Ion Mobility Workshop

Future of Ion Mobility Mass Spectrometry

--- To Biological Problems

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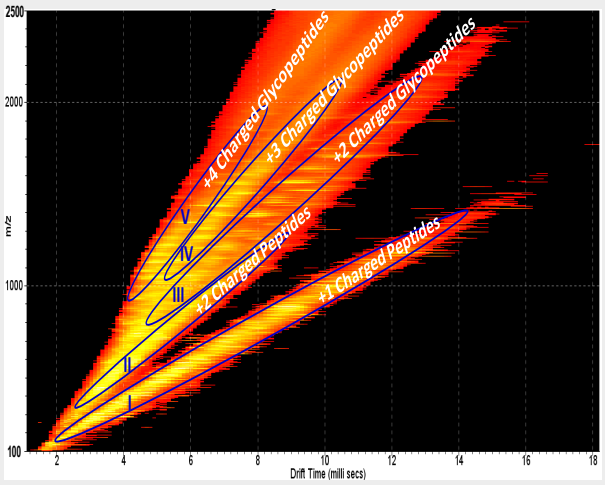
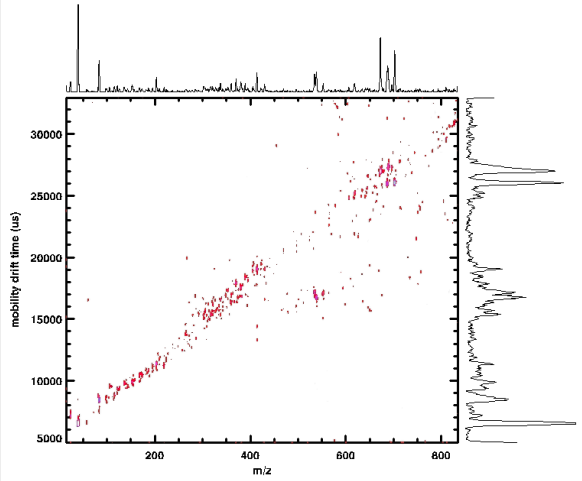
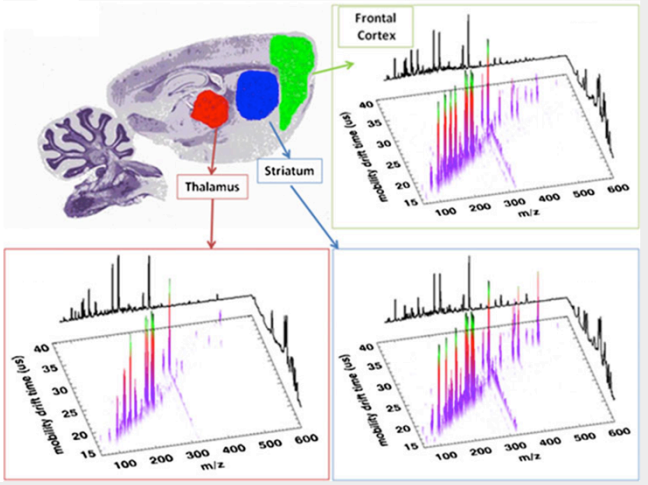
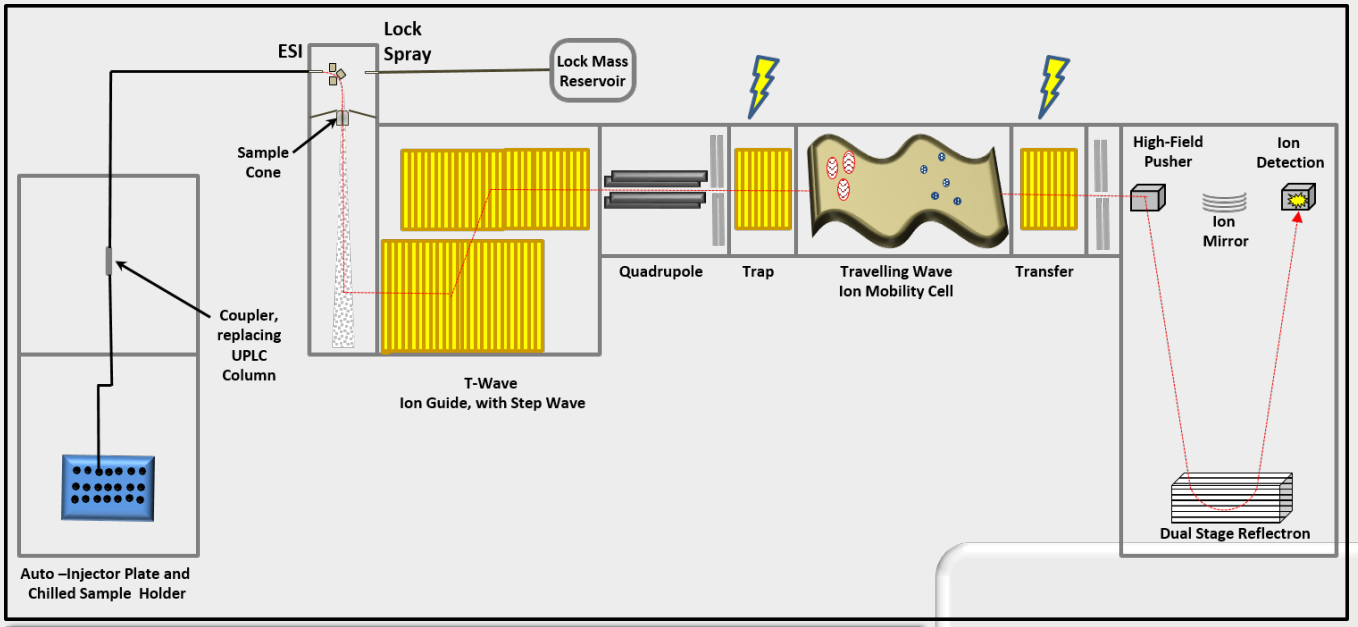


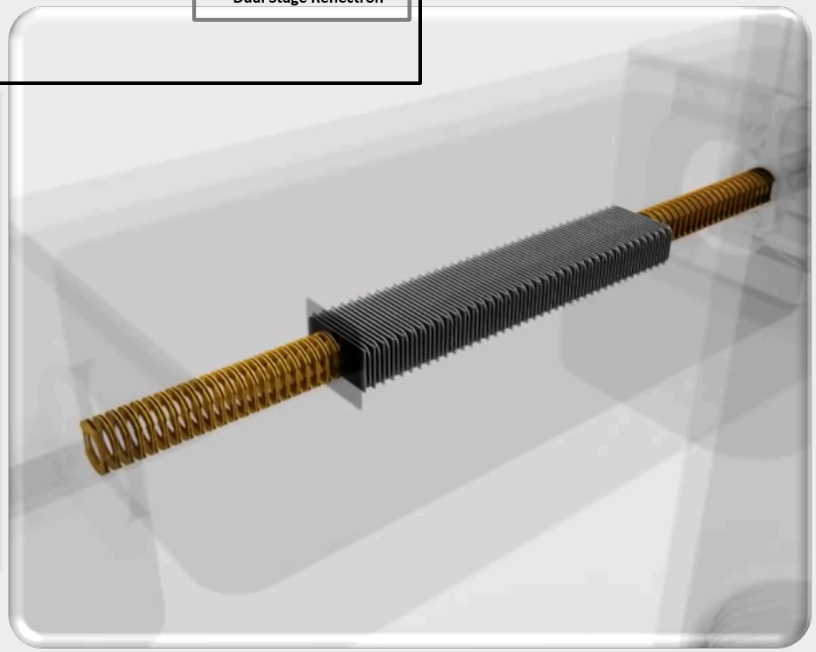




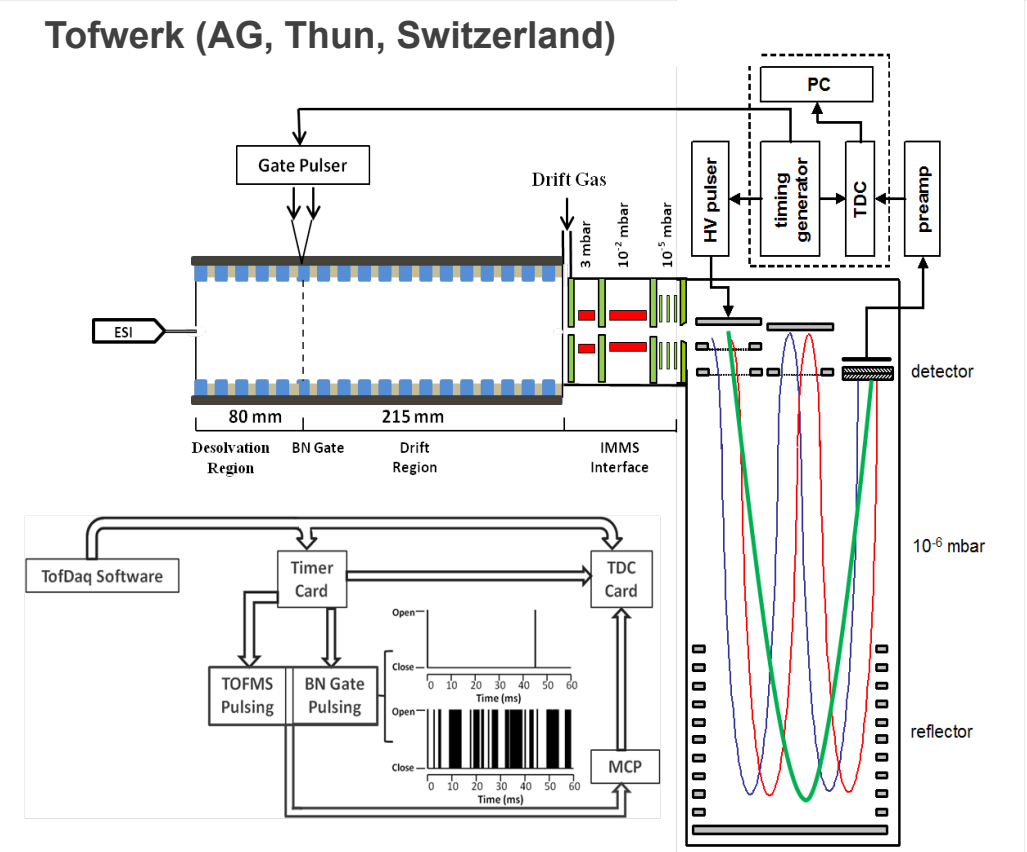
Synapt G2-S HDMS

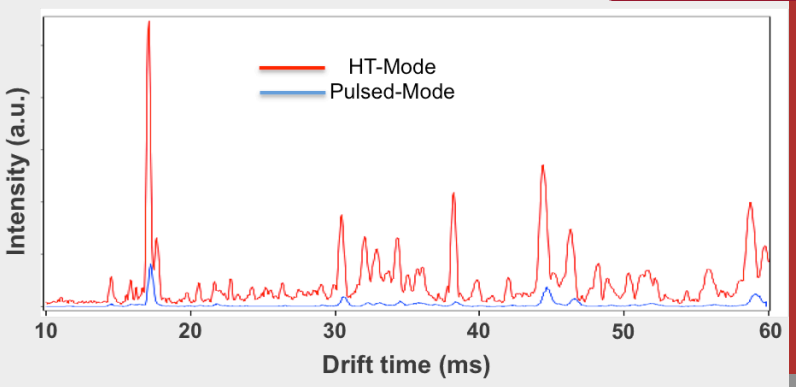


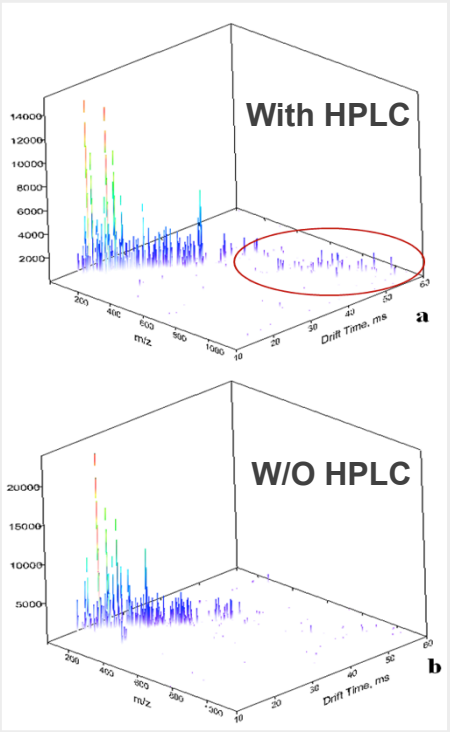
- **Synapt G2-S HDMS system**
  - Operated in the Mobility-Mass mode with TOF section in "V", or "resolution" configuration
  - TWIMMS separates ions, as they "surf" along a pulsed, time varying electric field, according to size and charge.
  - Direct infusion was achieved by use of a Waters ACQUITY UPLC
    - In place of column a VALCO coupler is placed in line to allow direct infusion.
  - Reduced pressure, 3-4 mbar Nitrogen
  - Moving electric field
  - Resolving power is relatively low (30-40)
  - Fewer Collisions with Drift Gas



High Throughput Metabolomics analysis---HT-apIMMS

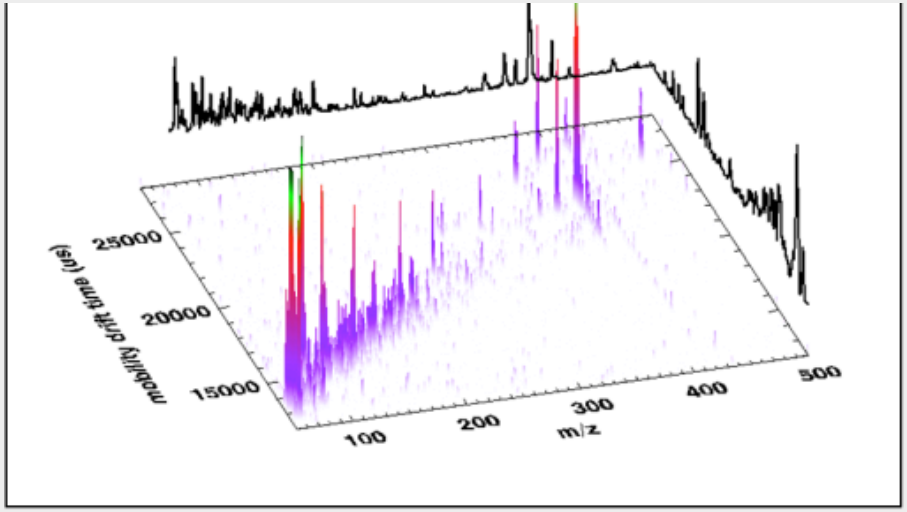


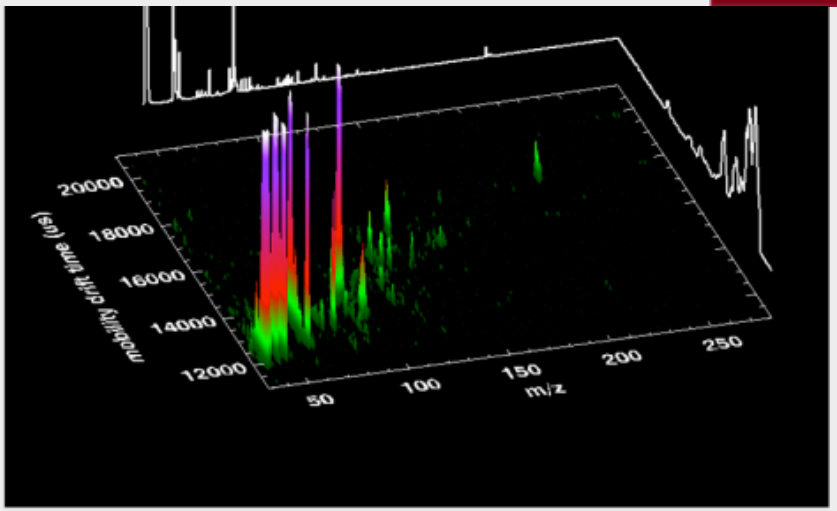


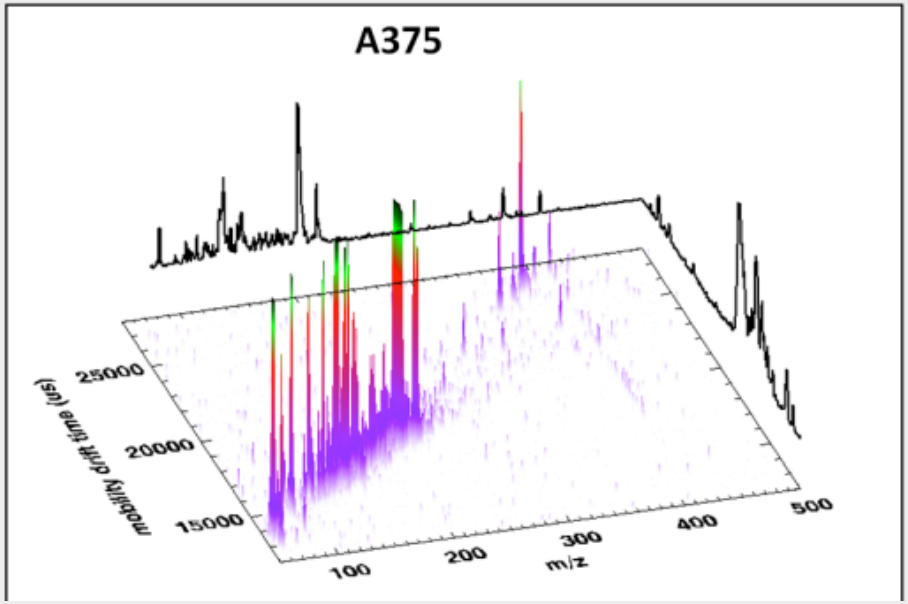


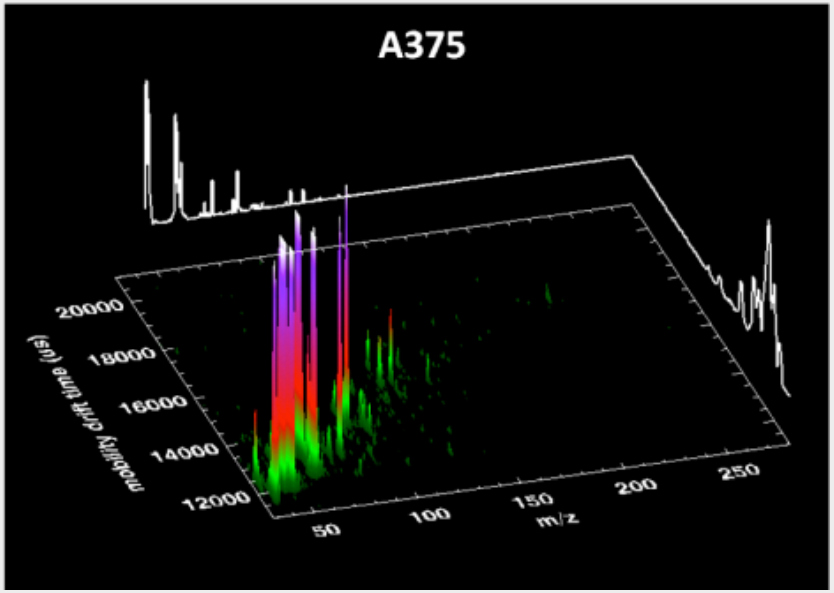
Zhang et al. *Analytical Chemistry.* 2014, 86, 1661−1670.

Melanoma Cancer Cell

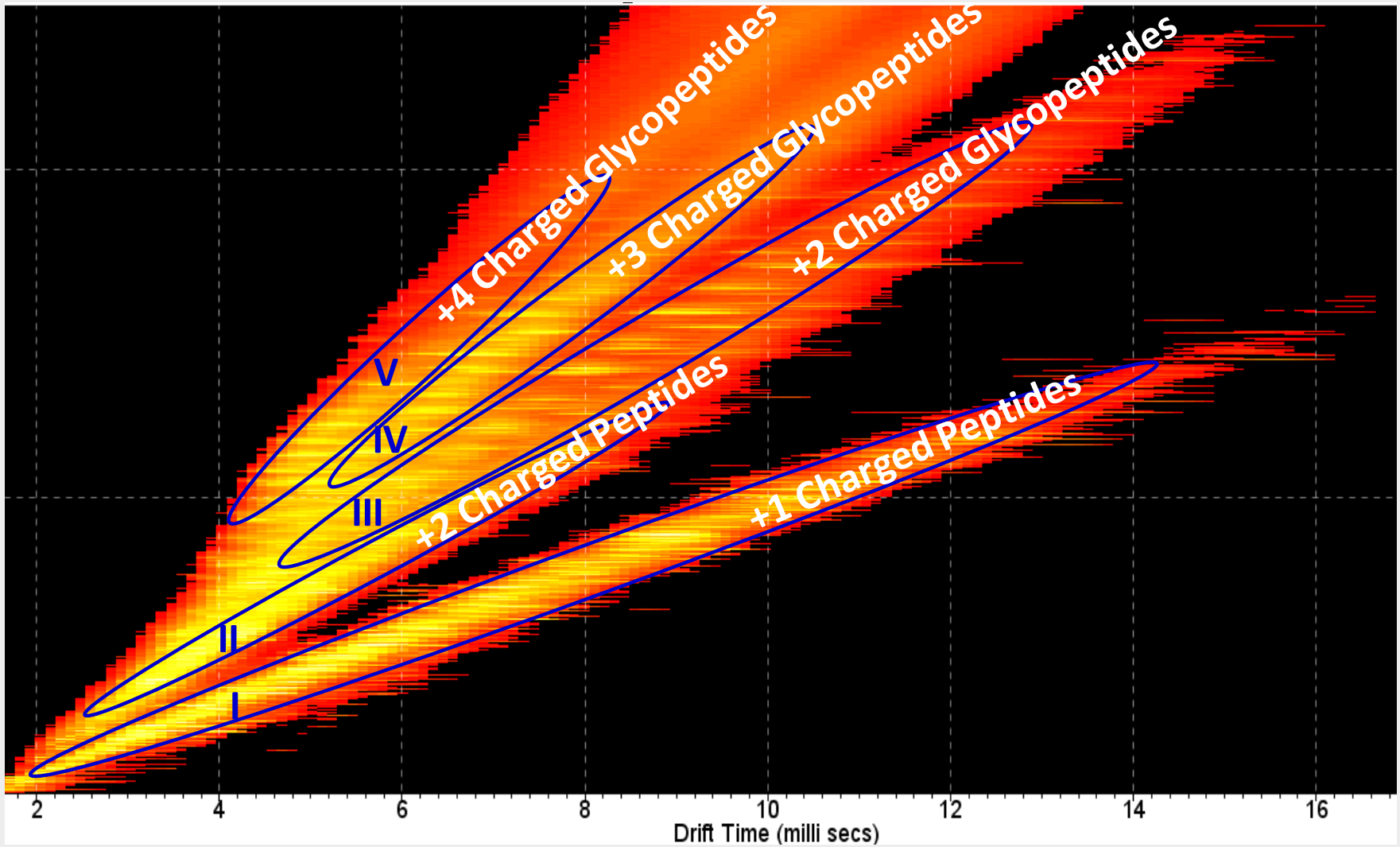




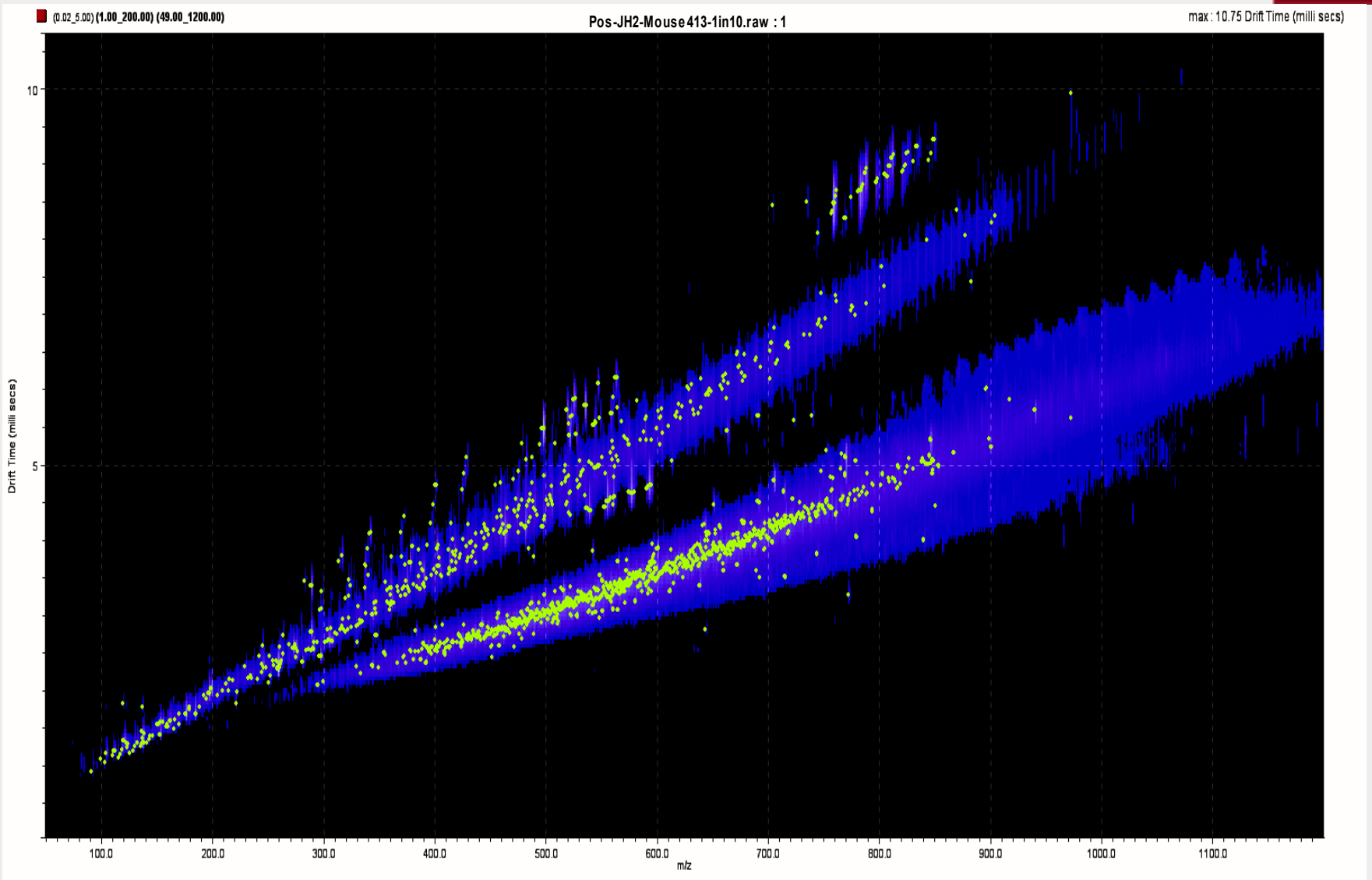




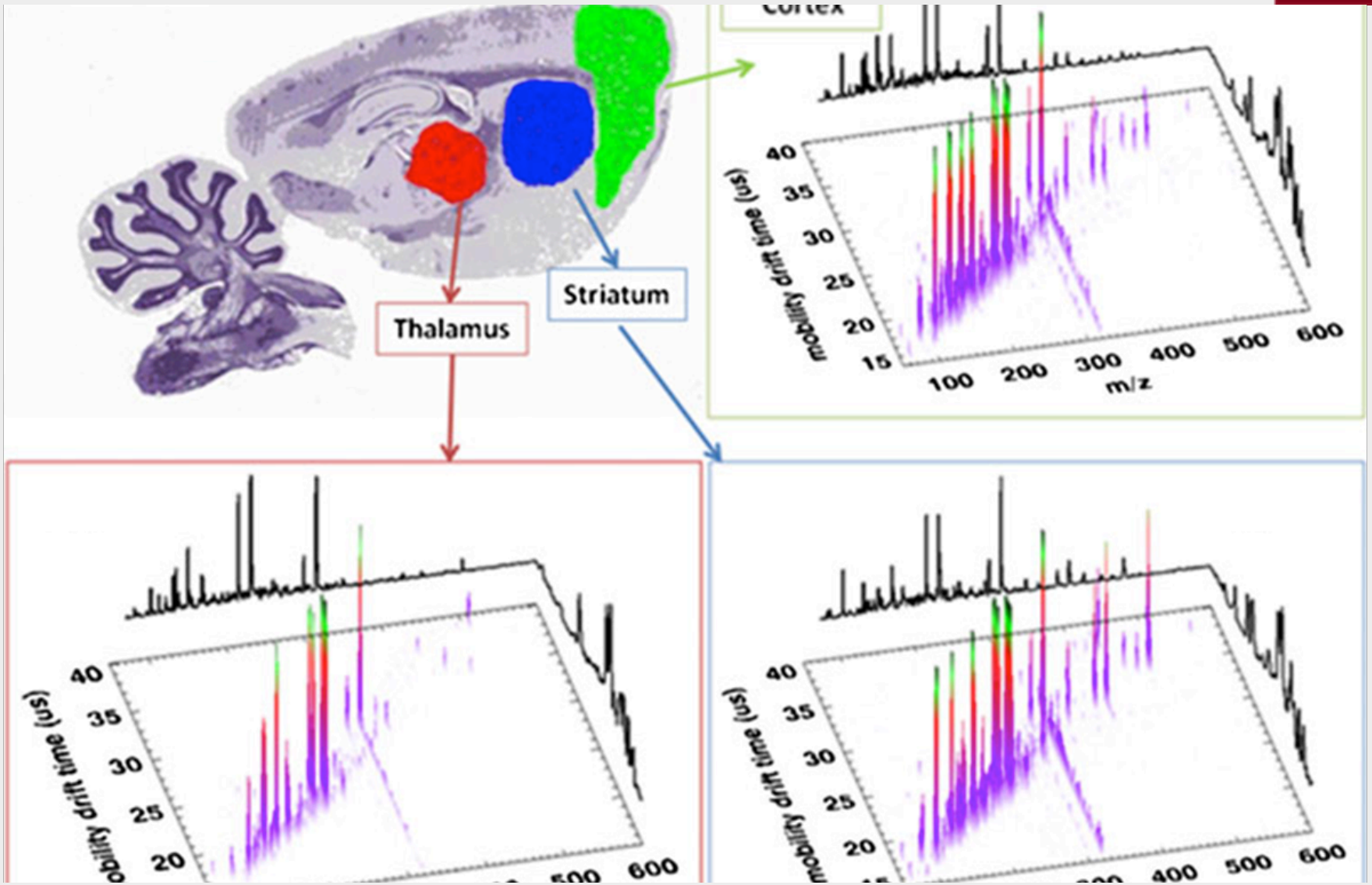
Glycopetides



Colorectal Cancer Tissue



Brain Tissue



Metabolome of Human Blood

Few Drops of Blood

Extracted with MeOH/Water

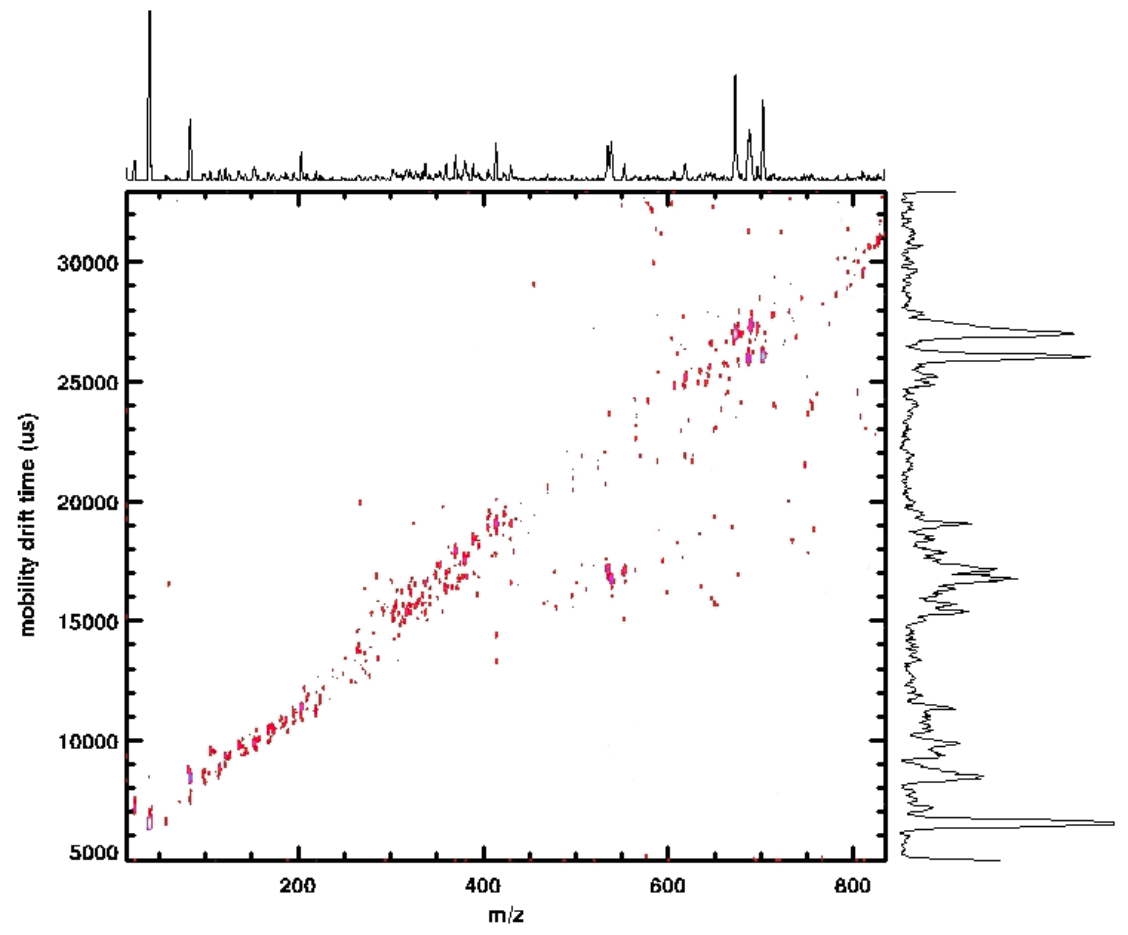
Centrifuged

ESI-IMS-TOF

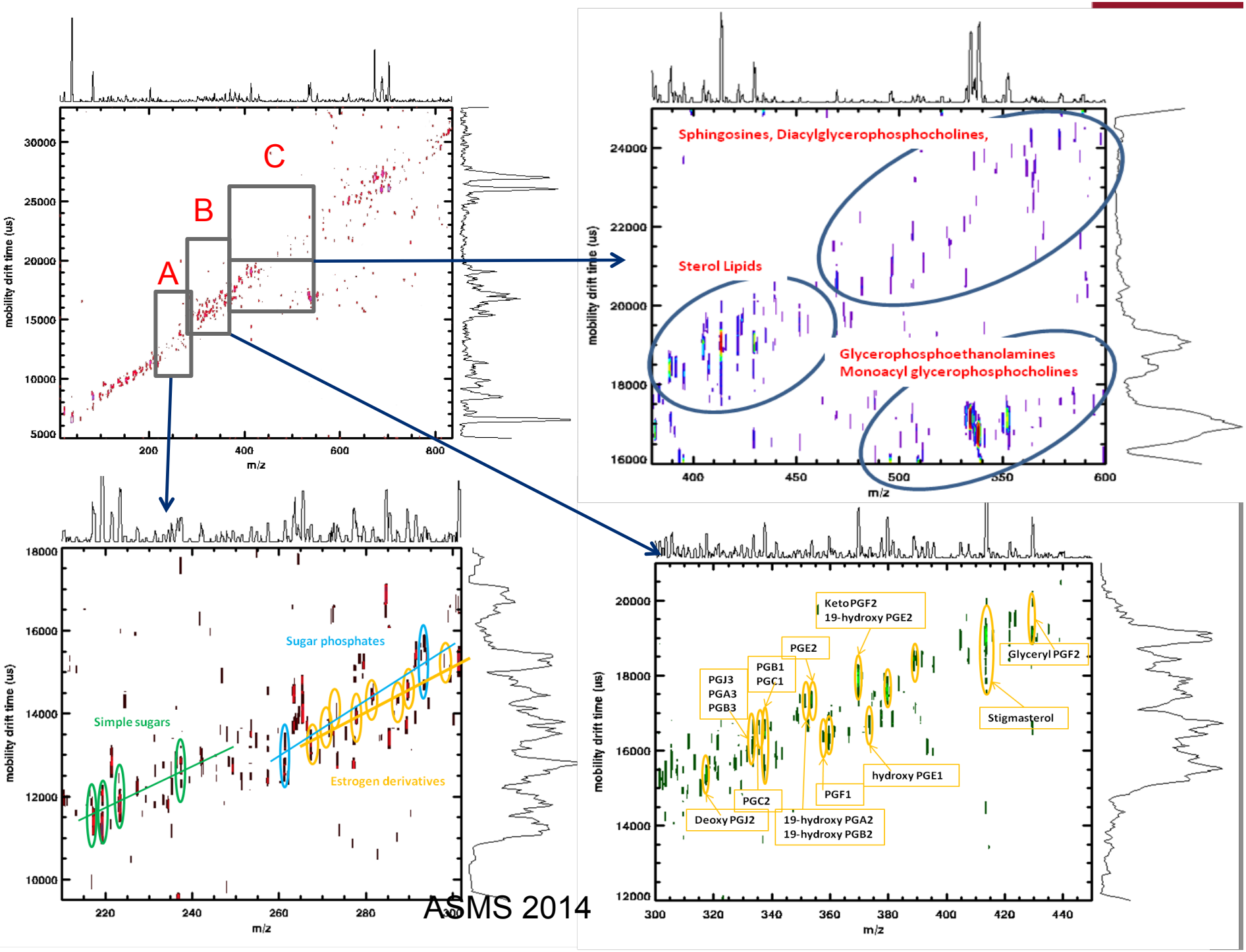
30 minutes

10 nM to 10μM

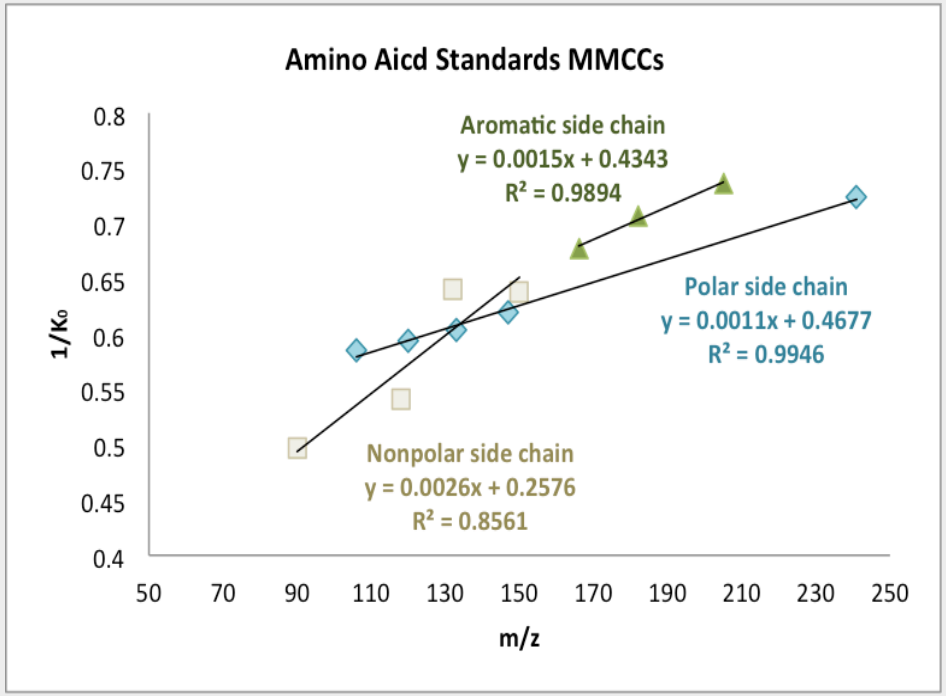
200 isobars

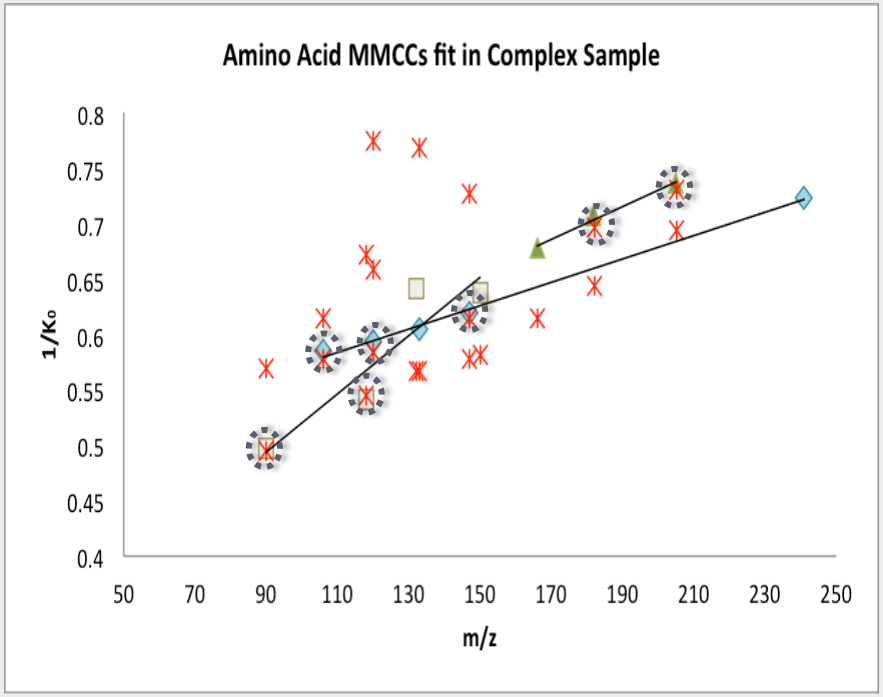


Metabolic profiling of human blood by high-resolution ion mobility mass spectrometry (IM-MS), P. Dwivedi, J. A. Schultz, H. H. Hill Jr, Int. J. Mass Spectrom. 298 (2010) 78-90.

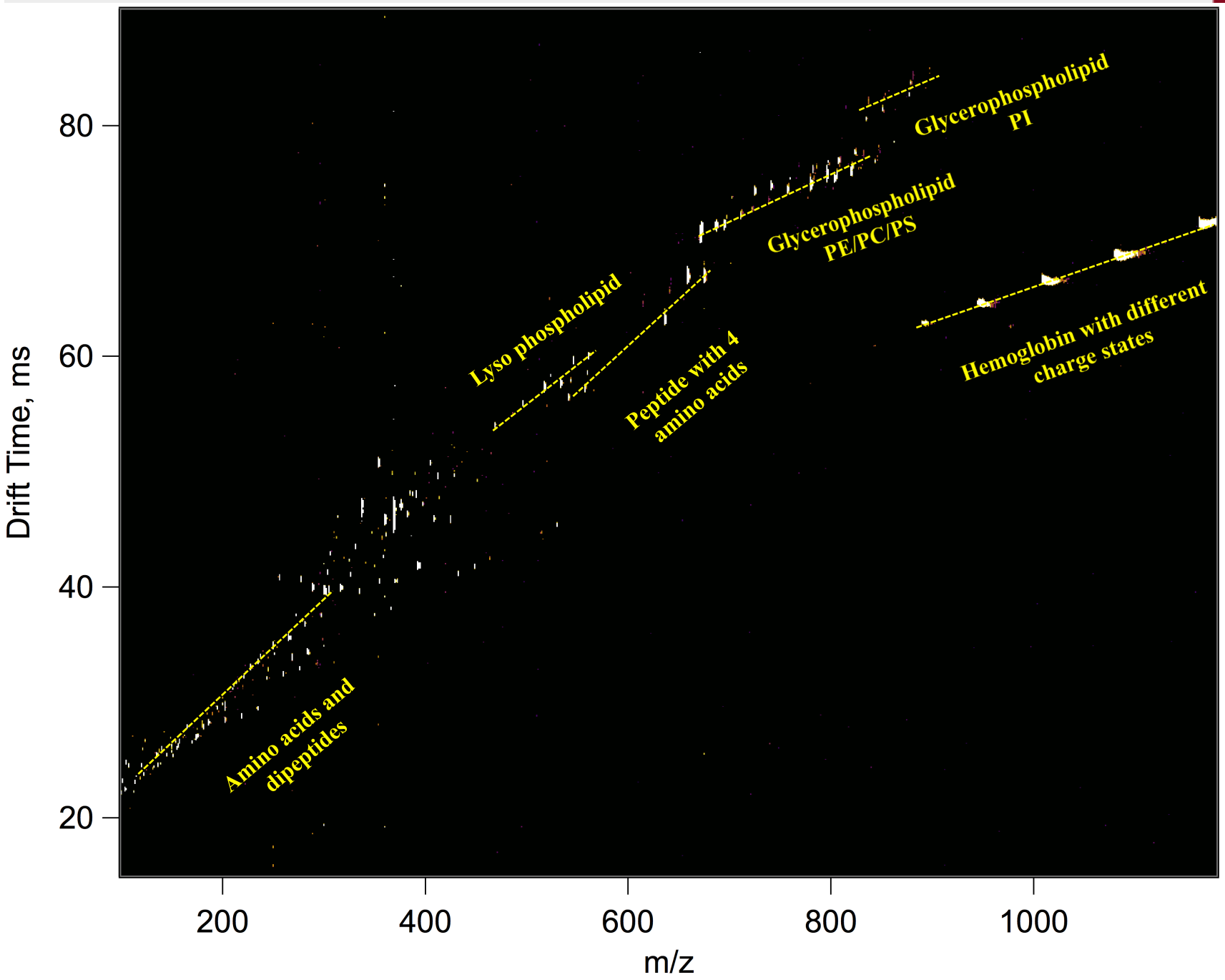

A
B
C
mobility drift time (us)
m/z
Sphingosines, Diacylglycerophosphocholines,
Sterol Lipids
Glycerophosphoethanolamines
Monoacyl glycerophosphocholines
Simple sugars
Sugar phosphates
Estrogen derivatives
Keto PGF2
19-hydroxy PGE2
PGE2
PGB1
PGC1
PGJ3
PGA3
PGB3
Glyceryl PGF2
Stigmasterol
hydroxy PGE1
PGF1
PGC2
Deoxy PGJ2
19-hydroxy PGA2
19-hydroxy PGB2

Structural Elucidation of Unknowns ---Mobility Mass Correlation Curves (MMCCs)

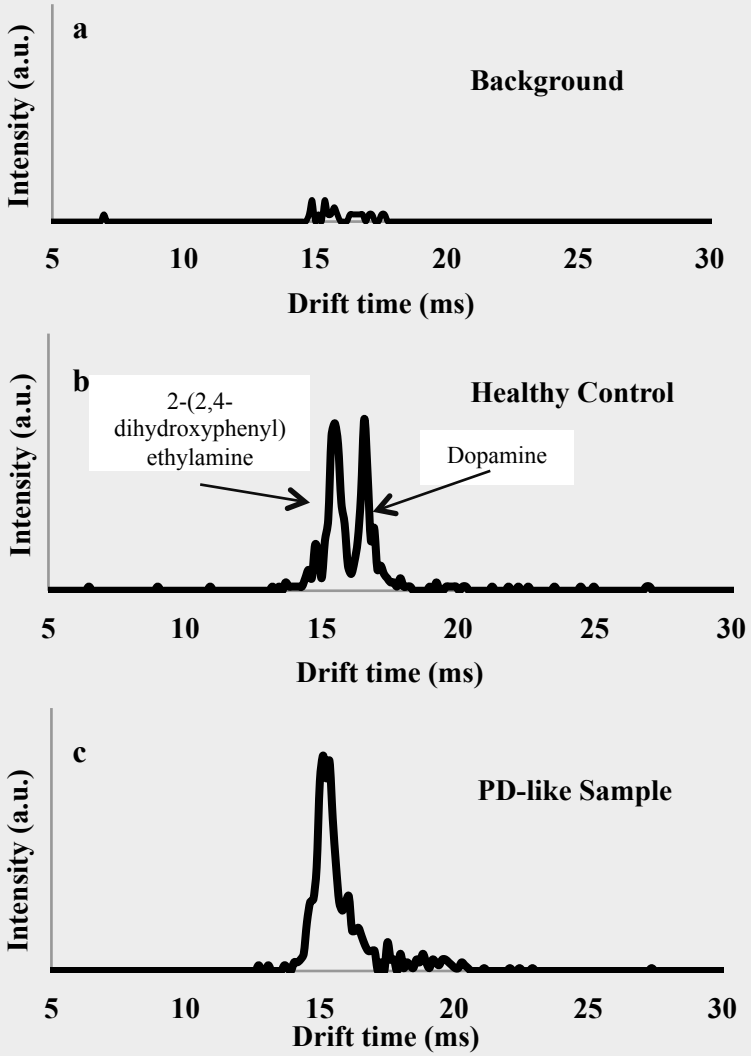




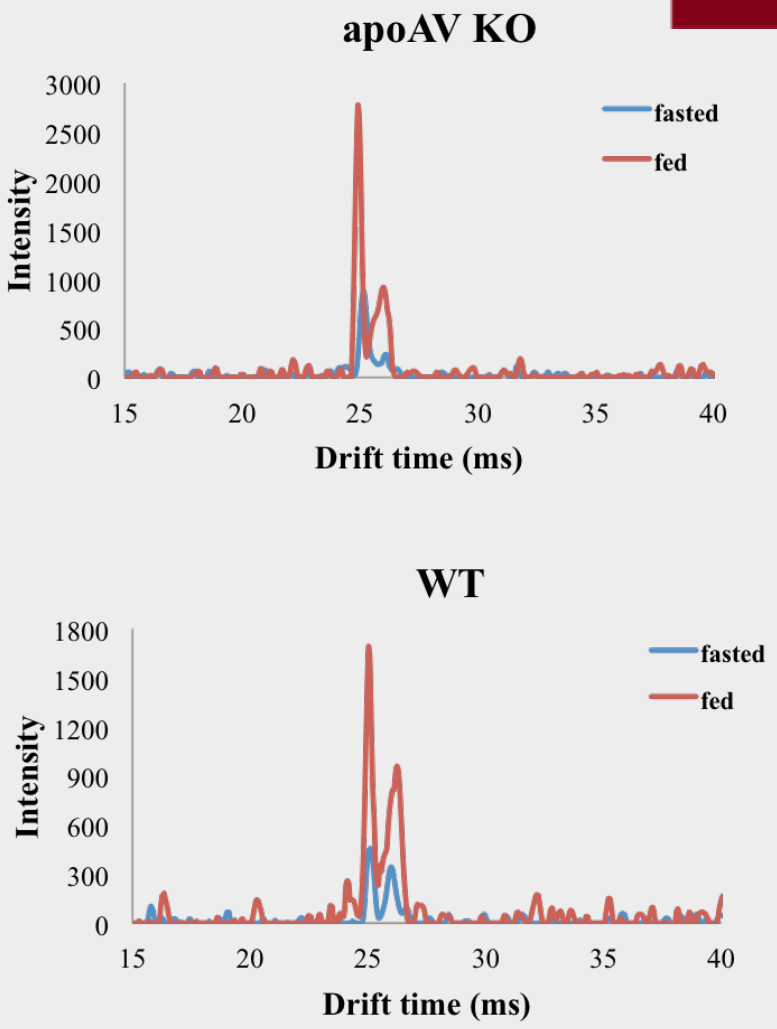
Identification of amino acids in brain tissue (striatum) using MMCCs obtained by standard analysis.


Drift Time, ms
80
60
40
20
200
400
600
800
1000
m/z
Glycerophospholipid
PI
Glycerophospholipid
PE/PC/PS
Lyso phospholipid
Peptide with 4
amino acids
Hemoglobin with different
charge states
Amino acids and
dipeptides

Isomeric Separations with High Resolving Power



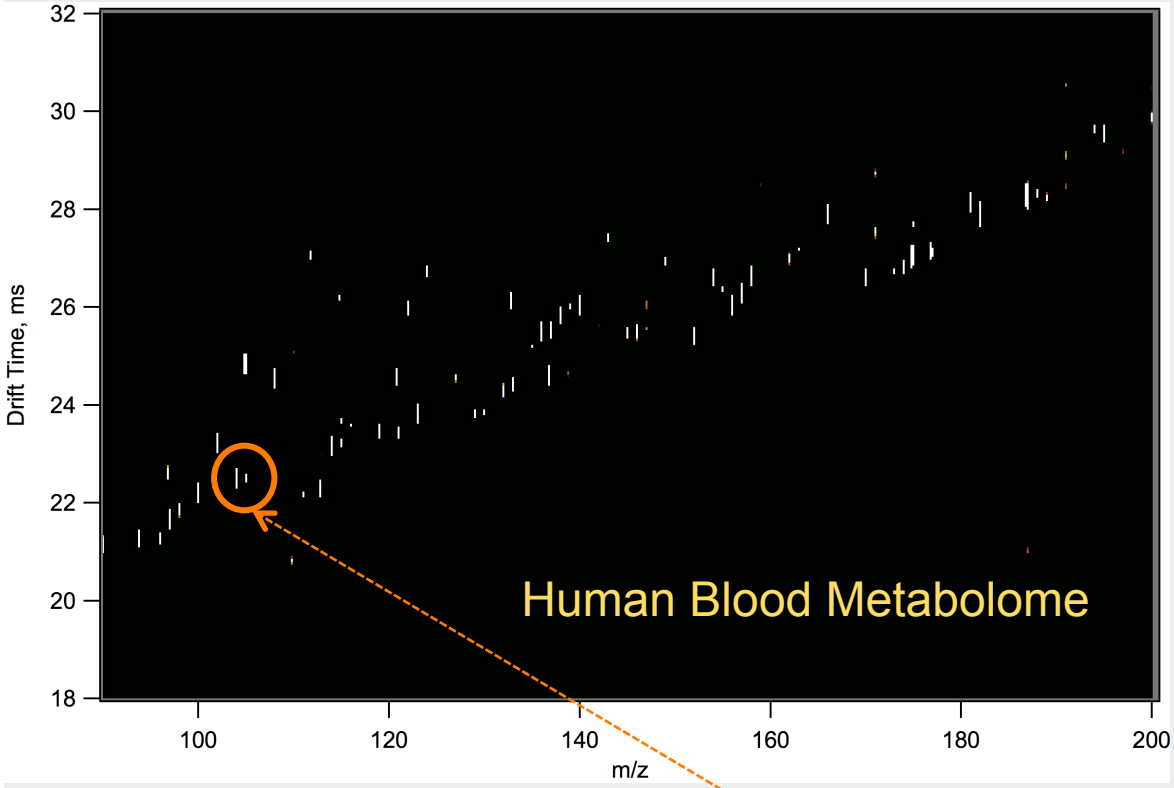
Detection of dopamine and its isomer in striatum from healthy control and PD-like sample

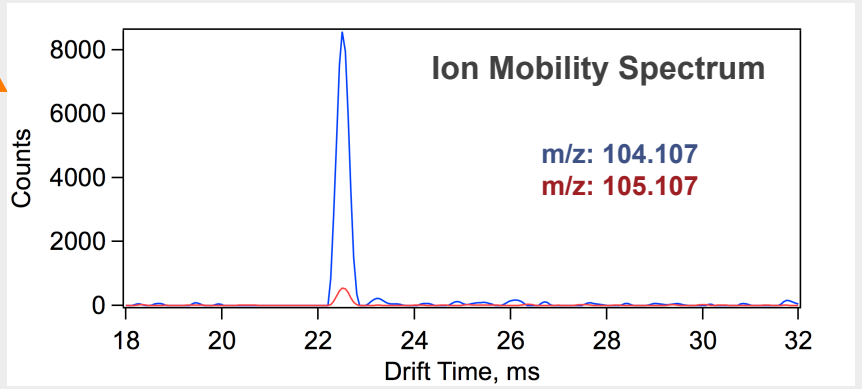


Detection of glucose and fructose in plasma fluids from apoAV KO mice and WT mice

Zhang et al. *Analytical Chemistry.* 2014, 86, 3075-3083.

Structural Elucidation of Unknowns ---Isotopic Ratio Analysis

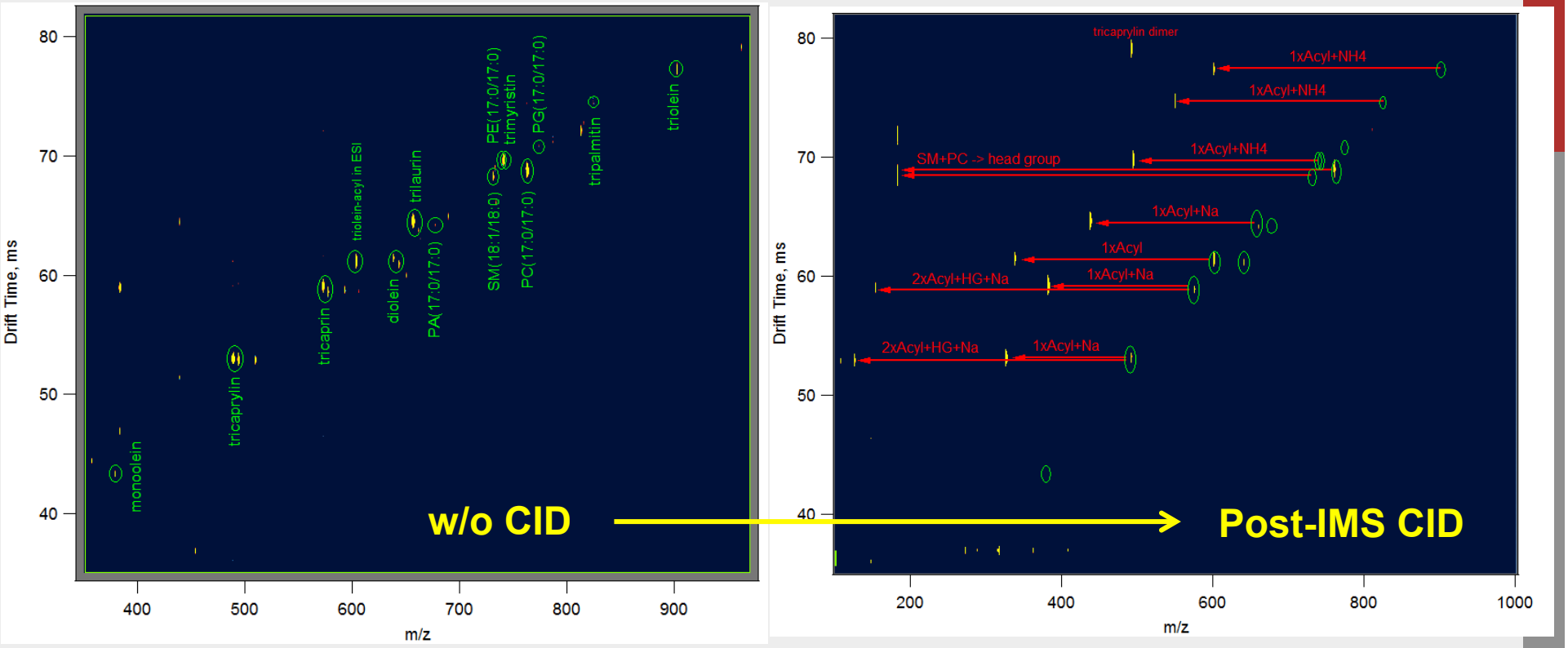




Choline

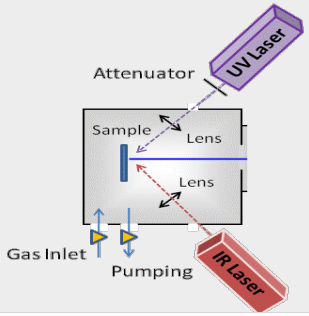
Isotopic ratio 100:5.5

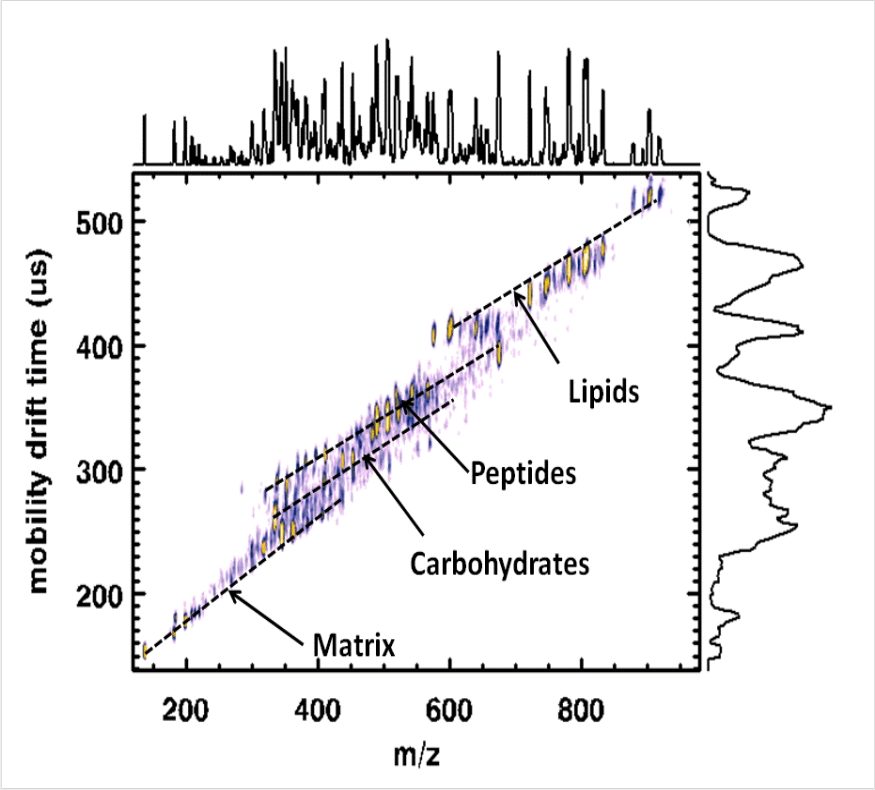
Structural Elucidation of Unknowns ---Fragmentation Analysis



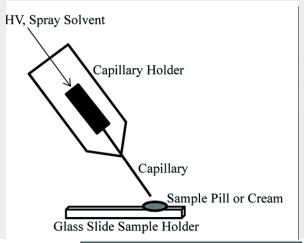
Provided by R. Knochenmuss. Tofwerk (AG, Thun, Switzerland)

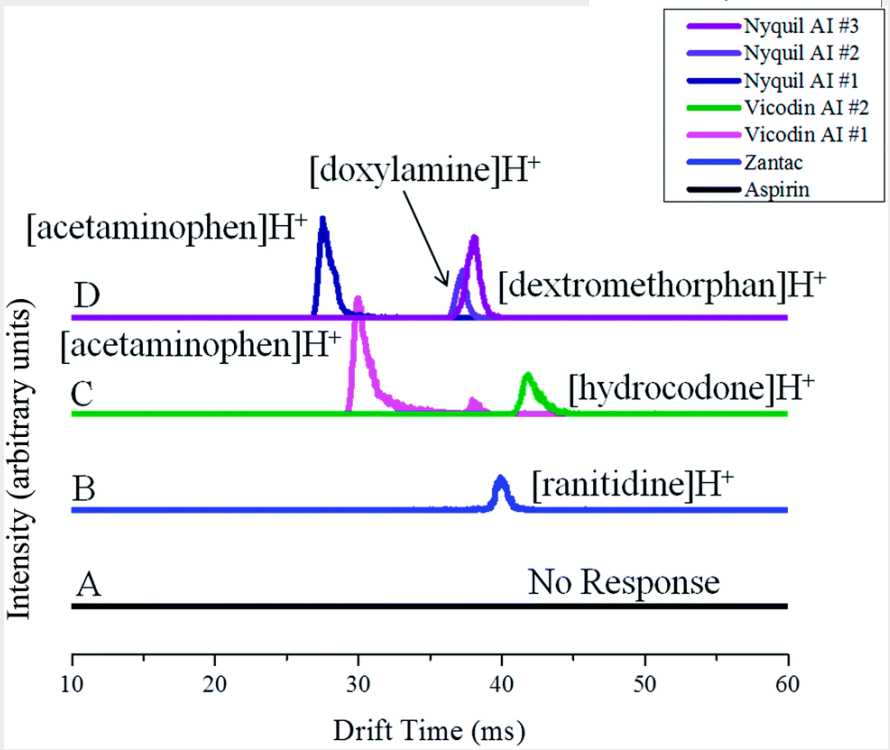
IMMS coupled with Surface Ionization
---Minimize Sample Preparation ---Imaging





MALDI-IMMS of mice lymph fluid





DESI-IMMS of drugs

Kaplan et al. *Int. J. Ion Mobil. Spec.* 2013, 16, 177-184.

Roscioli et al. *Analyst.* 2014, 139, 1740-1750.

IMMS Database with Accurate K_0 Measurement

Standards measured at 30°C, 477 V/cm, water < 1ppm$_v$

Standard	K_0	Literature K_0	Reference
PDO (- mode)	1.784 ± 0.001	--	--
PDO (+ mode) Monomer	1.853 ± 0.002	2.03 (200°C); 2.04 (200°C)	1, 2
PDO (+ mode) Dimer	1.476 ± 0.001	--	--
2,4-Lutidine Monomer	1.867 ± 0.002	1.84-2.07 (78°C-250°C)	3
2,4-Lutidine dimer	1.404 ± 0.001	1.37-1.38 (37°C-38°C)	3
DtBP	1.480 ± 0.002	1.43-1.44 (37°C-250°C); 1.42 (25°C)	3, 4
DMMP Monomer	1.805 ± 0.002	1.80-2.05 (37°C-250°C); 1.74-1.80 (25°C)	3, 4
DMMP Dimer	1.429 ± 0.001	1.39-1.40 (95°C-150°C); 1.38-1.39 (25°C)	3, 4

1. Karpas et al. *Int. J. Mass Spectrom. Ion Processes.*1991, 107, 435-440.
2. Berant et al. *J. Am. Chem. Soc*. 1989, 111, 3819-3824.
3. Eiceman et al. *Anal. Chim. Acta.* 2003, 493, 185-194.
4. Viitanen et al. *Talanta.* 2008, 76, 1218-1223.

IMMS Database with Collision Cross Sections (CCS)

$$\frac{\Omega}{z} = \frac{3}{4}\left(\frac{e}{\mu v_T K_0 N_0}\right)$$

	m / Da	Z	Ω_{He} / nm^2	Ω_{N2} / nm^2
GRGDS	490	1	1.32	2.06
		2	1.39	2.56
SDGRG	490	1	1.30	2.04
		2	1.42	2.59
Angiotensin fragment 1-7	898	2	2.26	3.34
RASG-1	1 000	2	2.25	3.31
Angiotensin II	1 046	2	2.45	3.35
Bradykinin	1 060	2	2.37	3.44
Angiotensin I	1 296	3	3.28	4.74
Renin substate	1 758	3	3.80	5.22
Enolase T35	1 872	3	3.80	5.19
Enolase T37	2 827	3	4.65	-

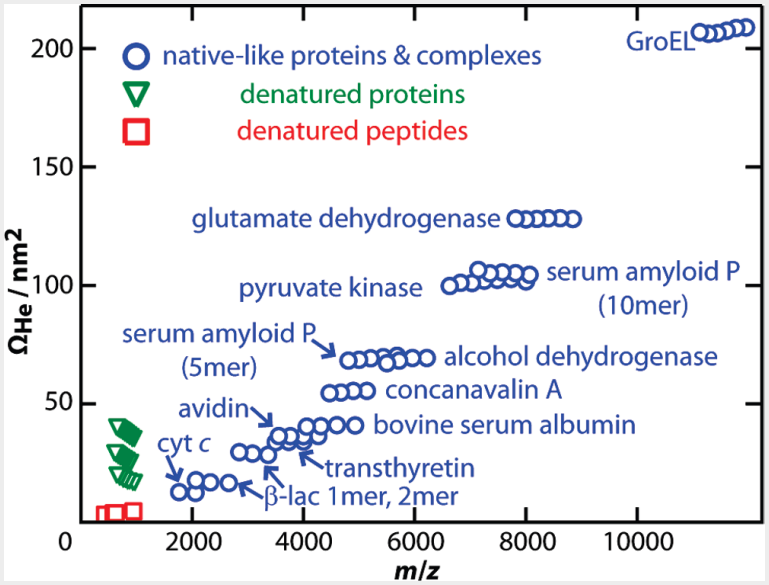
CCS values for proteins from TWIMMS (Waters)

name		exact mass [Da]	CCS (this work[a]) [Å^2]	CCS (literature[b]) [Å^2]	abs. percent difference[c] [%]
tetramethylammonium	TAA1	74.14		107.40	
tetraethylammonium	TAA2	130.25		122.20	
tetrapropylammonium	TAA3	186.36	144.1 ± 0.7 (23)	143.80	0.22
tetrabutylammonium	TAA4	242.46	166.6 ± 0.9 (16)	166.00	0.36
tetrapentylammonium	TAA5	298.57	190.1 ± 1.0 (28)	190.10	0.02
tetrahexylammonium	TAA6	354.68	213.5 ± 1.0 (31)	214.00	0.23
tetraheptylammonium	TAA7	410.78	236.4 ± 0.4 (31)	236.80	0.17
tetraoctylammonium	TAA8	466.54	256.6 ± 0.7 (31)	258.30	0.64
tetradecylammonium	TAA10	579.11	293.5 ± 0.7 (24)		
tetradodecylammonium	TAA12	691.32	319.0 ± 0.9 (24)		
tetrahexadecylammonium	TAA16	915.04	361.5 ± 0.9 (24)		
tetraoctadecylammonium	TAA18	1027.16	379.0 ± 1.7 (21)		

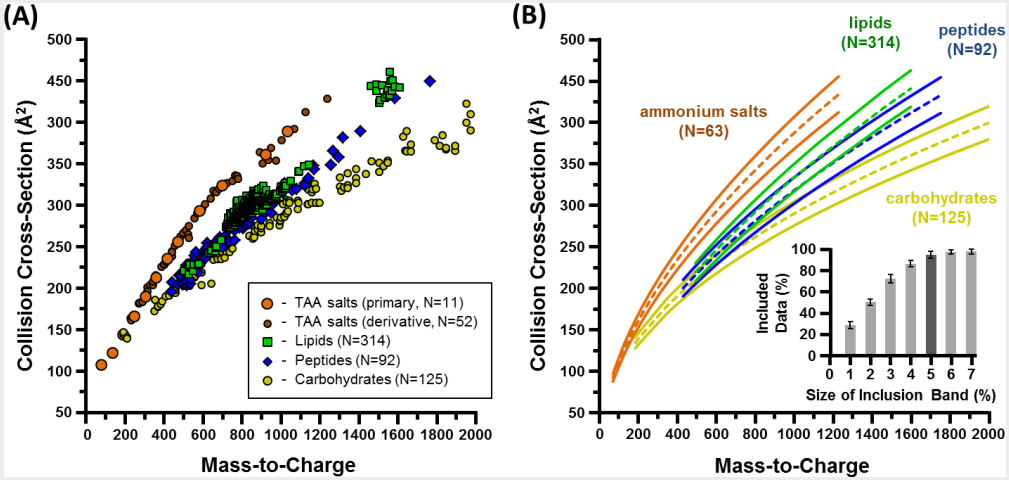
CCS values for TAA salts from IM-Q-TOFMS (Agilent)

May et al. *Anal. Chem.* 2014, 86, 2107-2116. Bush et al. *Anal. Chem.* 2010, 82, 9557-9565.

m/z *vs.* CCS Profiles for Different Classes



CCS values for proteins from TWIMMS (Waters)



CCS values for TAA salts from IM-Q-TOFMS (Agilent)

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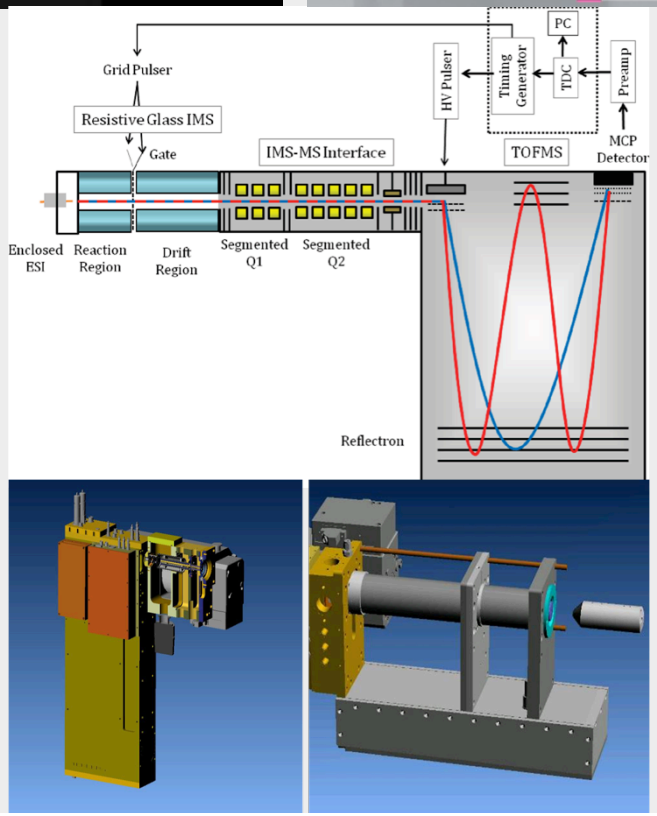
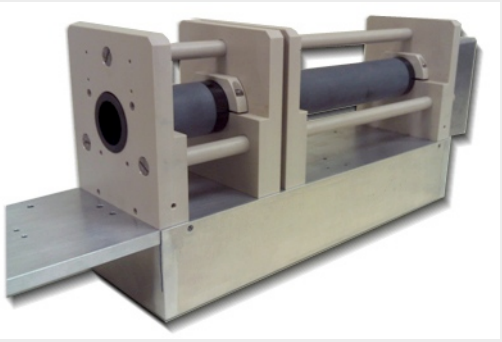
The Mobility Advantages

1. Wide Application (metabolomics, glycomics, proteomics, etc.)
2. High Throughput Analysis (rapid preseparations)
3. Isomer Separation
4. Conformer Separation
5. Size Selective Fragmentation
6. Isotope Ratios in Complex Mixtures
7. Mobility-Mass Correlation for Chemical Classes
8. Surface analysis (image analysis)
9. Charge State Separation
10. Accurate Mobility Measurements

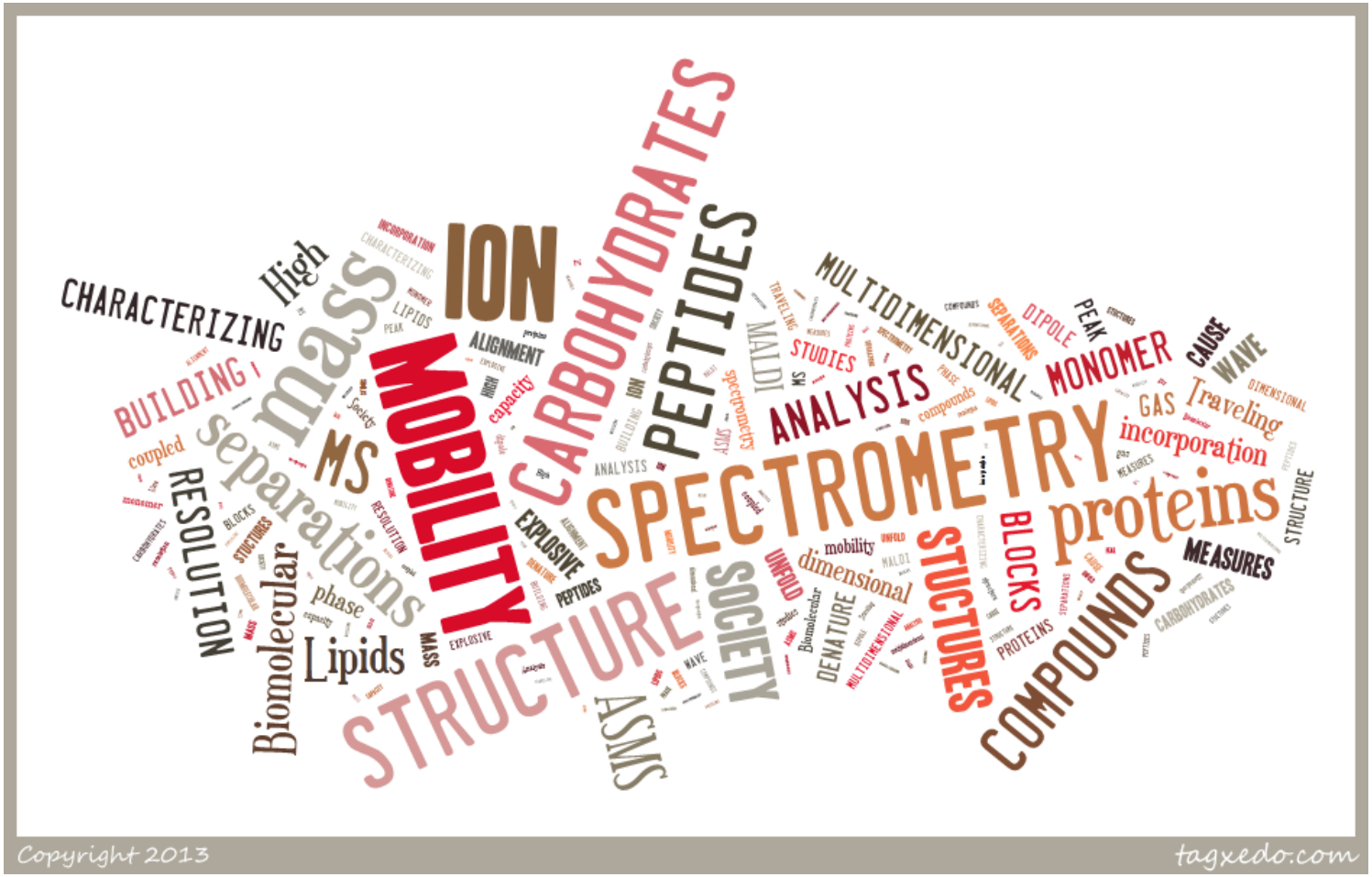
11. BUT THE MOST IMPORTANT MOBILITY ADVATAGE

IMMS Instruments Are Now Available





QUESTIONS?



2014

ASMS, Baltimore, MD