Improving the Selectivity of a High Pressure Mass Spectrometer

Andrew Hampton

September 14, 2015

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

Acknowledgements

COI Disclosures

Current Interactions

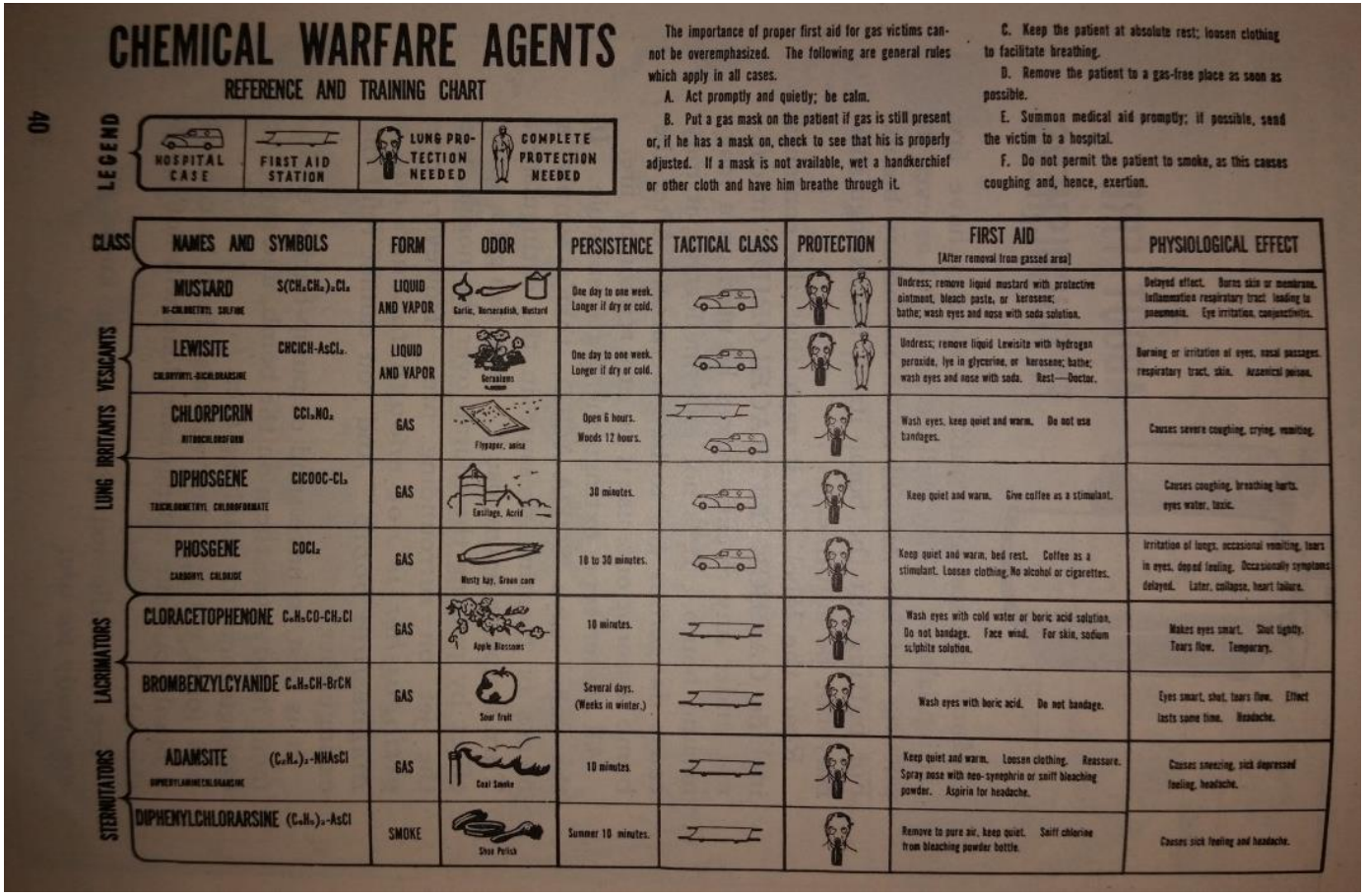
J. Michael Ramsey

908 Devices Inc.

- Scientific Founder
- Director
- Consultant
- Equity
- Receive royalties

DTRA Funding

Threat Detection



CHEMICAL WARFARE AGENTS

REFERENCE AND TRAINING CHART

40

LEGEND: HOSPITAL CASE | FIRST AID STATION | LUNG PROTECTION NEEDED | COMPLETE PROTECTION NEEDED

The importance of proper first aid for gas victims cannot be overemphasized. The following are general rules which apply in all cases.

A. Act promptly and quietly; be calm.

B. Put a gas mask on the patient if gas is still present or, if he has a mask on, check to see that his is properly adjusted. If a mask is not available, wet a handkerchief or other cloth and have him breathe through it.

C. Keep the patient at absolute rest; loosen clothing to facilitate breathing.

D. Remove the patient to a gas-free place as soon as possible.

E. Summon medical aid promptly; if possible, send the victim to a hospital.

F. Do not permit the patient to smoke, as this causes coughing and, hence, exertion.

CLASS	NAMES AND SYMBOLS	FORM	ODOR	PERSISTENCE	TACTICAL CLASS	PROTECTION	FIRST AID [After removal from gassed area]	PHYSIOLOGICAL EFFECT
VESICANTS	MUSTARD $S(CH_2CH_2)_2Cl_2$ DI-CHLORETHYL SULFIDE	LIQUID AND VAPOR	Garlic, Horseradish, Mustard	One day to one week. Longer if dry or cold.			Undress; remove liquid mustard with protective ointment, bleach paste, or kerosene; bathe; wash eyes and nose with soda solution.	Delayed effect. Burns skin or membrane. Inflammation respiratory tract leading to pneumonia. Eye irritation, conjunctivitis.
VESICANTS	LEWISITE $CHClCH\text{-}AsCl_2$ CHLOROVINYL-DICHLOROARSINE	LIQUID AND VAPOR	Geraniums	One day to one week. Longer if dry or cold.			Undress; remove liquid Lewisite with hydrogen peroxide, lye in glycerine, or kerosene; bathe; wash eyes and nose with soda. Rest—Doctor.	Burning or irritation of eyes, nasal passages, respiratory tract, skin. Arsenical poison.
LUNG IRRITANTS	CHLORPICRIN CCl_3NO_2 NITROCHLOROFORM	GAS	Flypaper, anise	Open 6 hours. Woods 12 hours.			Wash eyes, keep quiet and warm. Do not use bandages.	Causes severe coughing, crying, vomiting.
LUNG IRRITANTS	DIPHOSGENE $ClCOOC\text{-}Cl_3$ TRICHLOROMETHYL CHLOROFORMATE	GAS	Ensilage, Acrid	30 minutes.			Keep quiet and warm. Give coffee as a stimulant.	Causes coughing, breathing hurts, eyes water, toxic.
LUNG IRRITANTS	PHOSGENE $COCl_2$ CARBONYL CHLORIDE	GAS	Musty hay, Green corn	10 to 30 minutes.			Keep quiet and warm, bed rest. Coffee as a stimulant. Loosen clothing. No alcohol or cigarettes.	Irritation of lungs, occasional vomiting, tears in eyes, dopod feeling. Occasionally symptoms delayed. Later, collapse, heart failure.
LACRIMATORS	CLORACETOPHENONE $C_6H_5CO\text{-}CH_2Cl$	GAS	Apple Blossoms	10 minutes.			Wash eyes with cold water or boric acid solution. Do not bandage. Face wind. For skin, sodium sulphite solution.	Makes eyes smart. Shut tightly. Tears flow. Temporary.
LACRIMATORS	BROMBENZYLCYANIDE $C_6H_5CH\text{-}BrCN$	GAS	Sour fruit	Several days. (Weeks in winter.)			Wash eyes with boric acid. Do not bandage.	Eyes smart, shut, tears flow. Effect lasts some time. Headache.
STERNUTATORS	ADAMSITE $(C_6H_5)_2\text{-}NHAsCl$ DIPHENYLAMINECHLOROARSINE	GAS	Coal Smoke	10 minutes.			Keep quiet and warm. Loosen clothing. Reassure. Spray nose with neo-synephrin or sniff bleaching powder. Aspirin for headache.	Causes sneezing, sick depressed feeling, headache.
STERNUTATORS	DIPHENYLCHLORARSINE $(C_6H_5)_2\text{-}AsCl$	SMOKE	Shoe Polish	Summer 10 minutes.			Remove to pure air, keep quiet. Sniff chlorine from bleaching powder bottle.	Causes sick feeling and headache.

SS	NAMES AND SYMBOLS	FORM	ODOR	PROTECTION	FIRST AID [After removal from gassed area]	PHYSIOLOGICAL EFFECT
	MUSTARD $S(CH_2CH_2)_2Cl_2$ DI-CHLORETHYL SULFIDE	LIQUID AND VAPOR	Garlic, Horseradish, Mustard		Undress; remove liquid mustard with protective ointment, bleach paste, or kerosene; bathe; wash eyes and nose with soda solution.	Delayed effect. Burns skin or membrane. Inflammation respiratory tract leading to pneumonia. Eye irritation, conjunctivitis.

Taking Action

Threats

- CWAs
  - Blister
  - Blood
  - Nerve
- BWAs
- TICs

Responses

- Ger
  Pro
- Spe
- Tar
  Cle
- Eva

High Pressure Ion Trap Theory

$$\frac{m}{\Delta m} \propto \frac{\Omega}{P}$$

≈ 1 Torr

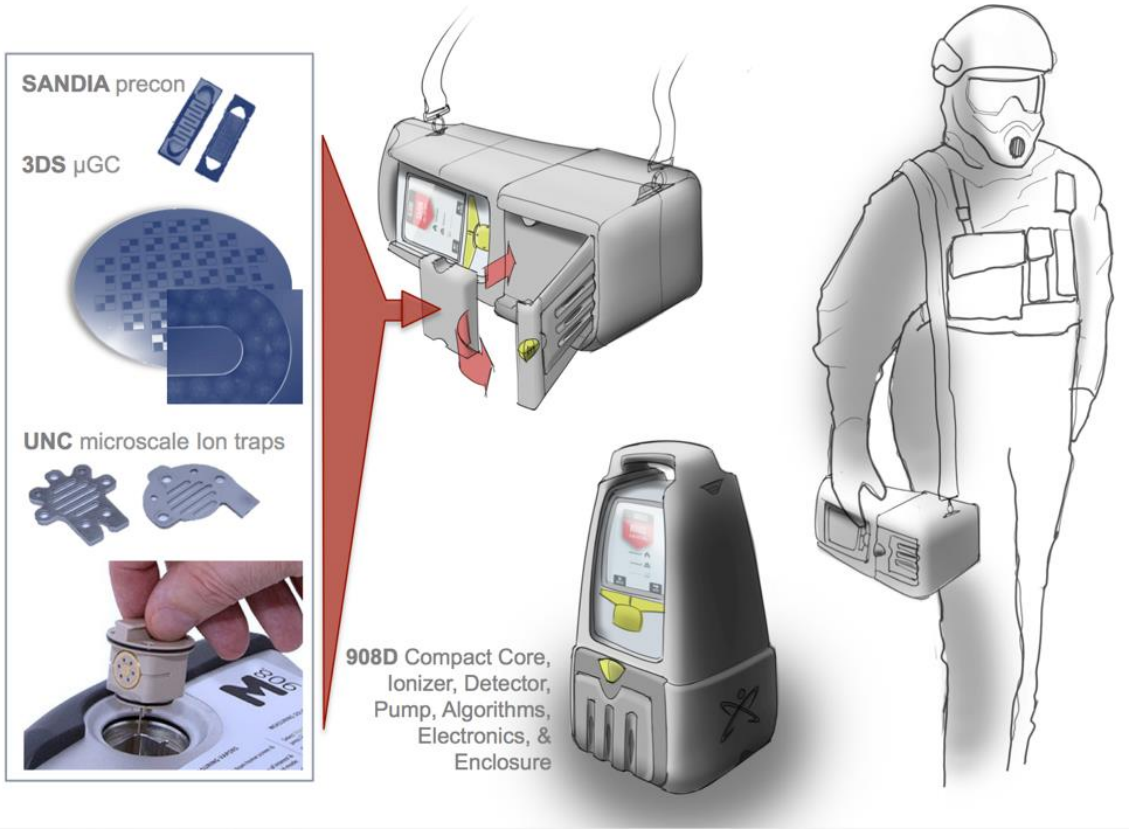
e = elementary charge
V = RF Amplitude (0-p)
m = ion mass (Daltons)
r_o = trap radius
$2z_o$ = endcap separation
Ω = 2πf, f = RF frequency
P = Pressure
$q_{max} < 0.908$

$$\left(\frac{m}{e}\right)_{max} = \frac{8\,V_{max}}{q_{max}\Omega^2(r_o^{\,2} + 2\,z_o^{\,2})}$$

Goeringer, D. E. et al. *Anal Chem.* **1992,** *64,* 1434-1439

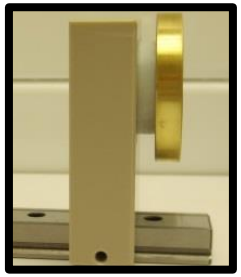
Enhancing Selectivity

- Gas Chromatography
  - Enables complex mixture analysis
  - Adds chemical information
- Tandem MS
  - Reduces chemical noise
  - Gives structural information



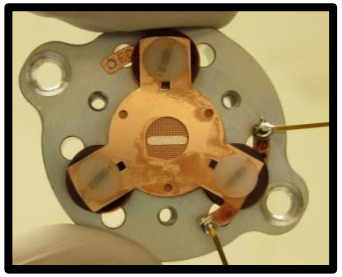
Breadboard Systems

Ion Source



Glow Discharge

Mass Analyzer



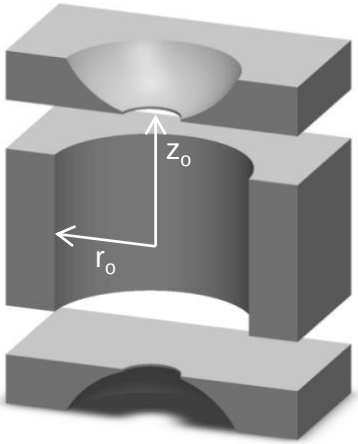
Microscale SLIT

~1 Torr

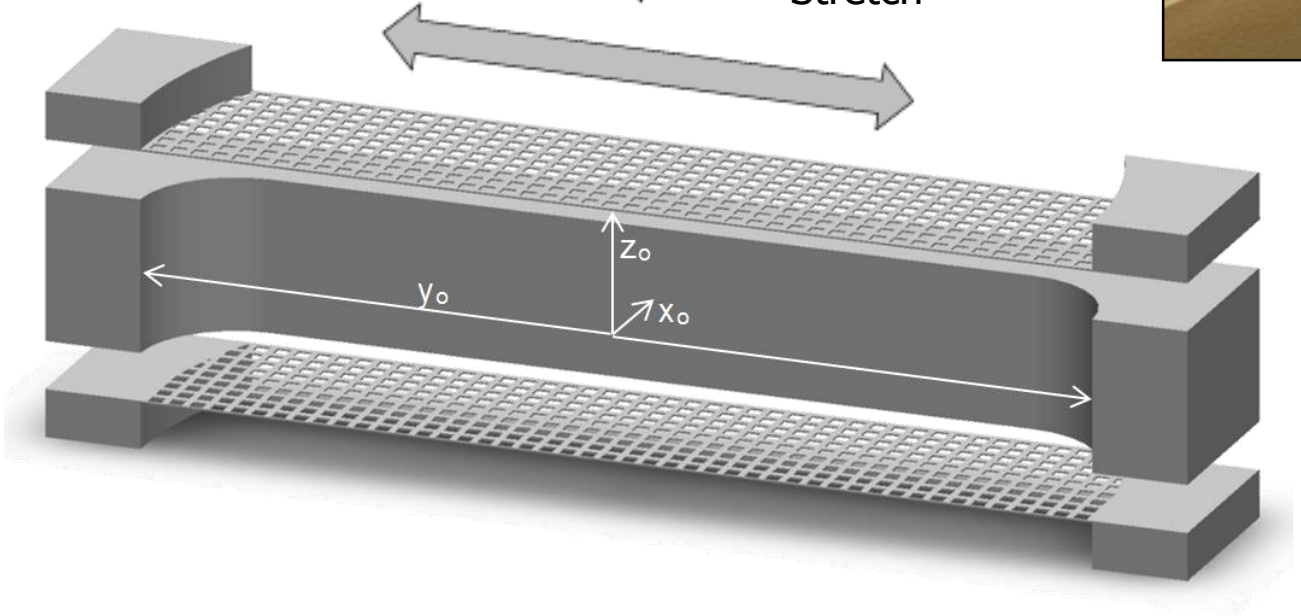
Detector

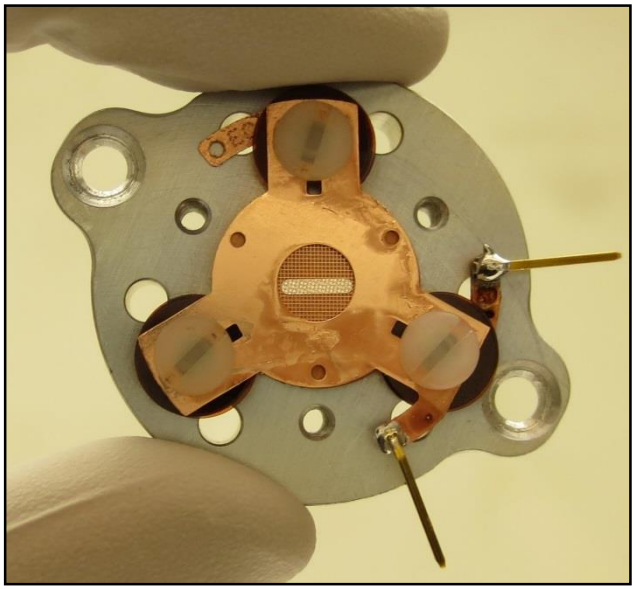
Faraday Cup

Stretched Length Ion Trap (SLIT)



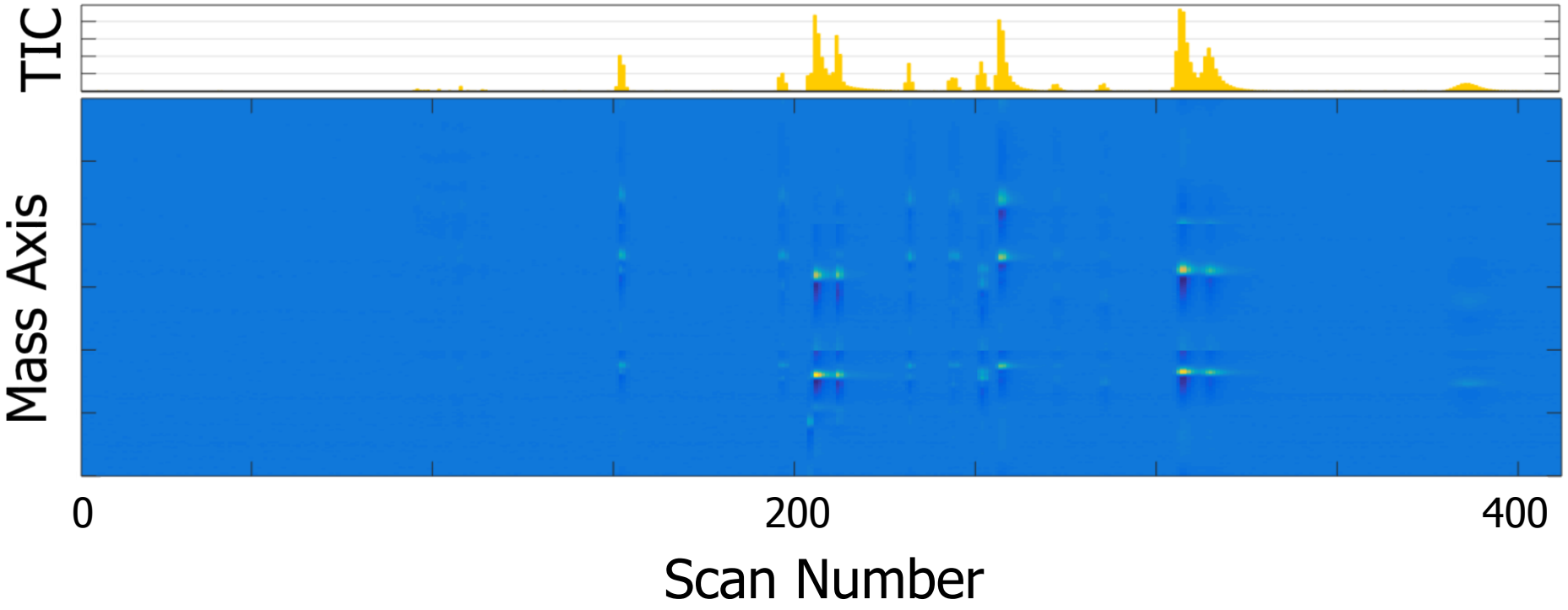
Y-Dimension Stretch



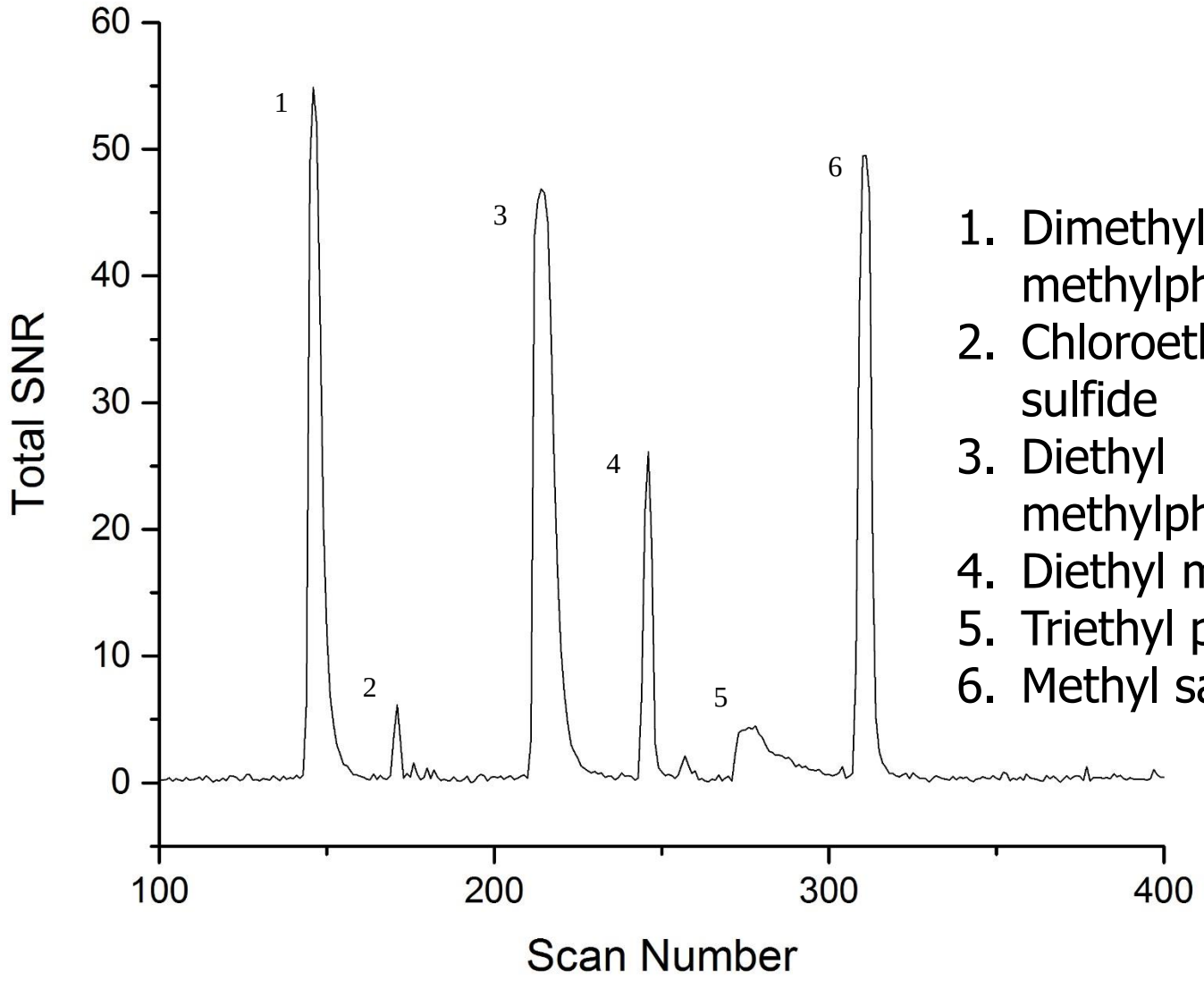


Courtesy Kevin Schultze

Separation of Complex Mixture

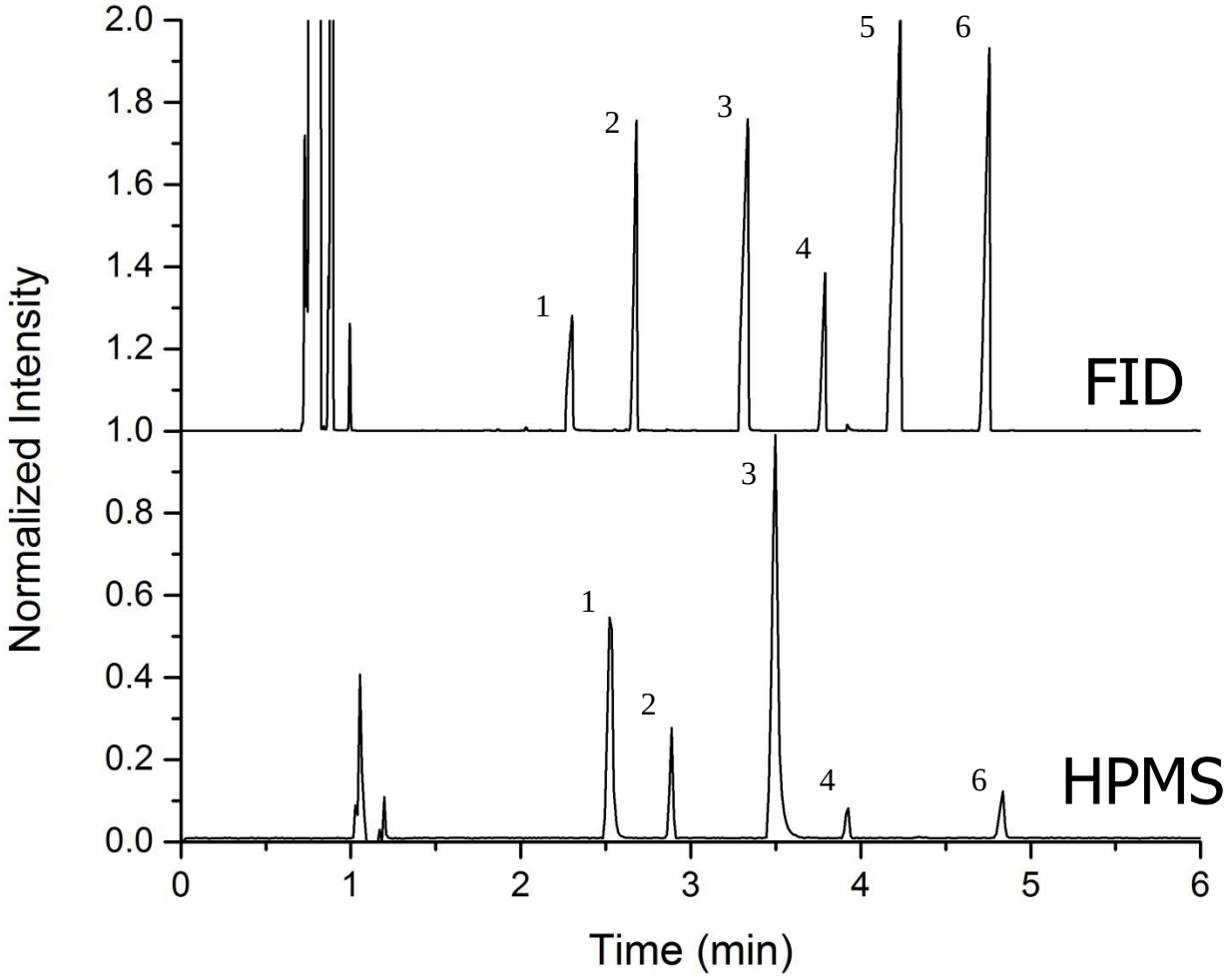


CWAS via GC-HPMS



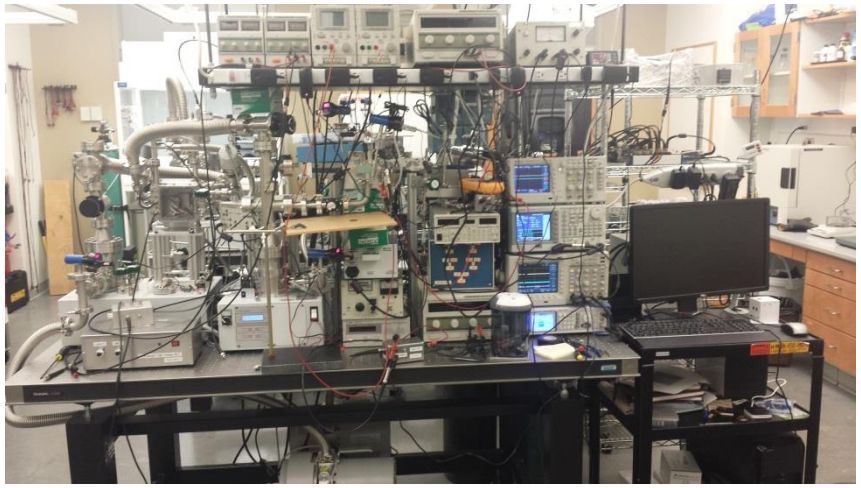
1. Dimethyl methylphosphonate
2. Chloroethyl ethyl sulfide
3. Diethyl methylphosphonate
4. Diethyl malonate
5. Triethyl phosphate
6. Methyl salicylate

CWASs Separation in Helium

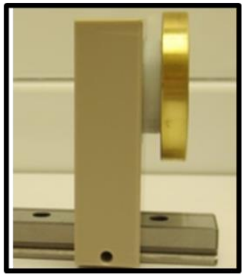


1. Dimethyl methylphosphonate
2. Chloroethyl ethyl sulfide
3. Diethyl methylphosphonate
4. Diethyl malonate
5. Triethyl phosphate
6. Methyl salicylate

Benchtop Systems

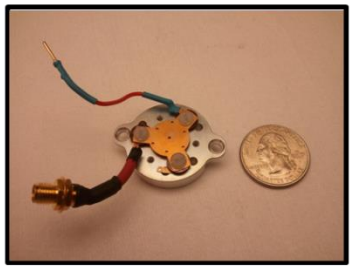


Ion Source



Electron Source

Mass Analyzer



CIT / SLIT

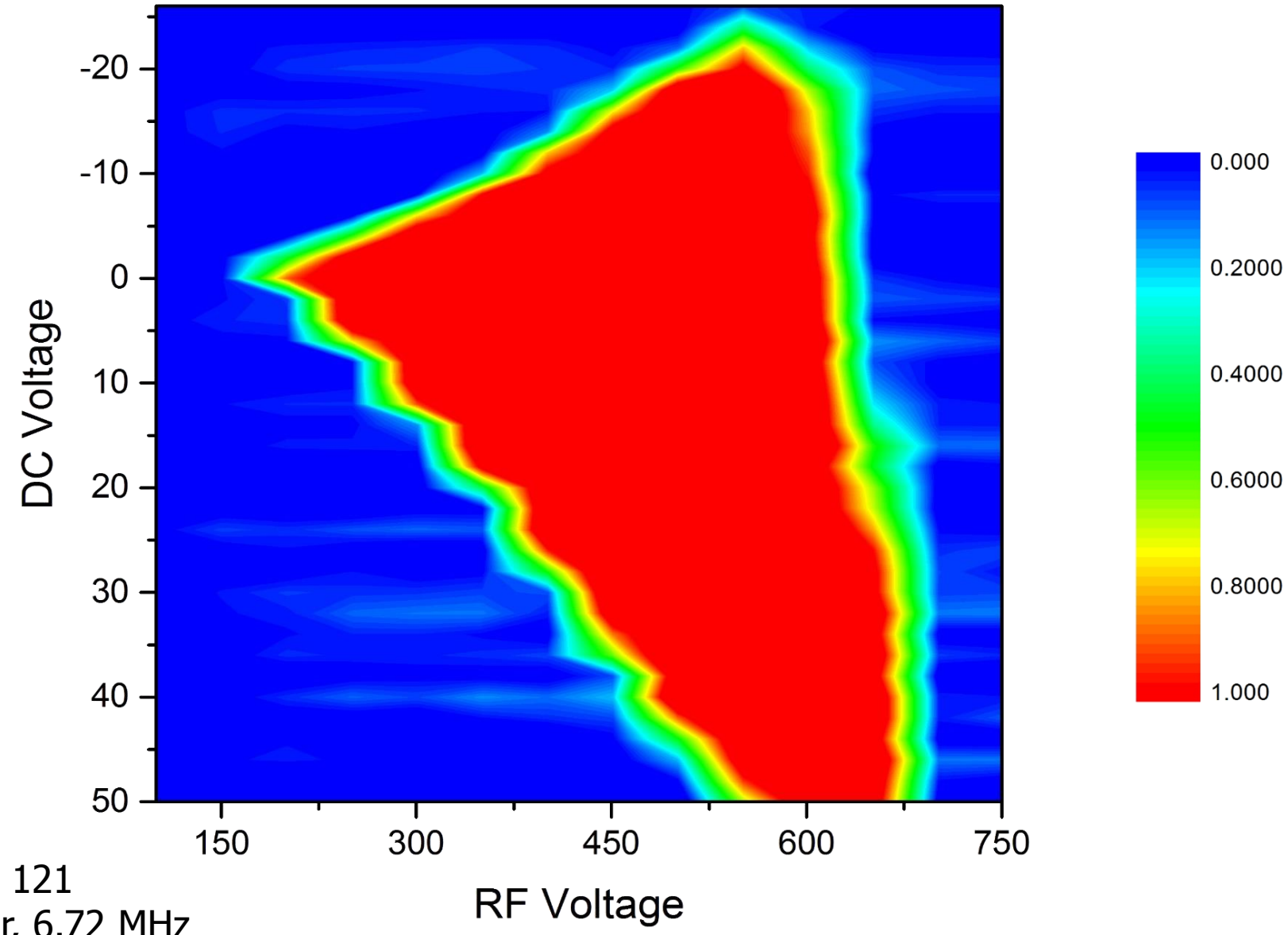
~ 1 Torr

Detector

Electron Multiplier

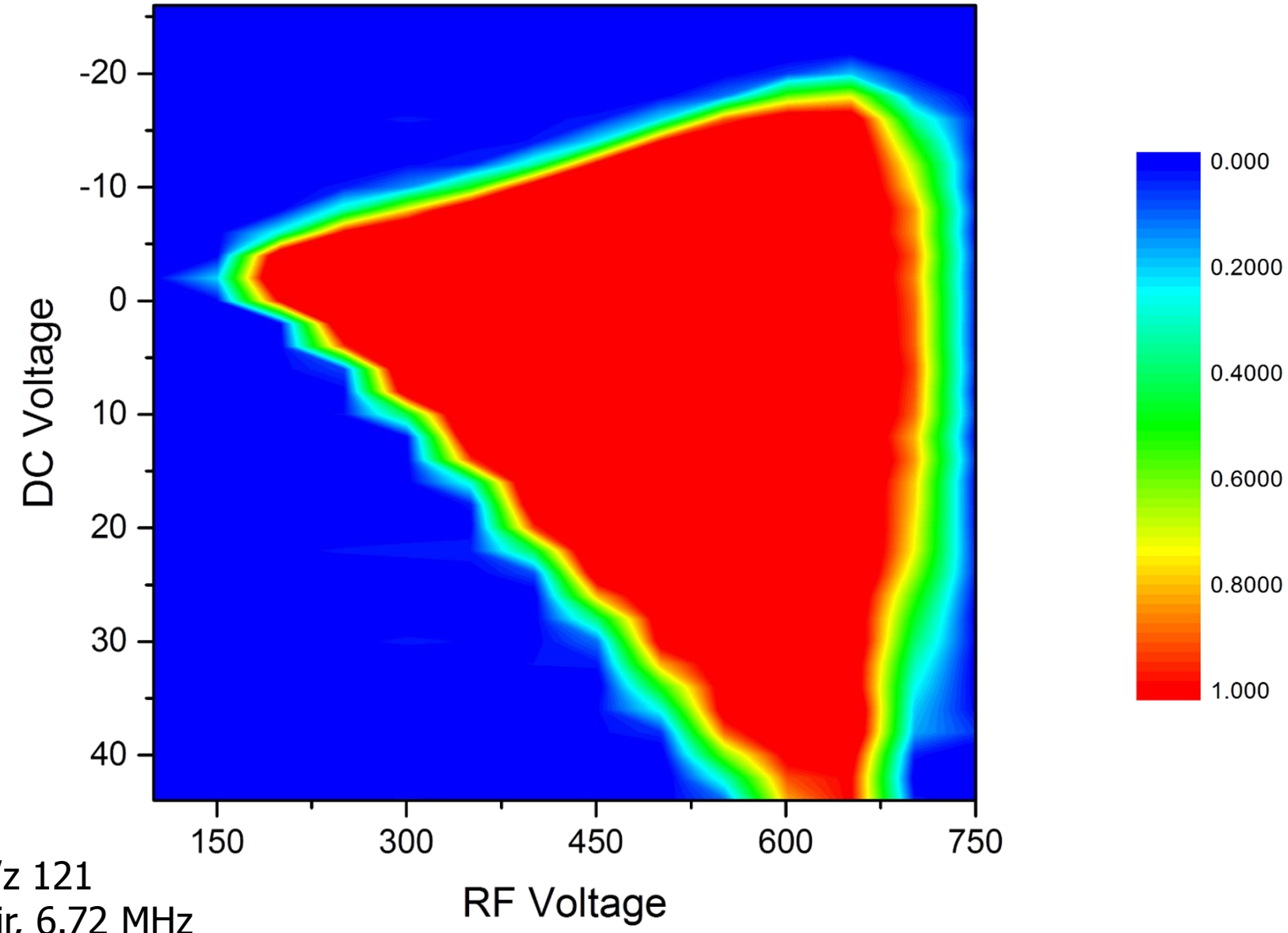
<10 mTorr

CIT Stability Diagram



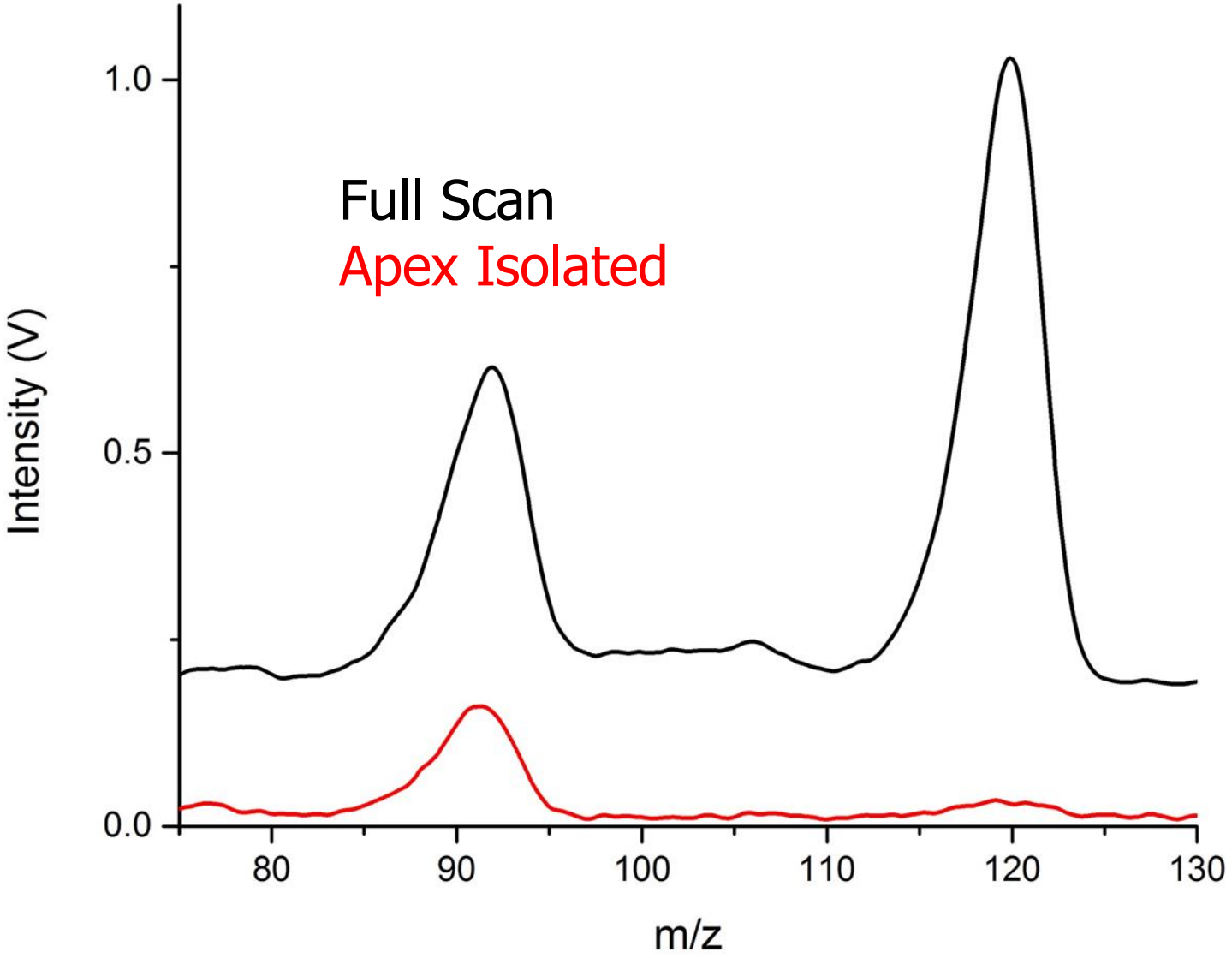
CIT, m/z 121
1 Torr Air, 6.72 MHz

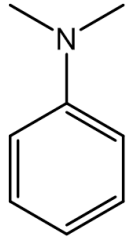
SLIT Stability Diagram

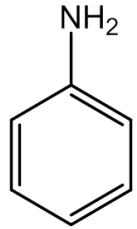


SLIT, m/z 121
1 Torr Air, 6.72 MHz

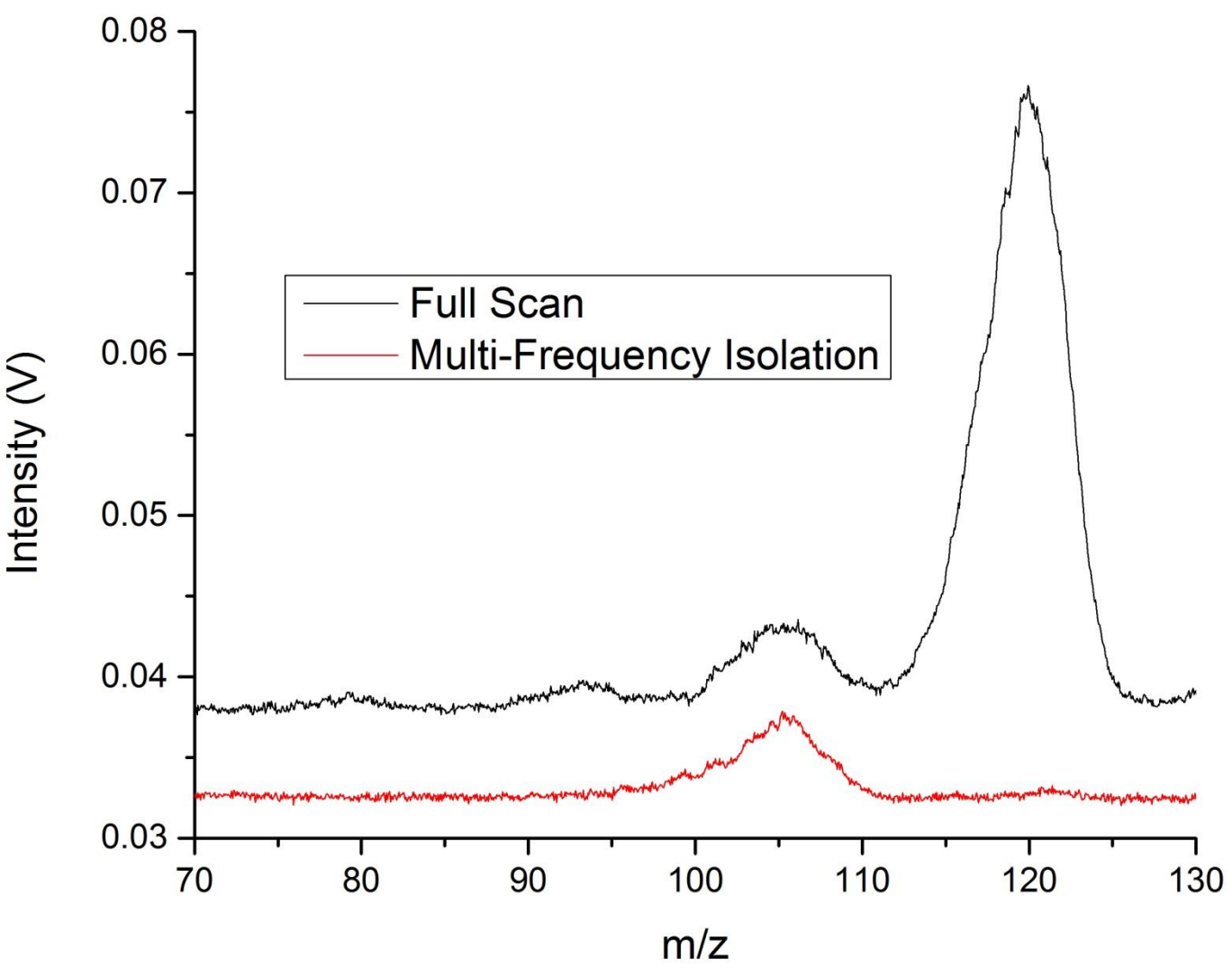
Apex Isolation

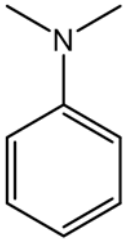






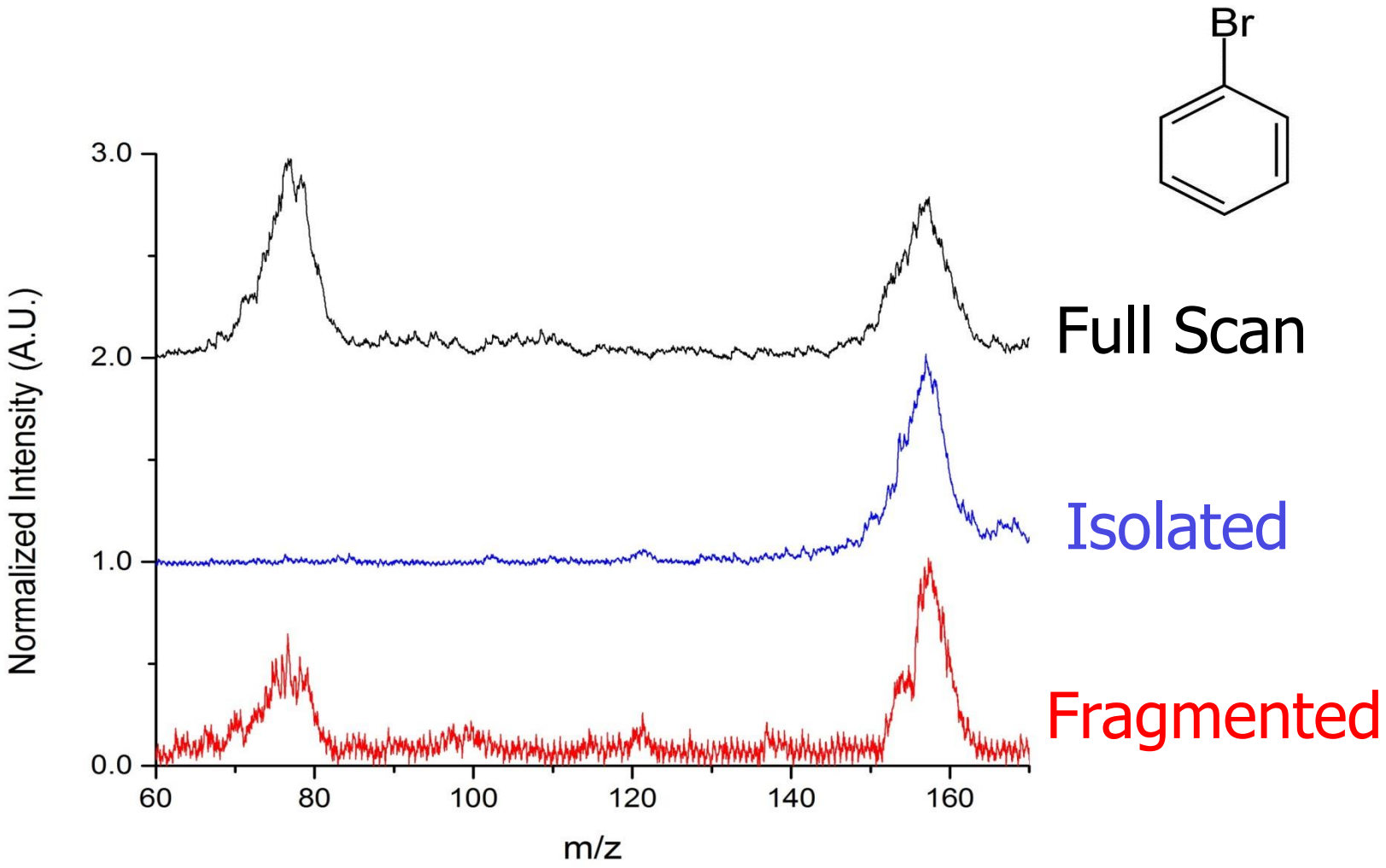
SWIFT-like Isolation



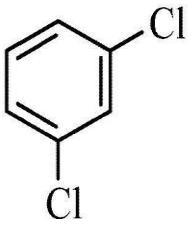


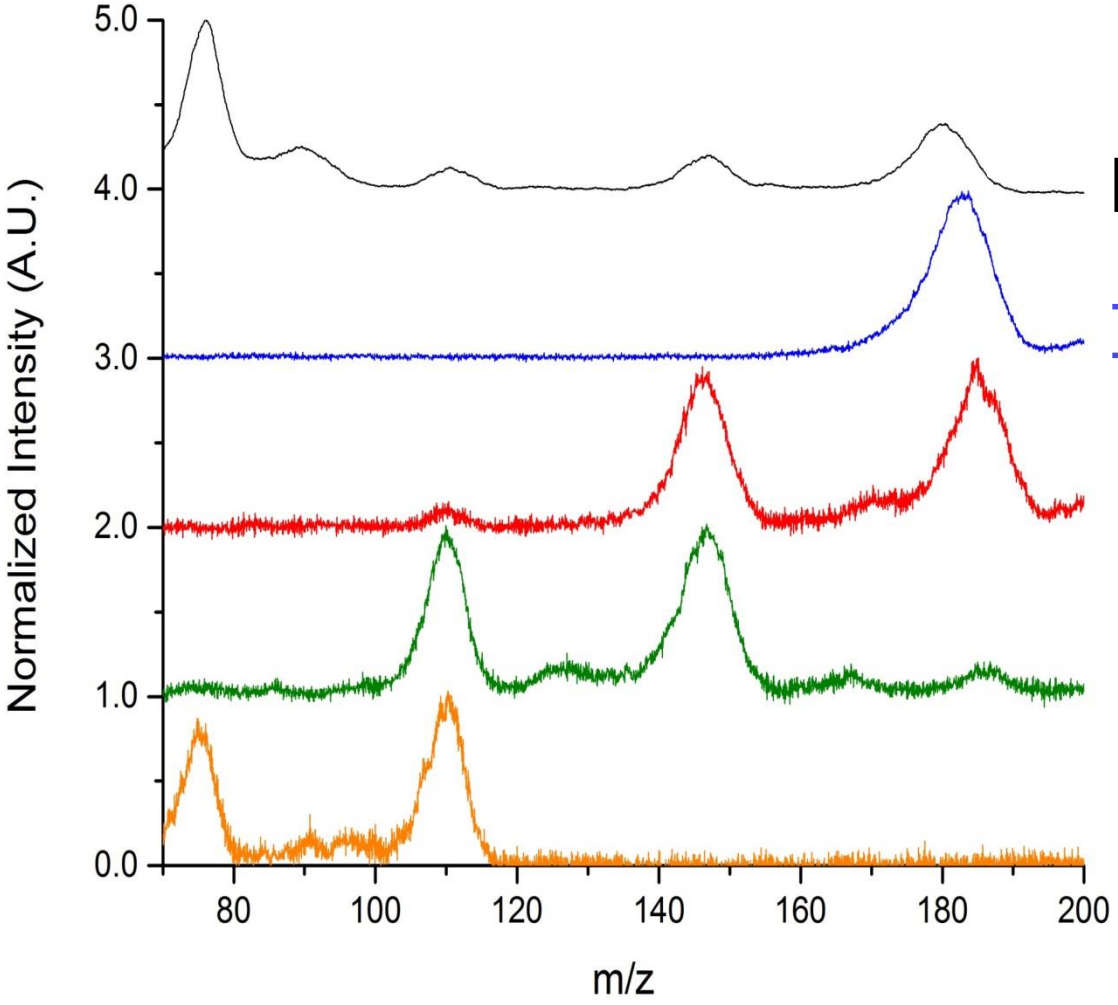
Isolation: 2.4, 4.8 MHz, 7.8 V, 0.6ms

Bromobenzene



1,3-Dichlorobenzene





Full Scan

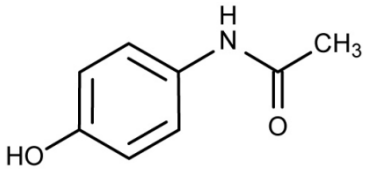
Isolated

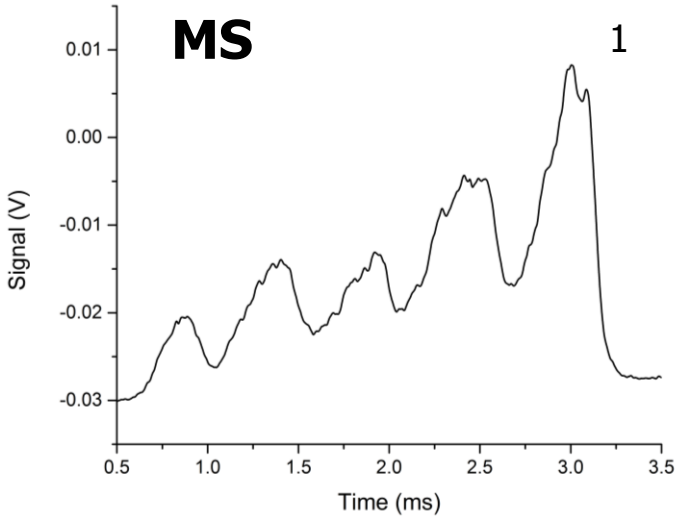
Fragmented

Fragmented

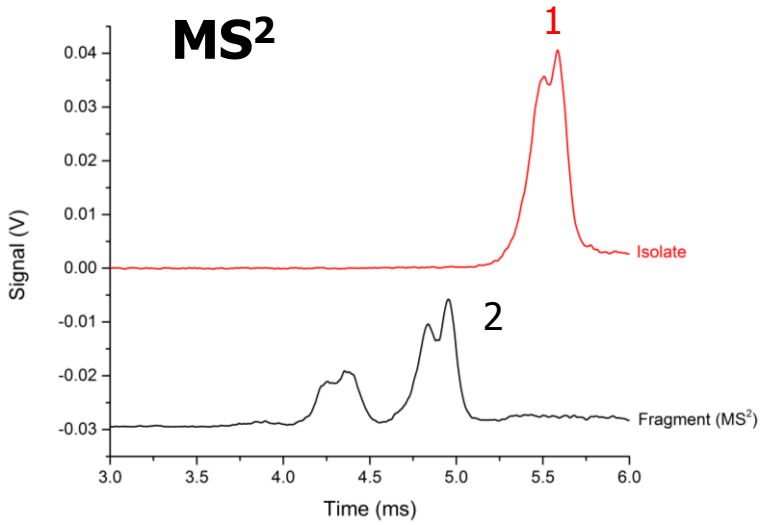
Fragmented

MS^4 with Acetaminophen

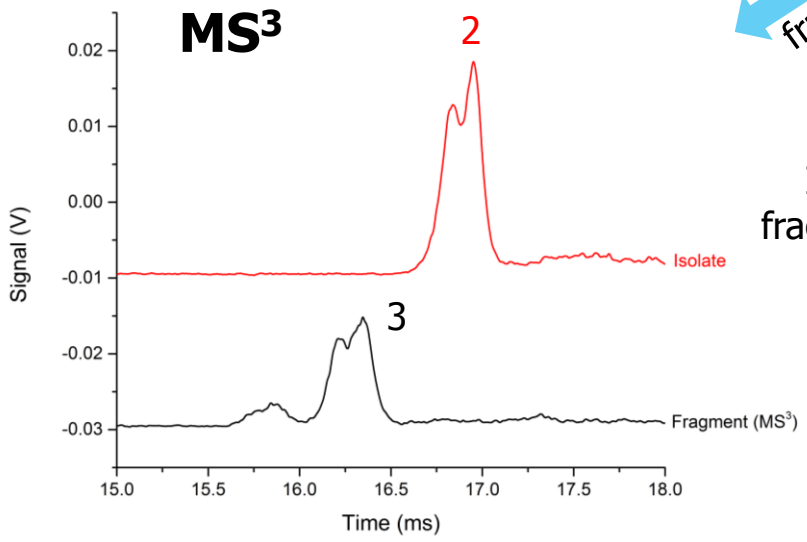




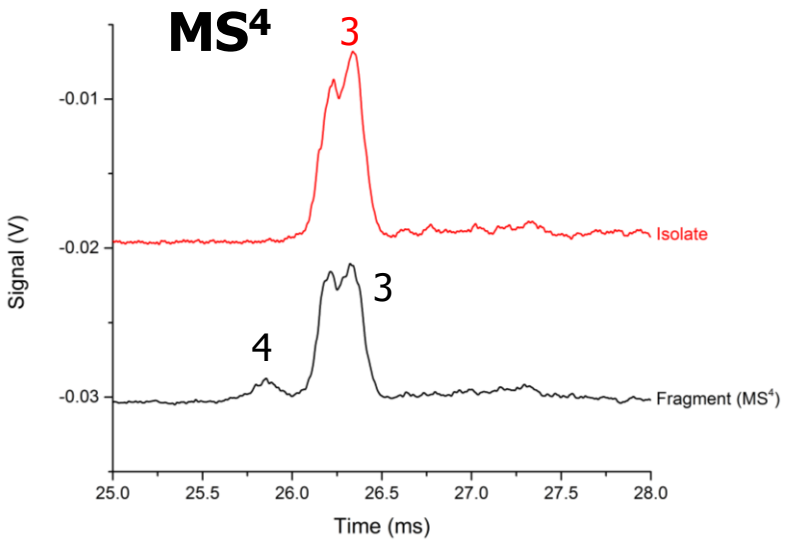
Isolate and fragment peak 1



Isolate and fragment peak 2



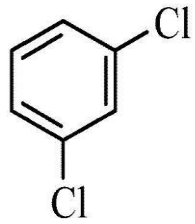
Isolate and fragment peak 3

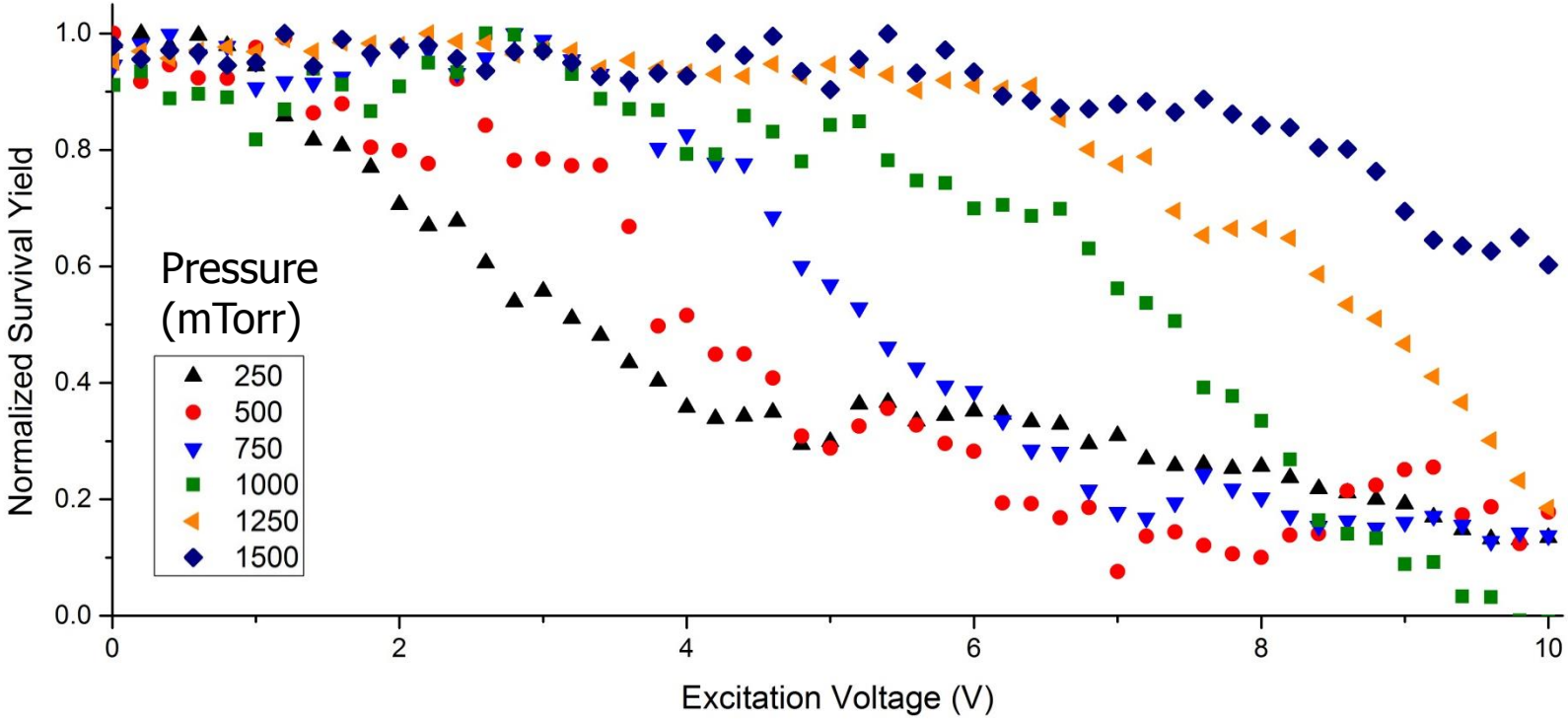


Excitation: 0.3 MHz, 8.3 V_{p-p}
1 Torr, ambient air, 10 µg/mL acetaminophen

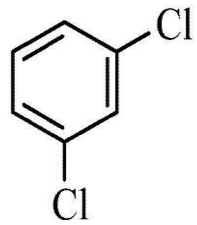
Thanks to Mac Gilliland

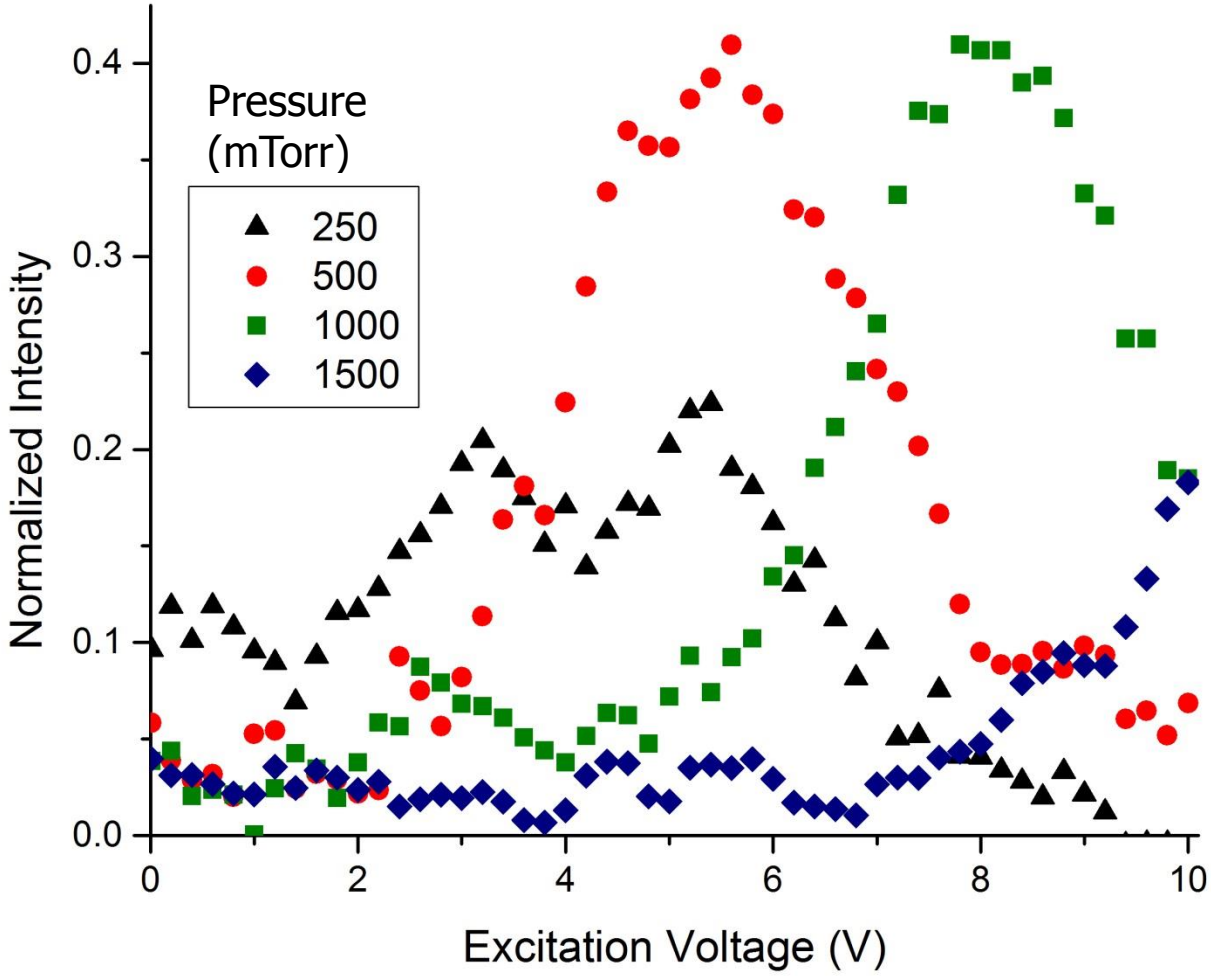
1,3 – Dichlorobenzene : 182 m/z Survival Yield Curves with Pressure



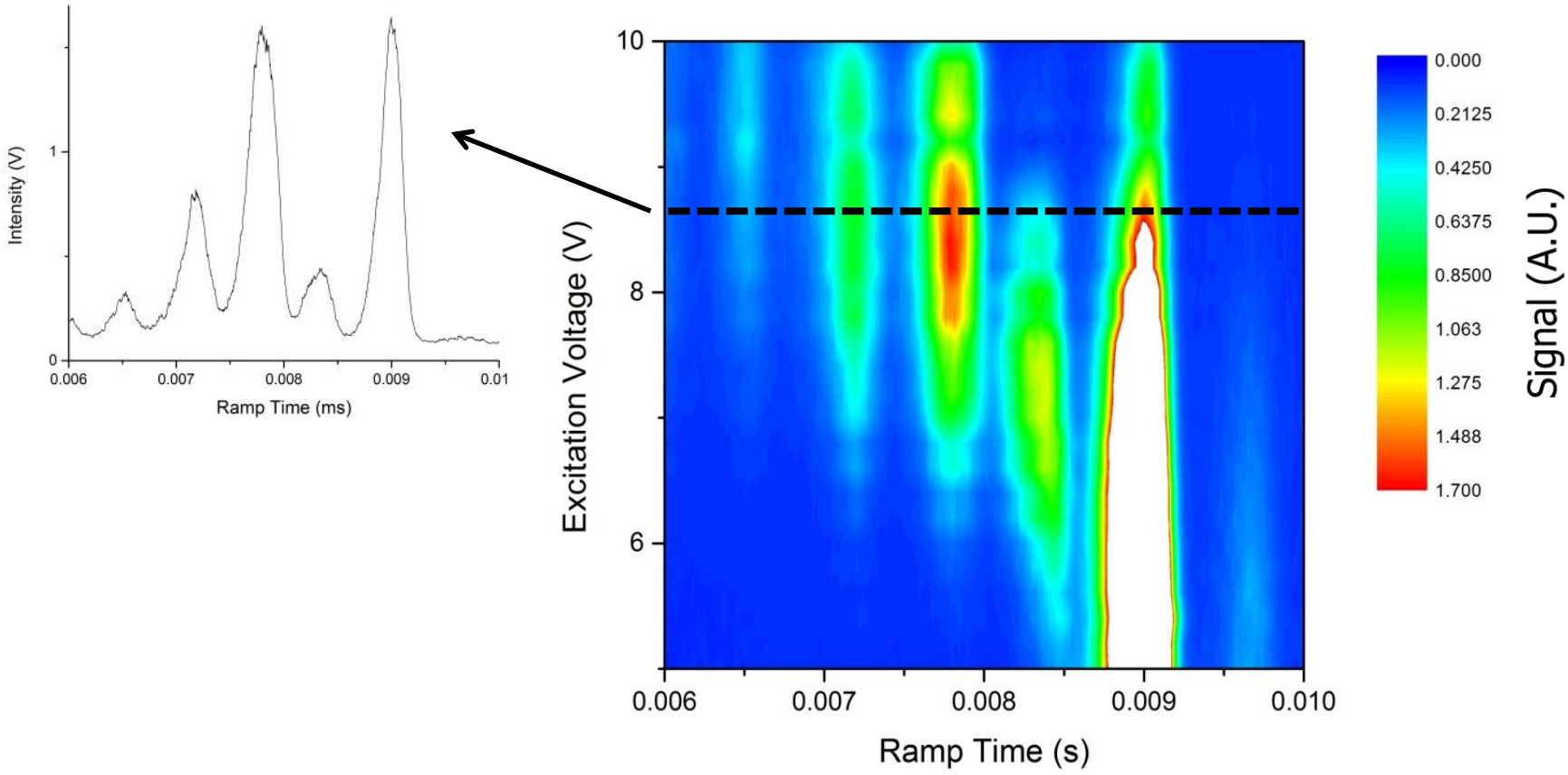


1,3 - Dichlorobenzene: 147 m/z Appearance Curves with Pressure



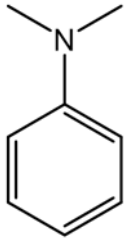


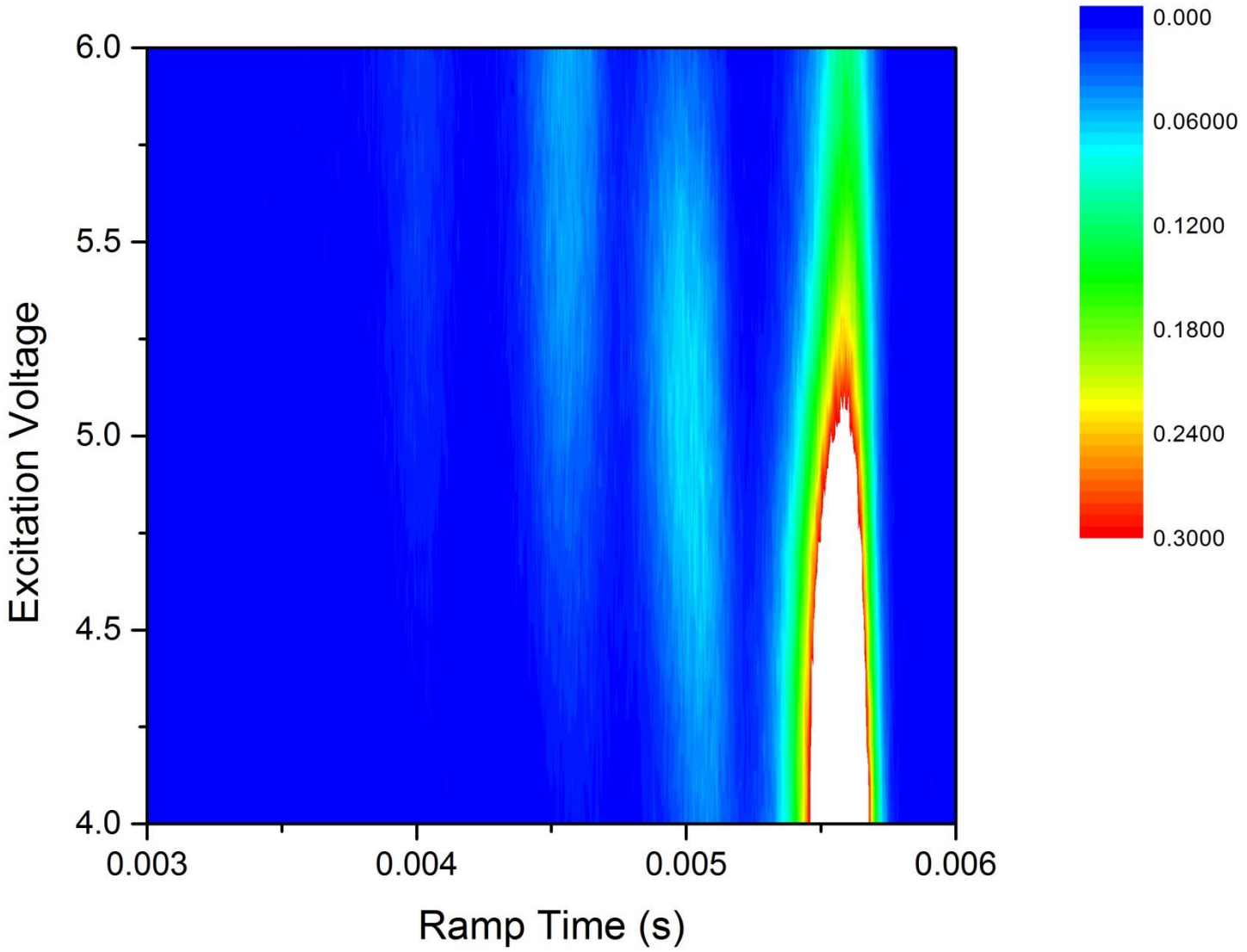
Tandem MS in False Color



11.23 MHz, 500 μm CIT
1.2 Torr Air
N,N-dimethylaniline

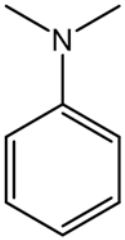
16 MHz Tandem MS

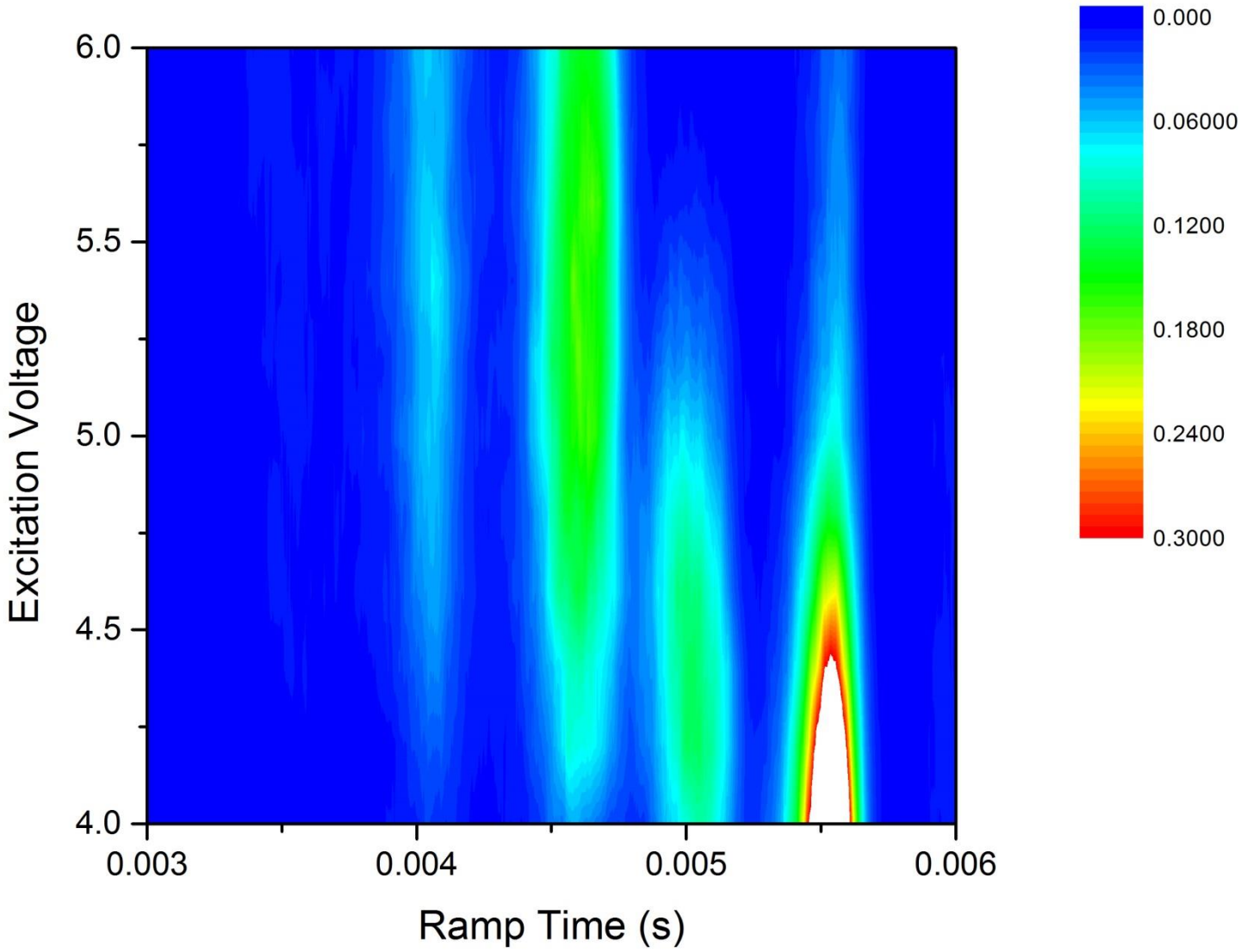




16.42 MHz

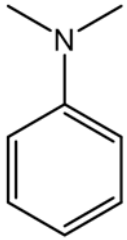
19 MHz Tandem MS

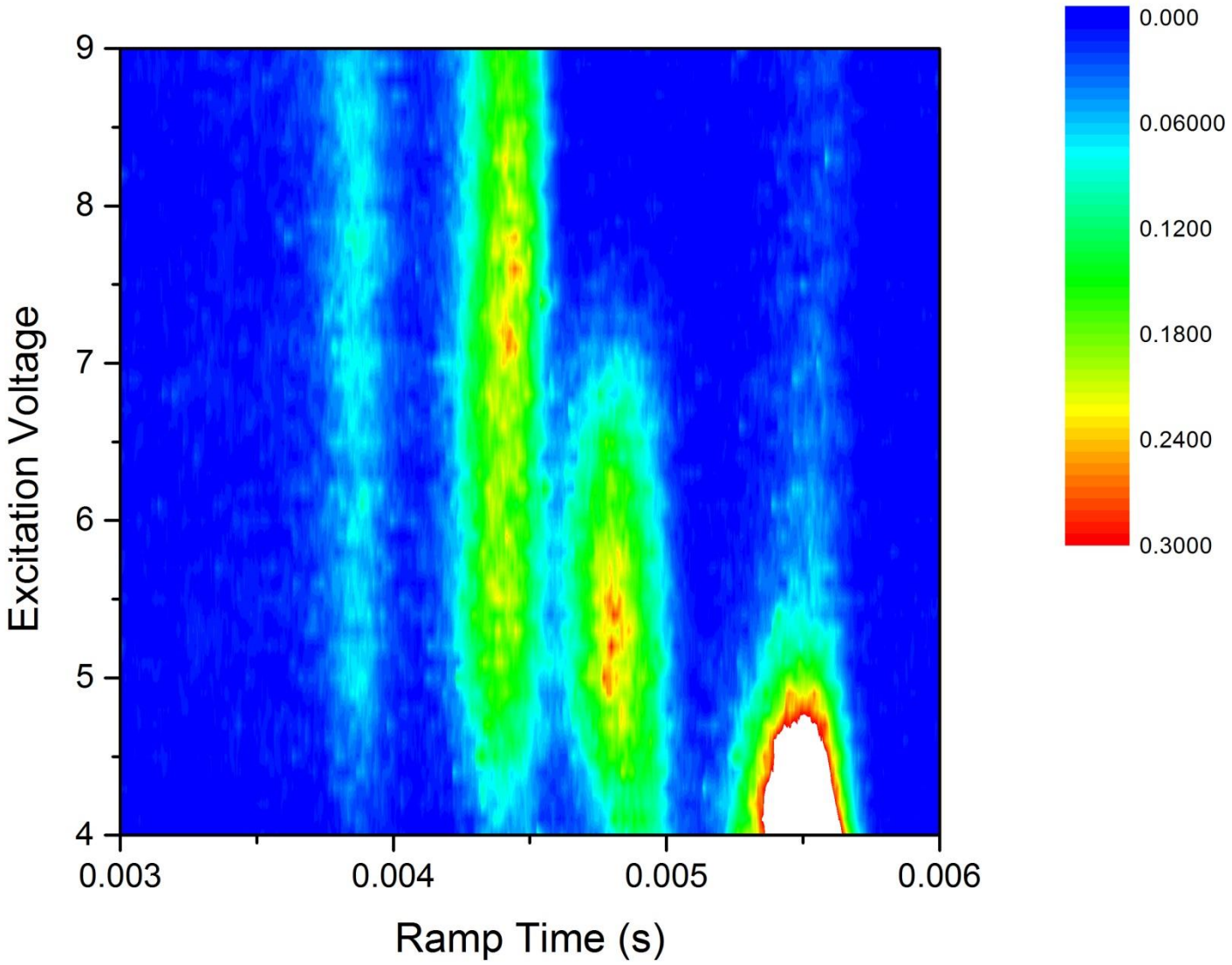




19.11 MHz

23 MHz Tandem MS





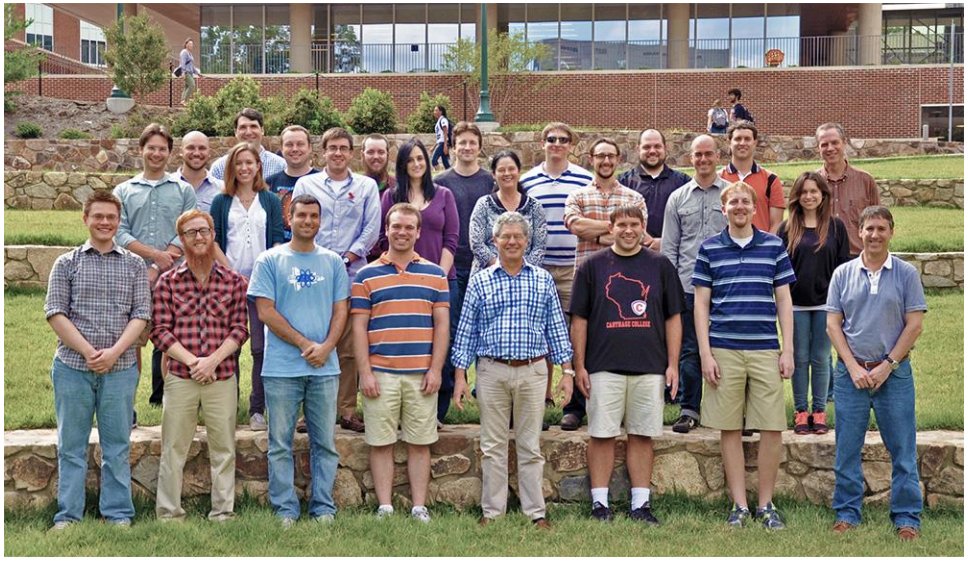
22.96 MHz

Future Directions

- Microscale Gas Chromatograph
  - Integrate with HPMS
  - Investigate LODs
- Tandem Mass Spectrometry
  - Improve Efficiency of Isolation/Fragmentation
  - Chief Targets:
    - Peptides, Proteins
    - CWA Simulants

Acknowledgments

- Dr. Ramsey
- J.P. Alarie
- Ramsey Group
- Micro Mass Spec Team
  - Kenion Blakeman
  - Russ Bornschein
  - Craig Cavanaugh
  - Dmitriy Chernookiy
  - Bruno Coupier
  - Zach Dyer
  - Mac Gililand
  - Rob Musser
  - Tina Stacy



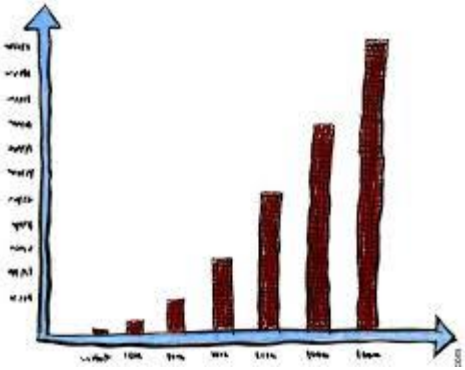
Funding

DTRA

Questions?

Discussions!

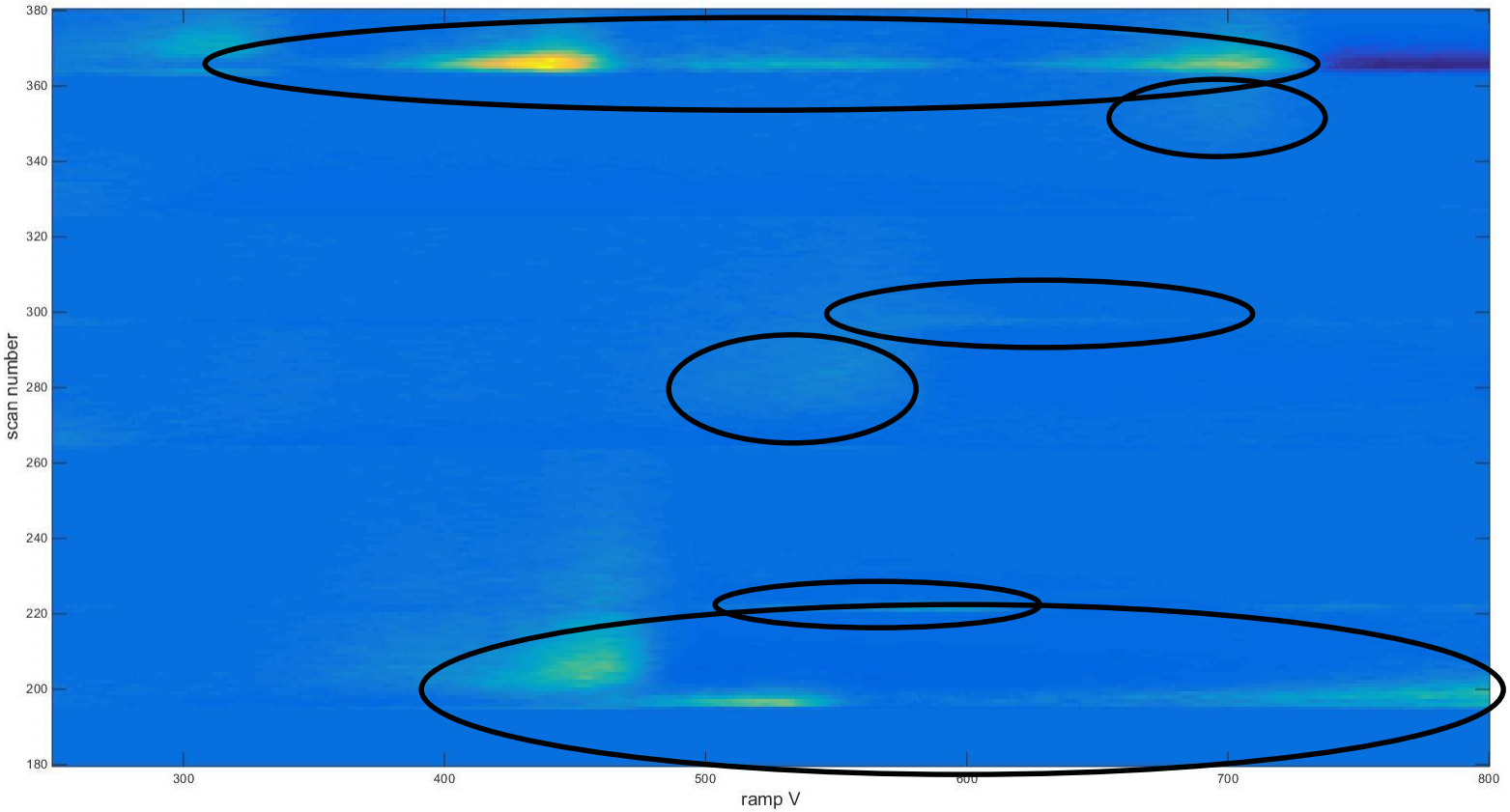
Analysis Paradigms



False Positives in Existing Technologies

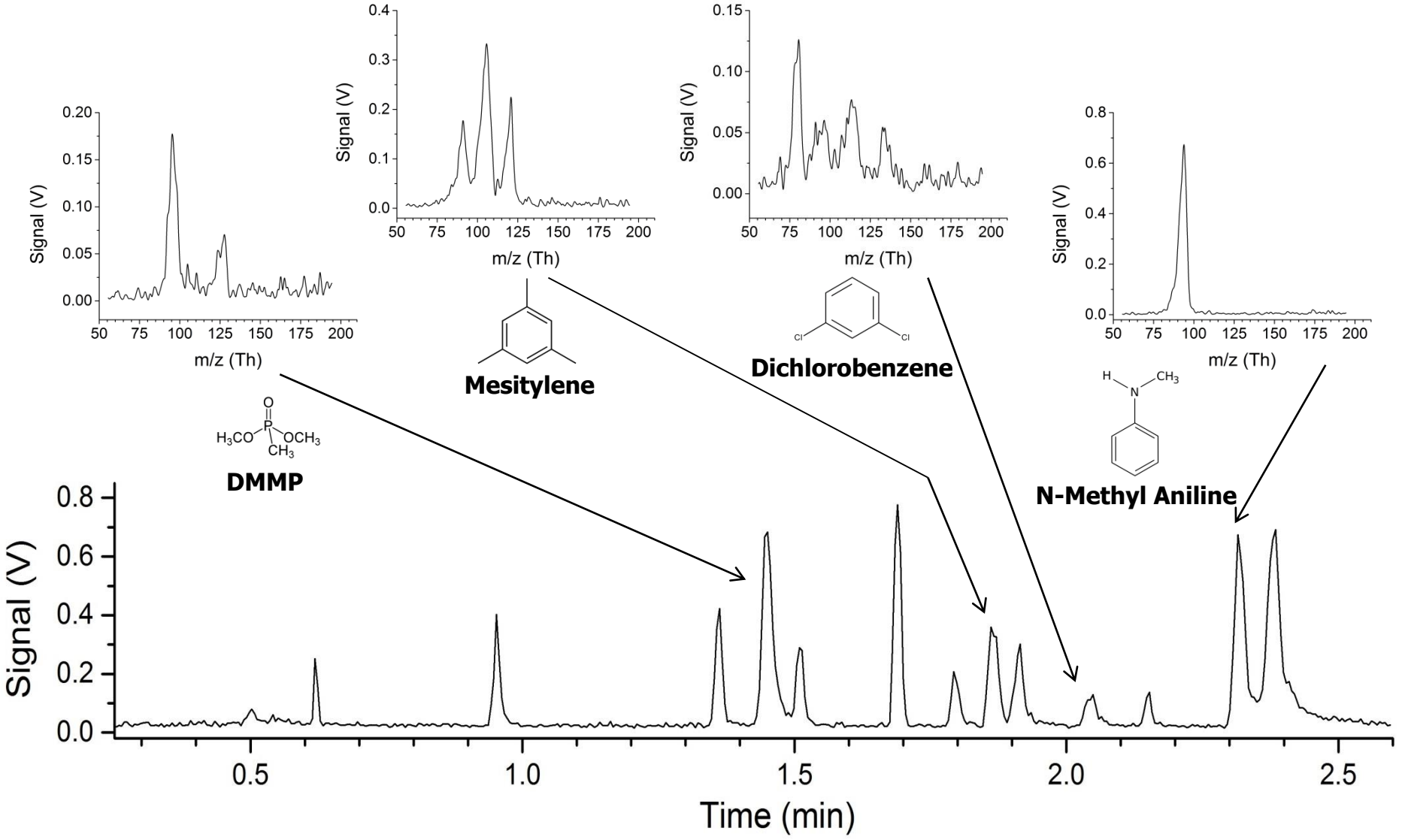
- IMS – Acetone, DMMP
- Detection paper – Organic solvents
- Flame photometric detector – DMMP
- Surface acoustic wavelength detector – Solvents

GC-HPMS of CWAS



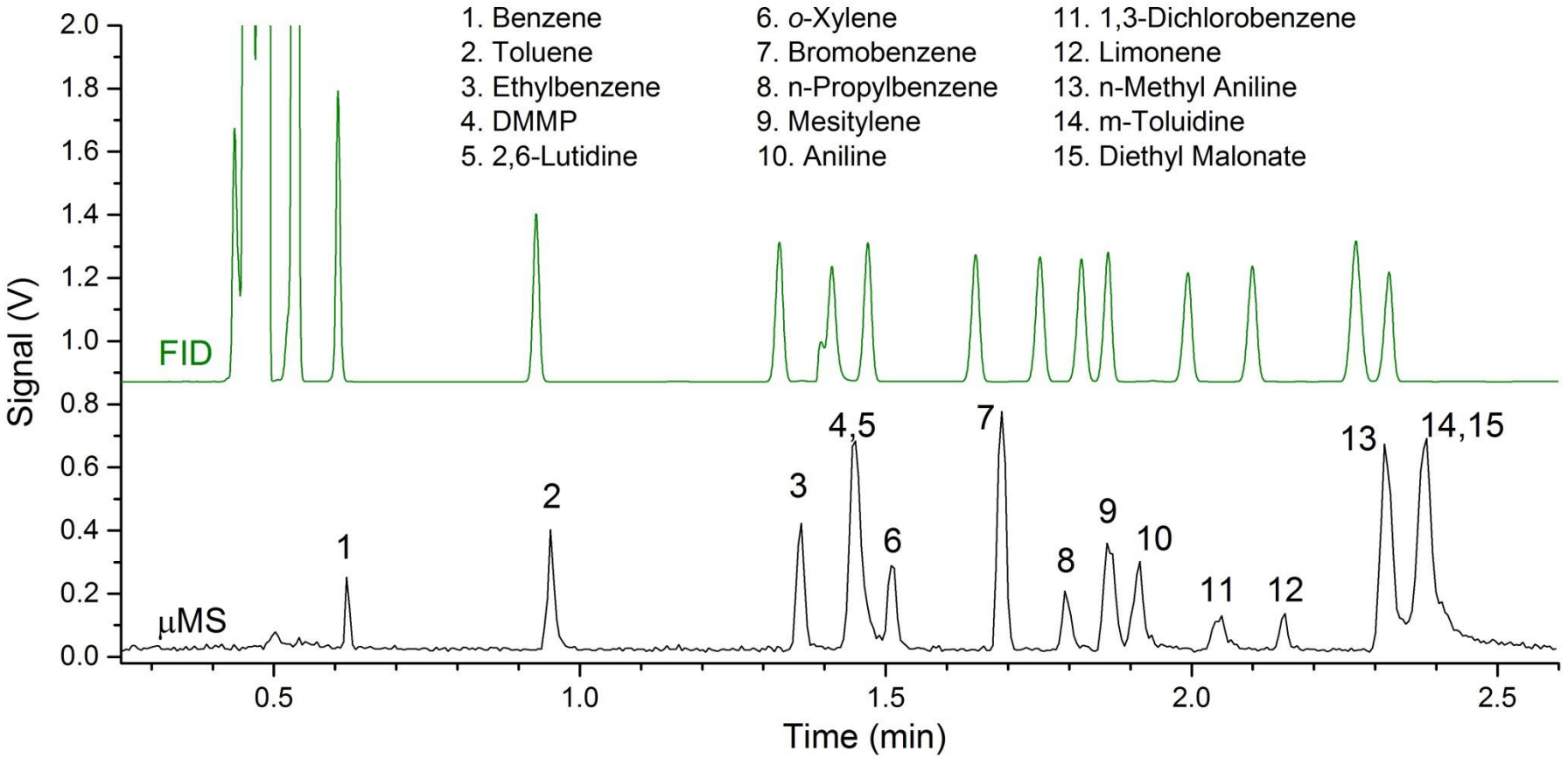
Electron Multiplier, Middle Frequency (6.00 MHz)
2 sccm Nitrogen,
1 µL CWAS1 Mixture (same as last slide)

GC-MS, Electron Multiplier Detection

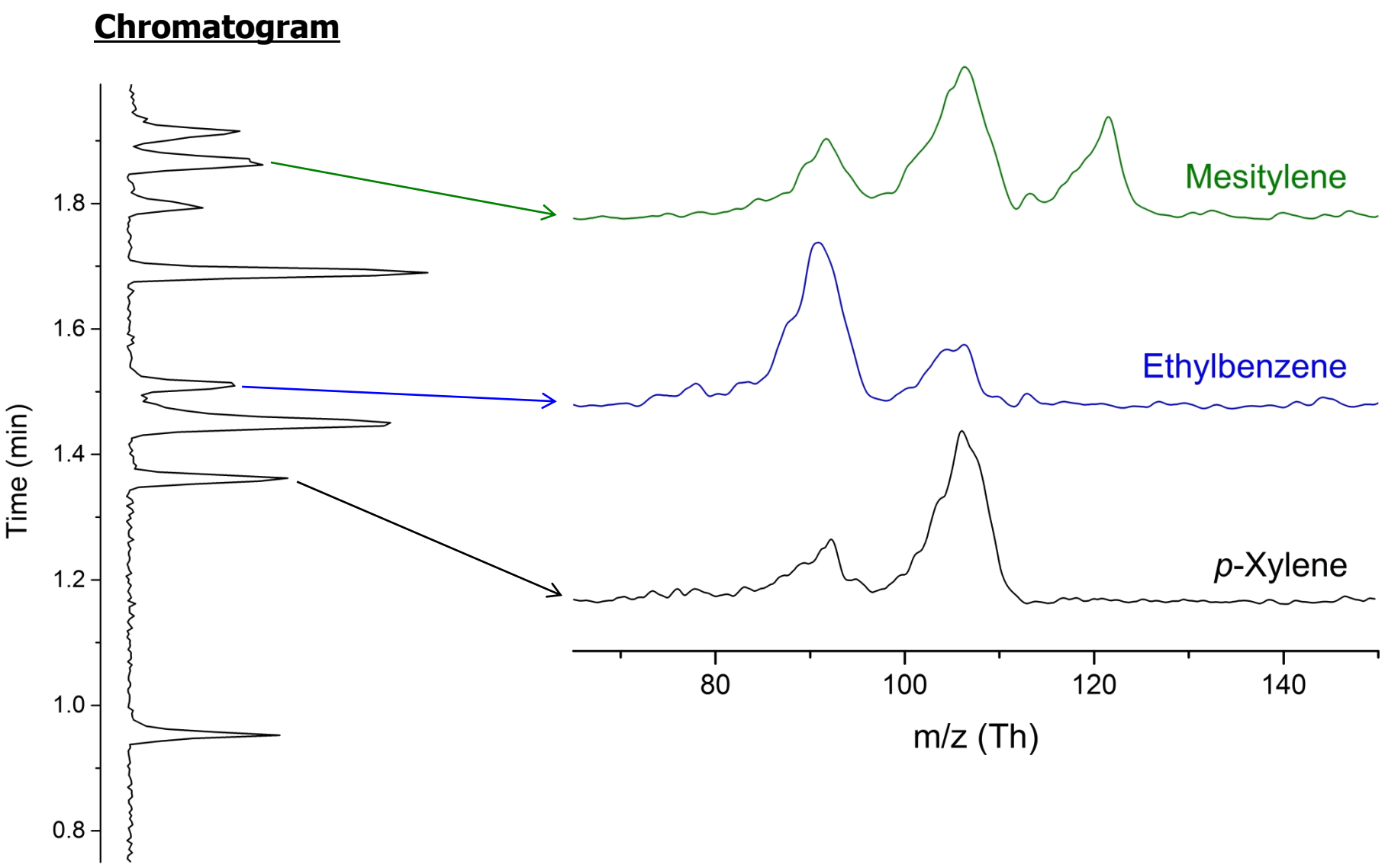


Courtesy Kevin Schultze

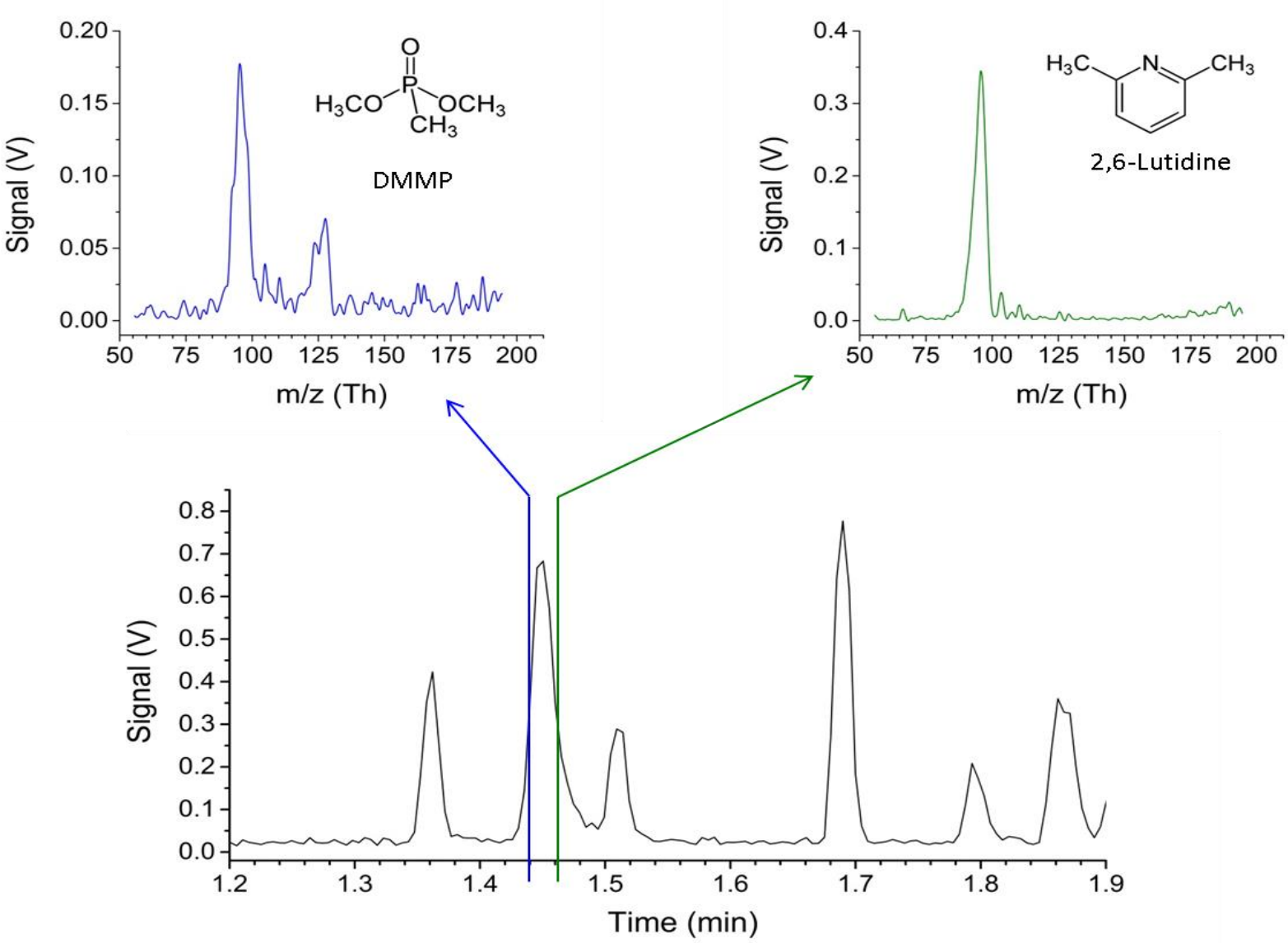
Commercial Detector Comparison



Separating Isobaric Compounds



Coeluting Peaks



Courtesy Kevin Schultze

Instrumentation Challenges

- Ionization
  - Pressure tolerance
  - Buffer gas compatibility
  - Power requirements

Filament

- CIT Operation
  - Traditional pressures ≈ 1 mTorr
  - Resolution loss with pressure
  - Fabrication

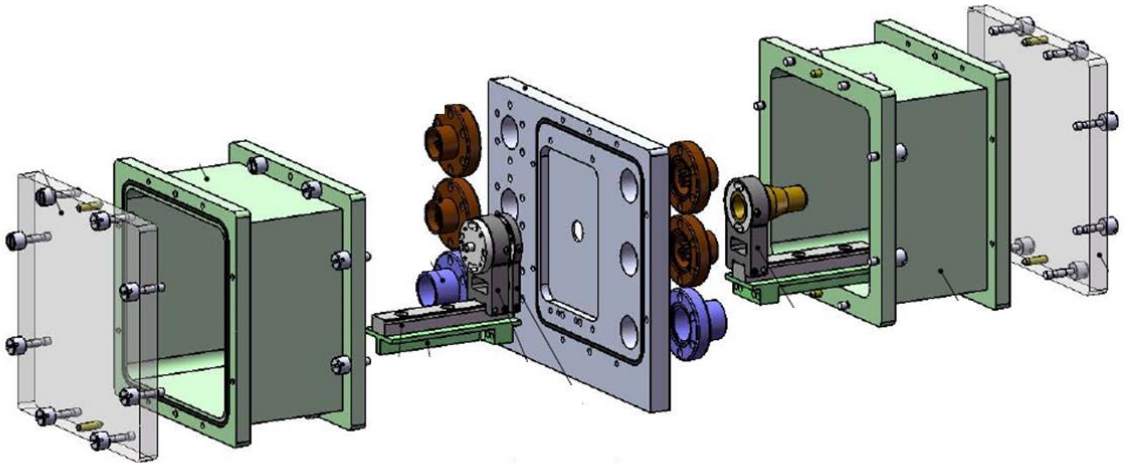
Hyperbolic Ion Trap

10 cm

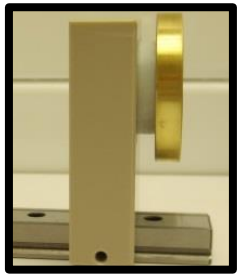
- Detection
  - Pressure tolerance
  - Sensitivity
  - Bandwidth

Electron Multiplier

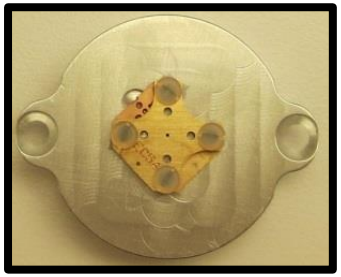
Differential Pressure Chamber



Ion Source **Mass Analyzer** **Detector**



Glow Discharge



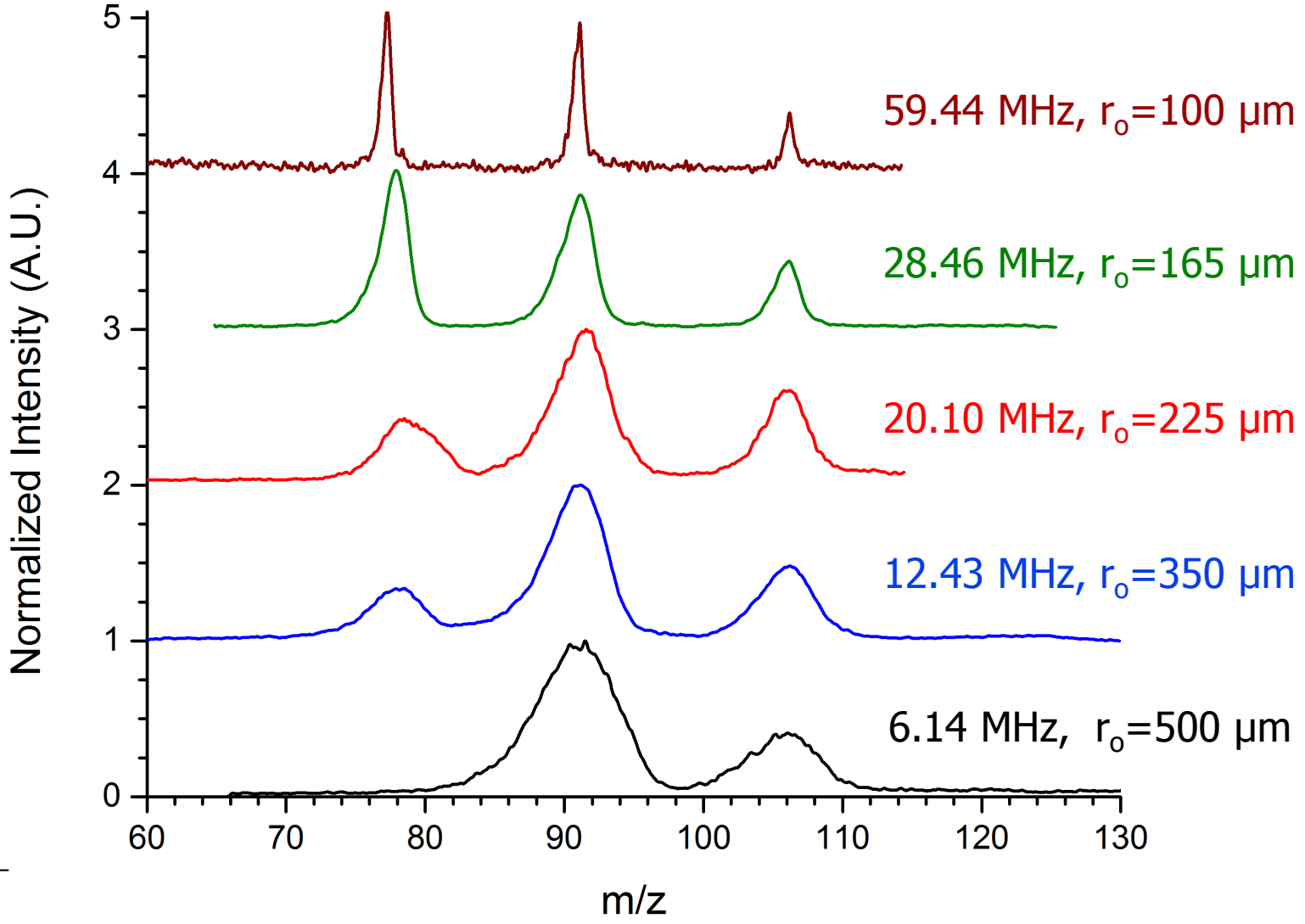
Microscale CIT

≈1 Torr

Electron Multiplier

≈10 mTorr

Trap Size and Frequency



p-Xylene, 1.0 Torr Ambient Air

Courtesy Kenion Blakeman

Buffer Gas

	He	N_2	O_2	Ar
Polarizability	0.205	1.740	1.581	1.641
Mass	4.002	28.01	32.00	39.95

MS of Complex Mixture

- Dynamic range
- Competitive ionization
- Overlapping peaks
- Chimeric interpretations

1,3-Dichlorobenzene: 112 Appearance Curve