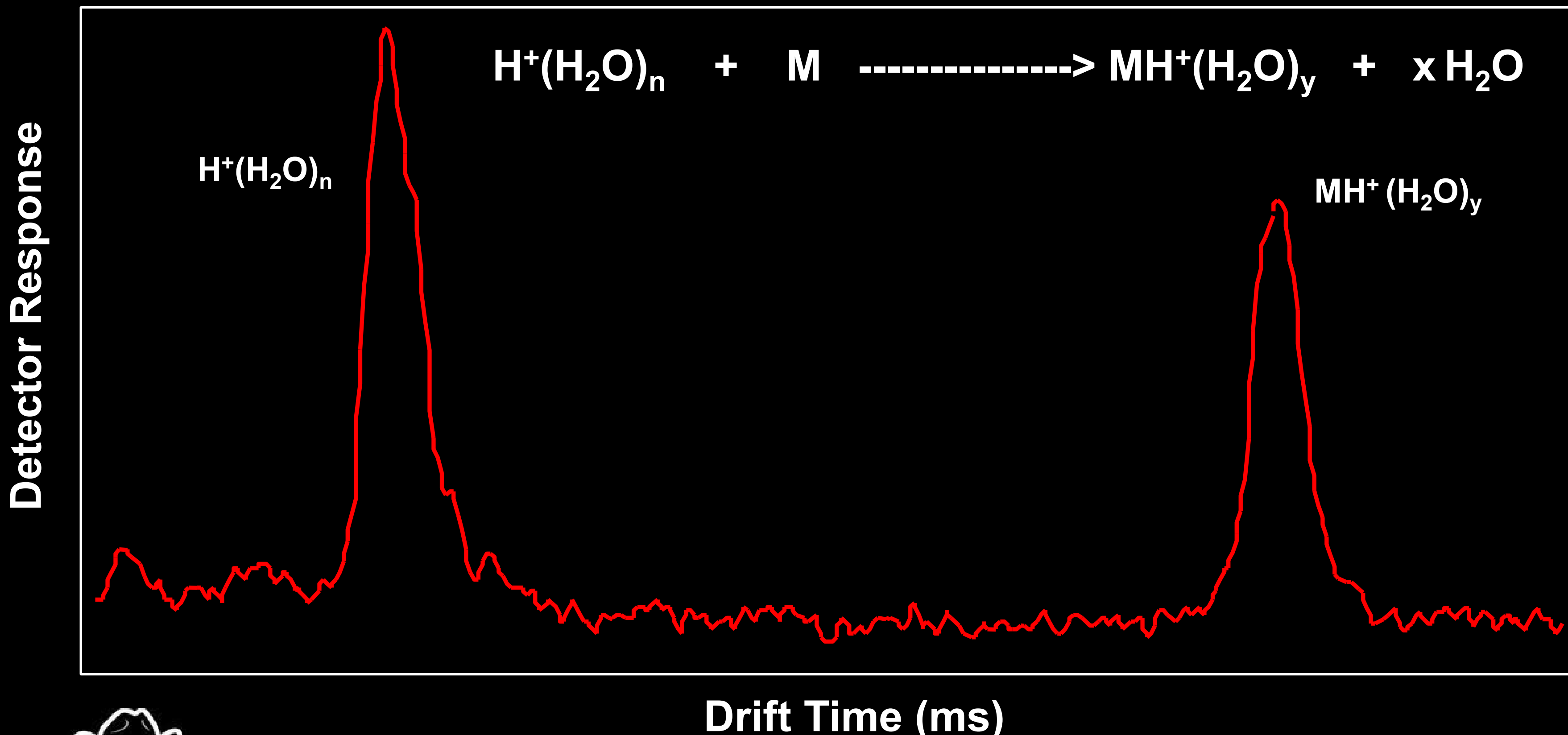
STRUCTURAL CONTENT IN FIELD INDUCED FRAGMENTATION (FIF) SPECTRA FROM TANDEM ION MOBILITY SPECTROMETRY TOWARD MOLECULAR IDENTIFICATION



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A SURPRISING RESULT (1999-2001)

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Analytica Chimica Acta 433 (2001) 53–70

ANALYTICA CHIMICA ACTA

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Chemical class information in ion mobility spectra at low and elevated temperatures

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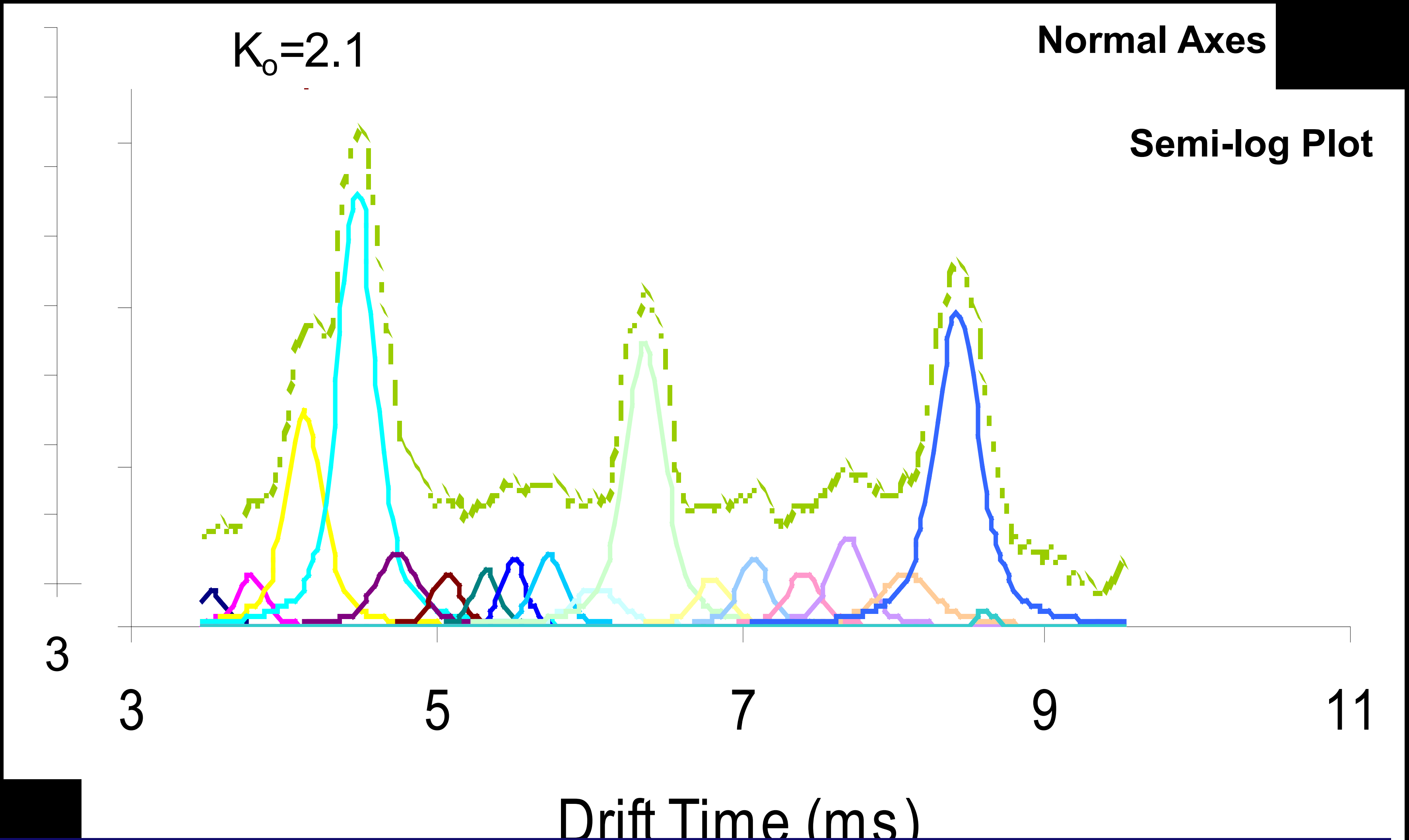
Abstract

Mobility spectra for organic compounds at temperatures of ~50°C and 175–250°C were catego
using back-propagation neural networks with the successful classification even of chemicals not f

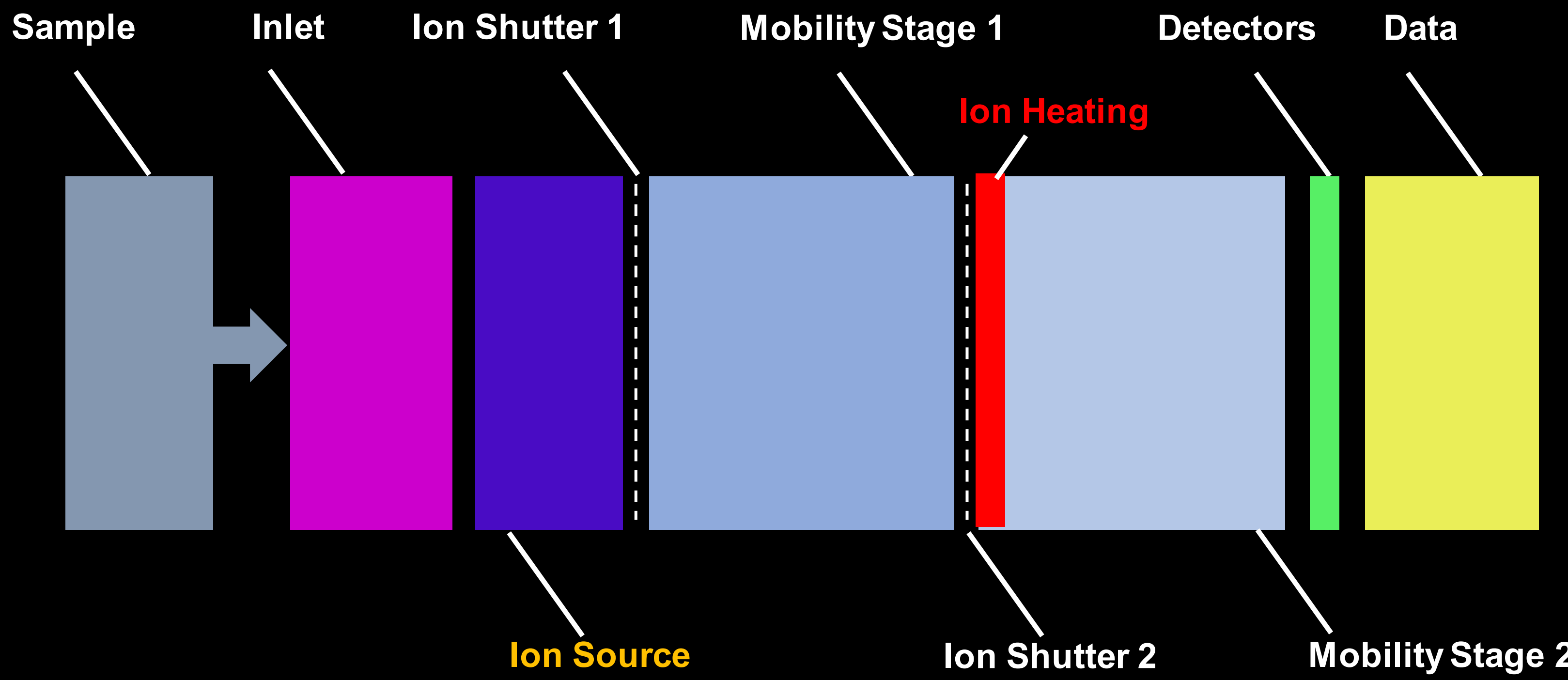
Somehow sufficient spectral detail was present for mobility spectra to be classify by Neural Nets into chemical families (>90%)

WE WERE DRAWN BY NEURAL NETWORK EXPERIMENTS TO SMALL IONS AT LOW ABUNDANCE



Were these ions "real" or only spectral artefacts?
How and where were they formed?

ADD REACTIVE STAGE AFTER SECOND ION SHUTTER

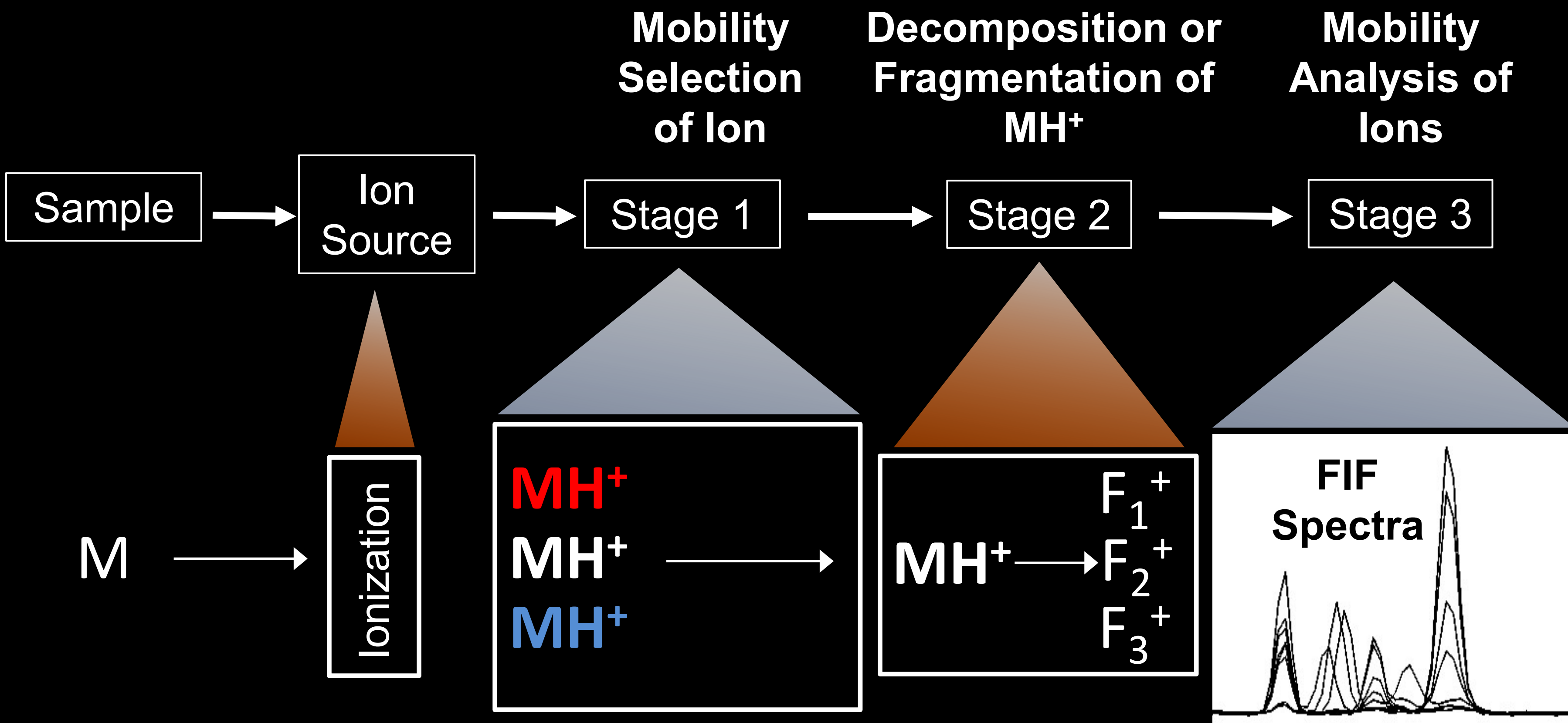


H. Shokri, M. Vuki, B.D. Gardner, H-C. Niu, U. Chiluwal, B.K. Gurung, D.B. Emery, G.A. Eiceman Reactive Tandem Ion Mobility Spectrometry with Electric Field Fragmentation of Alcohols at Ambient Pressure, *Analytical Chemistry* **2019**, 91(9), 6281-6287.

U. Chiluwal, G. Lee, Y. Rajapakse, T. Willy, S. Lukow, H. Schmidt, and G.A. Eiceman, Tandem Ion Mobility Spectrometry at Ambient Pressure and Field Fragmentation of Mobility Selected Ions of Explosives and Interferences, *Analyst* **2019**,**144**, 2052-2061

Ions undergo decomposition in symmetric waveforms
2 to 4 MHz with fields of 10 kV to 30 kV/cm (100 to ~250 Td)

FIELD INDUCED FRAGMENTATION (FIF) SPECTRA AND TANDEM MOBILITY METHODS AT AMBIENT PRESS.



Concept of FIF parallels Collision Induced Dissociation in Tandem MS

FUTURE DIRECTIONS (2019)

LOW COST "Tandem MS"

Tandem IMS | Low cost MS

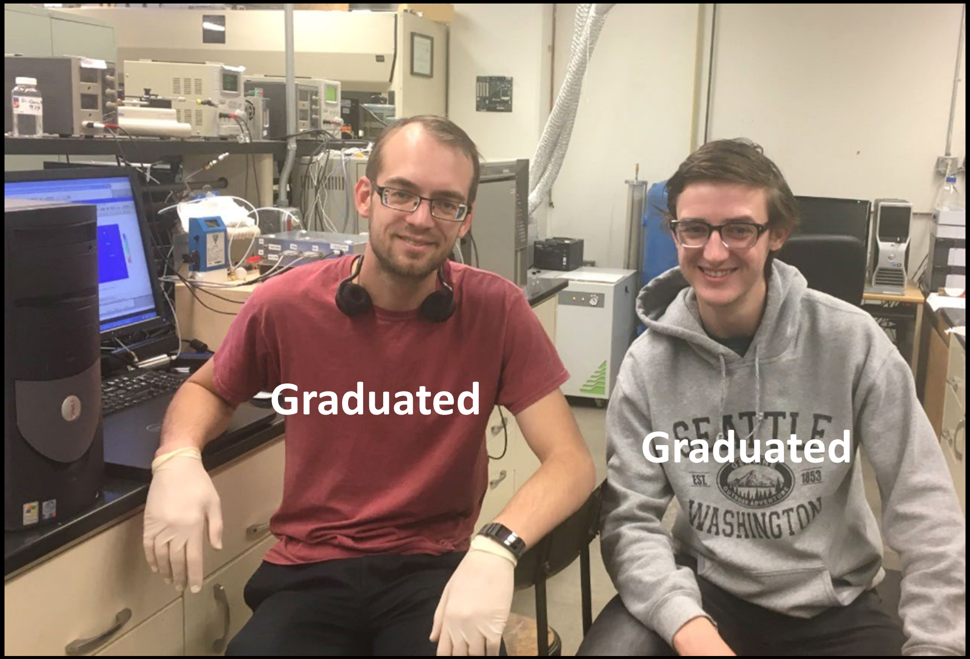
Tandem IMS | Low cost MS

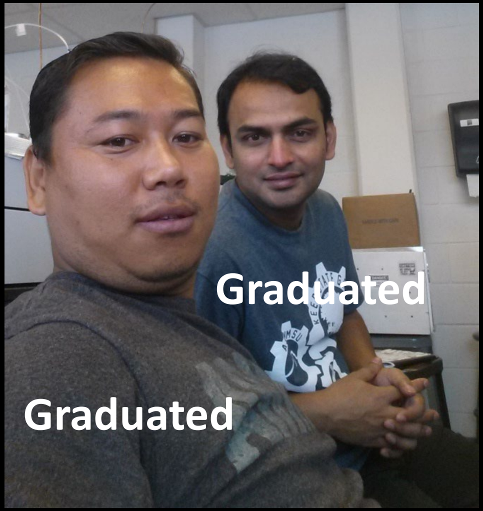
ADVANCES IN SCIENCE & TECH & PRACTICE

- Fragmentation Principles: Structures, mechanism, boundary conditions
- Algorithm or Neural Net for Molecular Identification?
- Advance TRL much
- Applications and compelling uses to initial commercial development

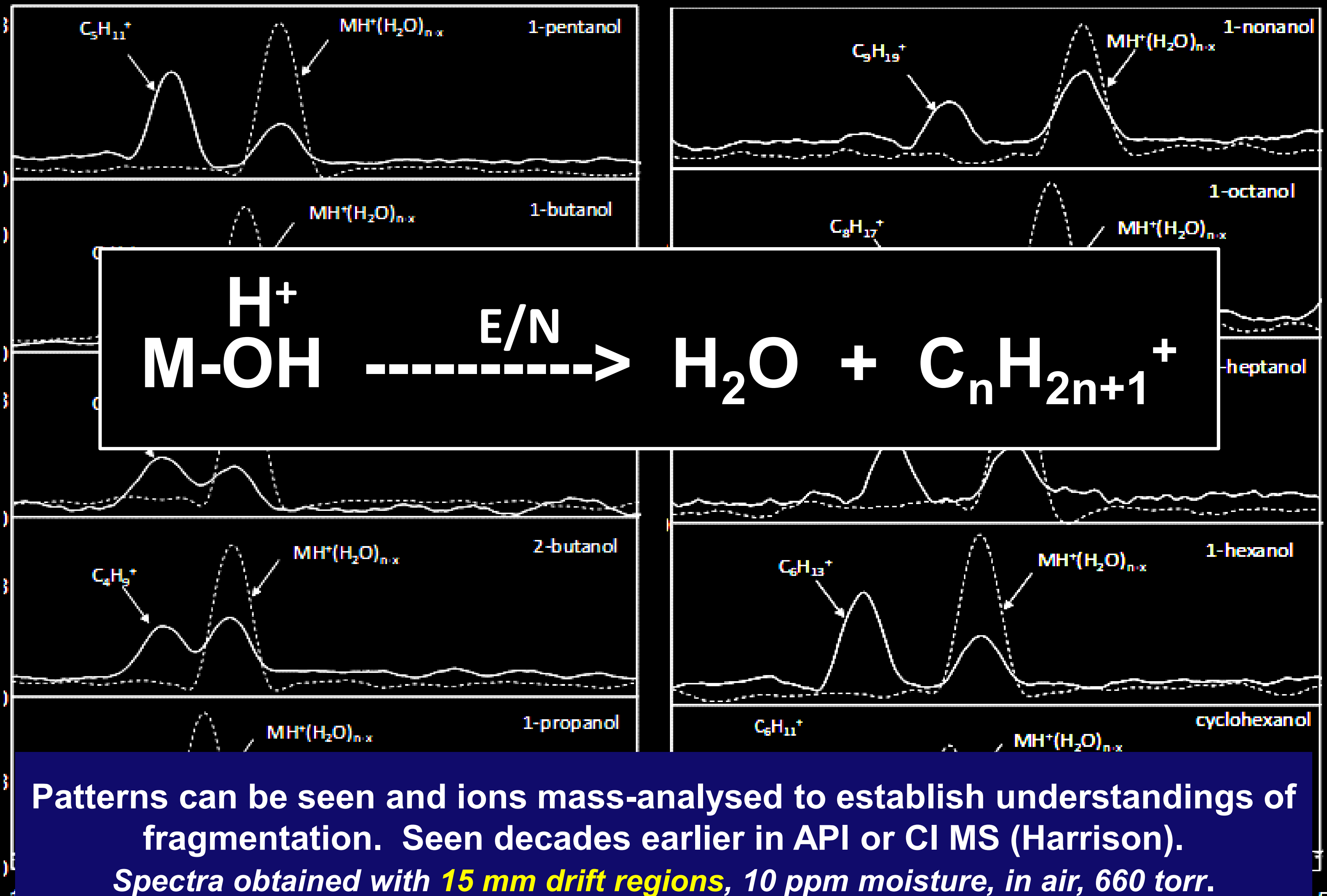
What have we learned since 2019?

STUDIES ON ION FRAGMENTATION (2016-2021)





FIF SPECTA FROM $MH^+(H_2O)_n$ OF n-ALCOHOLS



$$\overset{H^+}{\text{M-OH}} \xrightarrow{E/N} H_2O + C_nH_{2n+1}^+$$

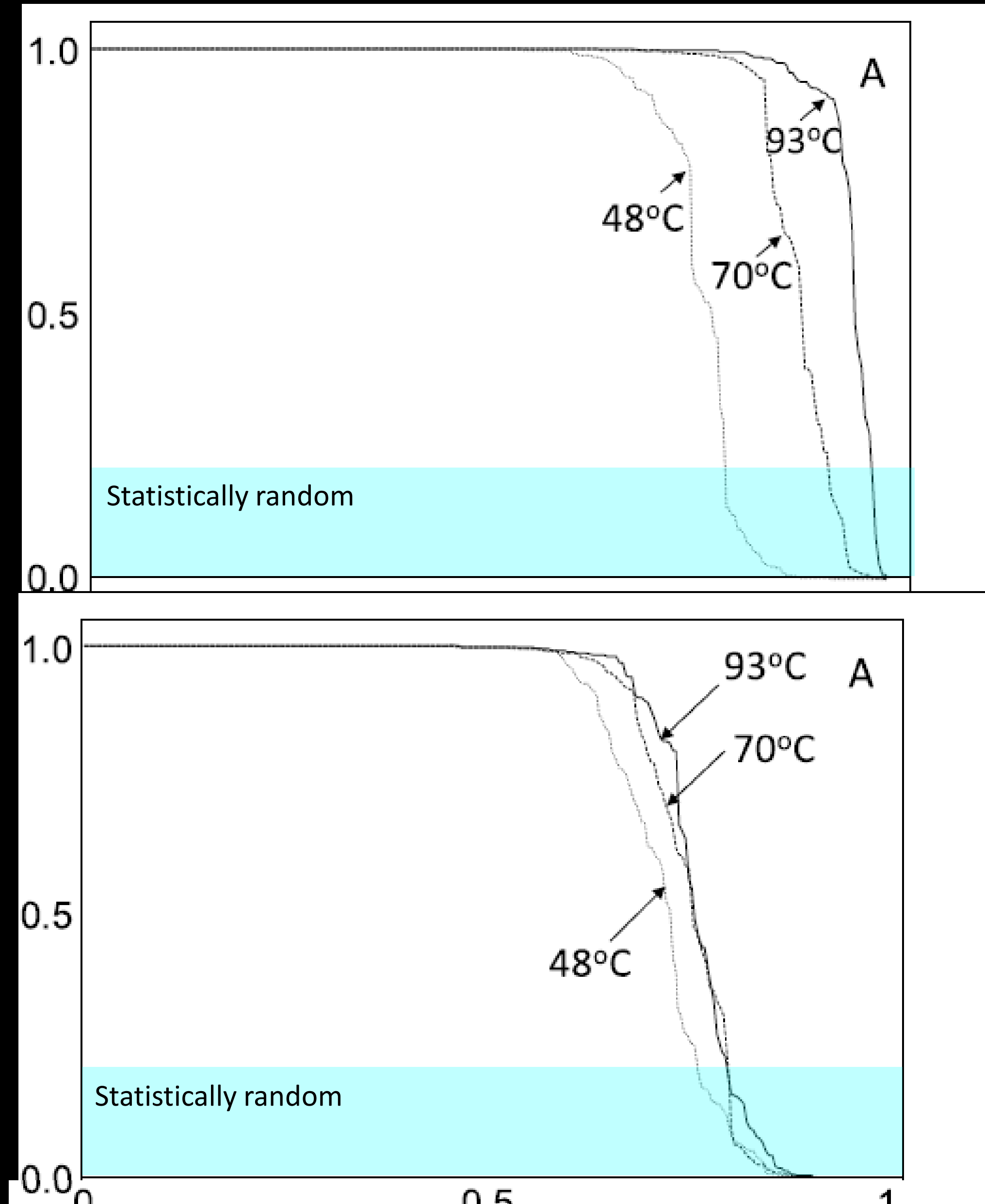
Patterns can be seen and ions mass-analysed to establish understandings of fragmentation. Seen decades earlier in API or CI MS (Harrison).

Spectra obtained with 15 mm drift regions, 10 ppm moisture, in air, 660 torr.

FAMILIAR COMPOUNDS

FIF Spectra

$MH^+(H_2O)_n$ only

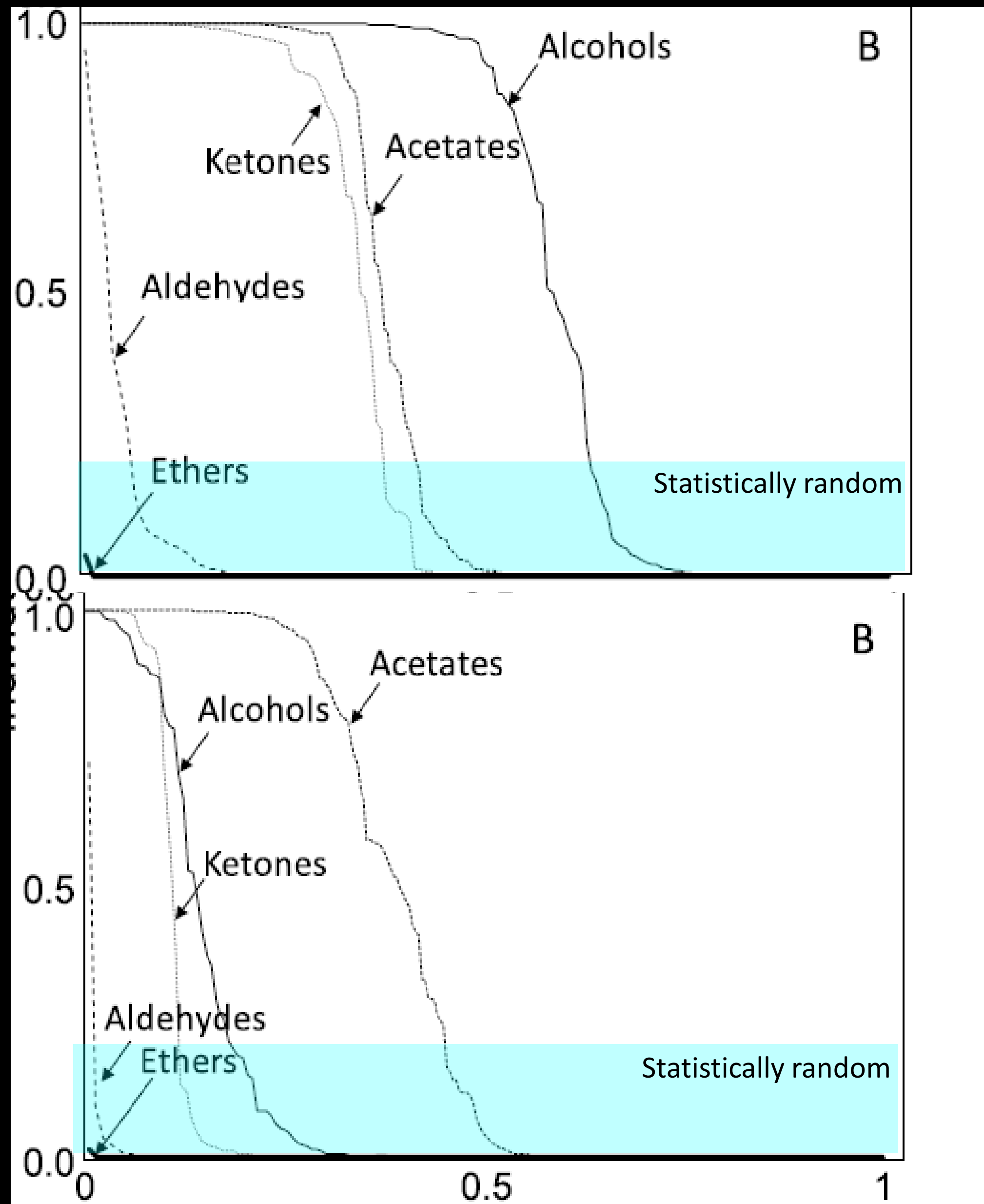


Ion energy (heat or field) matters. Even low E/N aids classification rates.
How to explain the Nnet performance? Fragment ion?

UNFAMILIAR COMPOUNDS

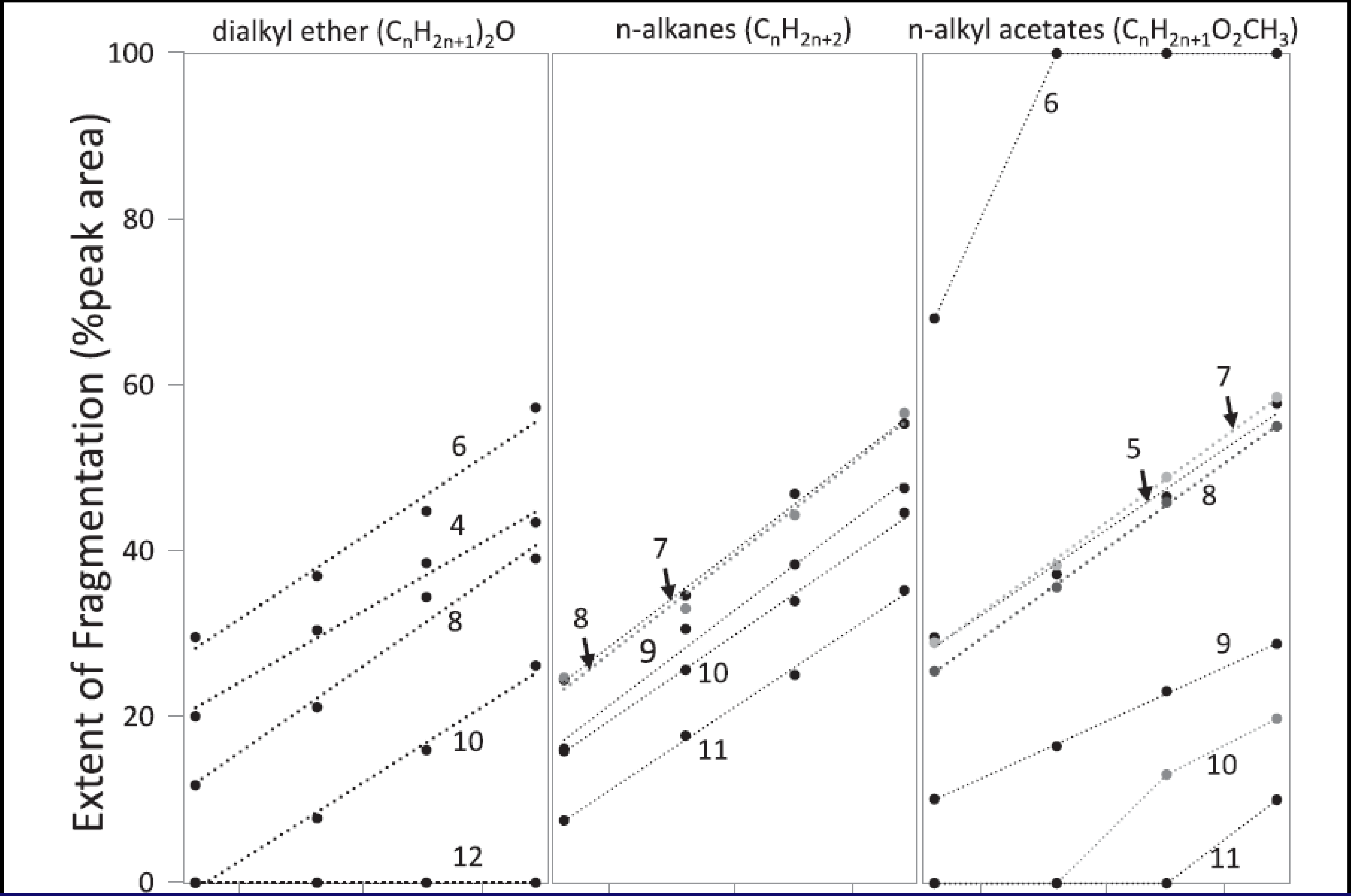
FIF Spectra

$MH^+(H_2O)_n$ only



Not all chemical classes are equal with Unfamiliar Compounds

FRAGMENTATION GOES WITH E/N "LINEARLY"



Fragmentation should go as E^2 over large range….. We are accessing a very narrow range of energies

ION ENERGIES IN "STRONG" ELECTRIC FIELDS

Lab Frame of Reference

$$KE_{ion} = 3/2\, k_B T + 1/2\, m_{ion} v_d^2 + 1/2\, m_b v_d^2$$

Thermal *Field Energy* *Neutrals collisions*

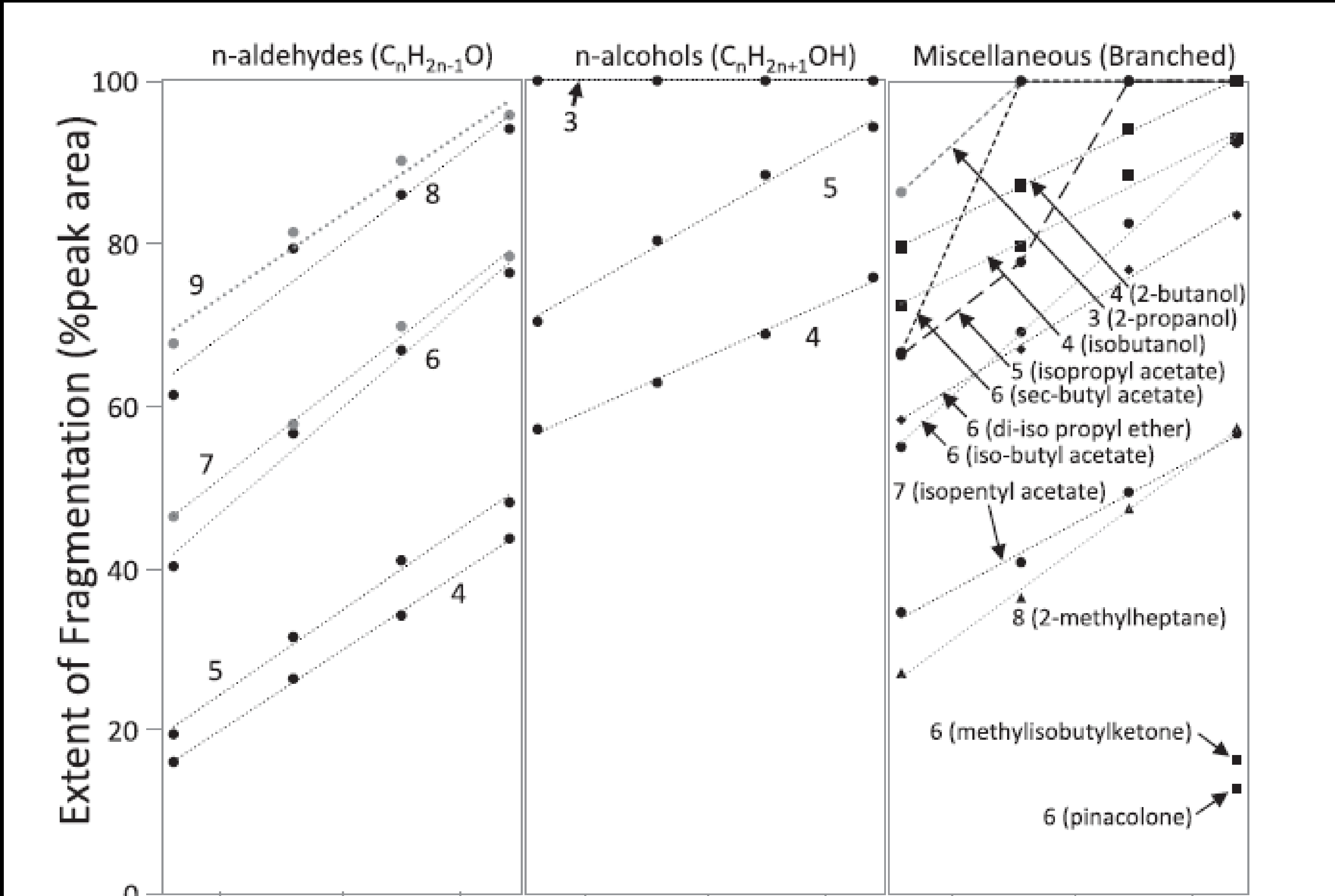
Center of Mass of Colliding System

$$KE_{\mathrm{CM}} = \frac{m_{\mathrm{n}}}{m_{\mathrm{ion}} + m_{\mathrm{n}}} \left(KE_{\mathrm{ion}} - \frac{3}{2} k_{\mathrm{B}} T \right) + \frac{3}{2} k_{\mathrm{B}} T$$

Andrew Ellis and Christopher Mayhew, Proton Transfer Mass Spectrometry, 2014, John Wiley and Son, pp72-73

D.J.Douglas, Applications of Collision Dynamics in Quadrupole Mass Spectrometry, JASMS 1998, 9 (2), 101-113

FRAGMENTATION CAN BE EXTENSIVE



We wish to reach 250 Td (ca. 30kV/cm) without arcs and sparks……we need new structures or principles needed.

WHAT DO NEURAL NET GET US WITH FIF SPECTRA?

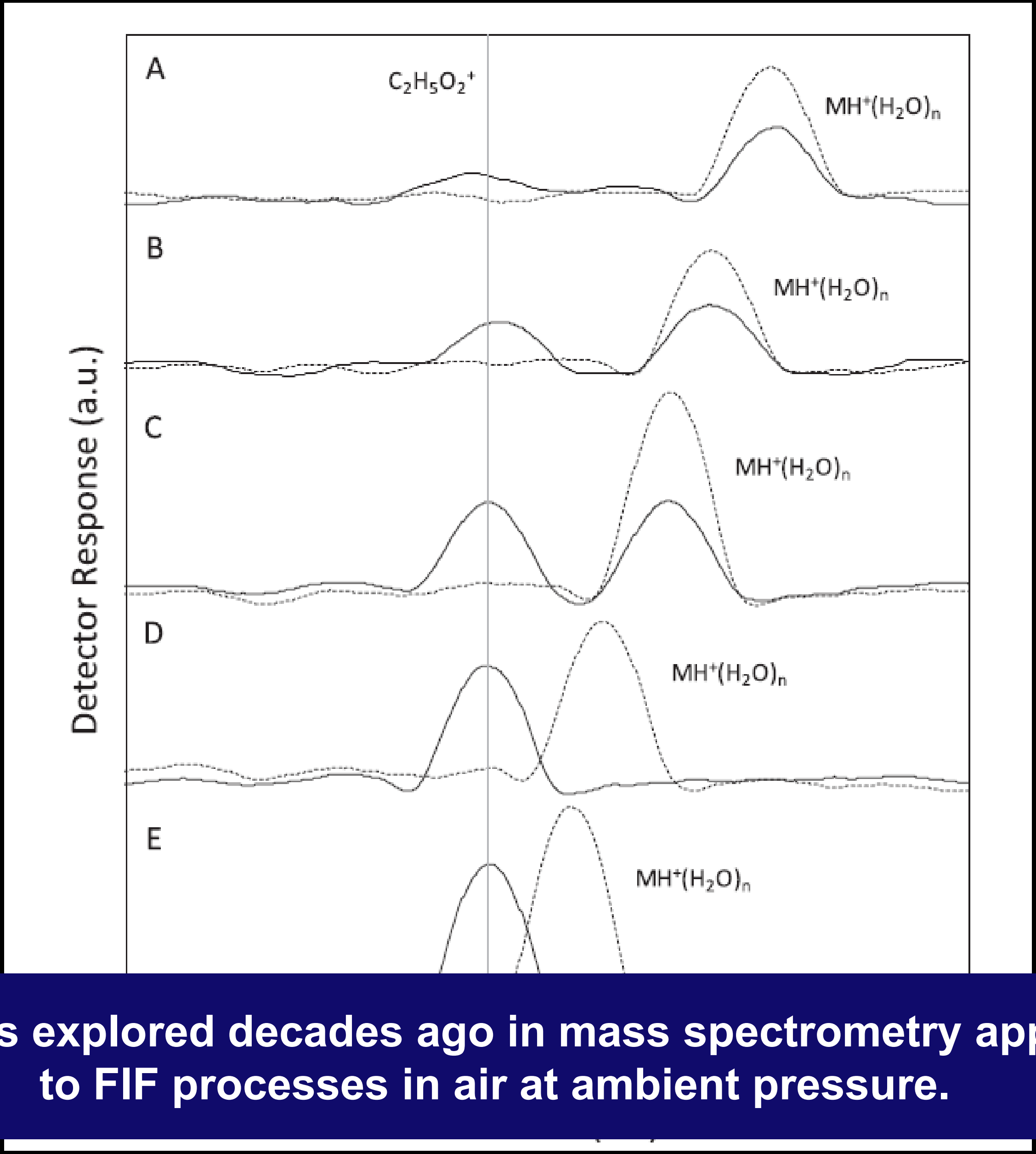
Acetates		
propyl acetate	1.000	1.000
isopropyl acetate	1.000	1.000
butyl acetate	1.000	1.000
isobutyl acetate	1.000	0.000
sec-butyl acetate	1.000	1.000
pentyl acetate	1.000	0.900
isopentyl acetate	1.000	0.632
hexyl acetate	1.000	0.000
heptyl acetate	1.000	0.000
octyl acetate	1.000	0.000
nonyl acetate	0.917	0.000
AVERAGE	0.992	0.503
Alcohols		
2-methyl-1-propanol	1.000	1.000
1-propanol	1.000	0.129
2-propanol	0.960	0.120
1-butanol	1.000	1.000
2-butanol	1.000	1.000
1-pentanol	1.000	0.000
AVERAGE	0.993	0.542
Aldehydes		
butanal	1.000	0.000
pentanal	0.960	0.000
hexanal	1.000	0.727
heptanal	1.000	0.238
octanal	1.000	0.571
nonanal	0.941	0.000
AVERAGE	0.984	0.256

Alkanes		
2-methyl-1-heptane	1.000	0.909
n-hexane	1.000	0.000
n-heptane	1.000	0.000
n-octane	1.000	0.850
n-nonane	1.000	0.000
n-decane	1.000	0.000
n-undecane	1.000	0.000
AVERAGE	1.000	0.251
Ethers		
diethyl ether	1.000	0.000
dipropyl ether	1.000	0.000
diisopropyl ether	1.000	0.000
dibutyl ether	1.000	0.000
dipentyl ether	1.000	0.000
dihexyl ether	1.000	0.000
AVERAGE	1.000	0.000
Ketones		
methylisobutylketone	1.000	1.000
2-butanone	0.971	0.000
2-pentanone	1.000	0.000
2-hexanone	1.000	1.000
2-heptanone	1.000	0.000
2-octanone	1.000	0.000
2-nonanone	1.000	0.000
2-decanone	1.000	0.000
pinacolone	1.000	0.929
AVERAGE	0.997	0.325

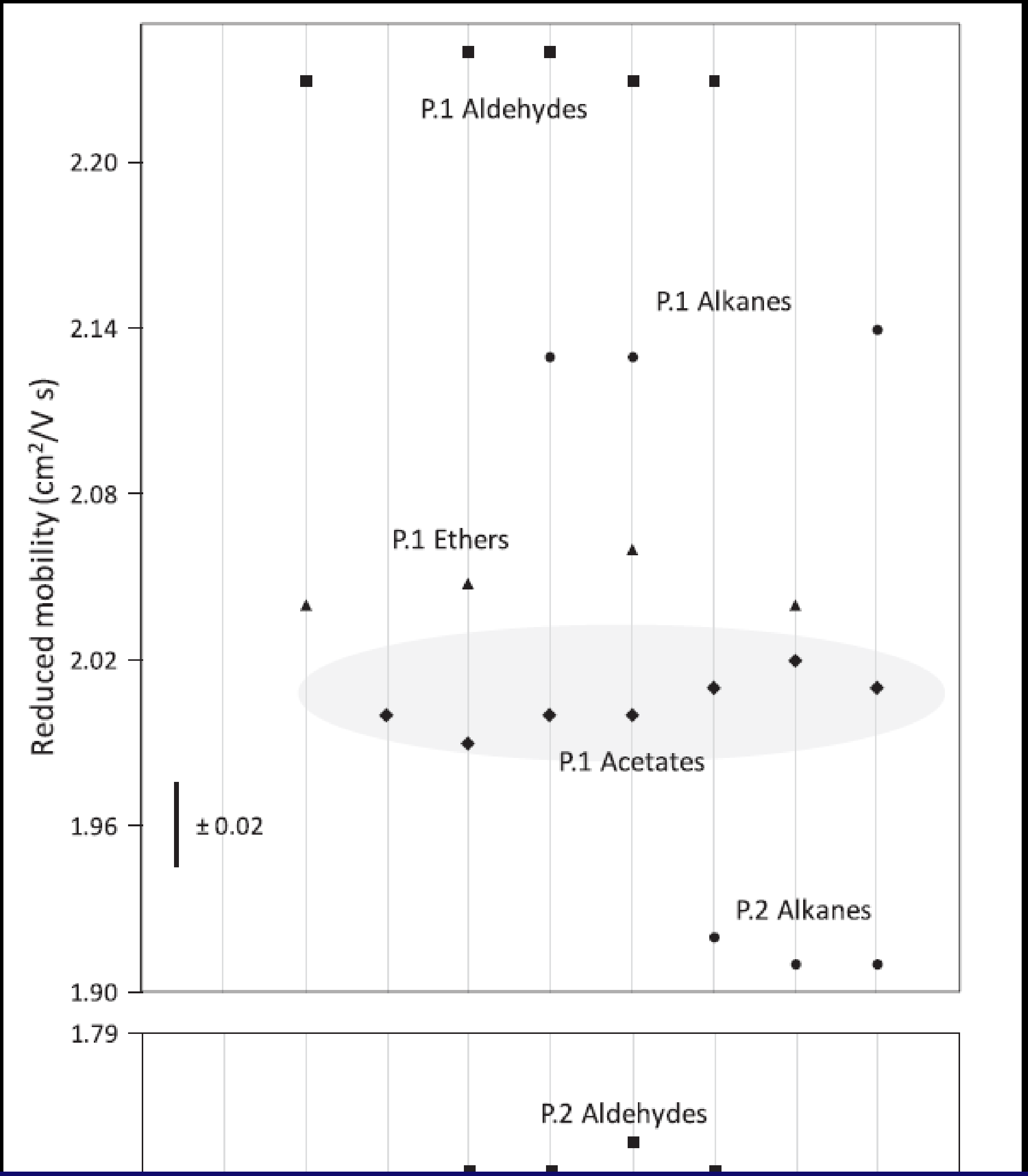
* All the improvements mention(AAV of FIF-A

Some numbers are very impressive.

REASONABLE EXPLANATIONS FOR NNET CLASSIFICATIONS CAN BE FOUND IN FRAGMENT IONS



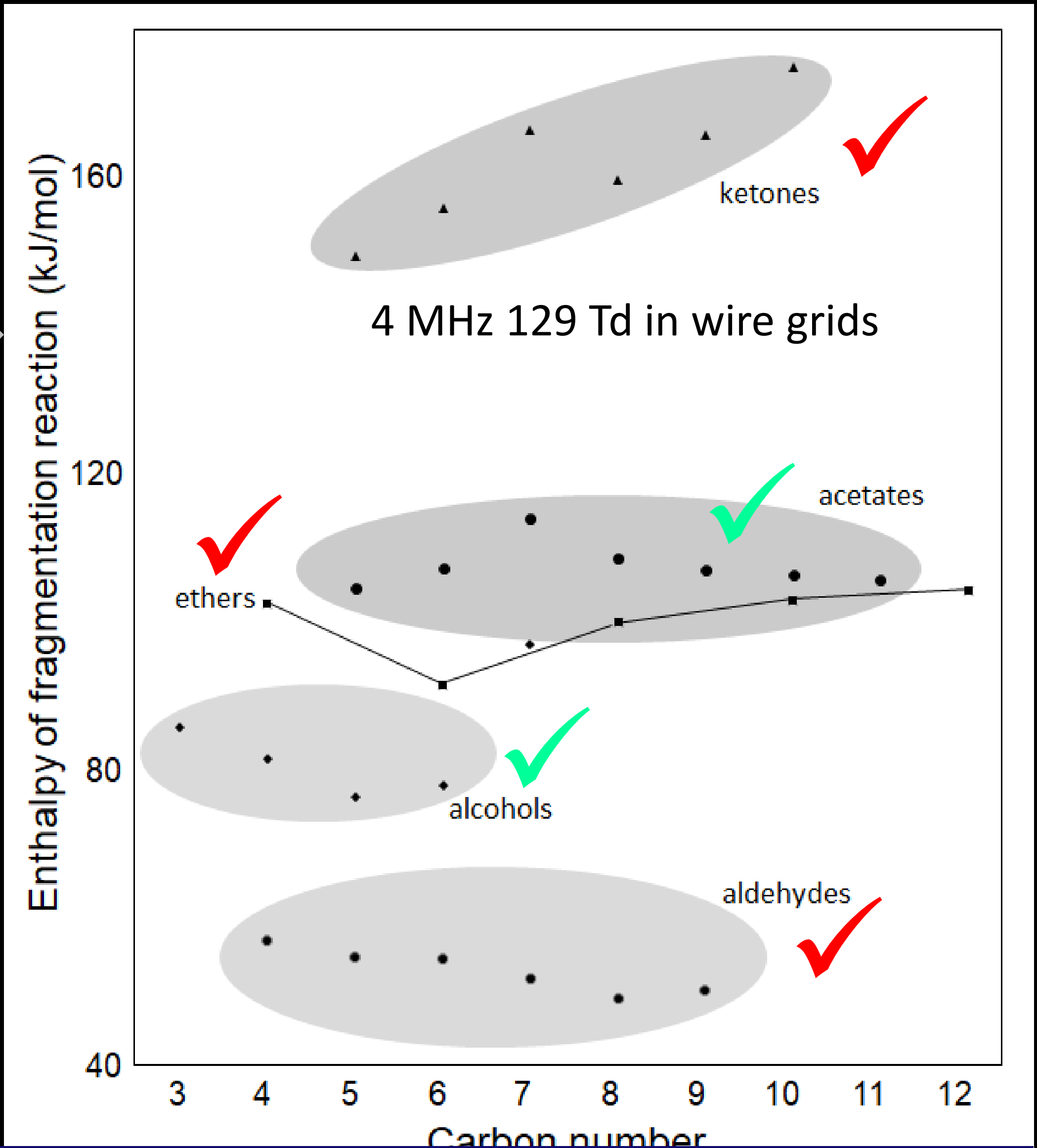
Fragmentations explored decades ago in mass spectrometry appear to apply to FIF processes in air at ambient pressure.



Patterns in IMS spectra seen in 2000 by Erkin Nazarov (and lost to time) re-established.

FRAGMENTATION ENTHALPY OR OTHER?

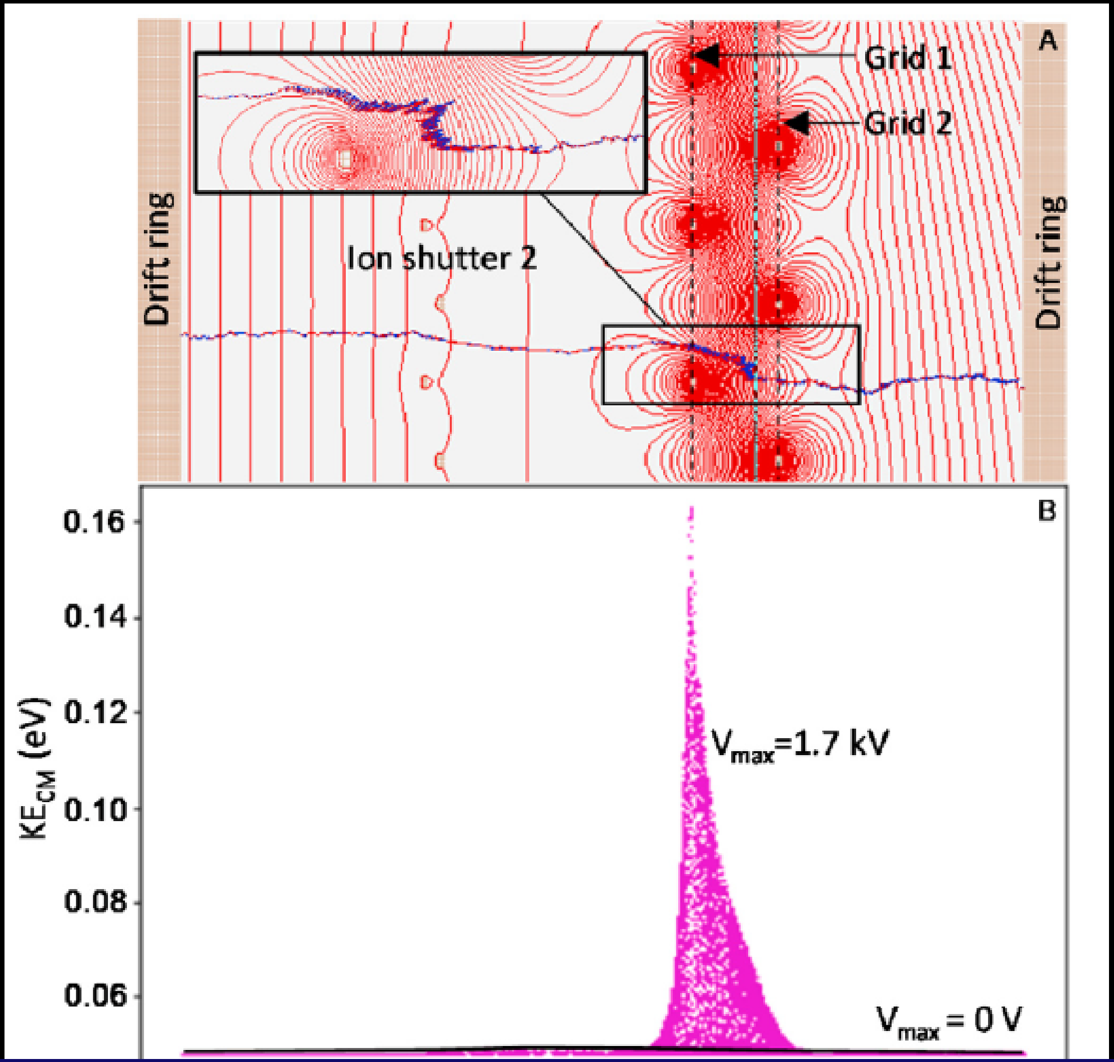
Gaussian DFT Modeling



Other

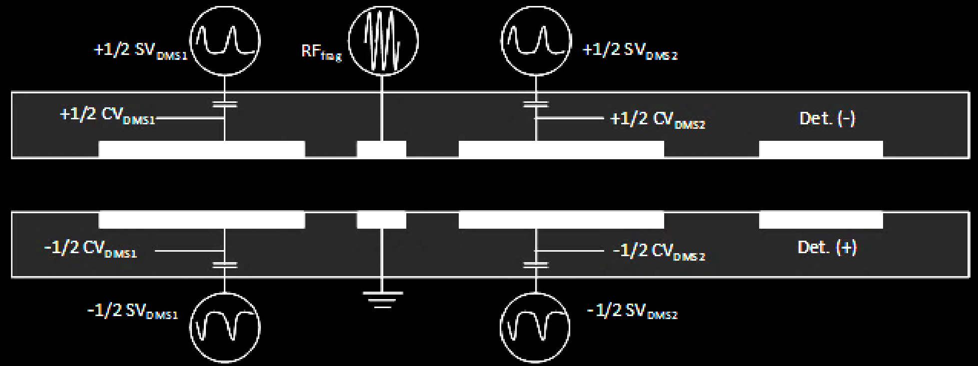
IONS IN RF "DANCE" AMONG THE WIRES

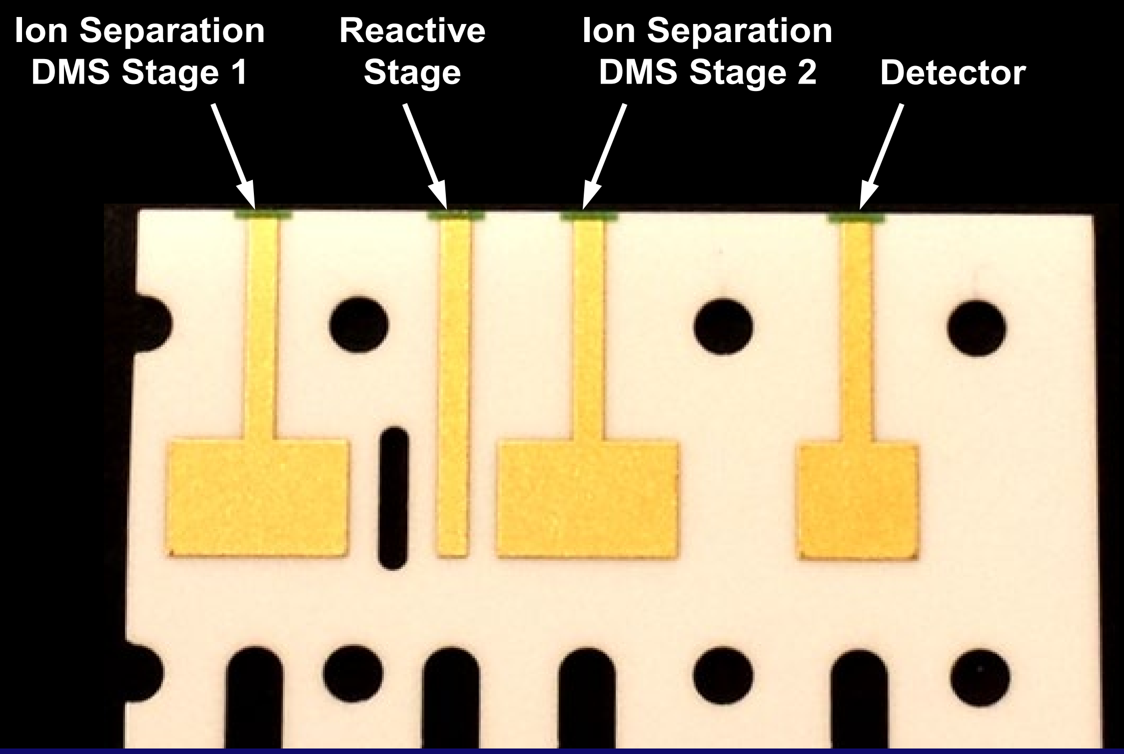
(>80% transmission efficiency)



Wire structures pretty acceptable for tandem IMS methods

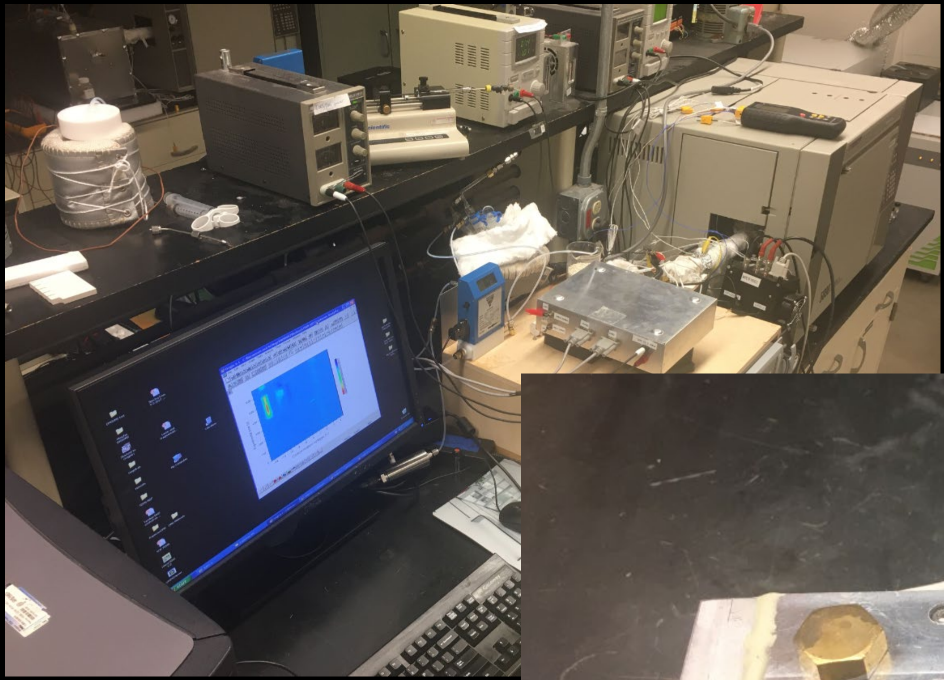
REACTIVE STAGE TANDEM DMS

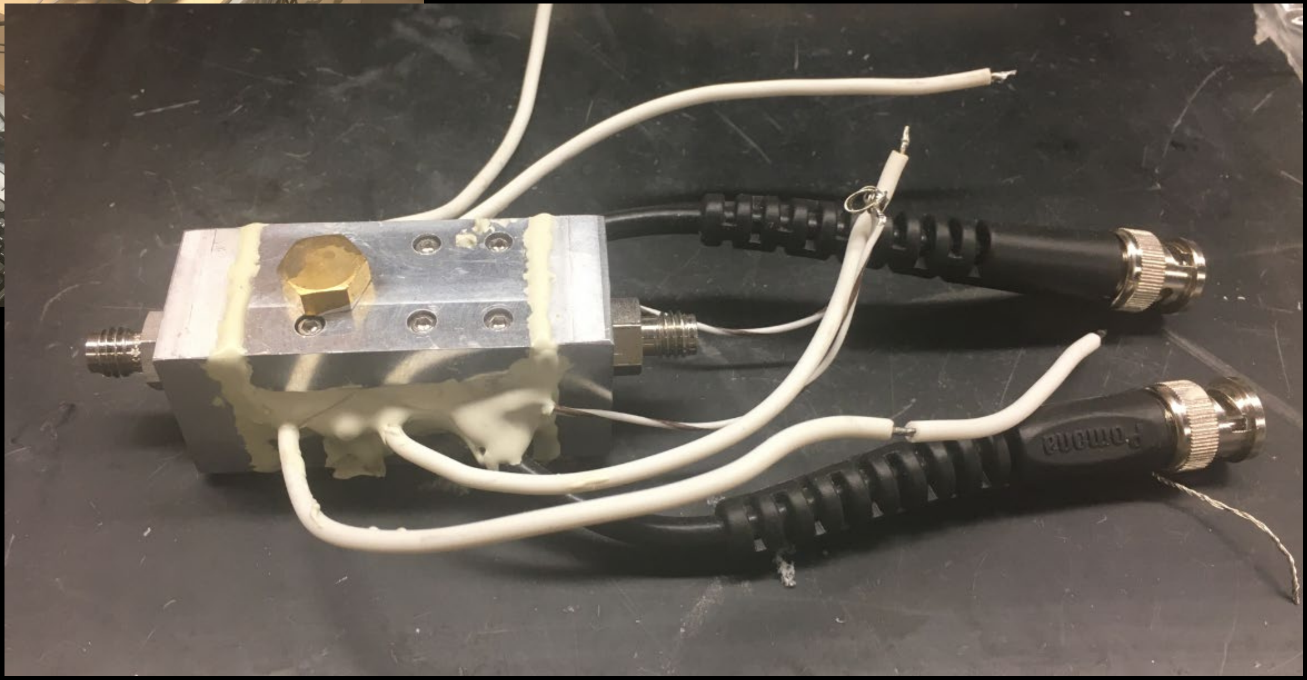




Simple technology new style of "fragmentor"

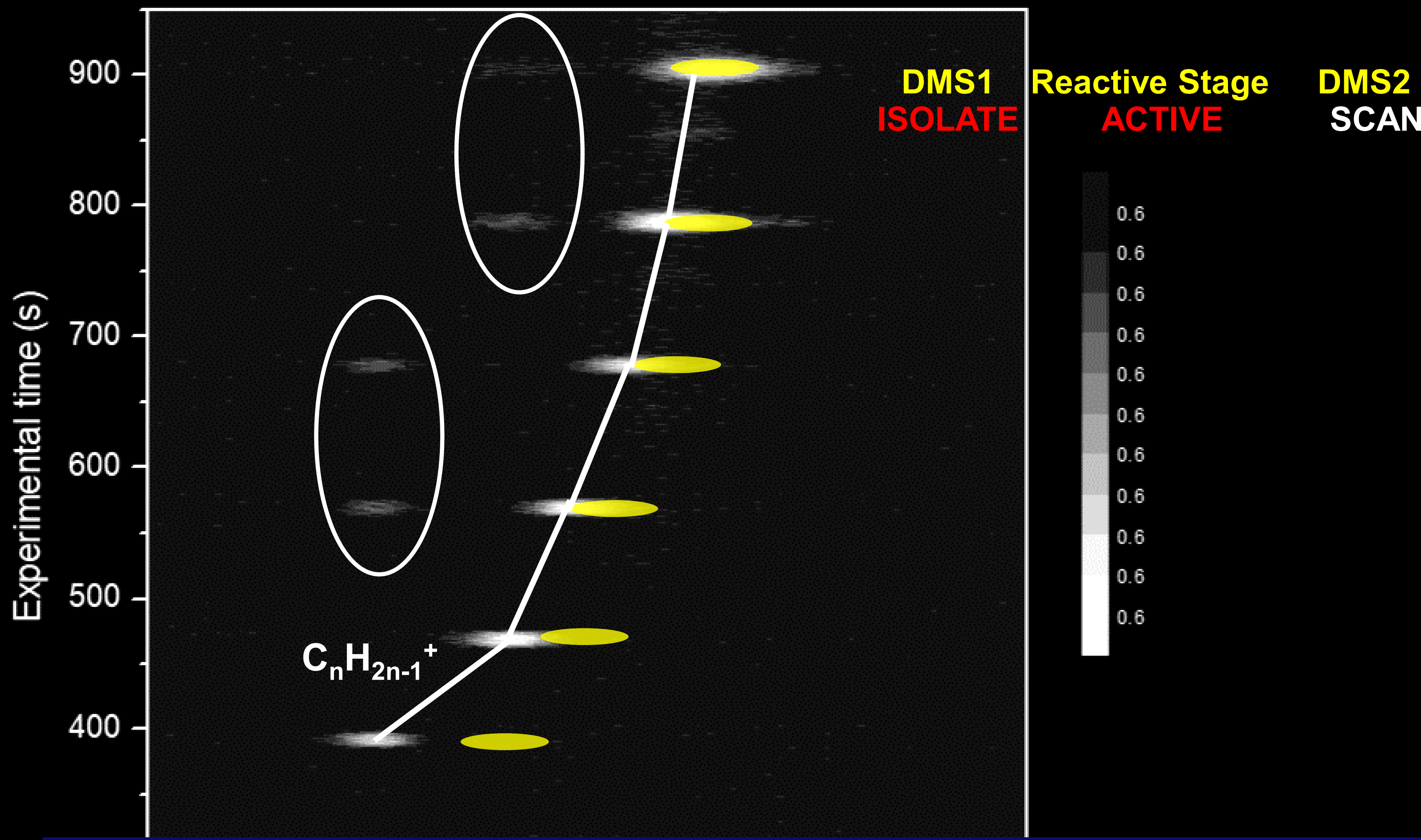
TANDEM DMS WITH REACTIVE STAGE





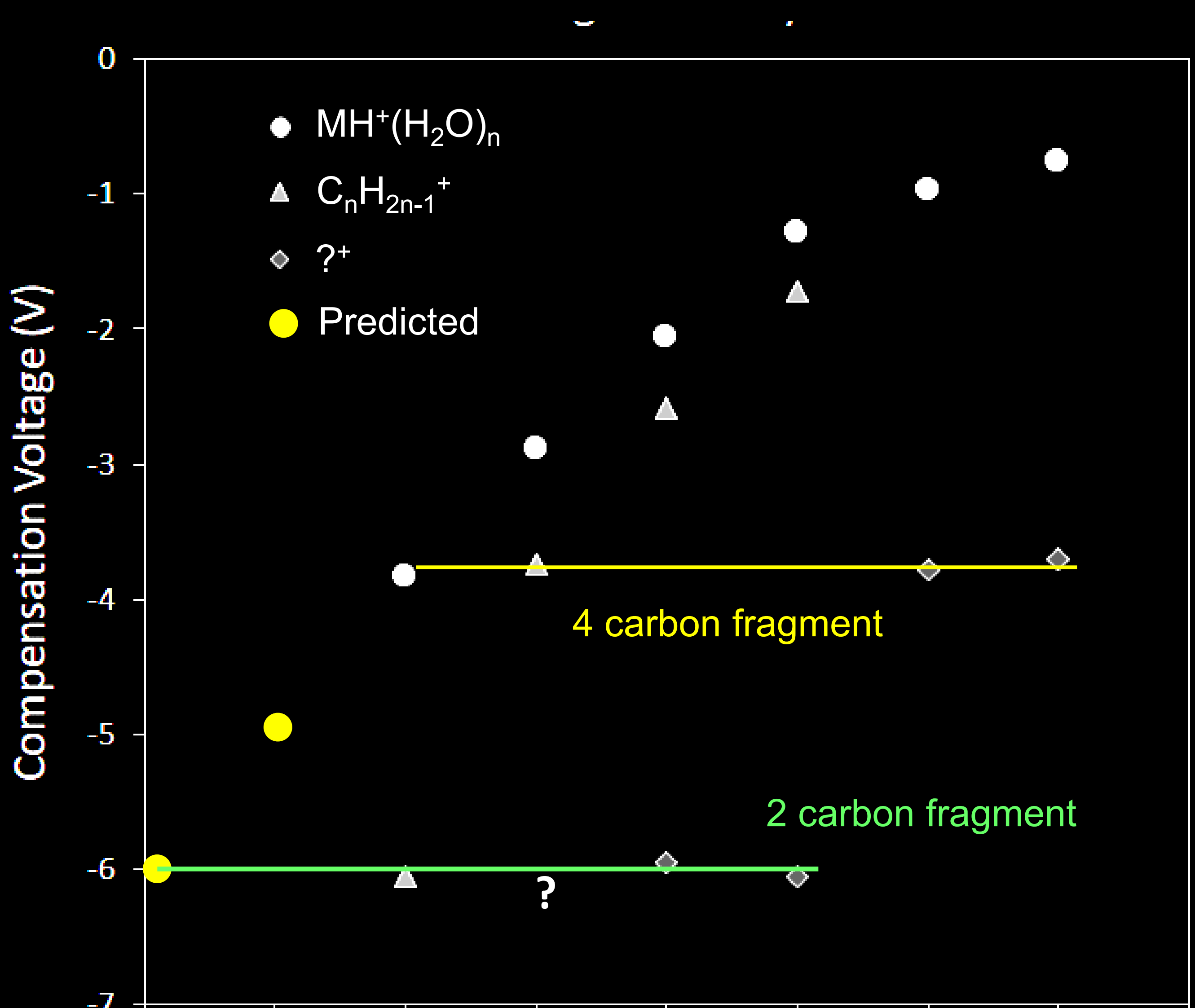
P.E. Fowler, J.Z. Pilgrim, G. Lee, and G.A. Eiceman, Field Induced Fragmentation Spectra from a Reactive Stage-Tandem Differential Mobility Spectrometry, Analyst, 2020,145, 5314-5324.

n-ALDEHYDES IN GC-TANDEM DMS
(DMS1 ISOLATE-REACTIVE STAGE ACTIVE-DMS2 SCAN)



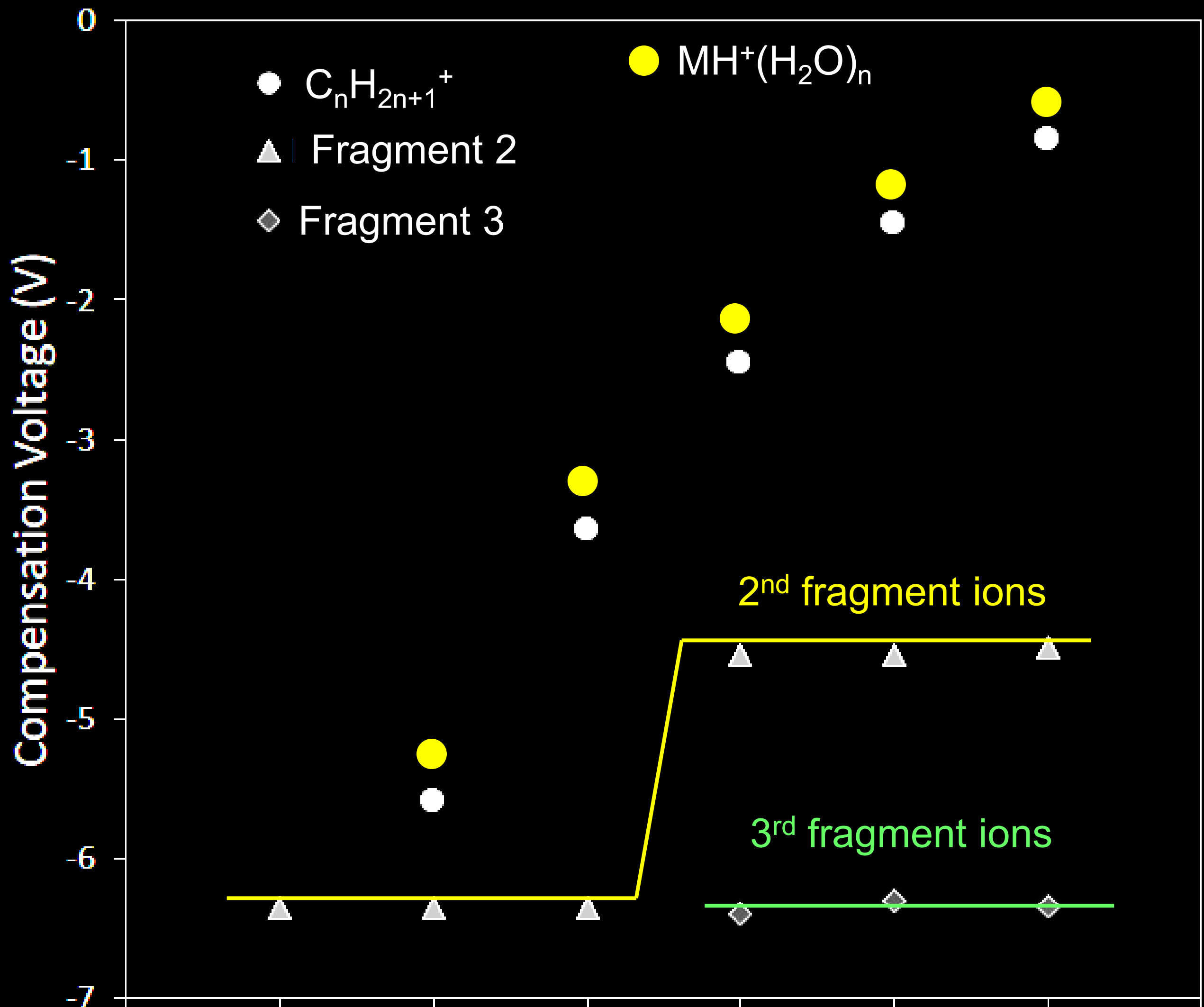
Planar fragmenter shows first and second levels of fragmentation of aldehydes (recall low level of fragmentation with wire grid design

n-ALDEHYDES WITH REACTIVE STAGE TANDEM DMS (COMMON IONS IN FIF SPECTRA)



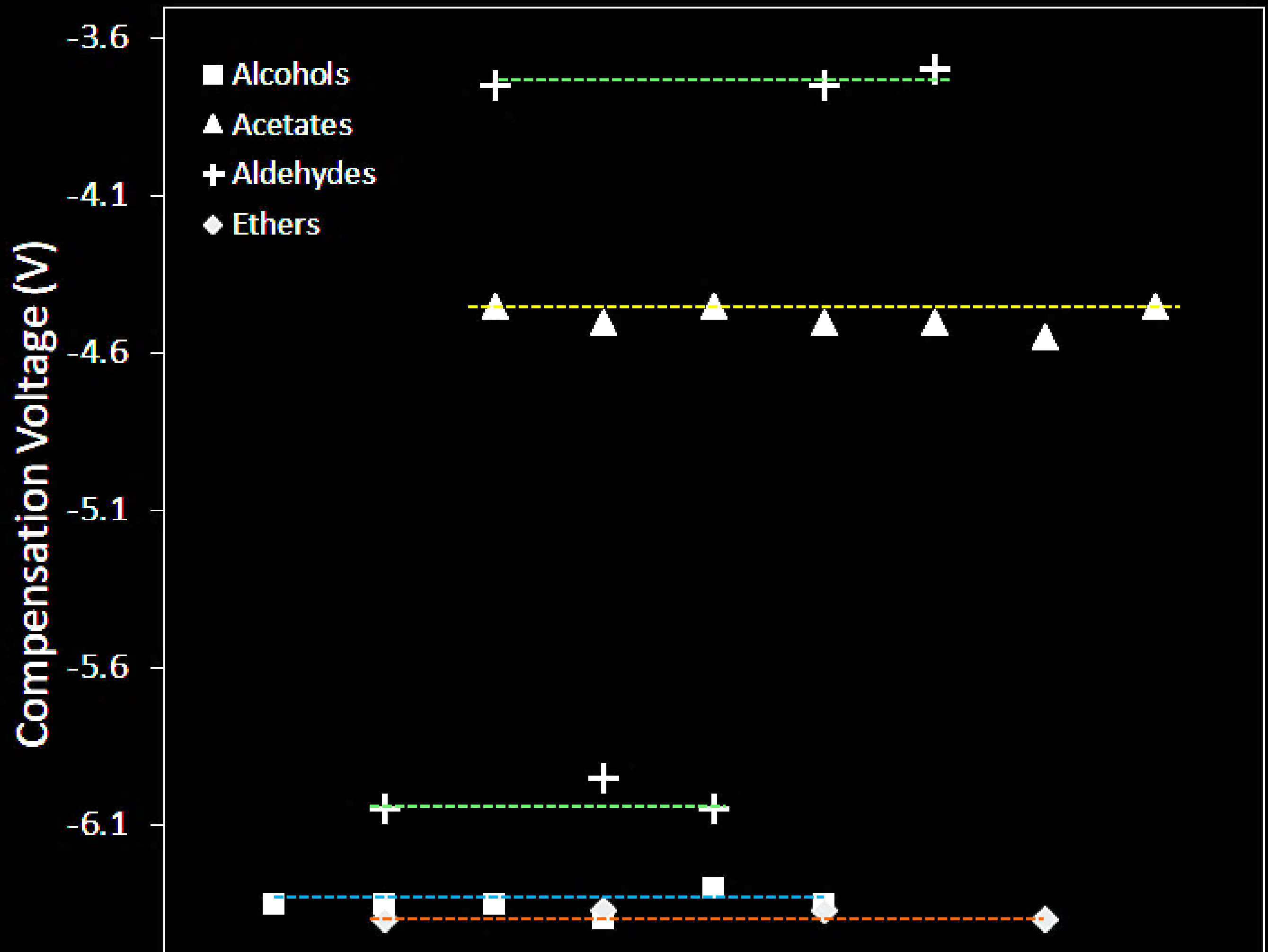
Another view of fragment ions within aldehydes

n-ALCOHOLS WITH REACTIVE STAGE TANDEM DMS (COMMON IONS IN FIF SPECTRA)



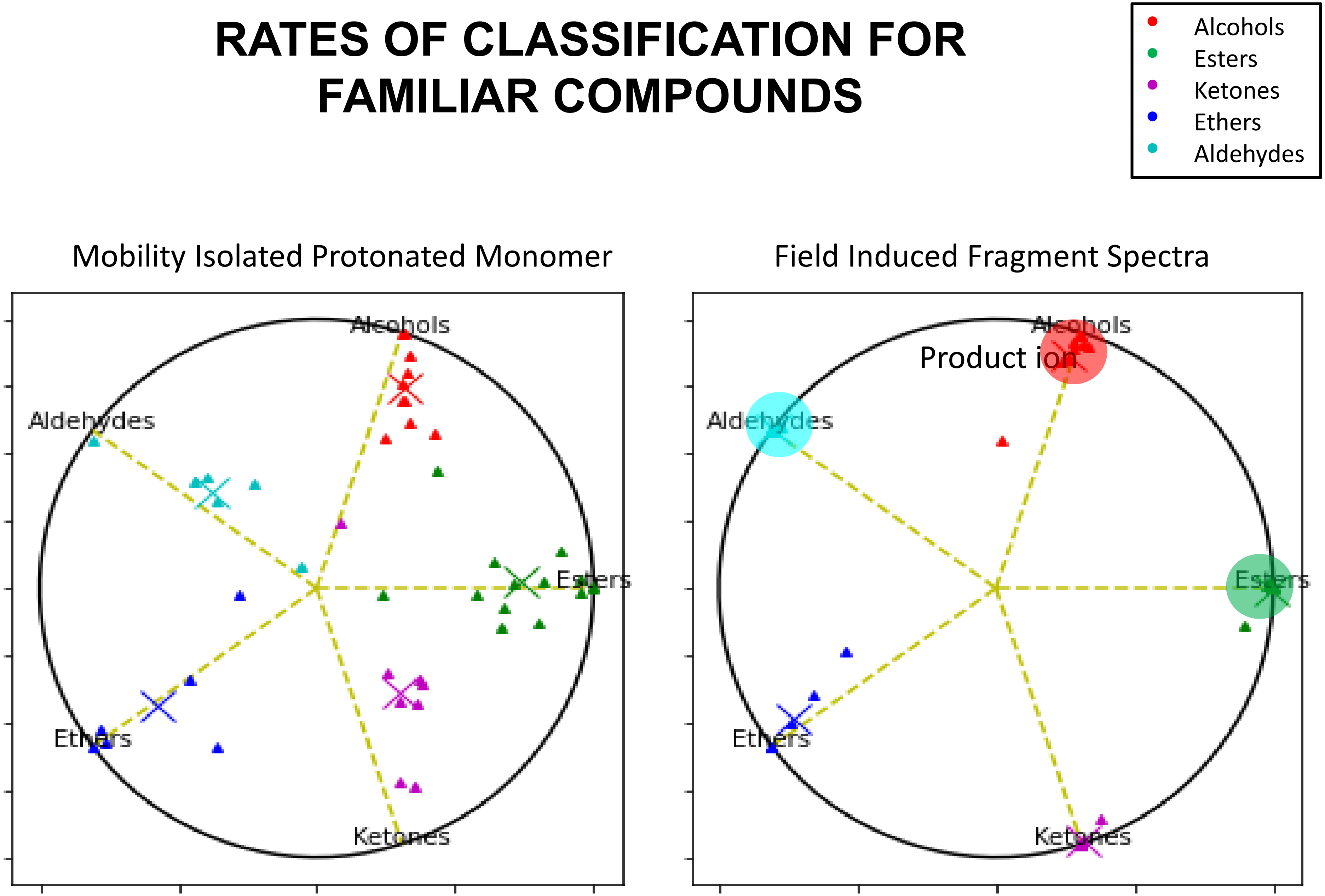
Another view of fragment ions within alcohols

CLASS CHARACTERISTIC FRAGMENT IONS IN FIF SPECTRA FROM TANDEM DMS



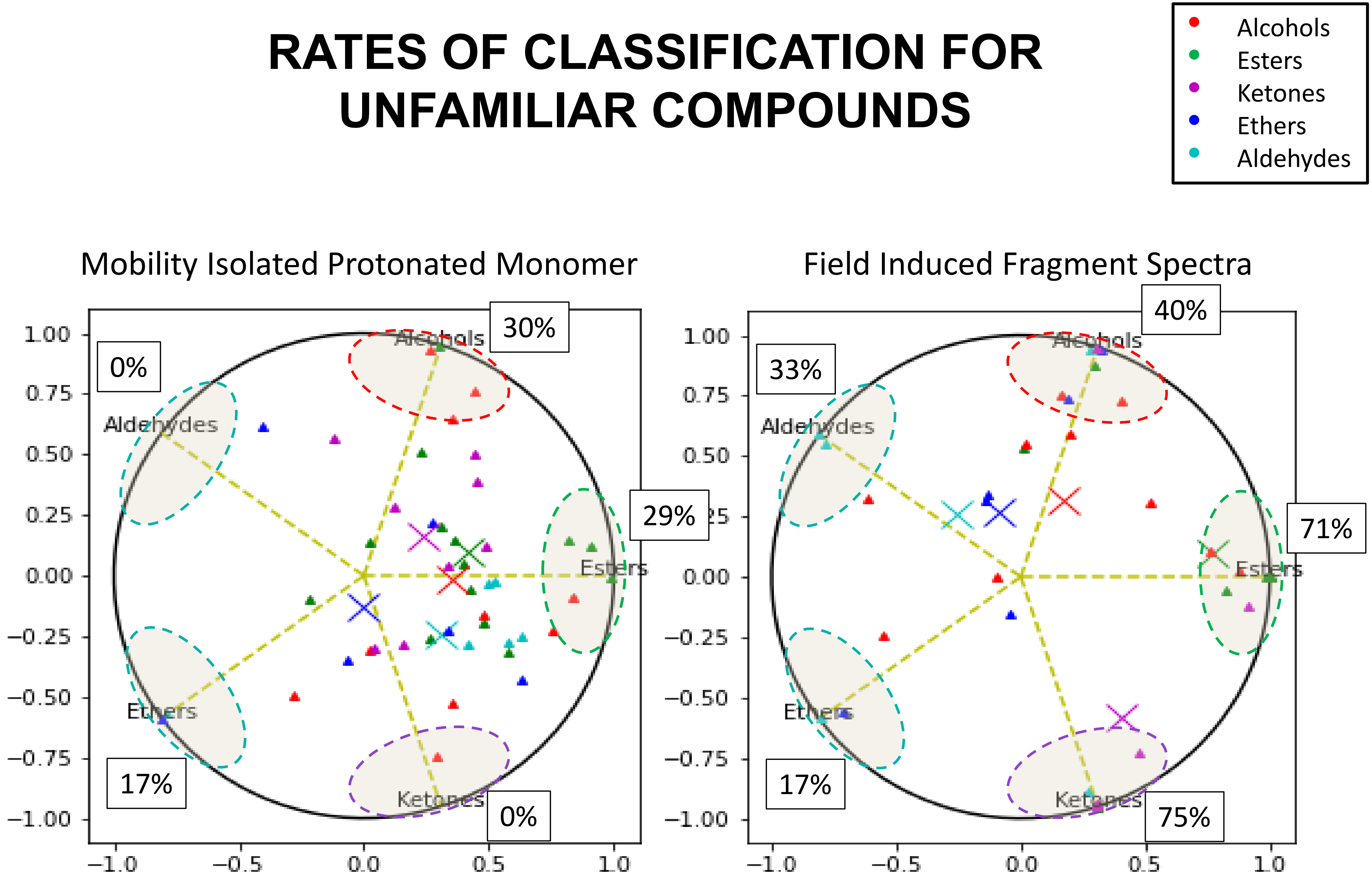
Fragment ions seen in FIF spectra are common within a chemical family and differ between chemical families. How widely will we find this?

RATES OF CLASSIFICATION FOR FAMILIAR COMPOUNDS

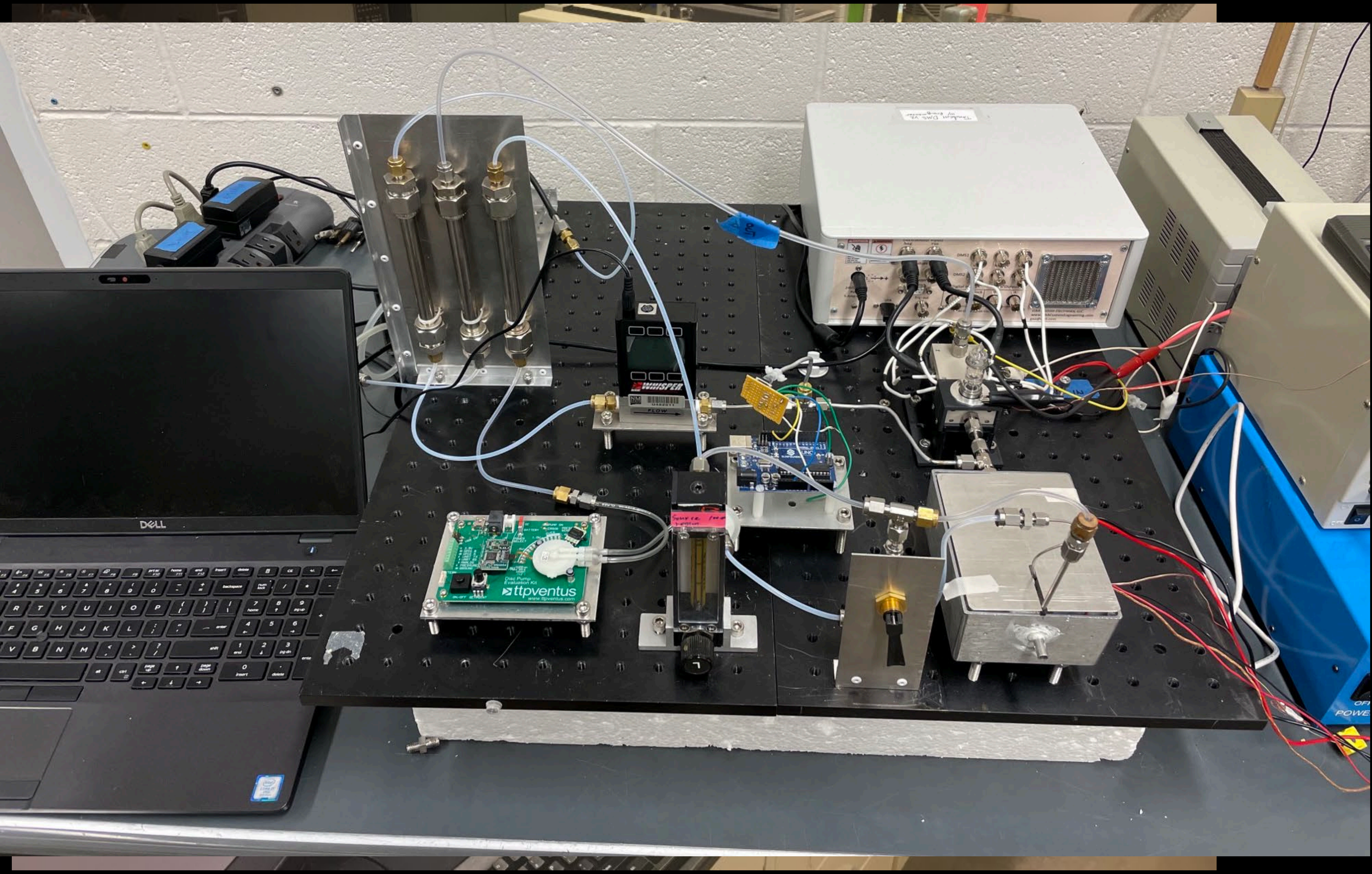


Radar Charts a new tool to probe classification and mis-classification

RATES OF CLASSIFICATION FOR UNFAMILIAR COMPOUNDS

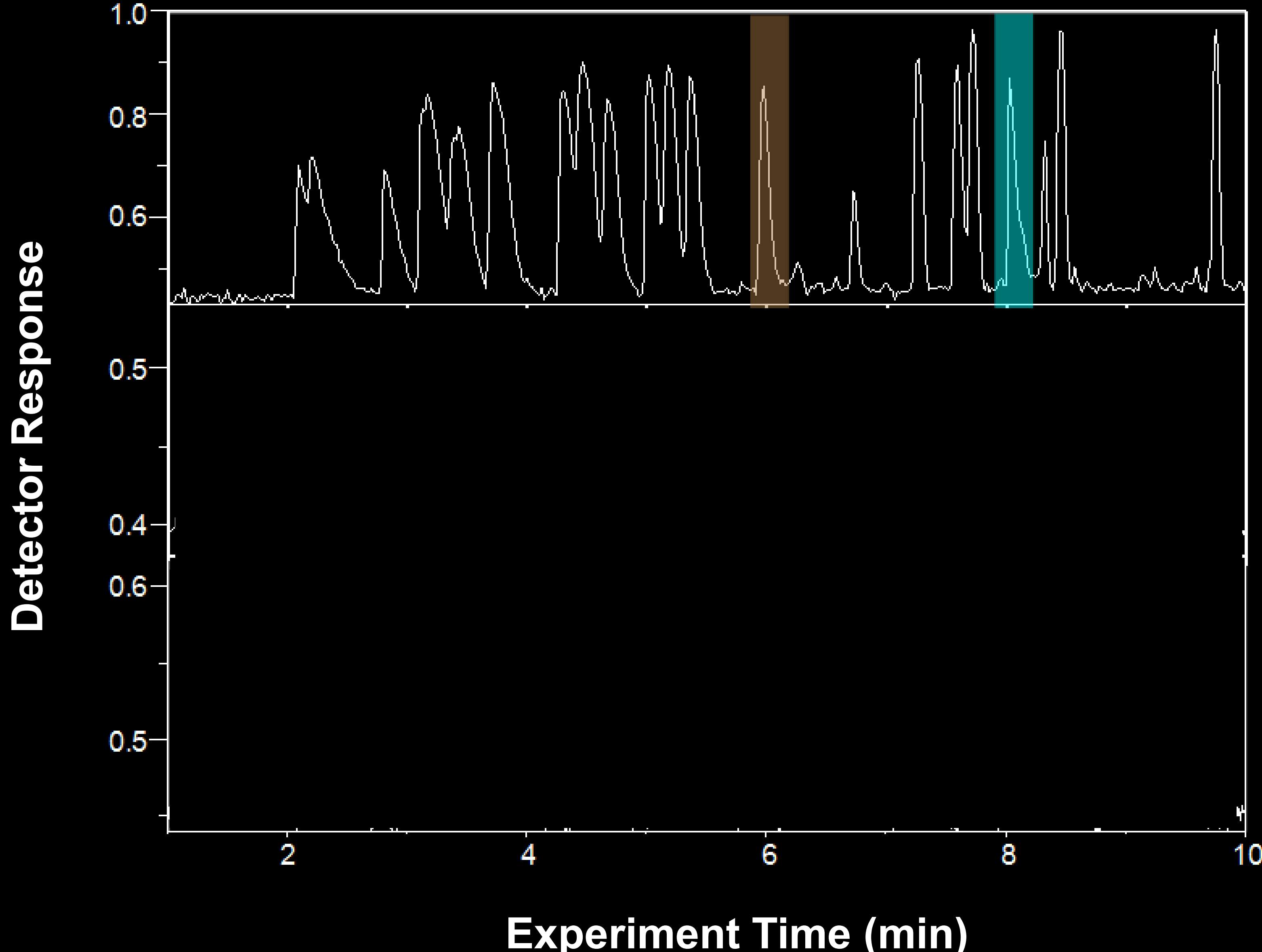


TECHNOLOGY: TRL 1/2 TO 3/4



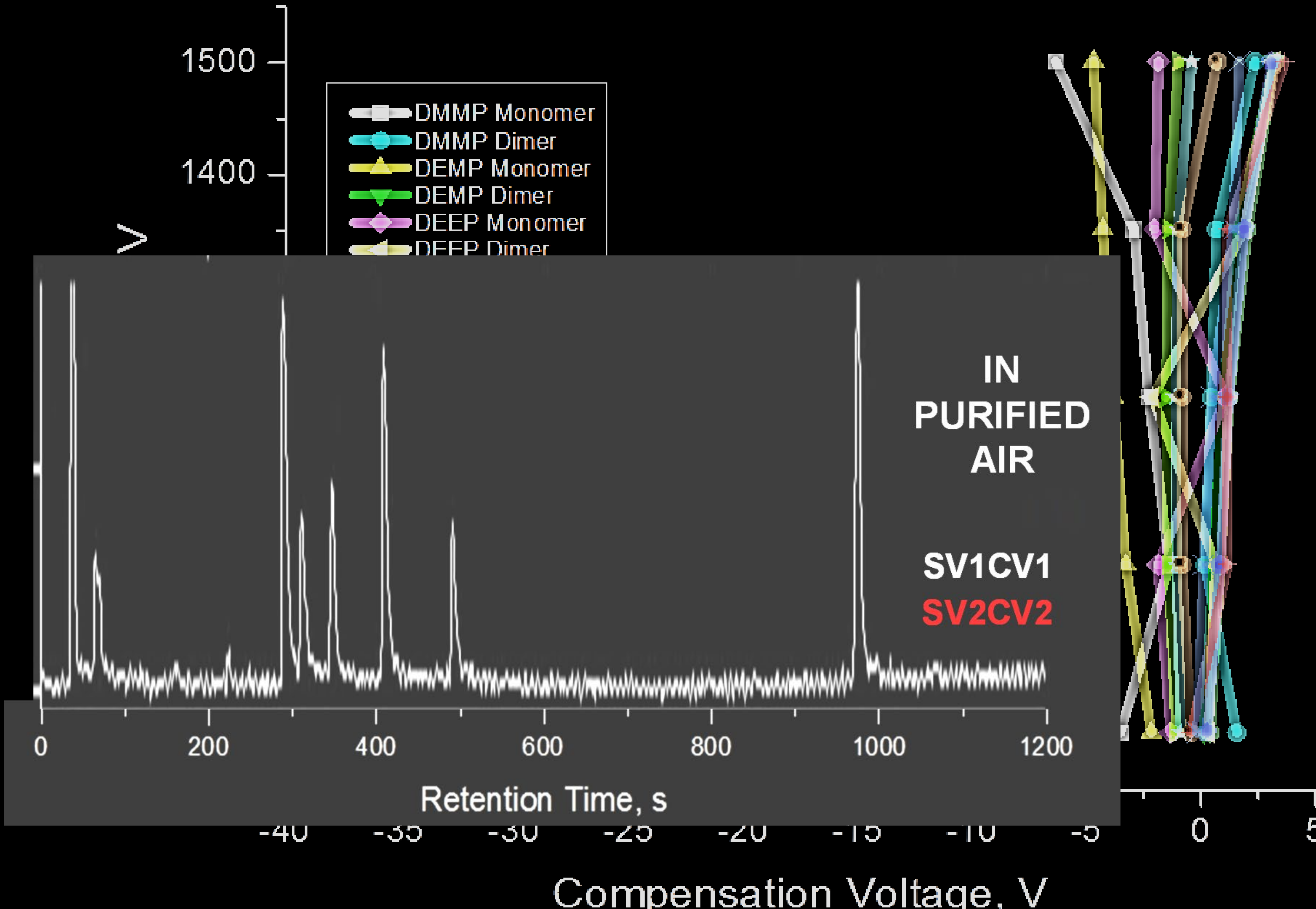
DUAL STAGE ION FILTERING BY α(*E/N*) ONLY

Menlyadiev, M.; Eiceman, G.A. Tandem Differential Mobility Spectrometry in Purified Air for High Speed Vapor Detection, Analyt. Chem. 2014, 86 (5): 2395-402



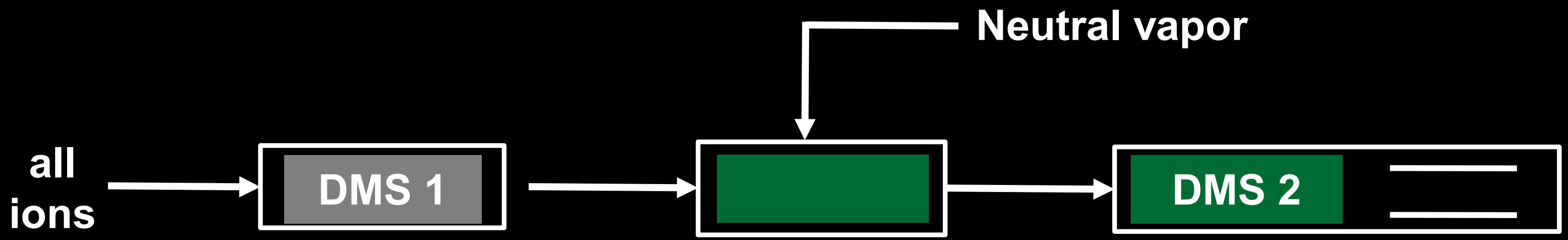
FLAT ALPHA FUNCTIONS WITH DMS:

$$K(E/N) = K_o\,[1 + \alpha(E/N)^2 + \ldots]$$



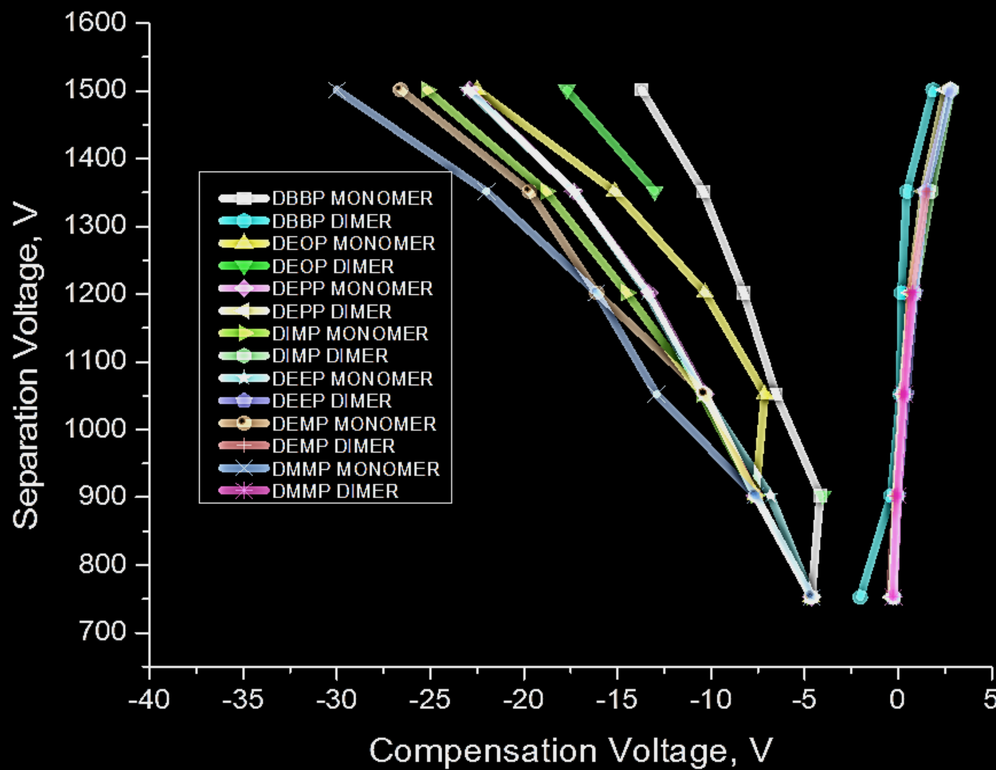
ALPHA MODIFICATION IN TANDEM DMS

Preserve ionization chemistry with modification of alpha functions



Modify Alpha Function

$$K(E/N) = K_o\ [1 + \alpha(E/N)^2 + \ldots]$$



Eiceman, et al. Separation of Ions from Explosives in Differential Mobility Spectrometry by Vapor-Modified Drift Gas, Analytical Chemistry **2004**, 76(17), 4937-4944

Rorrer and Yost, Solvent vapor effects on planar high-field asymmetric waveform ion mobility spectrometry, International Journal of Mass Spectrometry **2011**, 300, 173-181

Schneider, Covey, Nazarov, DMS-MS separations with different. transport gas modifiers, International Journal for Ion Mobility Spectrometry **2013**, 16(3), 207-216

Kafle, et al., Understanding gas phase modifier interactions in rapid analysis by Differential Mobility-Tandem Mass Spectrometry, J Am Soc. Mass Spectrom. **2014** Jul; 25(7): 1098–1113.

Conclusions as Sept 2022

- Pushing E/N above 150 Td was sufficient to fragment aldehydes and some ethers……ions for 2-ketones still un-fragmentated.
- Transition state and E_a apparently where control exists and where understanding is needed. Computational modeling underway…….non-trival.
- Radar charts provide tools to look at overall performance and give insights into mis-classifications.
- Fragment ions appear to be the source of Neural Net learning (and some memorization) and success at classification

Organ Mountains, Las Cruces, New Mexico

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Eiceman Research Group 1980 - 2022

Students and Colleagues