Two-dimensional mass spectrometry (2D MS/MS) on benchtop and portable ion trap mass spectrometers

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NASA Goddard Space Flight Center

PURDUE UNIVERSITY

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NASA

Why is portable MS important? **Security/Defense/Forensics**

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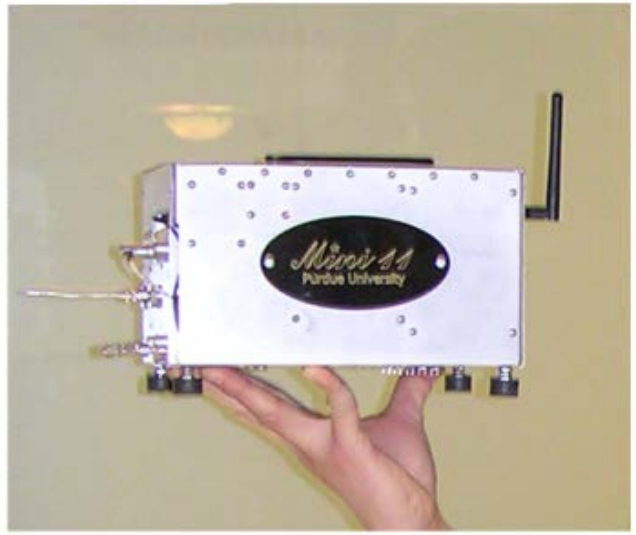
WORLD | HOSTAGE DRAMA IN MOSCOW: THE TOXIC AGENT

HOSTAGE DRAMA IN MOSCOW: THE TOXIC AGENT; U.S. Suspects Opiate in Gas In Russia Raid

By JUDITH MILLER and WILLIAM J. BROAD OCT. 29, 2002

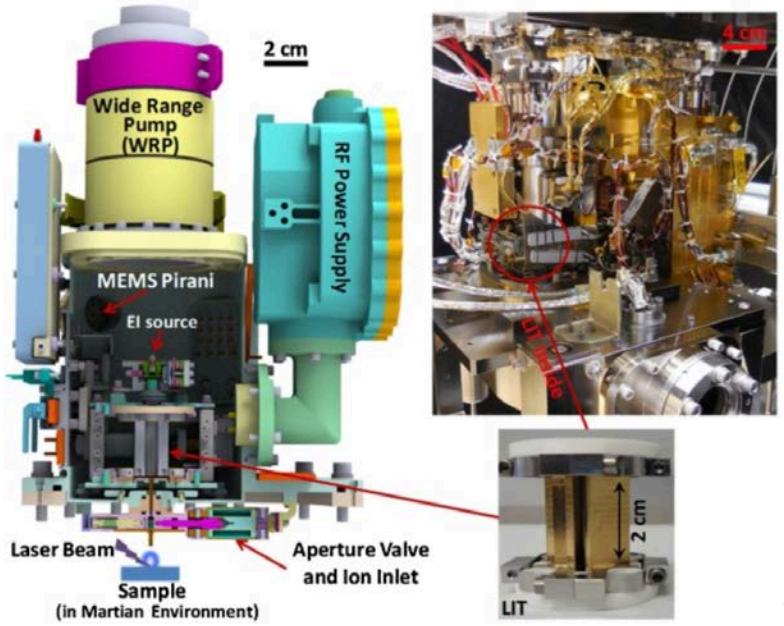
Aerosolized carfentanil

> 100 dead



Mini 11
Purdue University

Why is portable MS important? **Origin-of-life**



MOMA Linear Ion Trap (2020 launch) *IJMS* Vol 22, pp 177-187

nature
International journal of science

Letter | Published: 27 June 2018

Macromolecular organic compounds from the depths of Enceladus

Frank Postberg, Nozair Khawaja, Bernd Abel, Gael Choblet, Christopher R. Glein, Murthy S. Gudipati, Bryana L. Henderson, Hsiang-Wen Hsu, Sascha Kempf, Fabian Klenner, Georg Moragas-Klostermeyer, Brian Magee, Lenz Nölle, Mark Perry, René Reviol, Jürgen Schmidt, Ralf Srama, Ferdinand Stolz, Gabriel Tobie, Mario Trieloff & J. Hunter Waite

New ion trap method sets its sights on Mars

BY REBECCA BRODIE

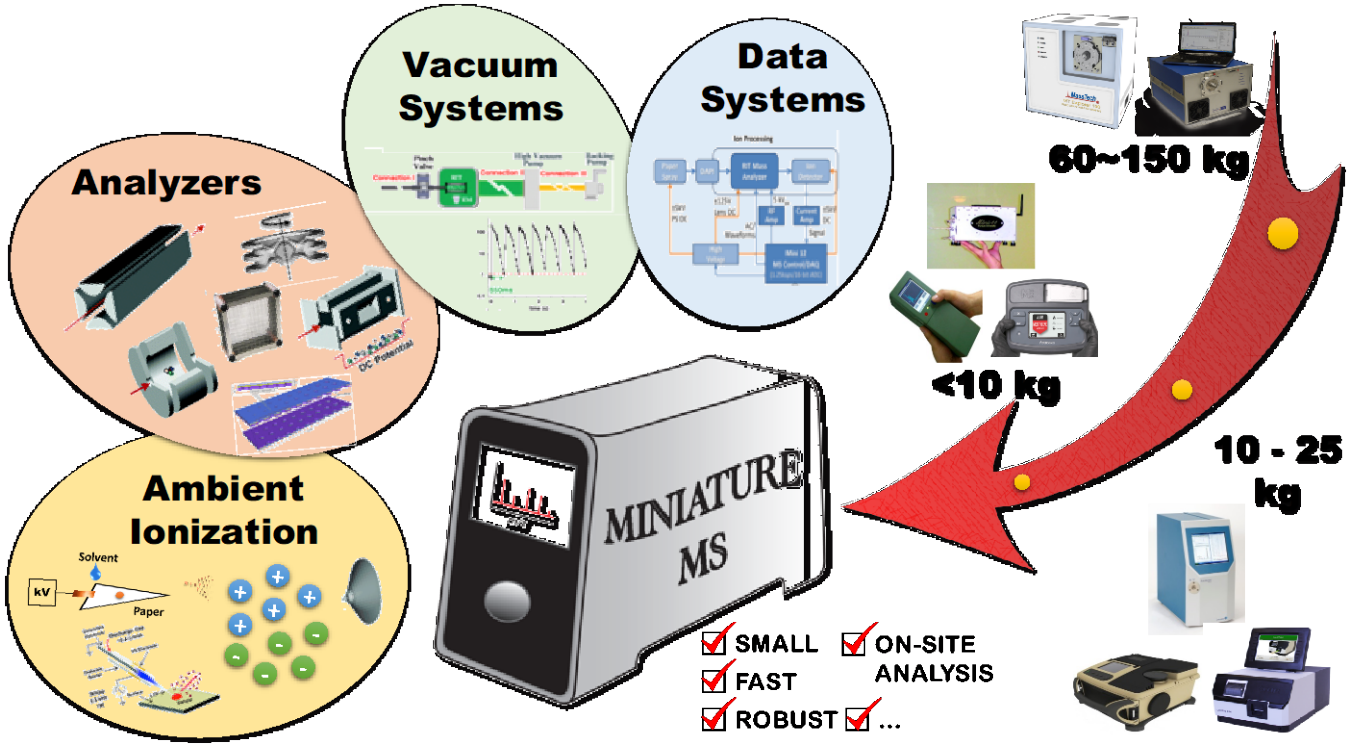
Technique that extends capabilities of existing instruments without physically modifying them could benefit origin-of-life studies on Mars

From Chemistry World

NASA PICASSO Motivation

The Planetary Instrument Concepts for the Advancement of Solar System Observations (PICASSO) Program supports the development of ***spacecraft-based instrument systems that show promise for use in future planetary missions***

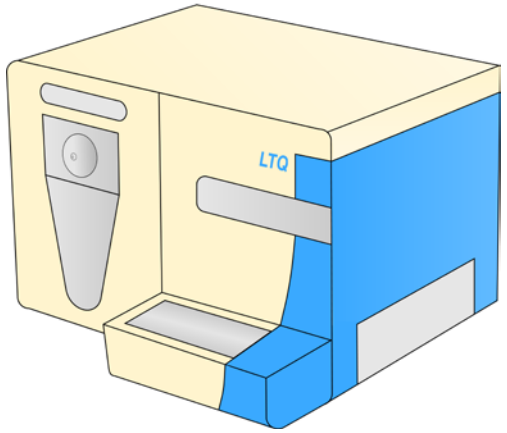
- lightweight
- robust
- lenient vacuum
- **small**
- **low power consumption**
- **simple**
- **MS/MS capabilities for origin-of-life studies**
- *Must think about sample, power, and weight constraints!*
- *Ion trap is obvious candidate*

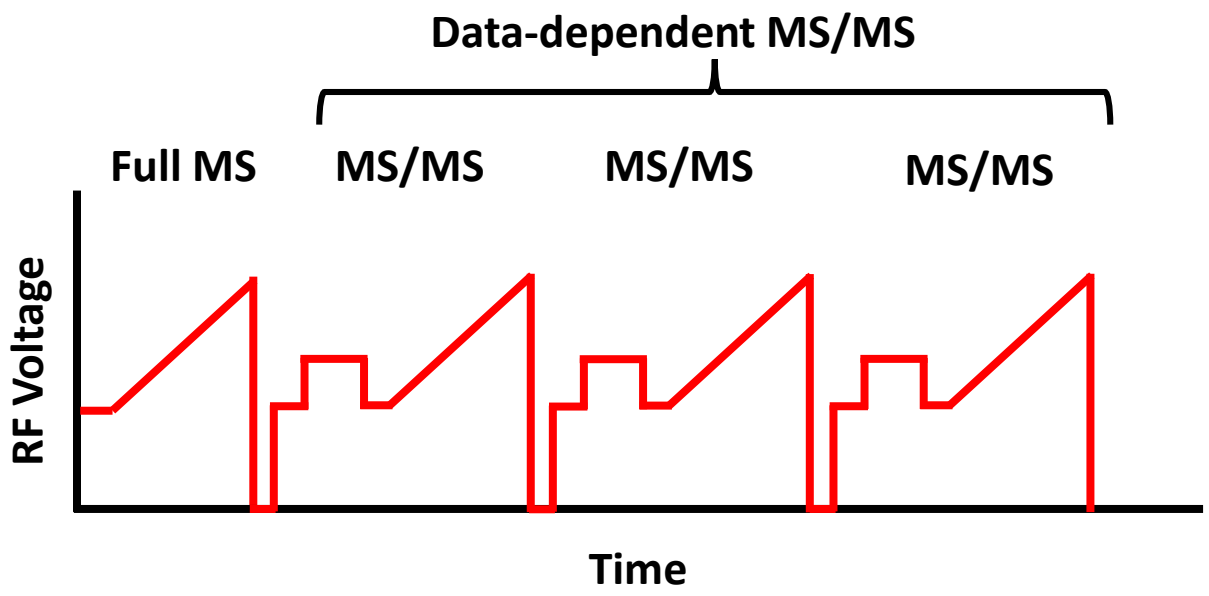


Snyder, D. T.; Pulliam, C. J.; Cooks, R. G. *Anal. Chem.* **2016**, *88*, 2-29. Invited review.

Benchtop vs. portable MS & MS/MS

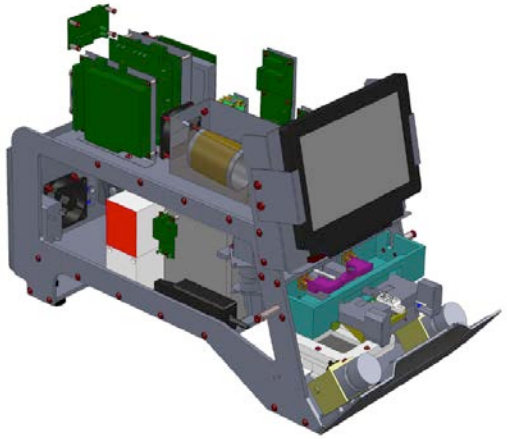
Benchtop LTQ

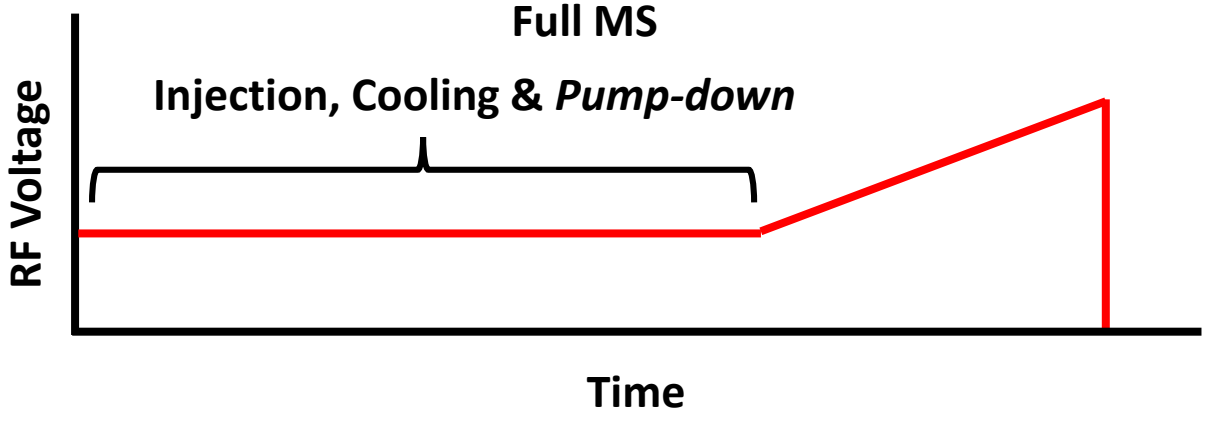




1 MS & 3 MS/MS per second

Mini 12





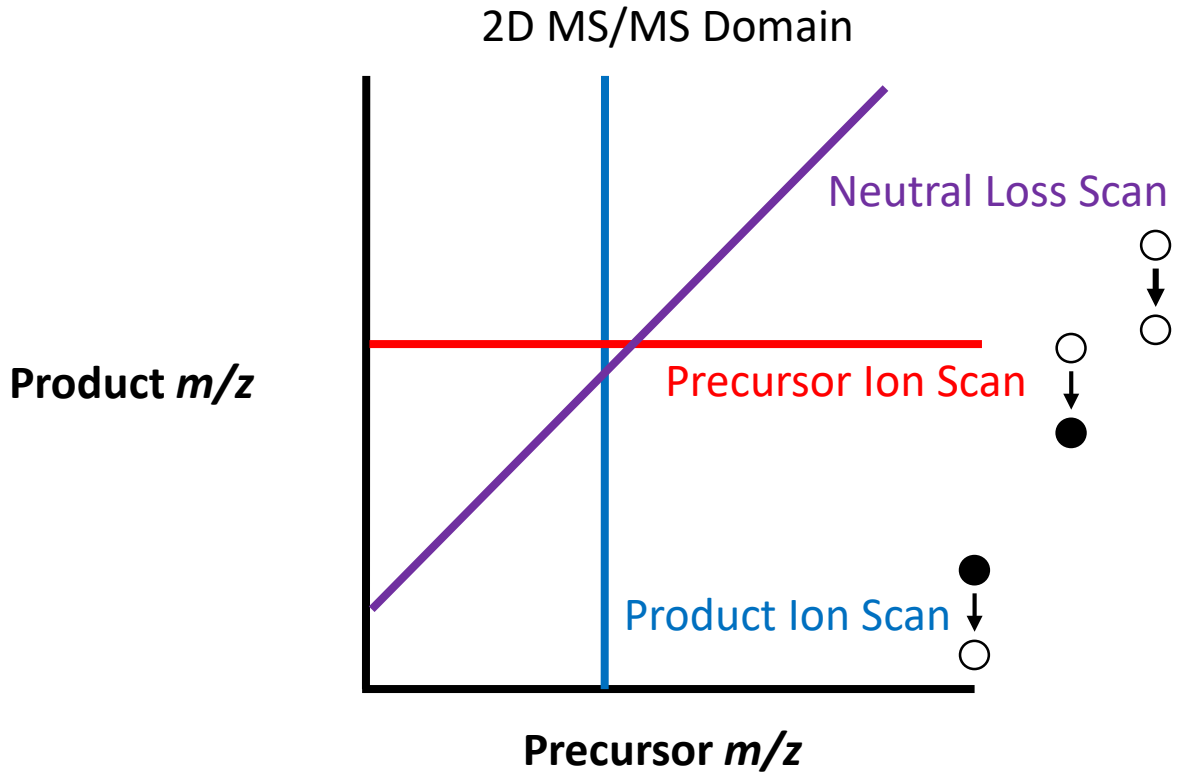
1 MS or MS/MS per second

Data-dependent MS/MS on miniature systems can be slow!

Portable ion traps must be more efficient with time, power, and MS/MS acquisition.

Solution: obtain the entire 2D MS/MS domain with one scan

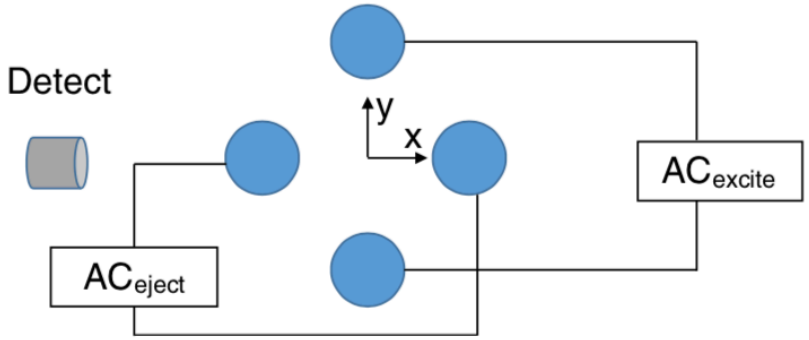
- 2D FT-ICR MS correlates precursor and product ions without isolation
- Is 2D MS/MS - using one scan - possible in a quadrupole ion trap?
- Must traverse every scan line simultaneously to obtain
  - 1. Precursor m/z
  - 2. Product m/z
  - 3. Precursor->Product correlation



M.A. van Agthoven et al. / International Journal of Mass Spectrometry 370 (2014) 114–124

What does a 2D MS/MS scan table look like?

Orthogonal double resonance

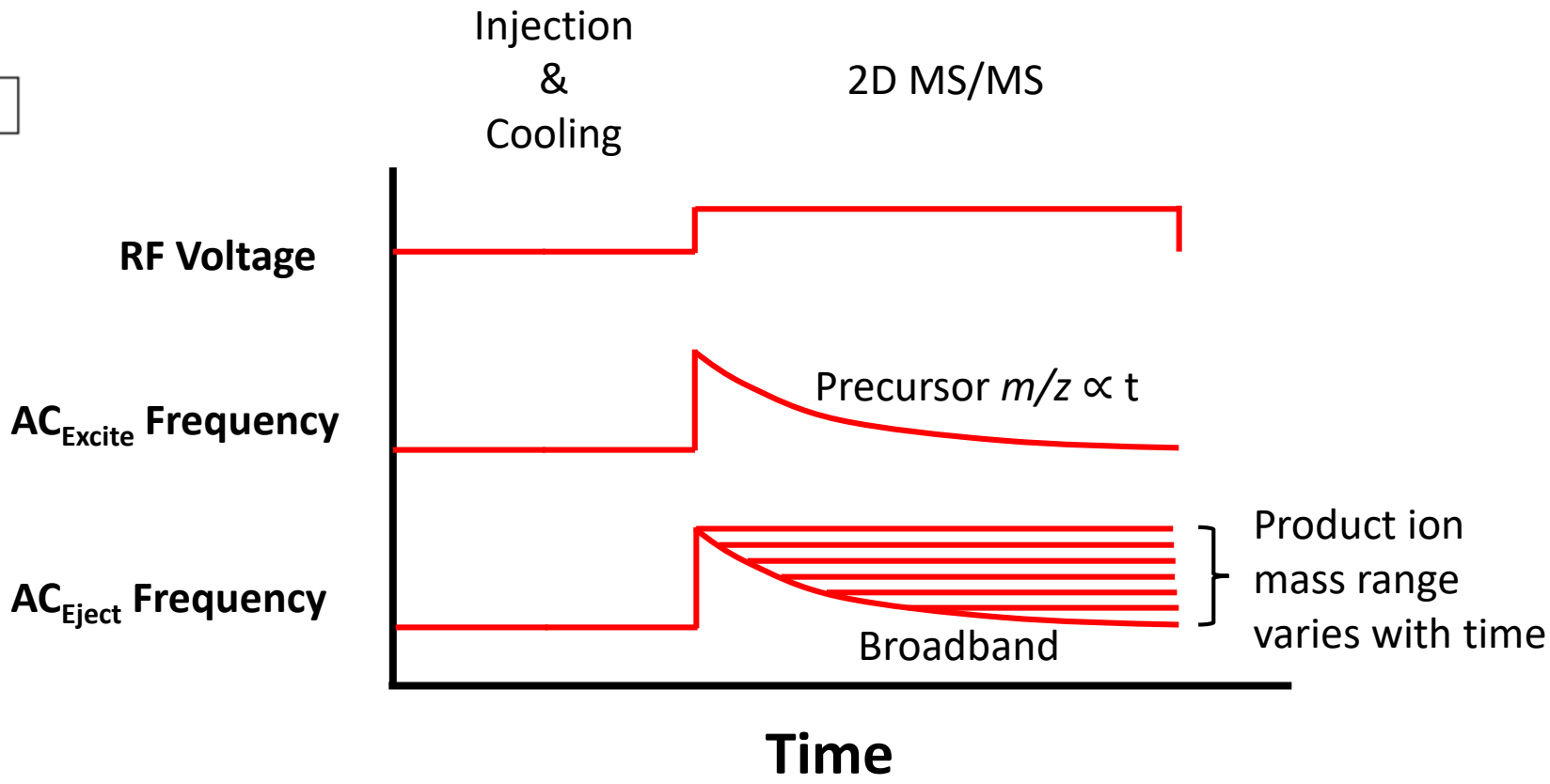


How do we recover precursor and product *m/z*?

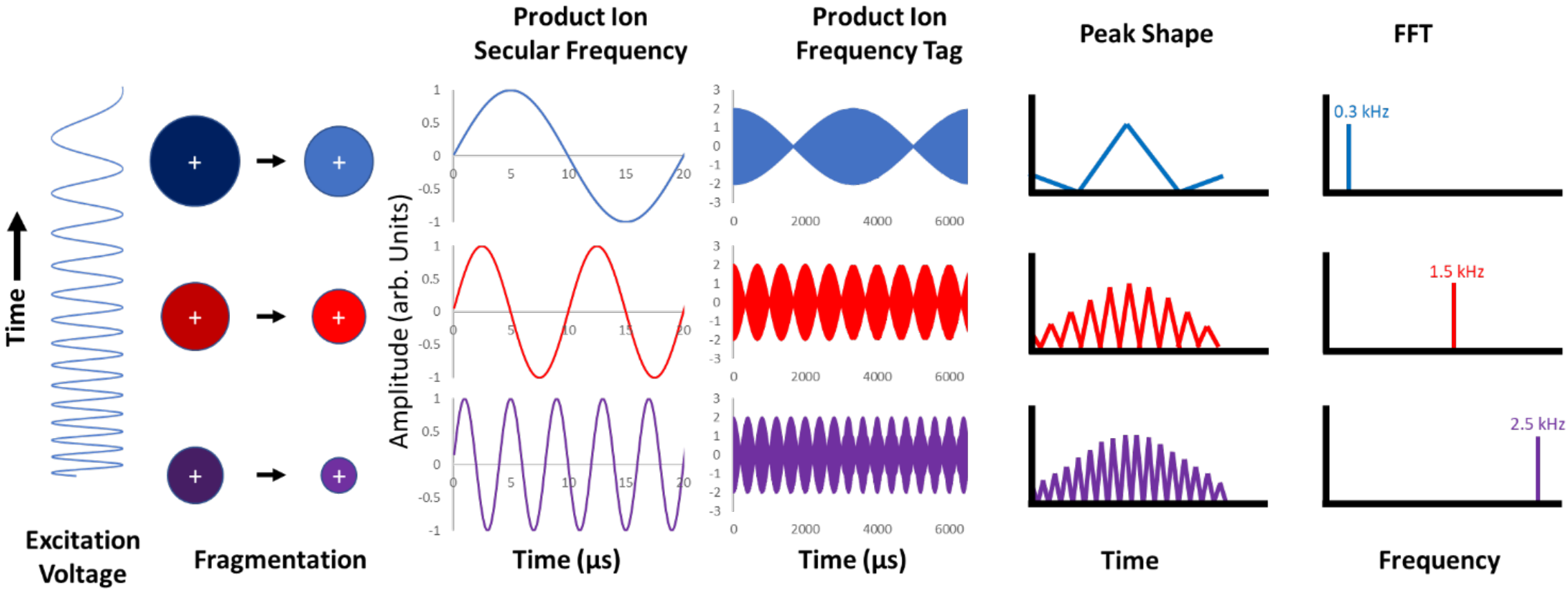
1. **Precursor *m/z* ∝ time**
2. **Product ions are ejected exactly when they are formed, maintaining their relationship with precursor *m/z*.**
3. **How do we determine product *m/z*???**

1. **'Frequency tagging'**
2. **Micropackets**

Simultaneous excitation of precursor ions and ejection of product ions



1. 2D MS/MS using frequency tagging

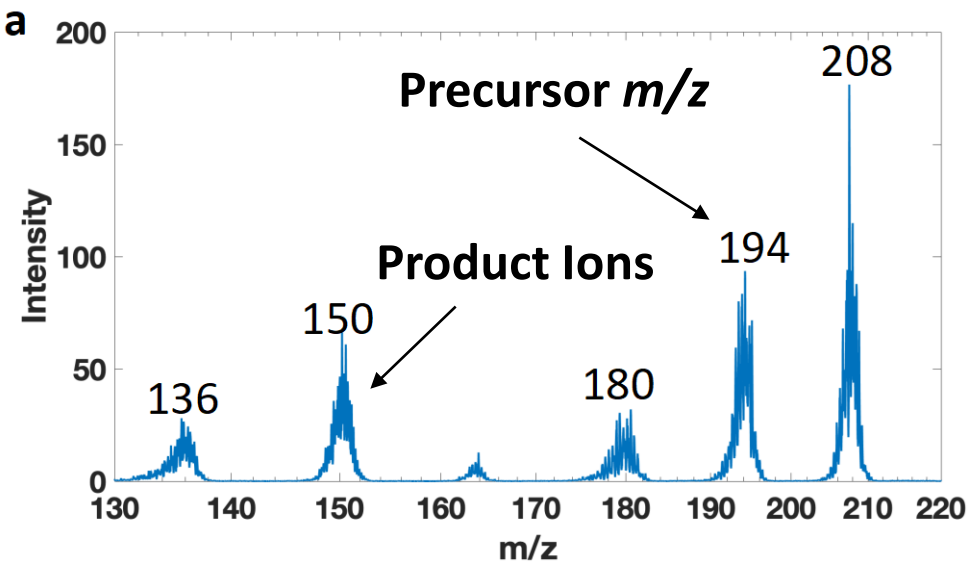


1. Precursor *m/z* ∝ fragmentation time

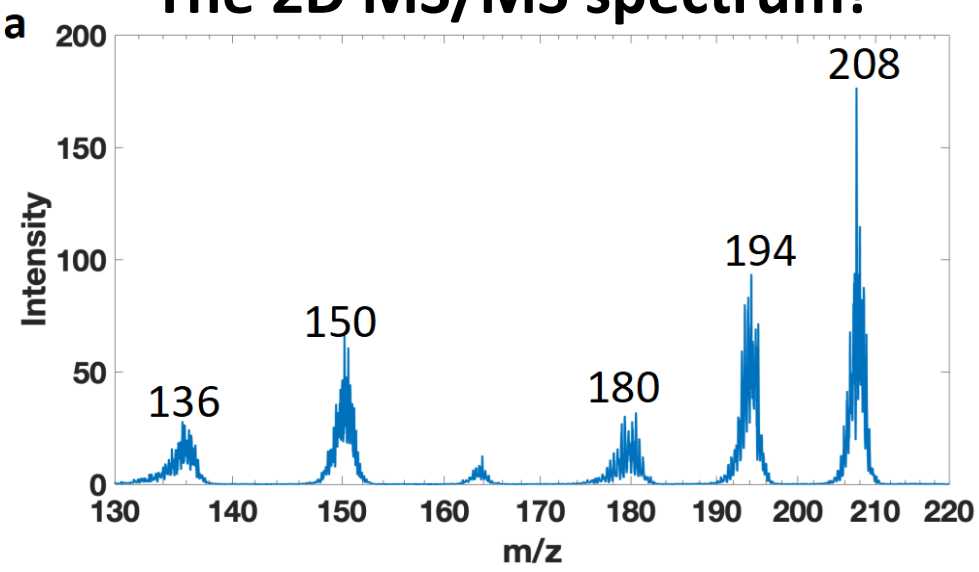
2. Product ions are ejected with a simultaneously applied broadband waveform

3. Beat frequency ∝ Secular frequency ∝ (Product *m/z*)$^{-1}$

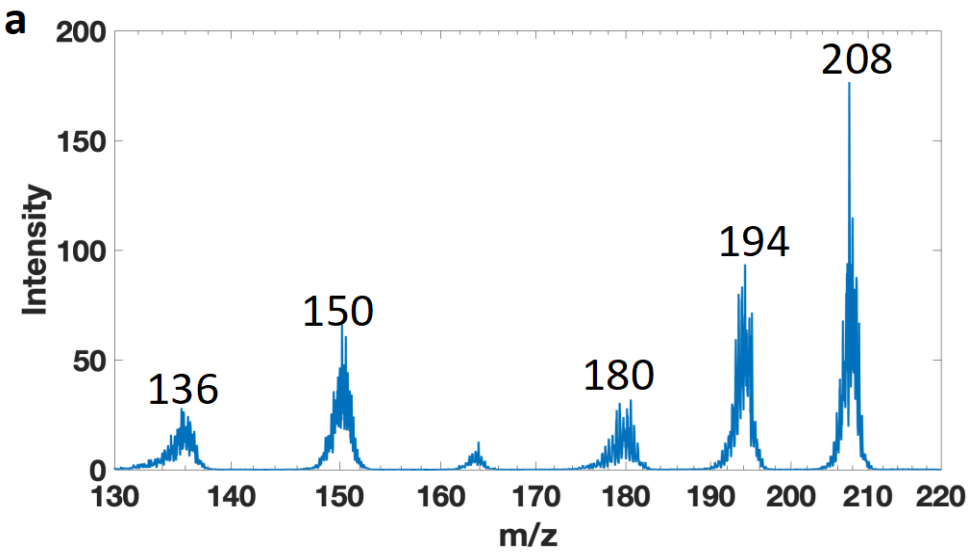
Precursor *m/z* ∝ fragmentation time



The 2D MS/MS spectrum!

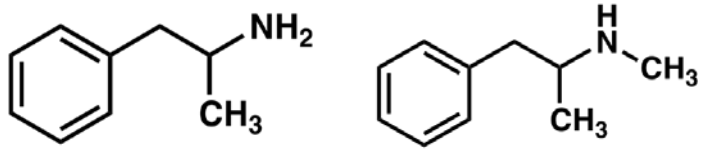


Beat frequency ∝ Secular frequency ∝ (Product *m/z*)$^{-1}$

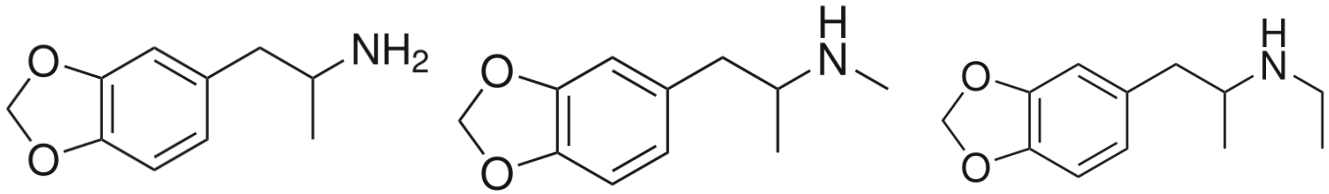


All LTQ data using N_2

5 amphetamines

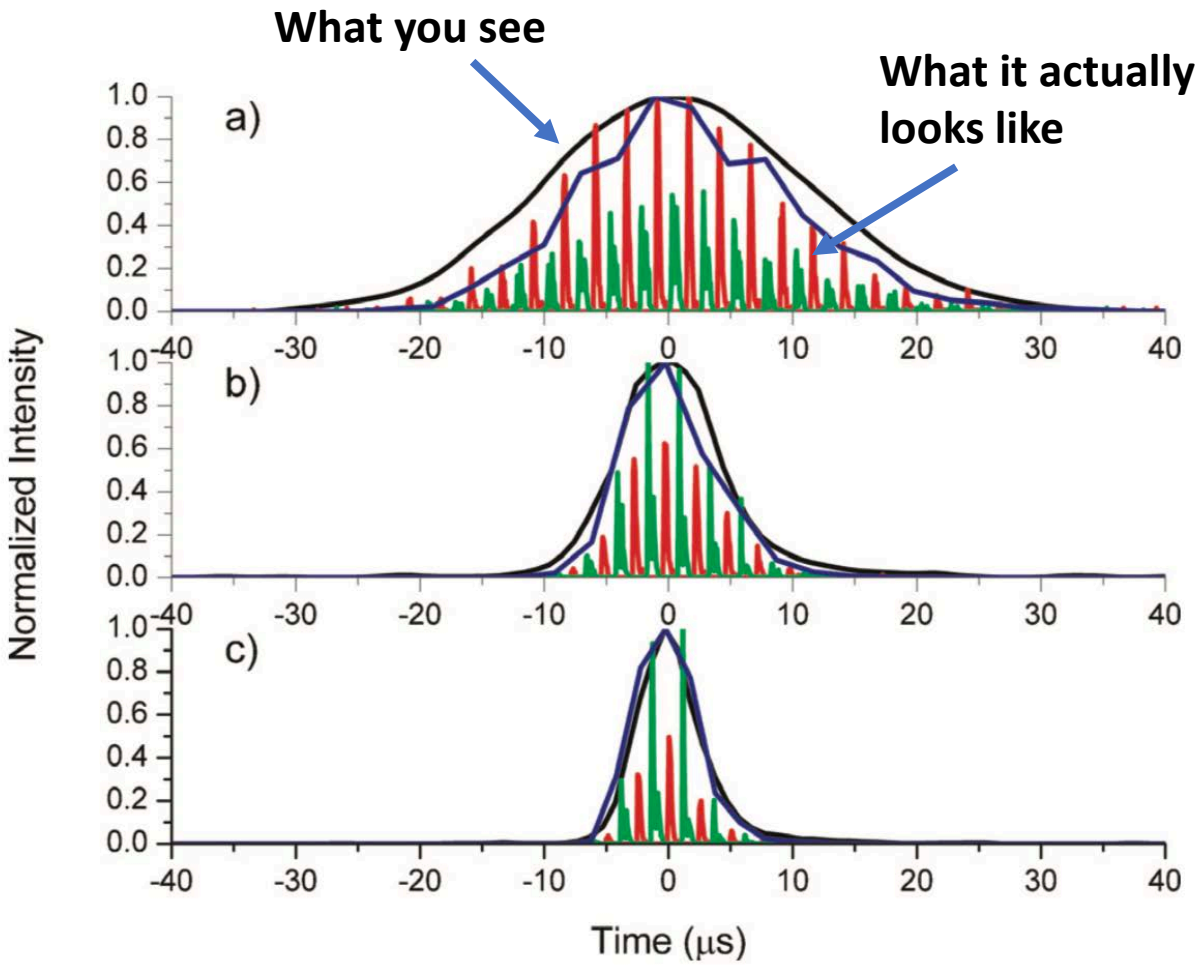


m/z 136 *m/z* 150



m/z 180 *m/z* 194 *m/z* 208

2. An alternate ‘encoding’ scheme – ion micropackets

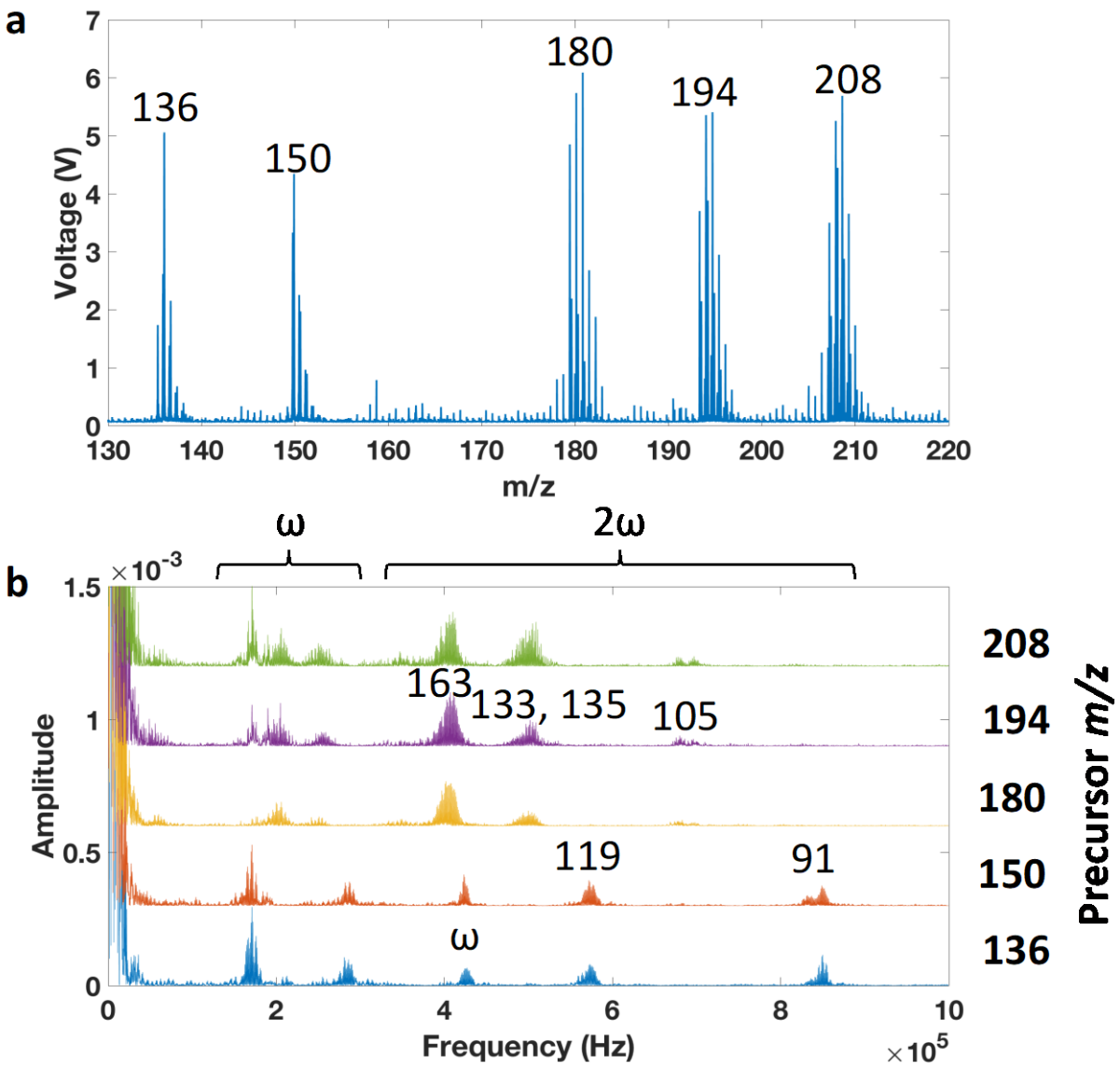


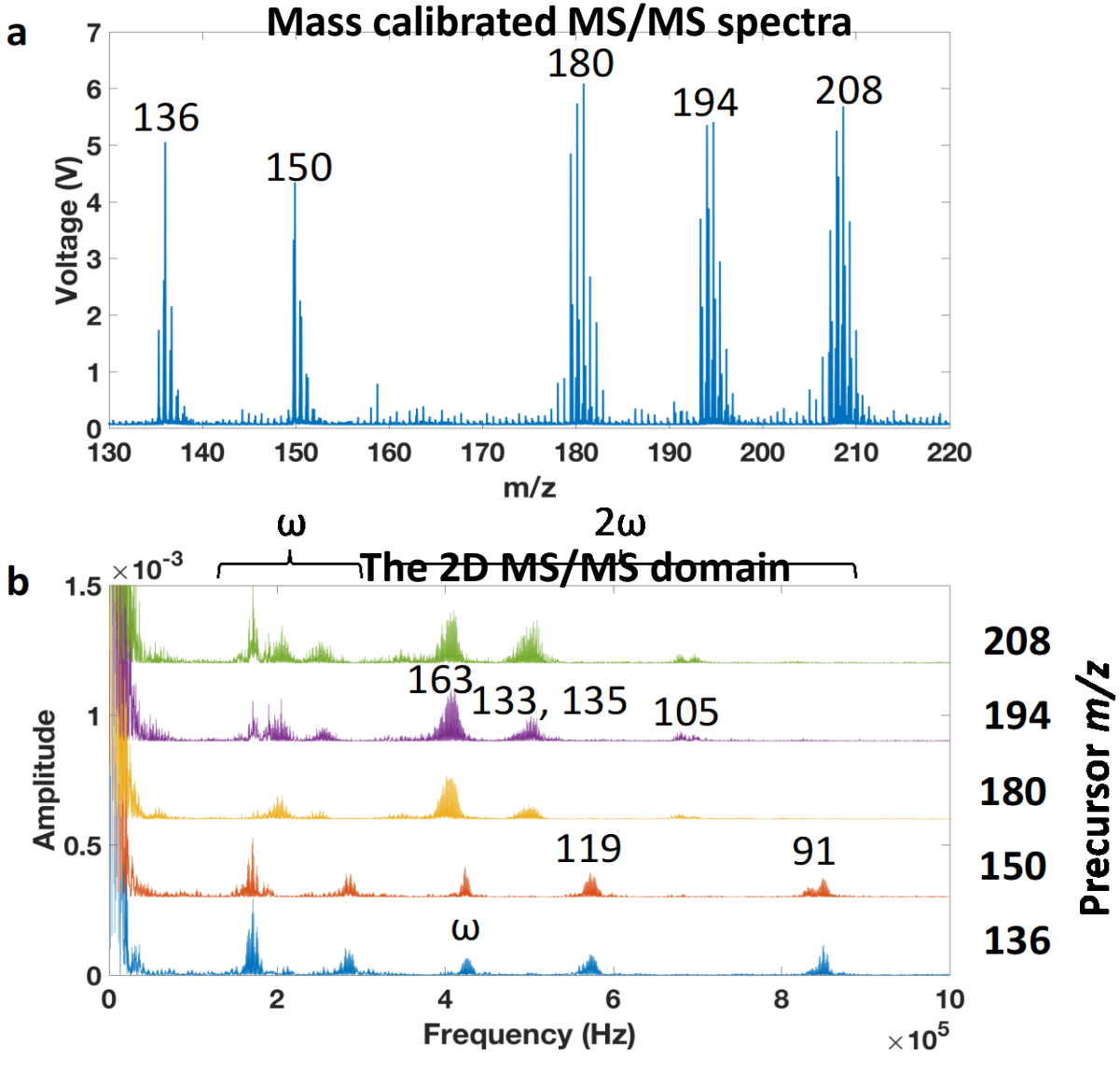
P.M. Remes et al. / International Journal of Mass Spectrometry 370 (2014) 44–57

If the product ions are ejected at different frequencies (their secular frequencies), then we can differentiate them and determine their *m/z* values through FFT & frequency to *m/z* conversion.

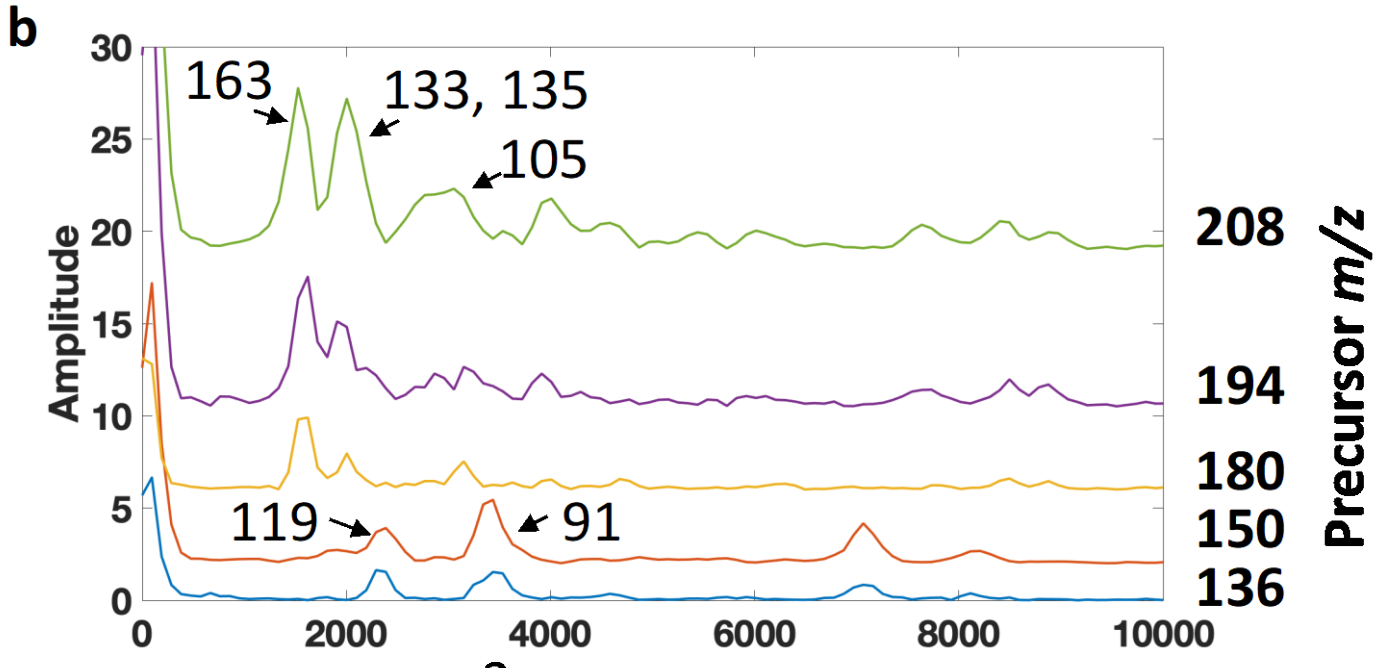
In this case we don’t need frequency tags, so the broadband has even frequency spacing. Otherwise the experiment is the same as before.

2. 2D MS/MS using ion micropackets

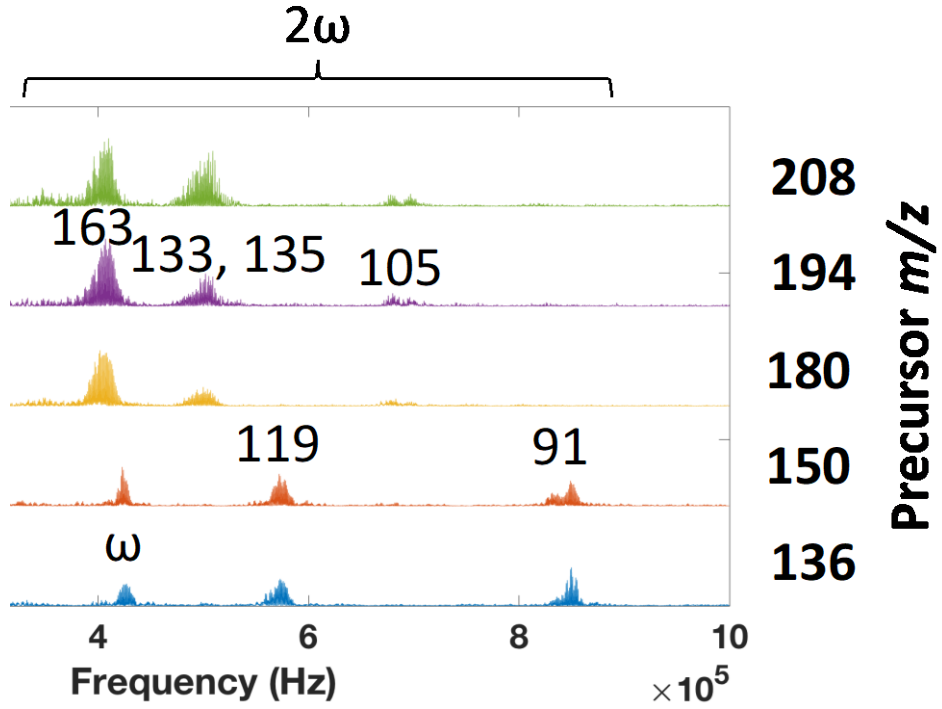




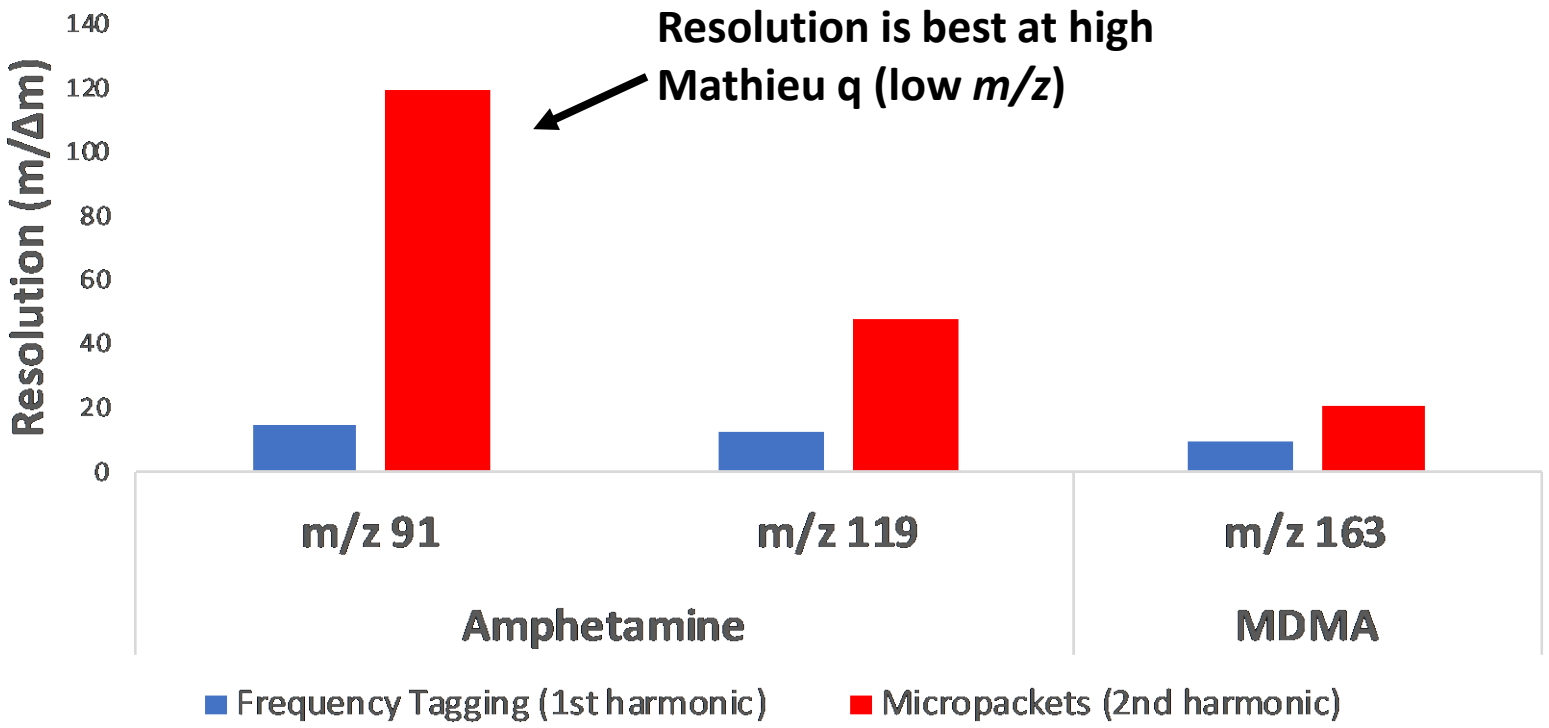
Frequency Tagging



Micropackets



2D MS/MS: Frequency Tagging vs. Micropackets

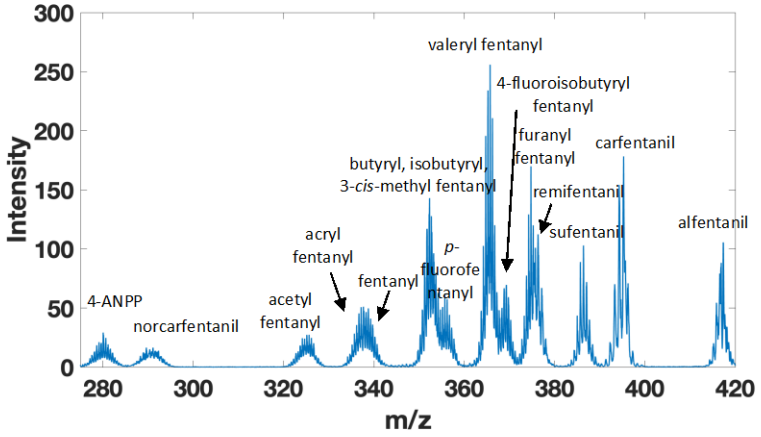


Resolution increases by measuring the ions' 10^2 kHz ejection frequencies instead of artificial 10^0 kHz beat frequencies.

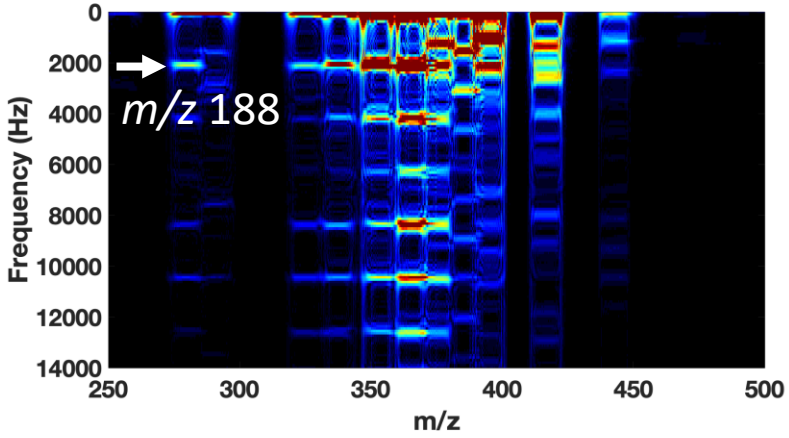
Higher frequency = Higher resolution

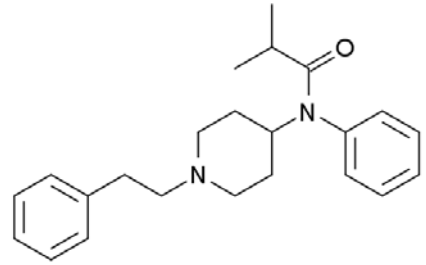
2D MS/MS applied to 16 fentanyl opioids (**FT**)

a

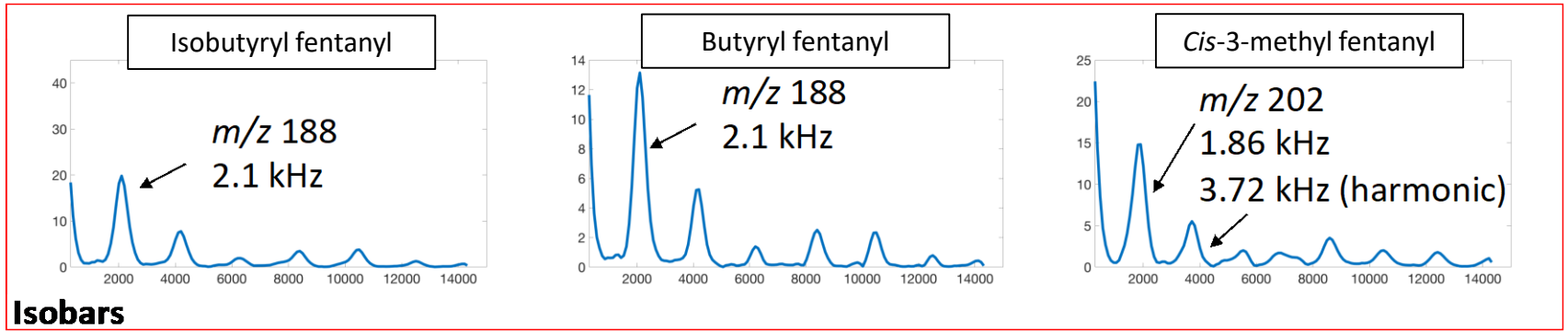


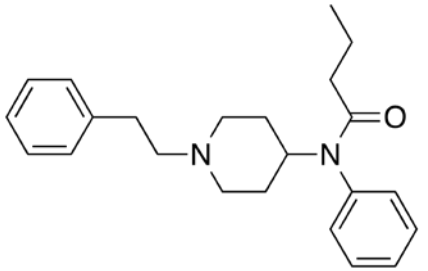
b

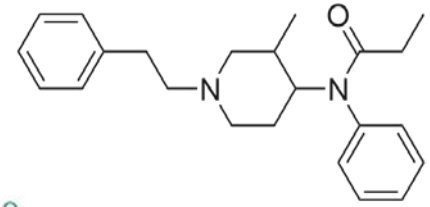




c

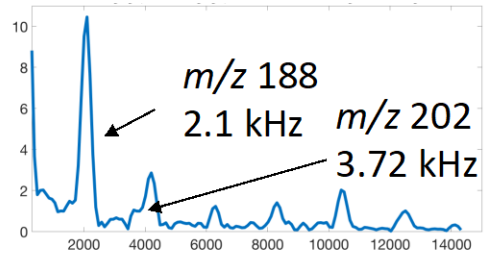




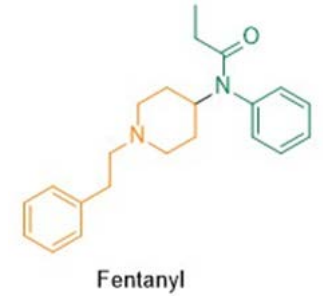


Intensity

Isobaric mix



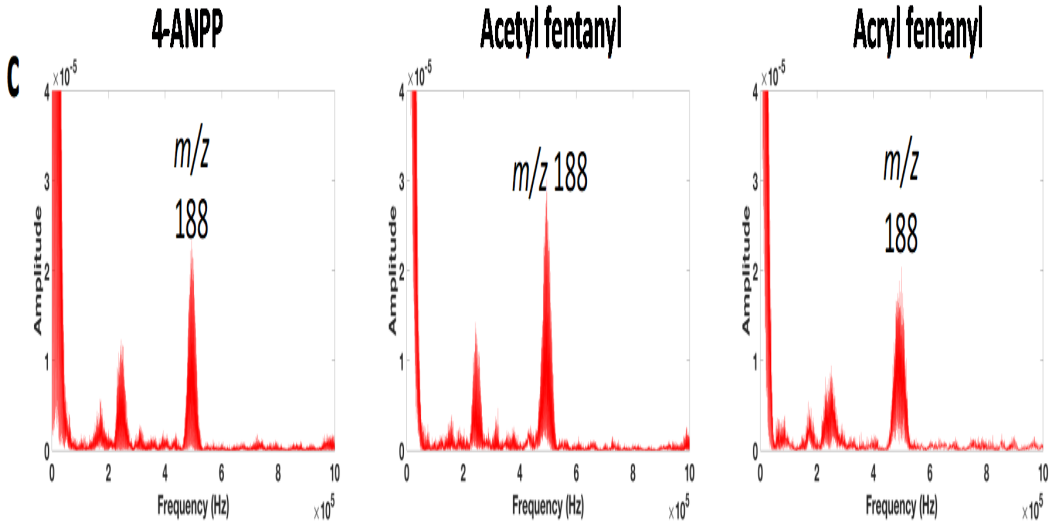
m_2^+
m/z 188



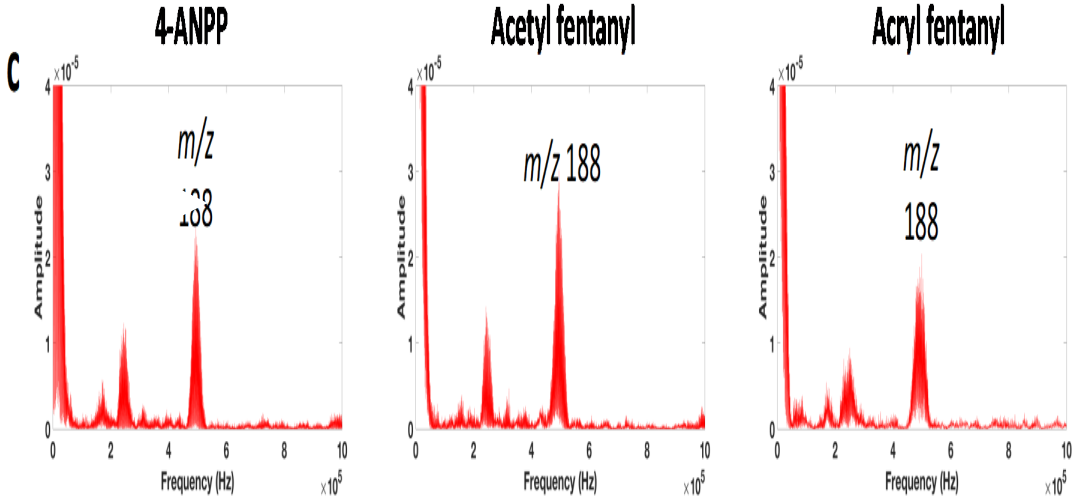
m_3
148 amu

2D MS/MS applied to 16 fentanyl opioids (**MP**)

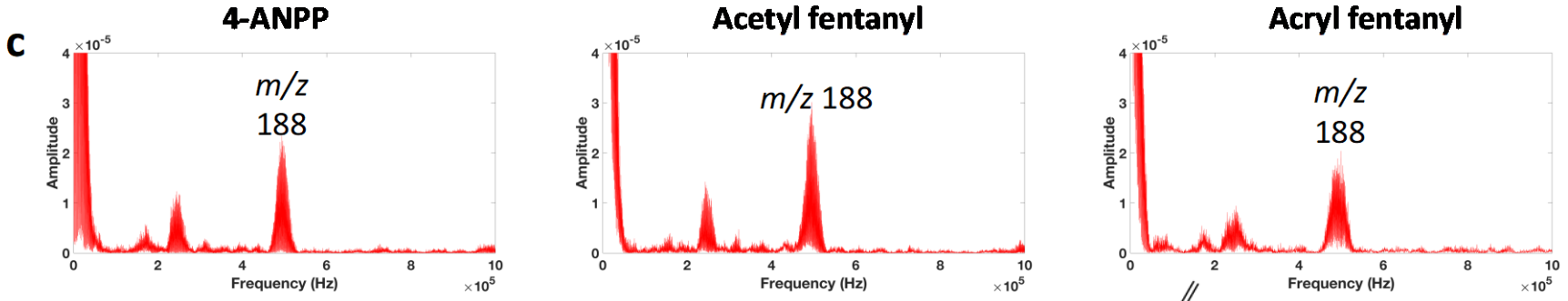
Full MS

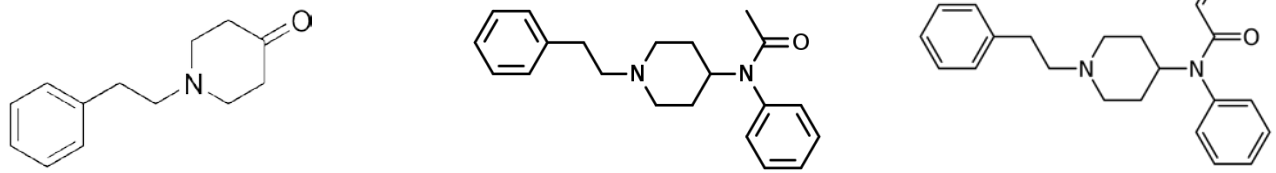


2D Representation

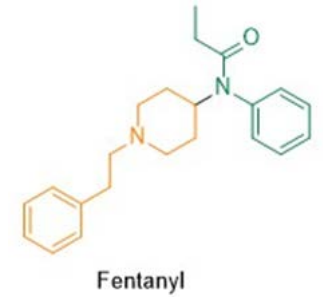


Extracted Product Ion Scans



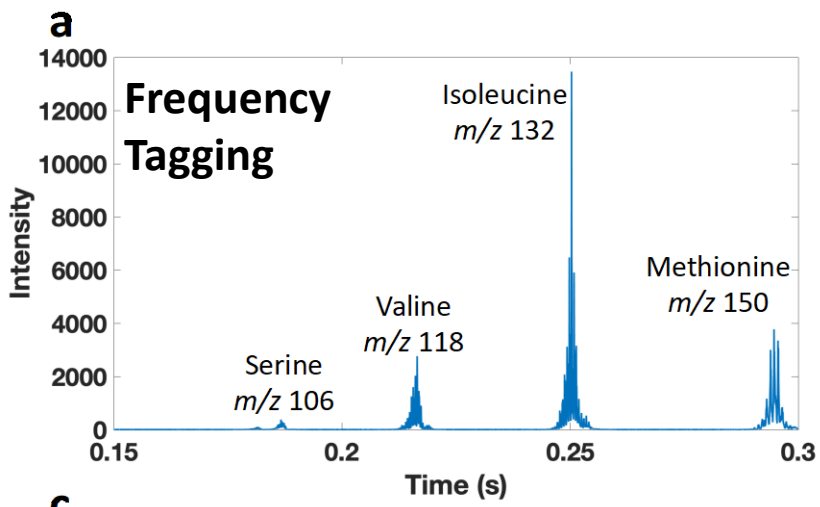


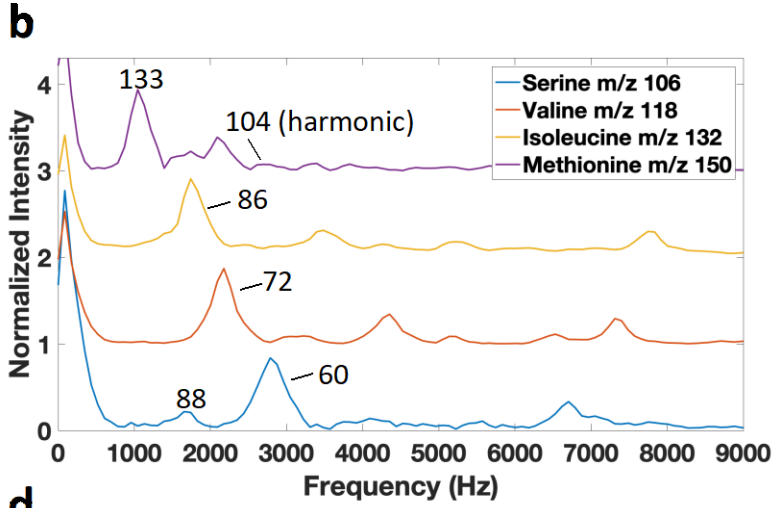
m_2^+
m/z 188

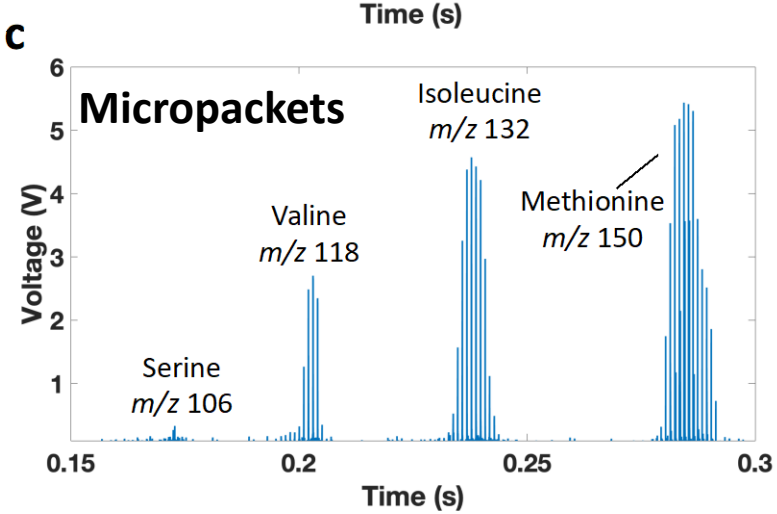


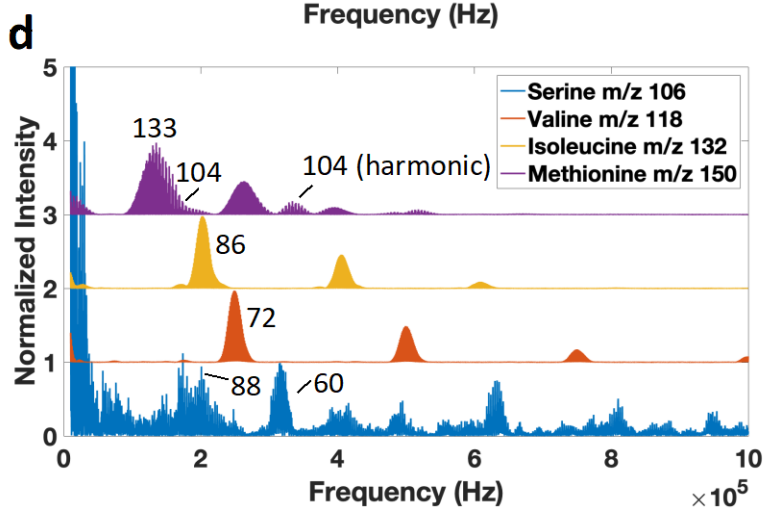
m_3
148 amu

An origin-of-life application: organics on **Mars/Europa/Titan/Enceladus**

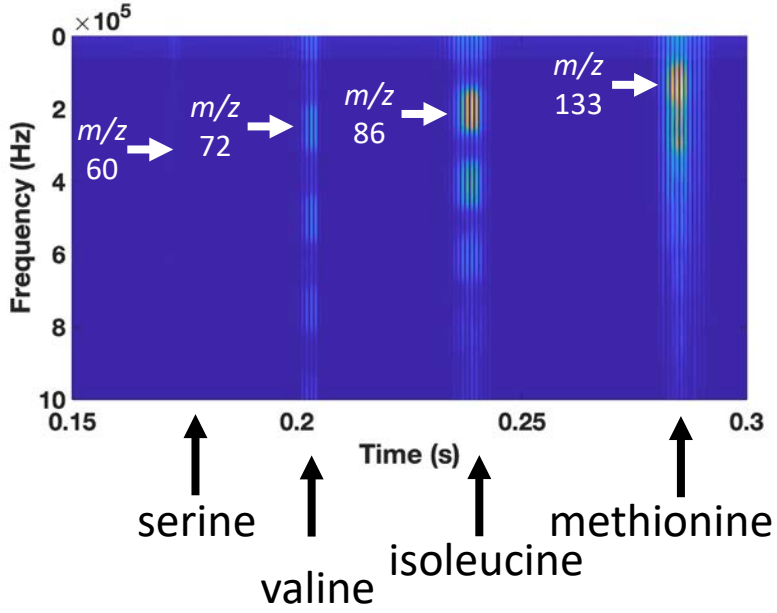








Vizualized as a 2D Mass Spectrum!



Both 2D MS/MS spectra are remarkably similar, despite resulting from different encoding schemes.

Conclusion & Outlook

- 2D MS/MS is yet another extraordinary capability of ion traps & is an efficient means of collecting MS & MS/MS data
- A *single scan* can collect the entire 2D MS/MS data domain!
- Next step – 2D MS/MS on a portable instrument
- Improvements need to be made
  - Broadband phasing, frequency spacing, amplitude, construction, etc.
  - Optimize precursor and product mass resolution
    - **Perhaps optimal to use 2D MS/MS as a survey scan and then use data-dependent MS/MS to obtain better resolution on product ions**
  - Optimize fragmentation efficiency while maintaining good resolution
    - Impossible to do this if ion trap CID is the activation method
  - How do we filter and process the data?

Acknowledgements

- NASA Planetary Sciences Division (PICASSO NNX16AJ25G)
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