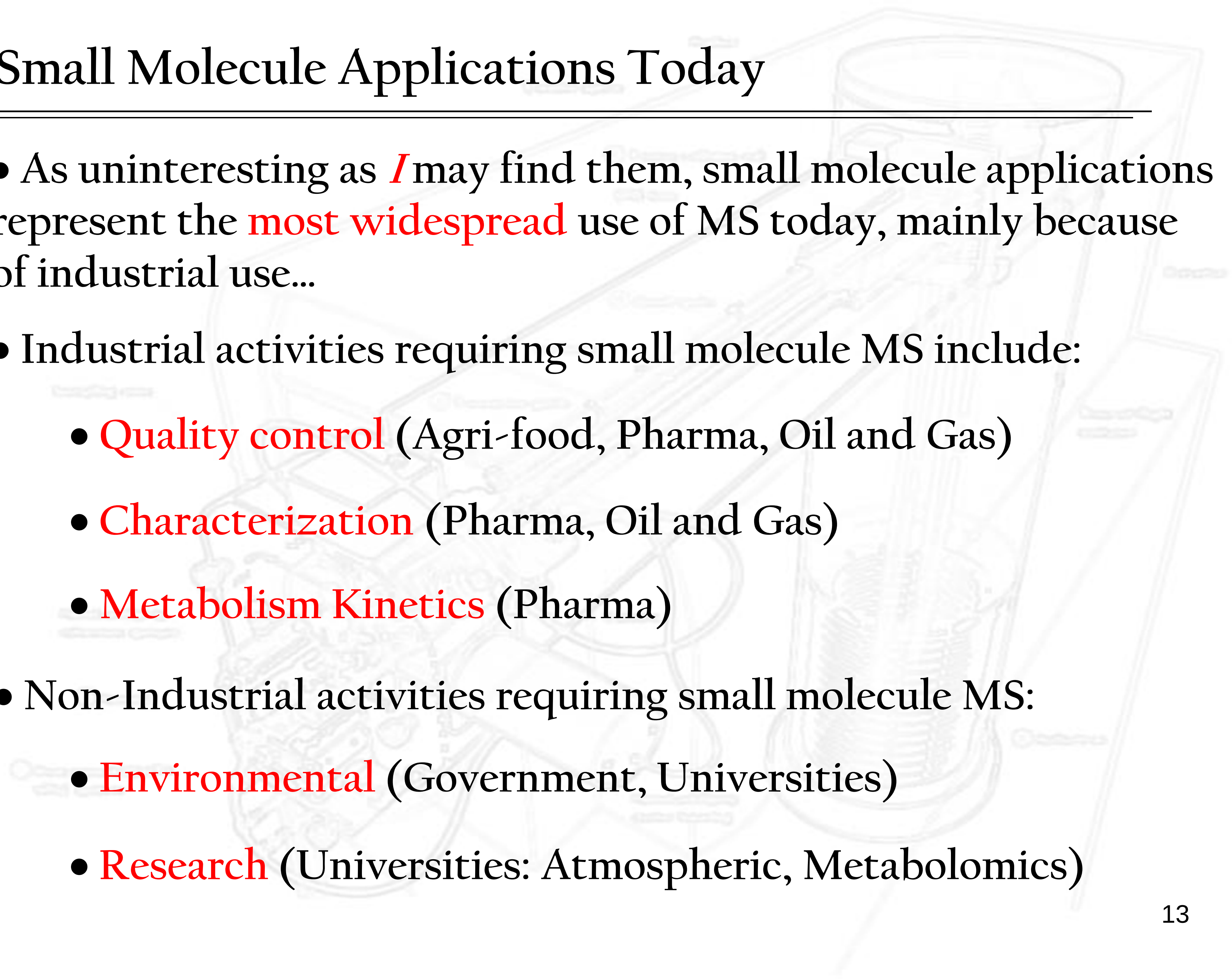
- Given that early ionization techniques tended to completely destroy analytes, especially big ones, mass spectrometry strated out as a tool for studying vaporous small molecules.

- We already learned about the first application of mass spectrometry: The characterization of stable isotopes in the periodic table.

- Next was preparative mass spectrometry to make ^{235}U for the bomb

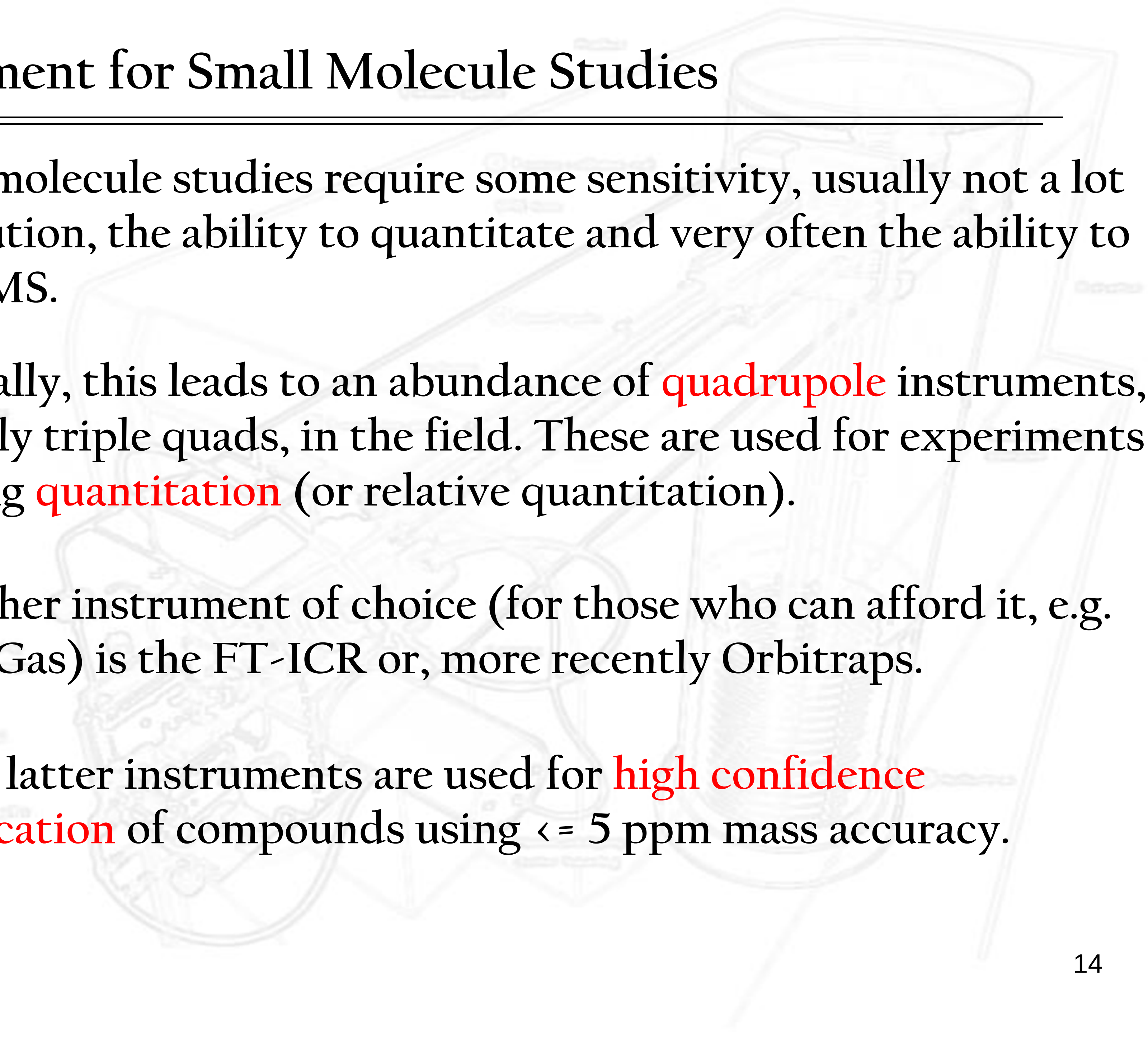
- And finally there was isotope ratio mass spectrometry which filled the intervening years (sortof) until softer ionization techniques revived the field.

Small Molecule Applications Today



- As uninteresting as *I* may find them, small molecule applications represent the most widespread use of MS today, mainly because of industrial use…
- Industrial activities requiring small molecule MS include:
  - Quality control (Agri-food, Pharma, Oil and Gas)
  - Characterization (Pharma, Oil and Gas)
  - Metabolism Kinetics (Pharma)
- Non-Industrial activities requiring small molecule MS:
  - Environmental (Government, Universities)
  - Research (Universities: Atmospheric, Metabolomics)

Equipment for Small Molecule Studies



- Small molecule studies require some sensitivity, usually not a lot of resolution, the ability to quantitate and very often the ability to do MS/MS.

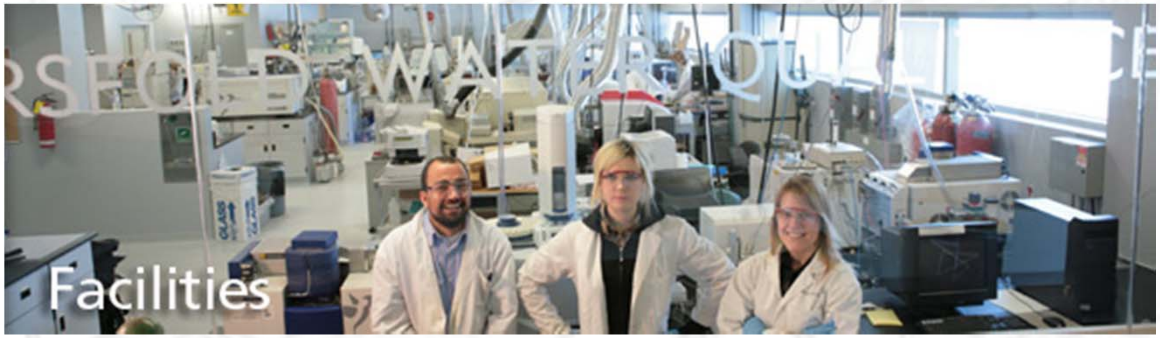
- Naturally, this leads to an abundance of quadrupole instruments, especially triple quads, in the field. These are used for experiments involving quantitation (or relative quantitation).

- The other instrument of choice (for those who can afford it, e.g. Oil and Gas) is the FT-ICR or, more recently Orbitraps.

- These latter instruments are used for high confidence identification of compounds using <= 5 ppm mass accuracy.

Case Study 1: The Water Quality Center at Trent

- The Trent Water Quality center is an example of a small molecule MS-centered research center. They focus on Environmental Analysis:

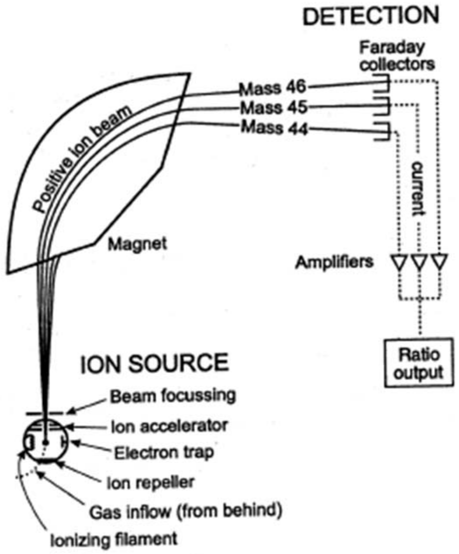


- Research Activities:
    - Isotope Analysis MS
    - Elemental Composition Analysis
    - Organic and Organometallic Contaminants

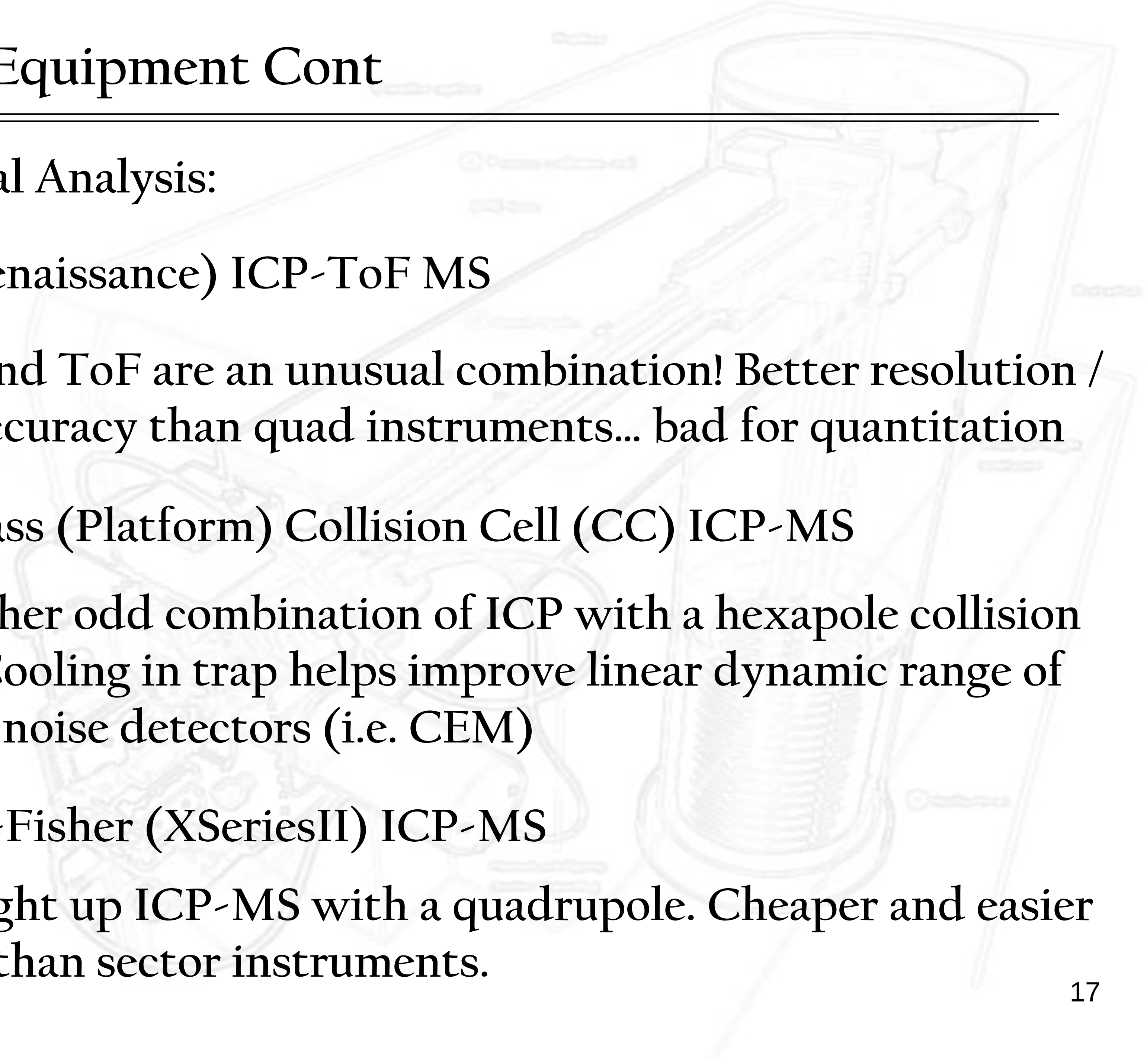
TWQC Equipment

- Isotope Analysis:

- Thermo-Finnigan (Neptune) Multicollector ICP-MS
  - This is an ICP-MS designed specifically for elemental analysis. The 'multicollector' feature refers to the use of two faraday cups...
  - Of course this means we have to split the beam by m/z... which we can do in a magnetic sector!
  - This Neptune is actually a double focusing sector instrument...
  - They also have a Micromass (Isoprime) CF-IRMS which does GC-MS... CF is for 'continuous flow'

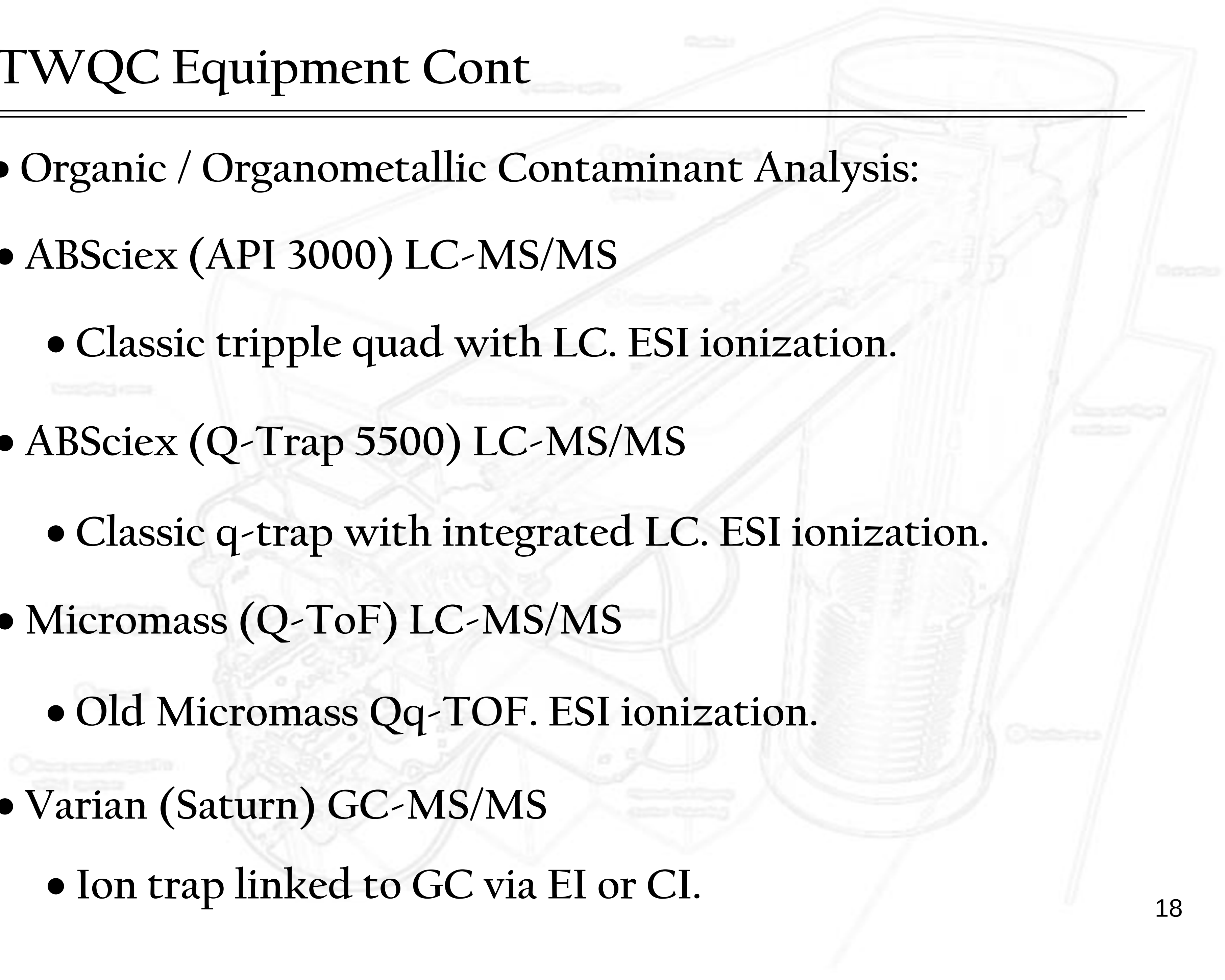


TWQC Equipment Cont



- Elemental Analysis:
- Leco (Renaissance) ICP-ToF MS
  - ICP and ToF are an unusual combination! Better resolution / mass accuracy than quad instruments… bad for quantitation
- Micromass (Platform) Collision Cell (CC) ICP-MS
  - Another odd combination of ICP with a hexapole collision cell… Cooling in trap helps improve linear dynamic range of higher noise detectors (i.e. CEM)
- Thermo-Fisher (XSeriesII) ICP-MS
  - Straight up ICP-MS with a quadrupole. Cheaper and easier to use than sector instruments.

TWQC Equipment Cont



- Organic / Organometallic Contaminant Analysis:
- ABSciex (API 3000) LC-MS/MS
  - Classic tripple quad with LC. ESI ionization.
- ABSciex (Q-Trap 5500) LC-MS/MS
  - Classic q-trap with integrated LC. ESI ionization.
- Micromass (Q-ToF) LC-MS/MS
  - Old Micromass Qq-TOF. ESI ionization.
- Varian (Saturn) GC-MS/MS
  - Ion trap linked to GC via EI or CI.

Isotope Ratios: Example Paper

- Title: ‘Determination of compound-specific Hg isotope ratios from transient signals using gas chromatography coupled to multicollector inductively coupled plasma mass spectrometry (MC-ICP/MS)’

- The Problem: No one had yet determined an easy way to measure heavy metal isotope ratios from ‘transient peaks’ associated with coupled separation techniques such as GC

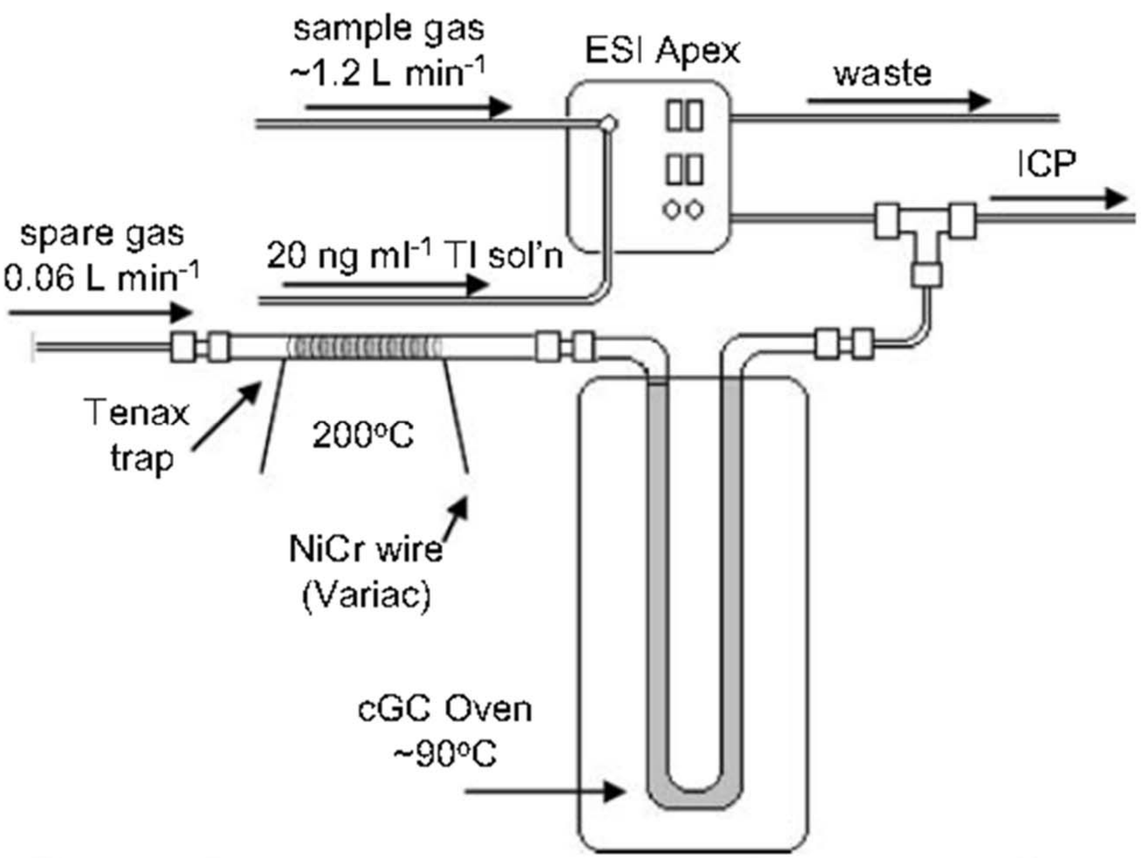
- Moreover, when people *did* do this, they found that the measured isotope ratios at the ‘start’ of the transient peak were different than the isotope ratios at the ‘end’ of the transient peak

The Aparatus...

- The experiments were conducted on the 'neptune' multicollector instrument

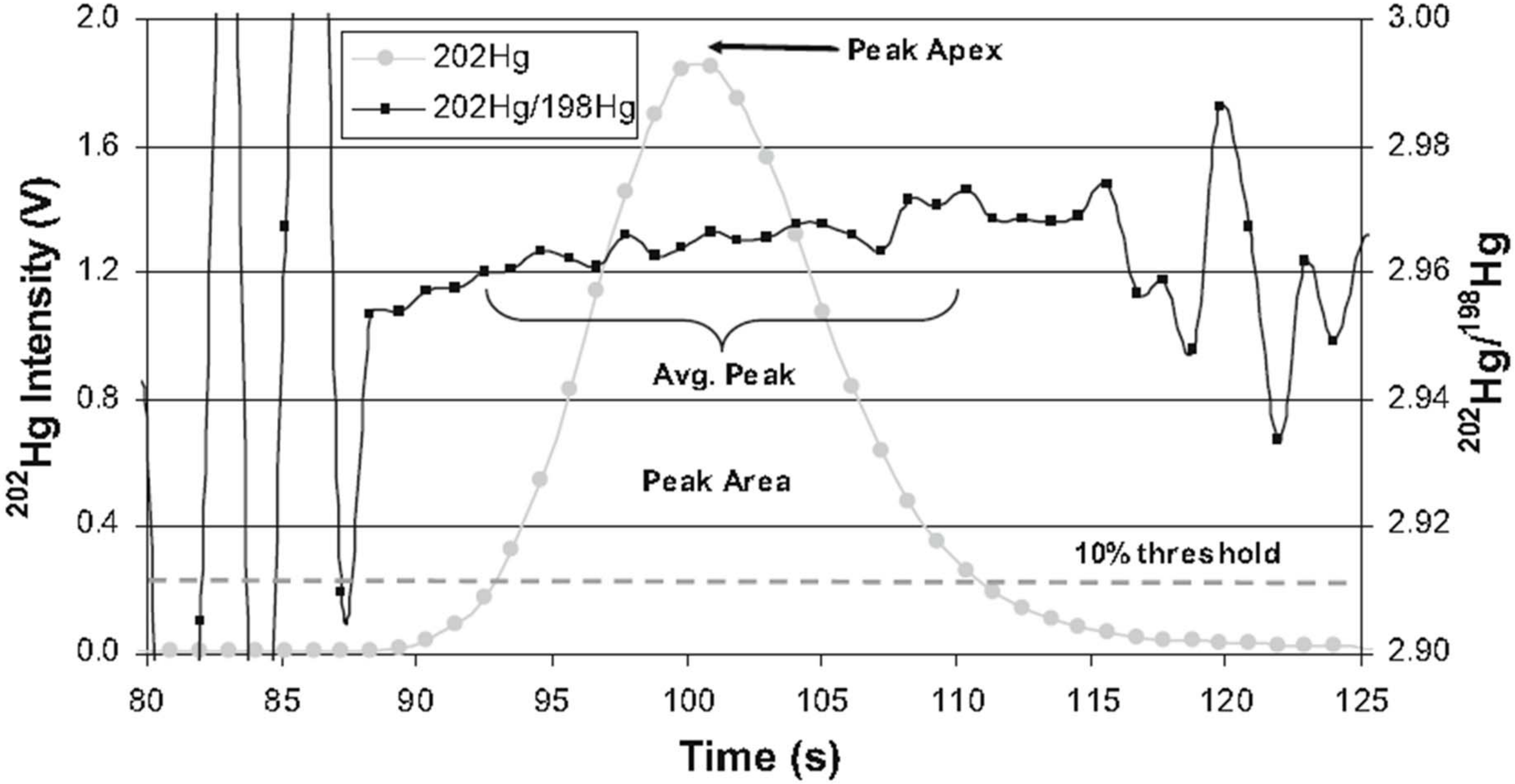
- Lets take a look at the apparatus:

- Ti not put through a GC was used to correct for mass bias in GC... the 'standard' ratio was ^{205}Tl / ^{203}Tl.



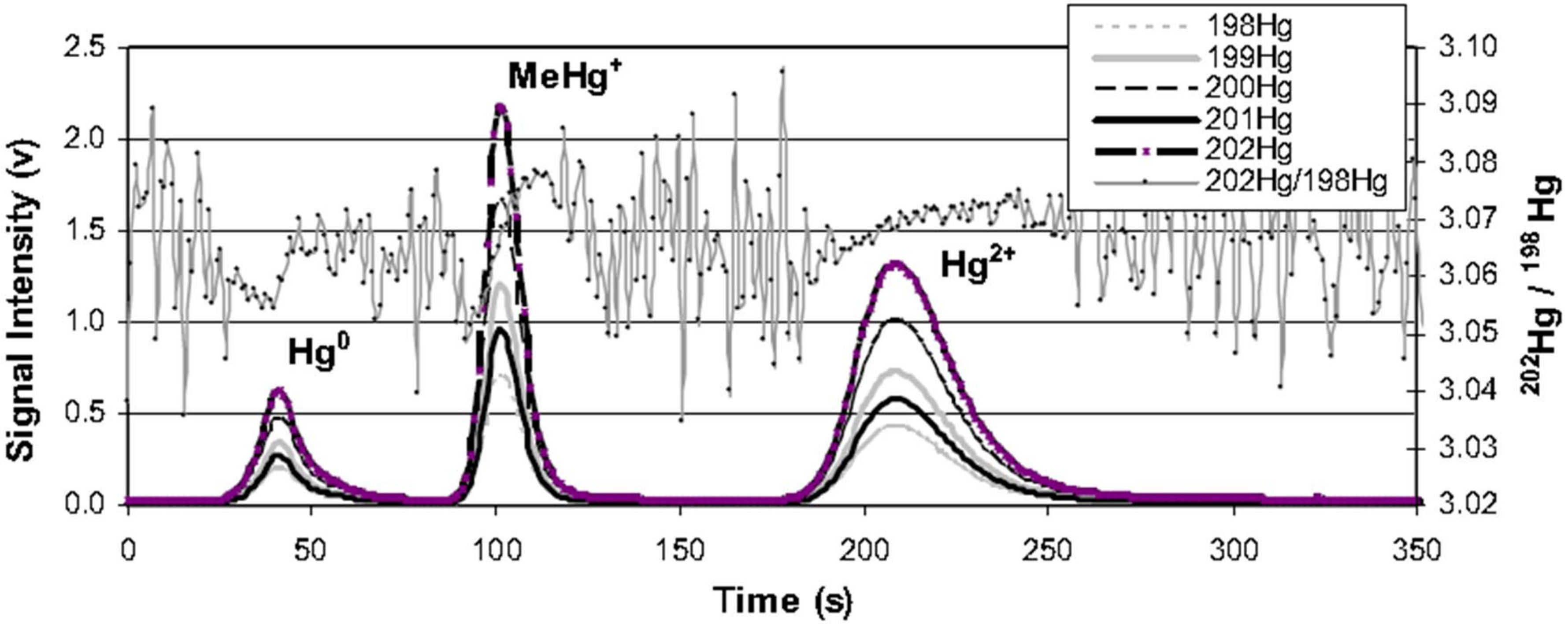
The Problem Illustrated…

- In the second Figure, they Illustrate the problem:

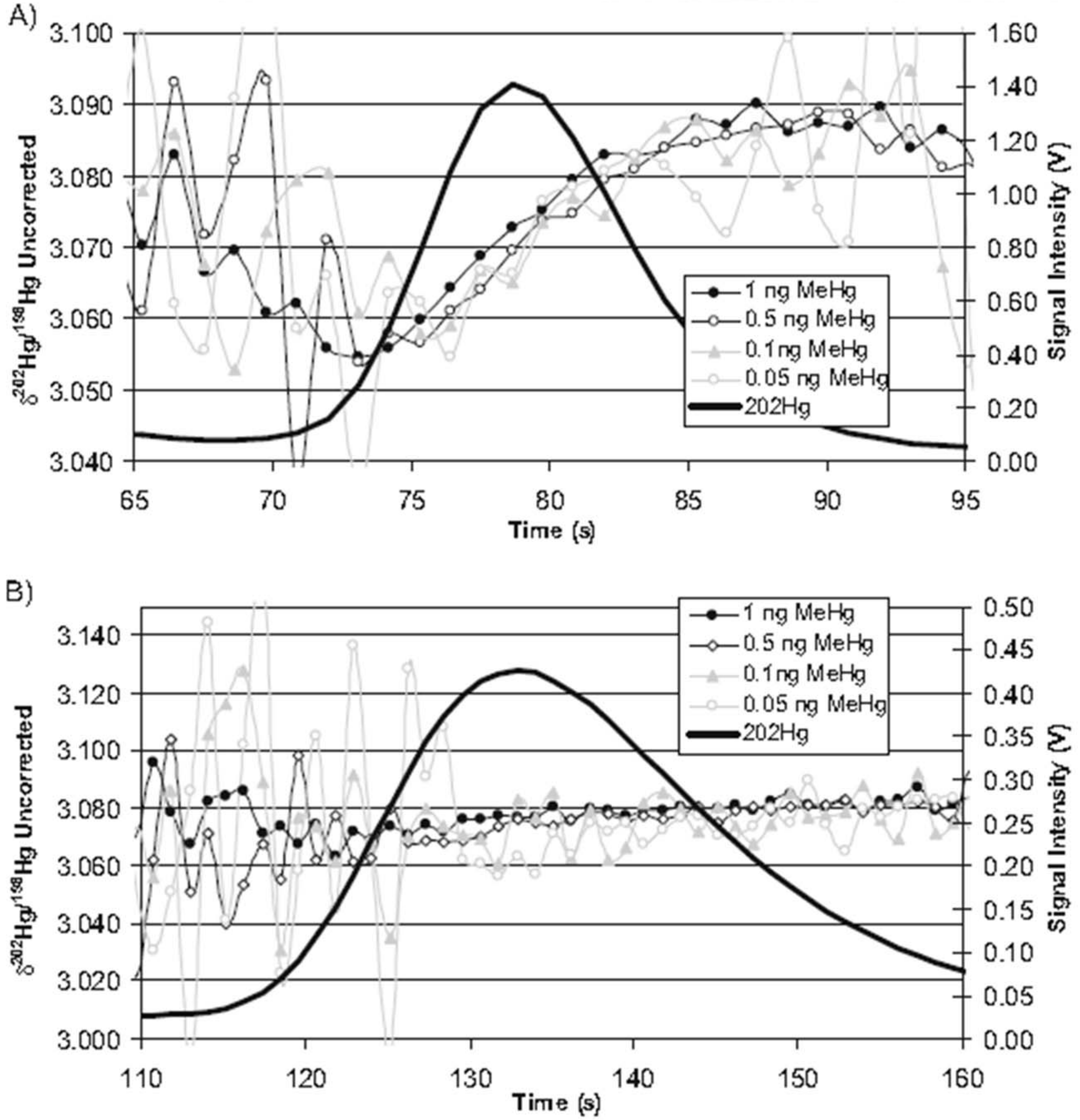


- Notice the drift in the isotope ratio (2.960 – 2.975) across the GC peak

- And Again, this time for all forms of Hg:



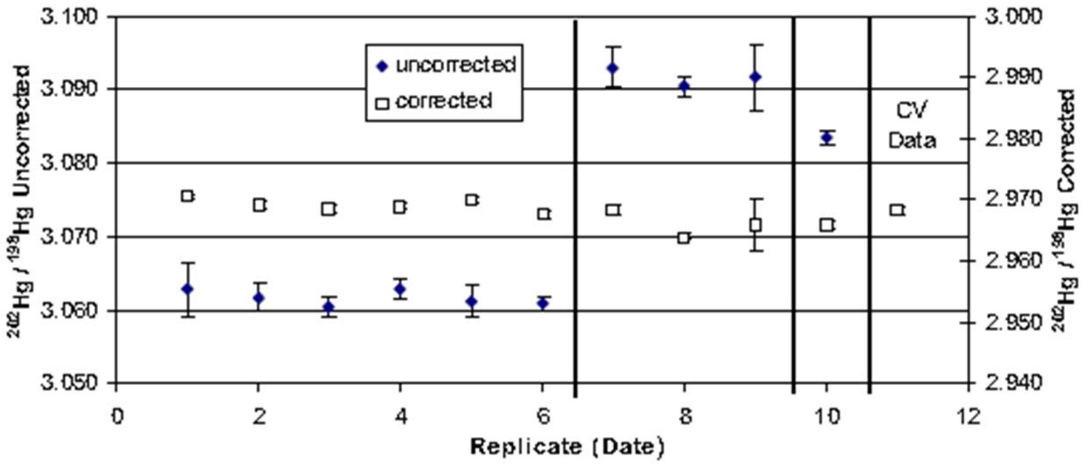
- **Problem is Worse for Methyl Mercury:**



Conclusions…

- With Tl-based mass correction, the average 202/198 Hg ratio comes out 2.96388 vs. 2.96410 or an error of 0.0006.

NRC THg



- Ratio is always lower in MeHg, suggesting enrichment of the light isotope in methylation

NRC MeHg