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Mixed Halogen Dioxins and Furans in Controlled Burn Samples Determined Using Gas Chromatography-Ion Mobility

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Overview

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- Human Exposure to Dioxins
- Simulated Burn Study
- Comparing Magnetic Sector to Tandem Quadrupole Data
- Ion Mobility Investigation
- Conclusion

Effect of Large Scale Fires

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- World Trade Center
  - New York City (2001)
  - 50,000 first responders
  - 19% increase in total cancer rates among exposed NYC firefighters
  - Prostate, thyroid, and multiple myeloma cancers most prominent
- Plastimet Fire
  - Hamilton, Ontario (1997)
  - 294 firefighters at scene

Owens, R.O. et al; *Lancet*, 378 (2011) 898-905

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What is something they all have in common?

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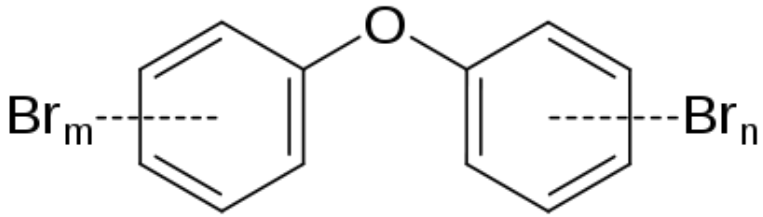
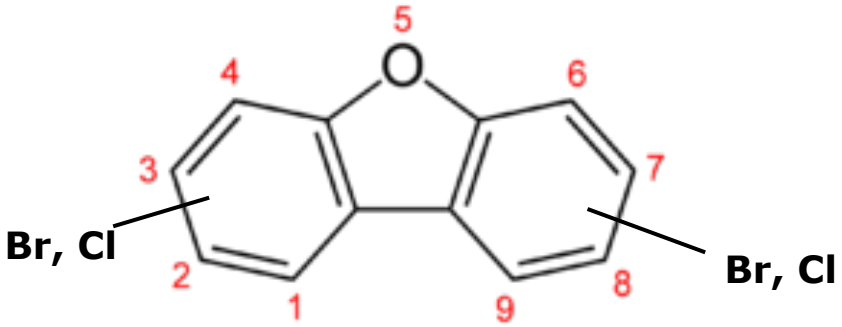
Brominated Flame Retardants



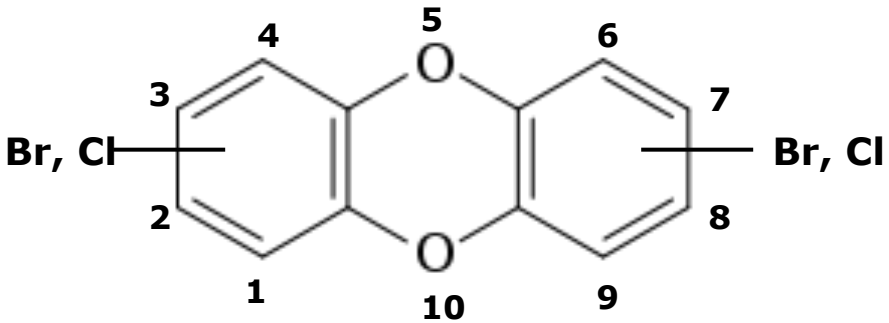
Polybrominated diphenyl ether (PBDE)

Δ
+ source of chlorine

Δ
+ source of chlorine



Dibenzofuran



Dibenzo-p-dioxin

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Potency studies in human liver cells

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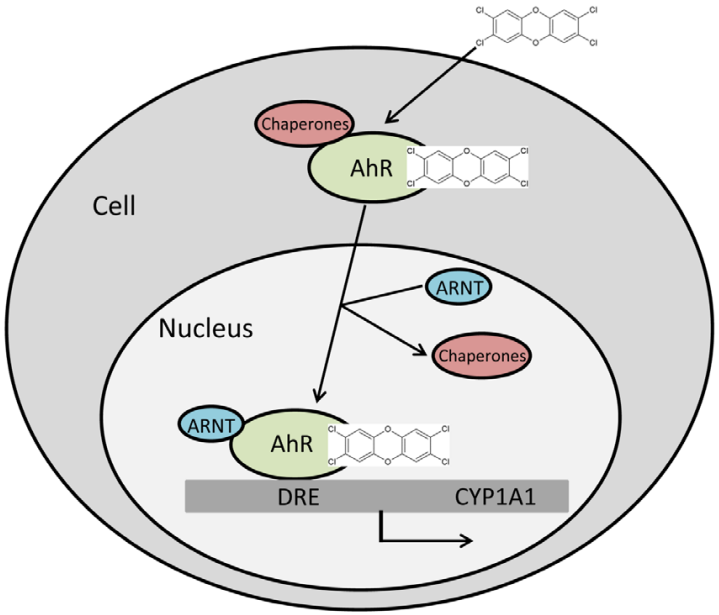
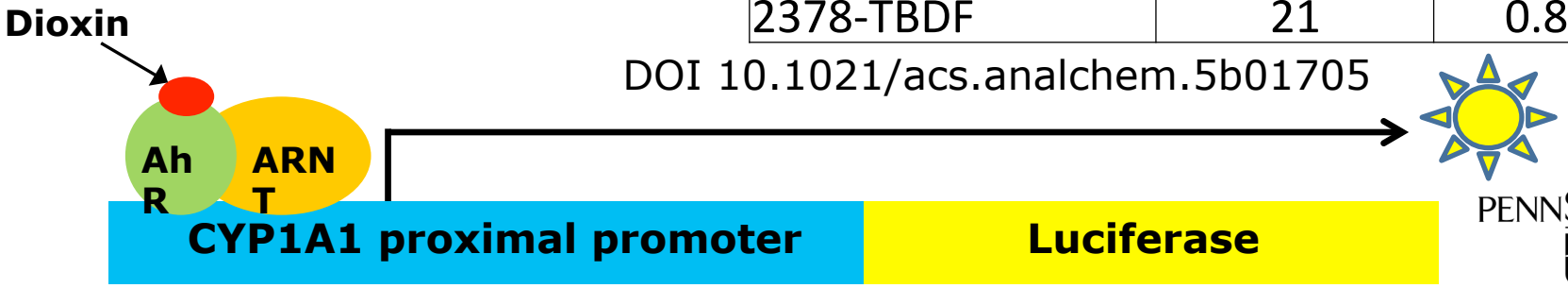


Compound	Number of replicates	Potency
2378-TCDD	21	1.00
2Br, 378Cl DD	18	0.99 ± .13
23Br, 78Cl DD	19	0.84 ± .10
2378-TBDD	17	0.77 ± .14
2378-TCDF	21	0.83 ± .07
3Br, 278Cl DF	20	0.97 ± .12
23Br, 78Cl DF	20	1.02 ± .15
2378-TBDF	21	0.86 ± .10

DOI 10.1021/acs.analchem.5b01705



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Simulated Burn Studies

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ELITE FIREFIGHTERS

2013

Household Fire
- Mattress
- Sofa Chair
- Vinyl / Wood Chair
- Carpet
- Pillows
- Television

Electronics Fire
- Televisions
- Microwave
- Printers
- Computer monitors
- Laptop
- Cables/Wires

2014

Household Fire
- 2 Sofa Chairs
- Vinyl and Metal Chair
- 2 Carpets
- Pillows and Cushions
- Coffee Table
- Vinyl Kitchen Chairs

Electronics Fire
- Televisions
- Microwave
- Computer Monitors
- Computer Towers
- VHS tapes
- Keyboards
- Used Ink Cartridges

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Can APGC/MS/MS be Qualified for Dioxin Analysis?

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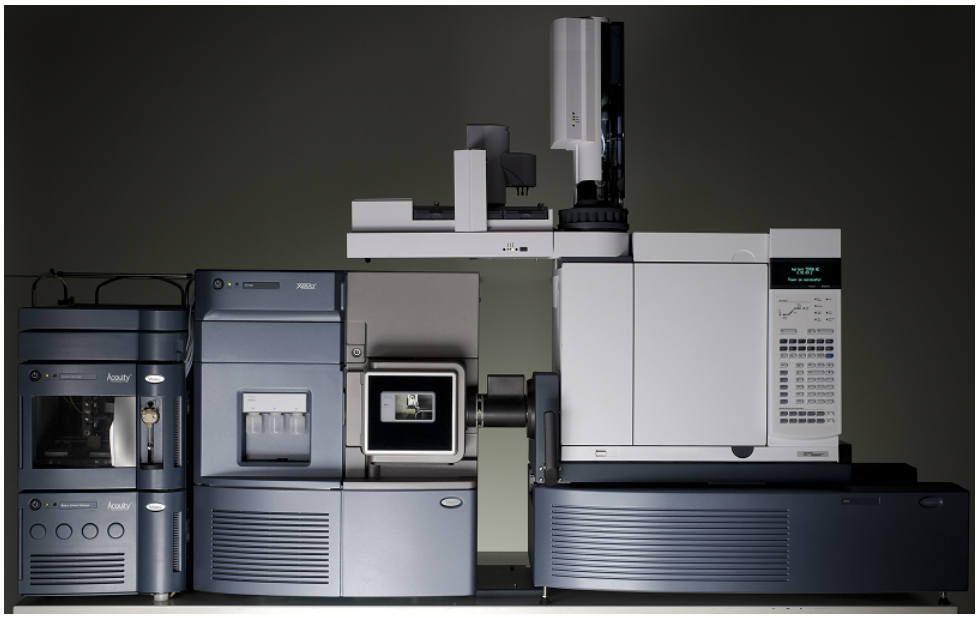
- Penn State and the Ontario Ministry of Environment
  - Compare reference materials run on both the Autospec and Xevo APGC-TQS



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Sensitivity Evaluation

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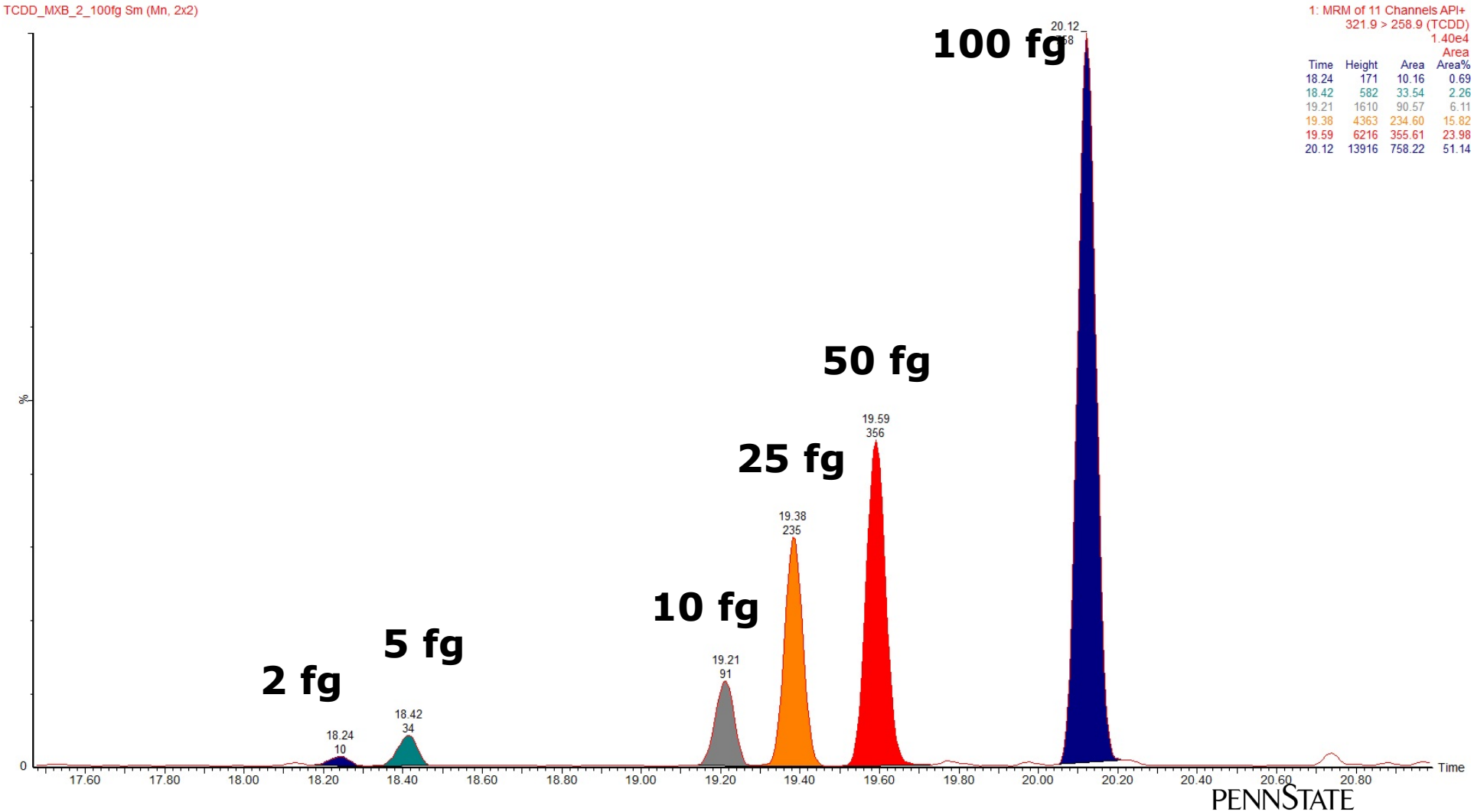

DOI 10.1021/acs.analchem.5b01705

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Magnetic Sector v. Tandem Quad

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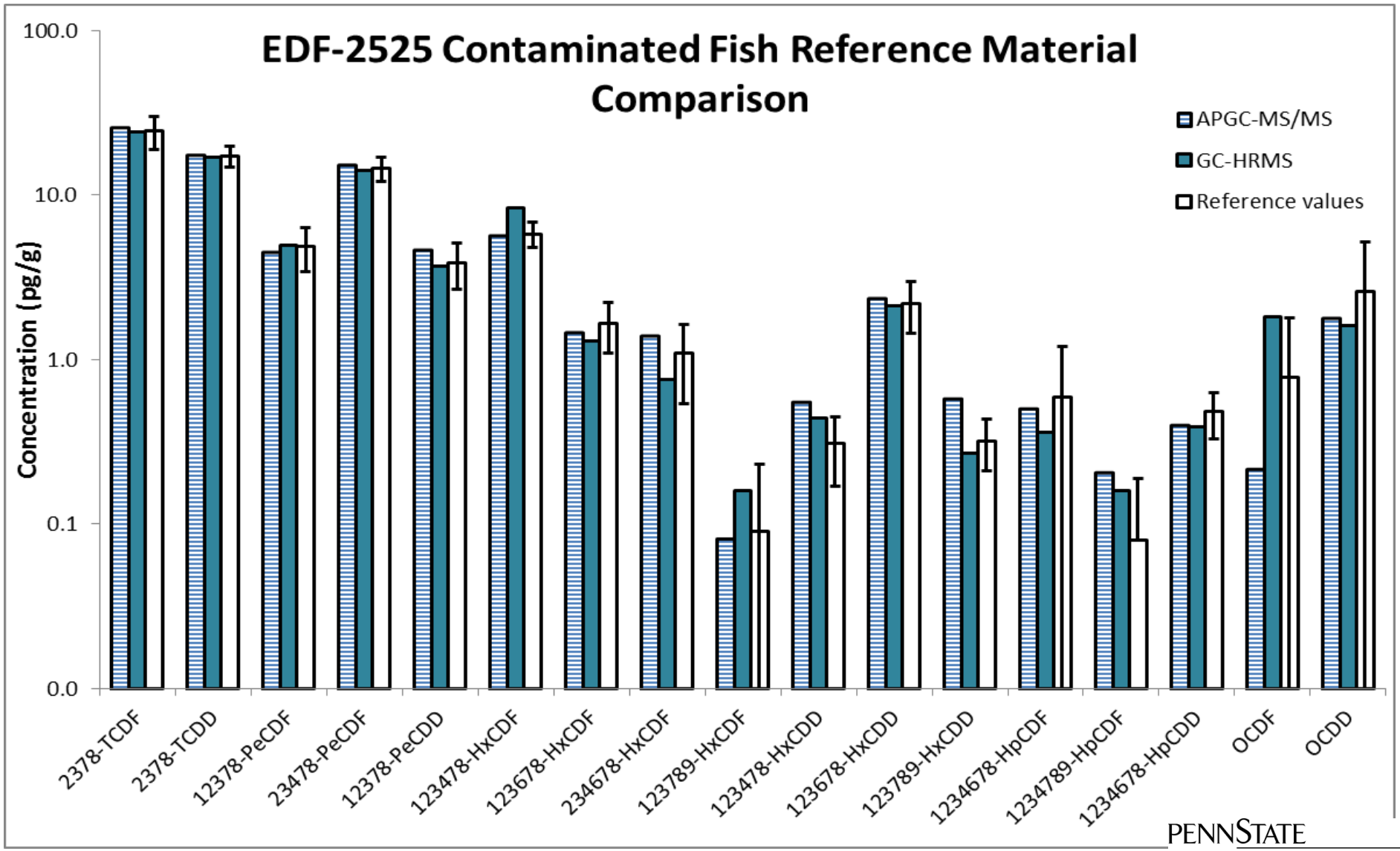

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Method Detection Limit (MDL)

TQ-S v. Autospec

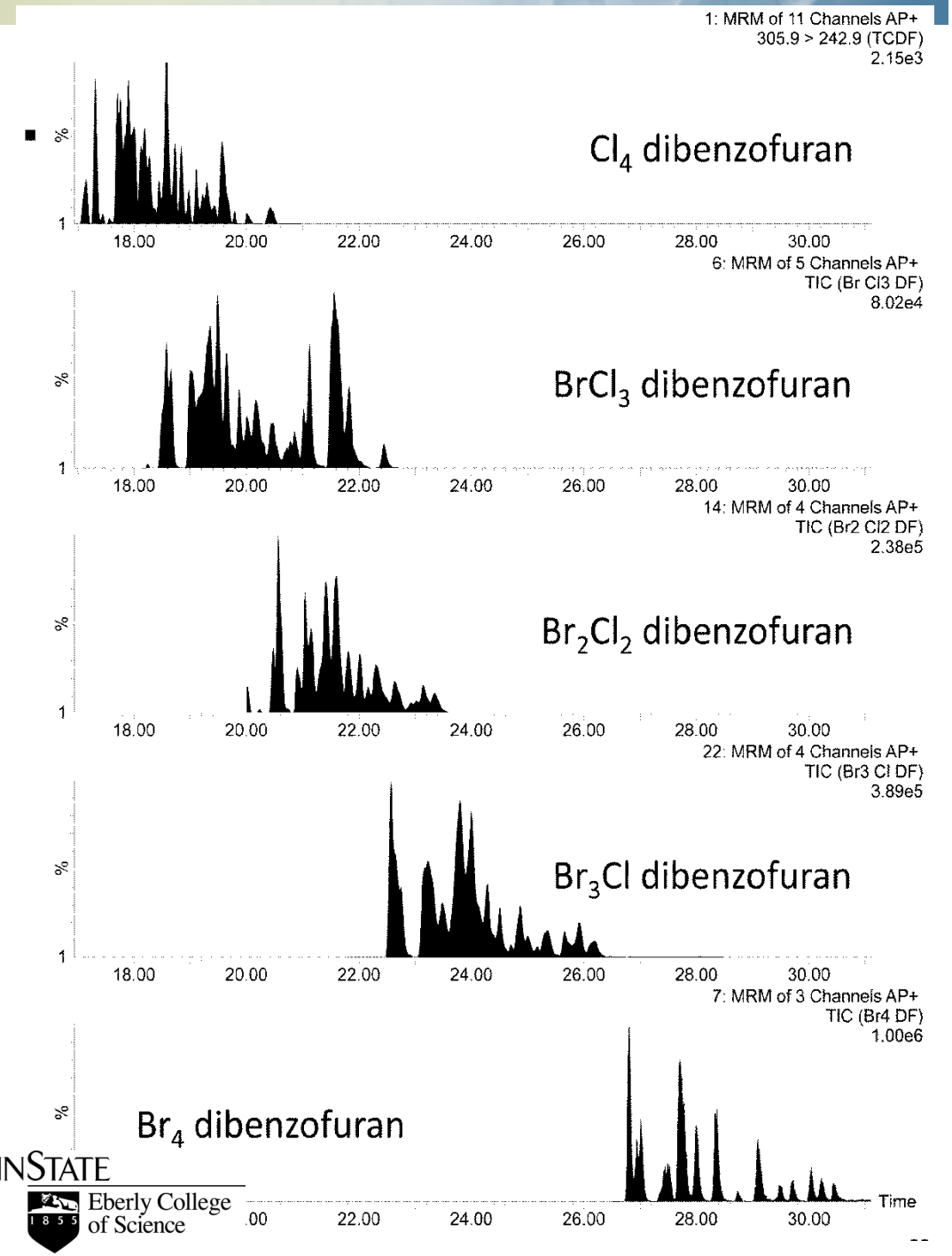
TQ-S MDLs 2 – 20

times lower

		Soil matrix (n=10)		Fish matrix (n=10)	
Compound	units	APGC-MS/MS MDL	GC-HRMS MDL	APGC-MS/MS MDL	GC-HRMS MDL
2,3,7,8-TCDF	pg/g	0.17	0.68	0.21	0.77
2,3,7,8-TCDD	pg/g	0.15	0.80	0.23	4.29
1,2,3,7,8-PeCDF	pg/g	1.32	2.64	1.96	3.47
2,3,4,7,8-PeCDF	pg/g	0.48	2.22	0.31	2.63
1,2,3,7,8-PeCDD	pg/g	0.39	3.85	0.55	1.83
1,2,3,4,7,8-HxCDF	pg/g	0.78	2.28	0.53	2.99
1,2,3,6,7,8-HxCDF	pg/g	0.54	1.01	0.30	2.65
1,2,3,7,8,9-HxCDF	pg/g	0.41	2.21	0.51	2.68
2,3,4,6,7,8-HxCDF	pg/g	0.37	2.30	0.54	1.86
1,2,3,4,7,8-HxCDD	pg/g	0.62	3.79	0.70	6.02
1,2,3,6,7,8-HxCDD	pg/g	0.40	3.01	0.40	0.82
1,2,3,7,8,9-HxCDD	pg/g	0.35	4.28	0.76	4.05
1,2,3,4,6,7,8-HpCDF	pg/g	0.28	3.36	0.50	5.79
1,2,3,4,7,8,9-HpCDF	pg/g	0.56	4.87	0.84	2.93
1,2,3,4,6,7,8-HpCDD	pg/g	0.41	1.62	1.24	4.80
OCDF	pg/g	0.74	4.85	1.99	3.71
OCDD	pg/g	1.42	4.49	1.26	7.46

Firefighter helmet wipes

- Model exposure of firefighters to PXDD/F's



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Detection of Mixed Halogenated Dioxins

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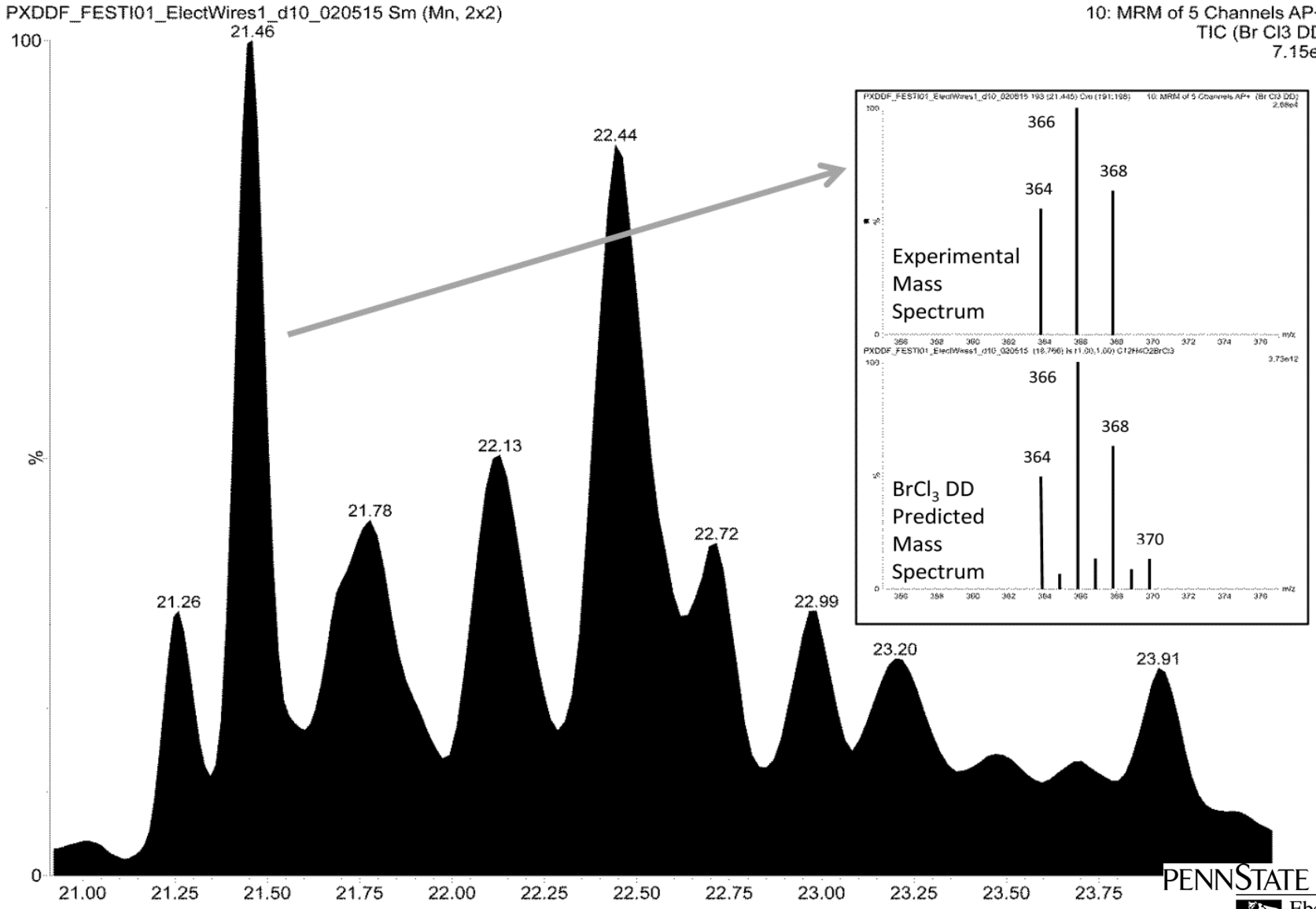

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QQQ v HRMS

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Goals of Combining HRMS with IMS

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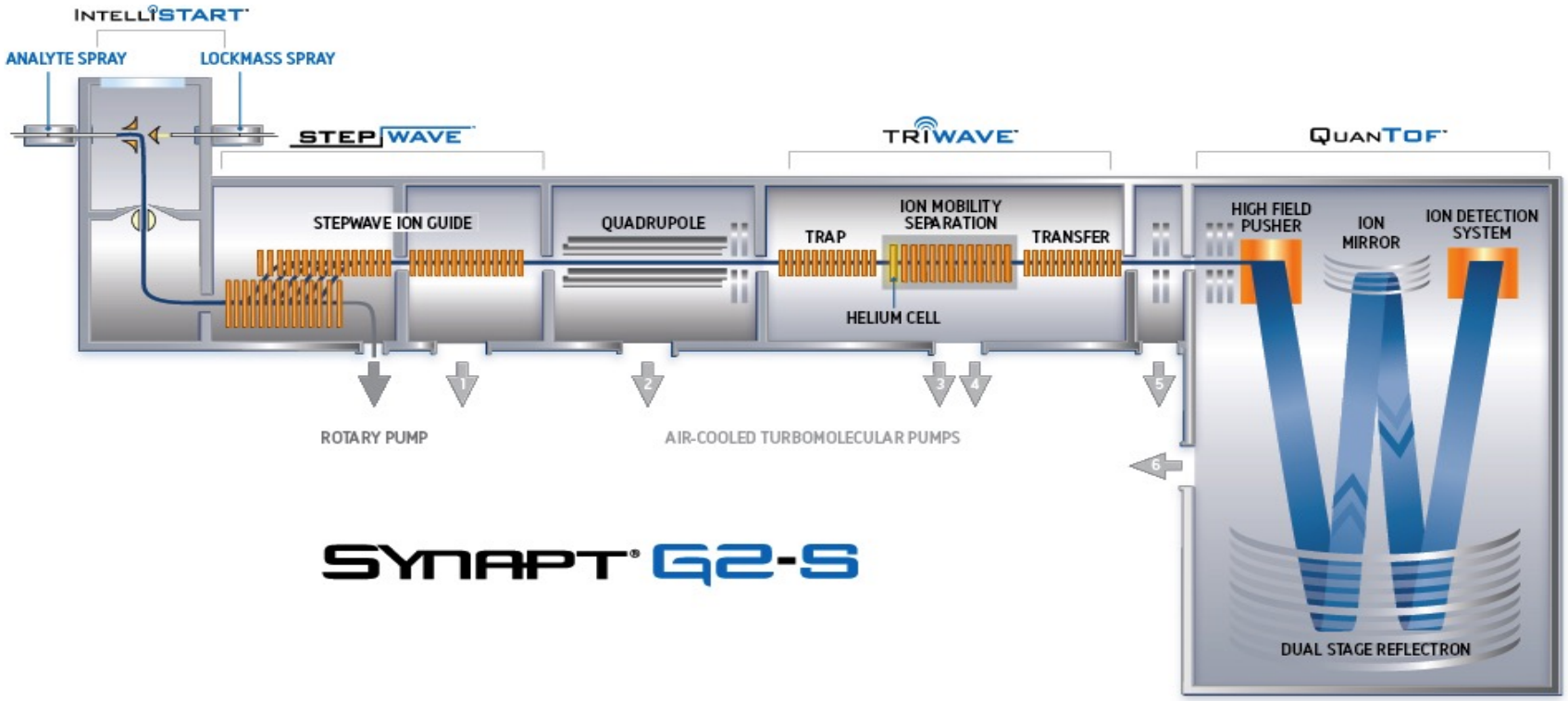
- IMS = additional separation based on size, shape and charge state of an analyte
  - Collisional Cross Section (CCS)



IMS Uses

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- Overcome chemical noise limits in MS/MS
- Improve MRM methods with <70 or > 120% recoveries
- Spectral clean up
- Avoid false positive/negative results
- Prevent unnecessary failure of biomarker validation
- ID relationships among analytes – compound class

- Resolve compounds chromatography does not as well as isomers, isobars, charge states, and protomers

Ion Mobility Overview

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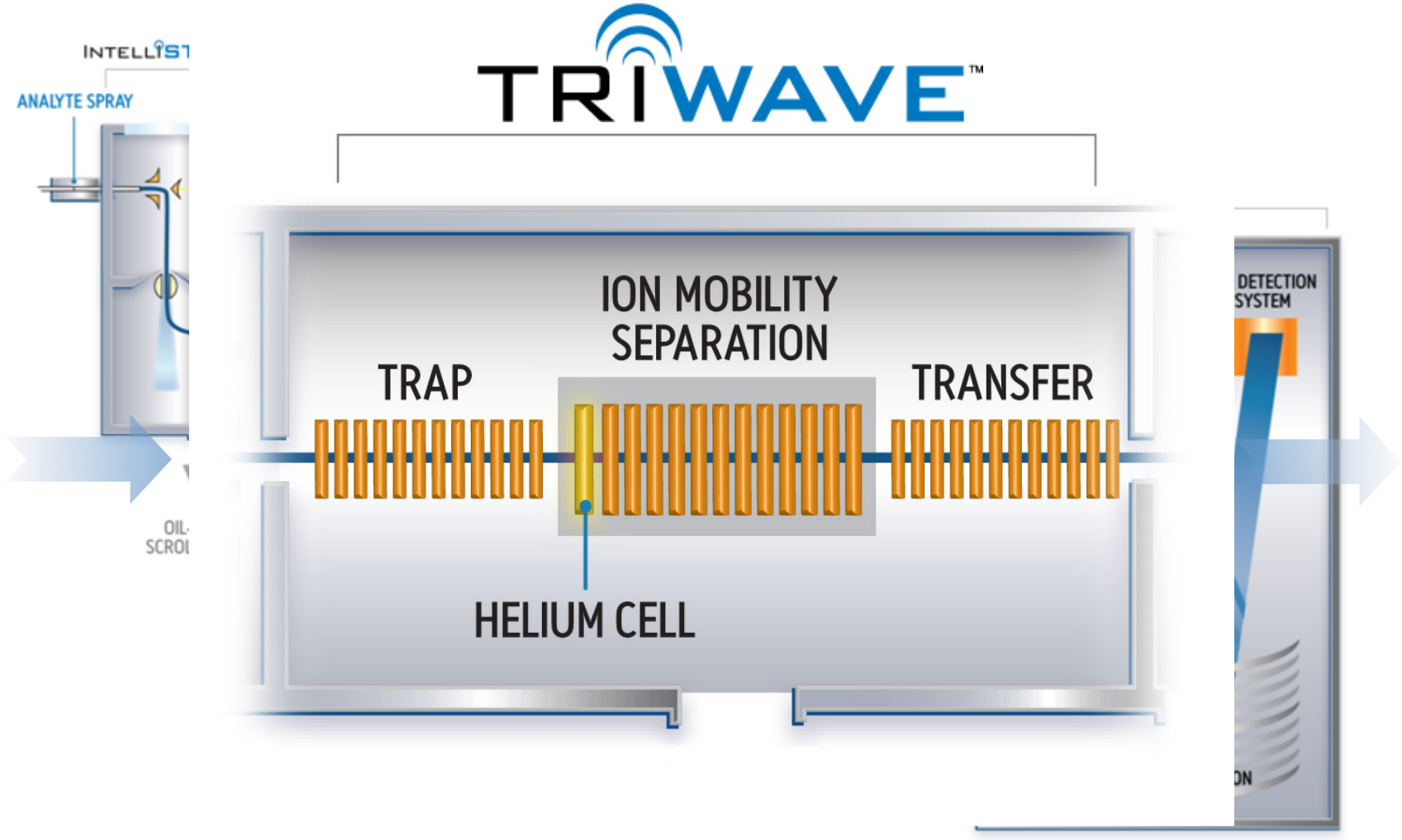

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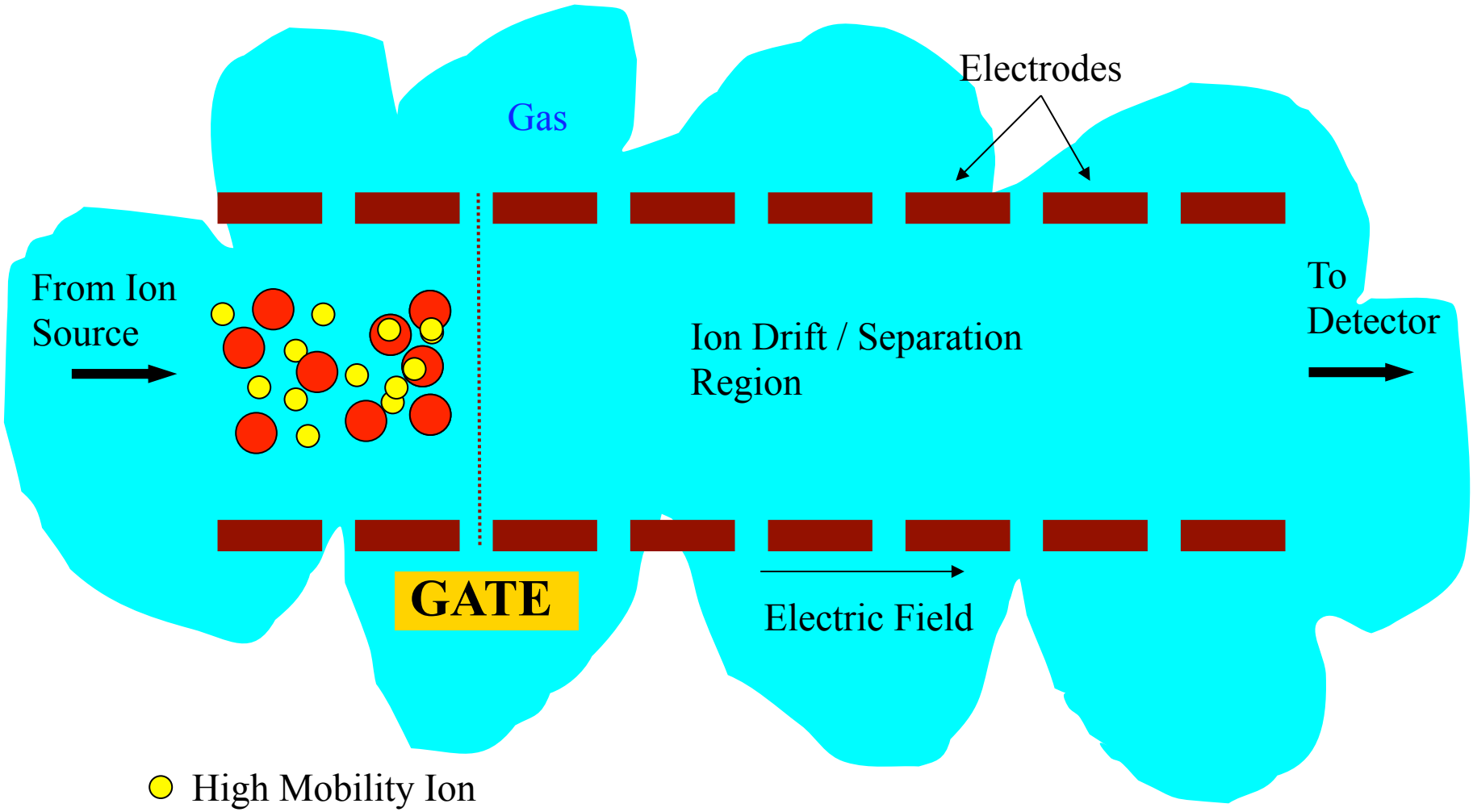

Ion Mobility Separation Isomers

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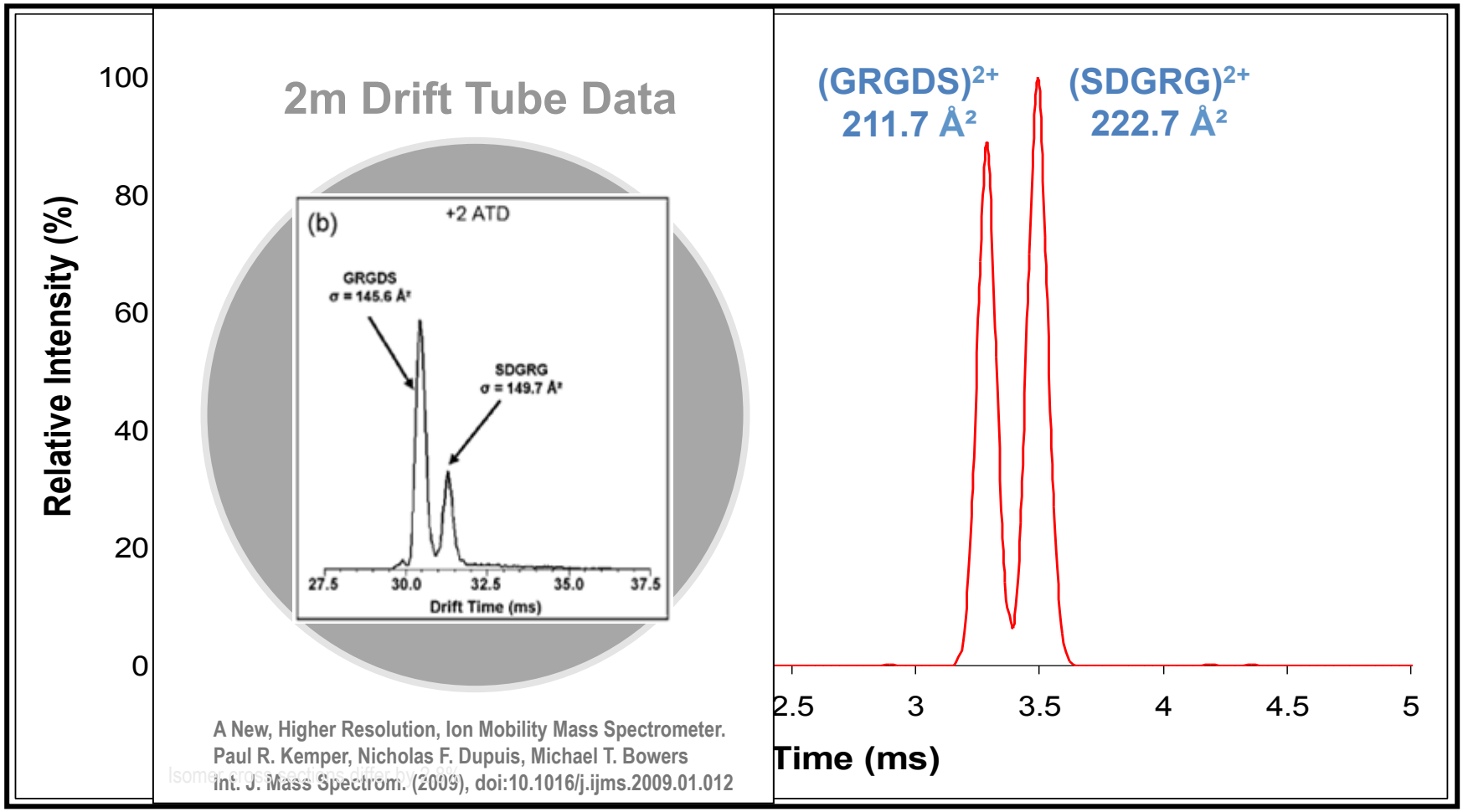

Where's Waldo?

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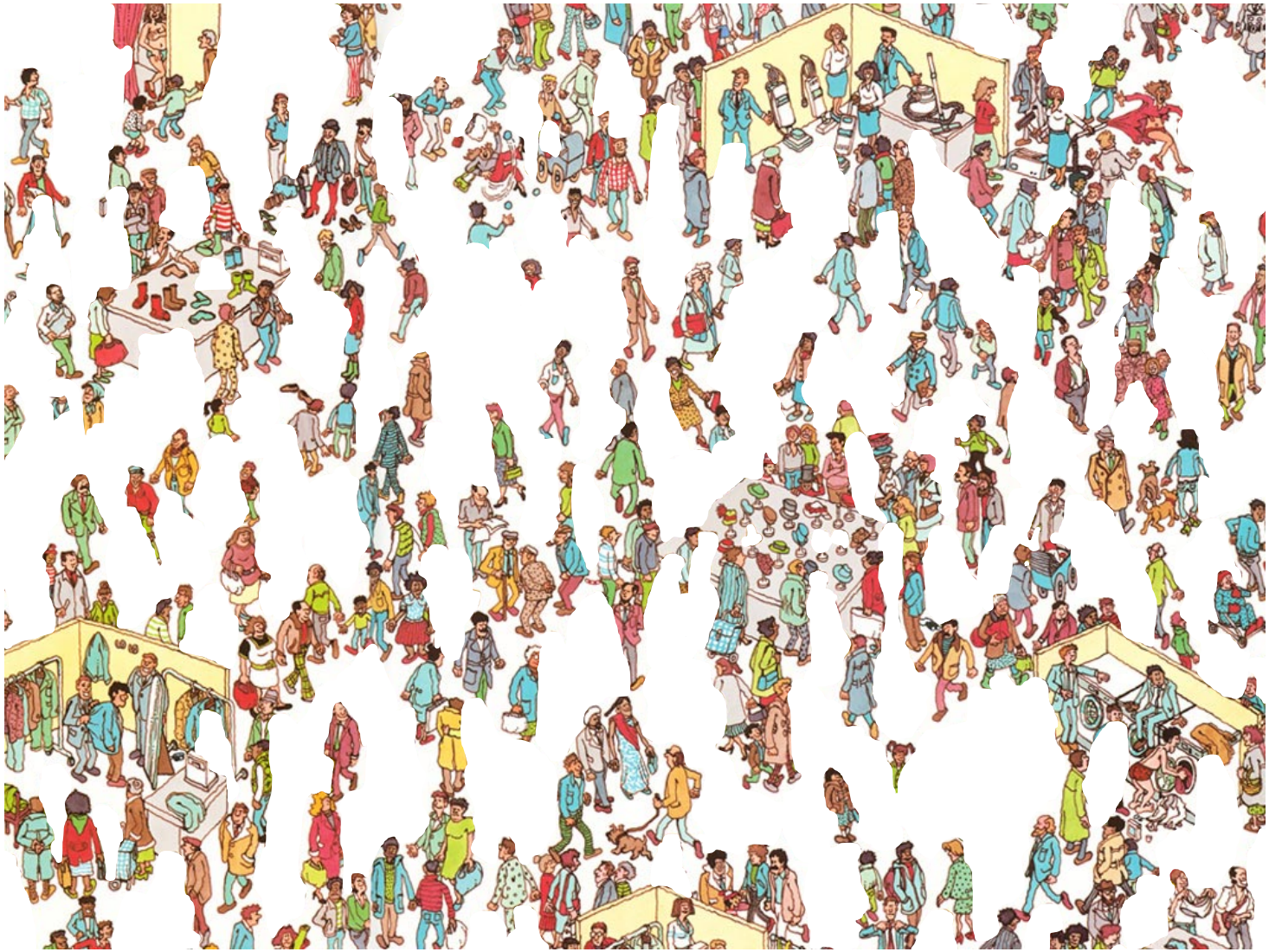

APGC

Where's Waldo?

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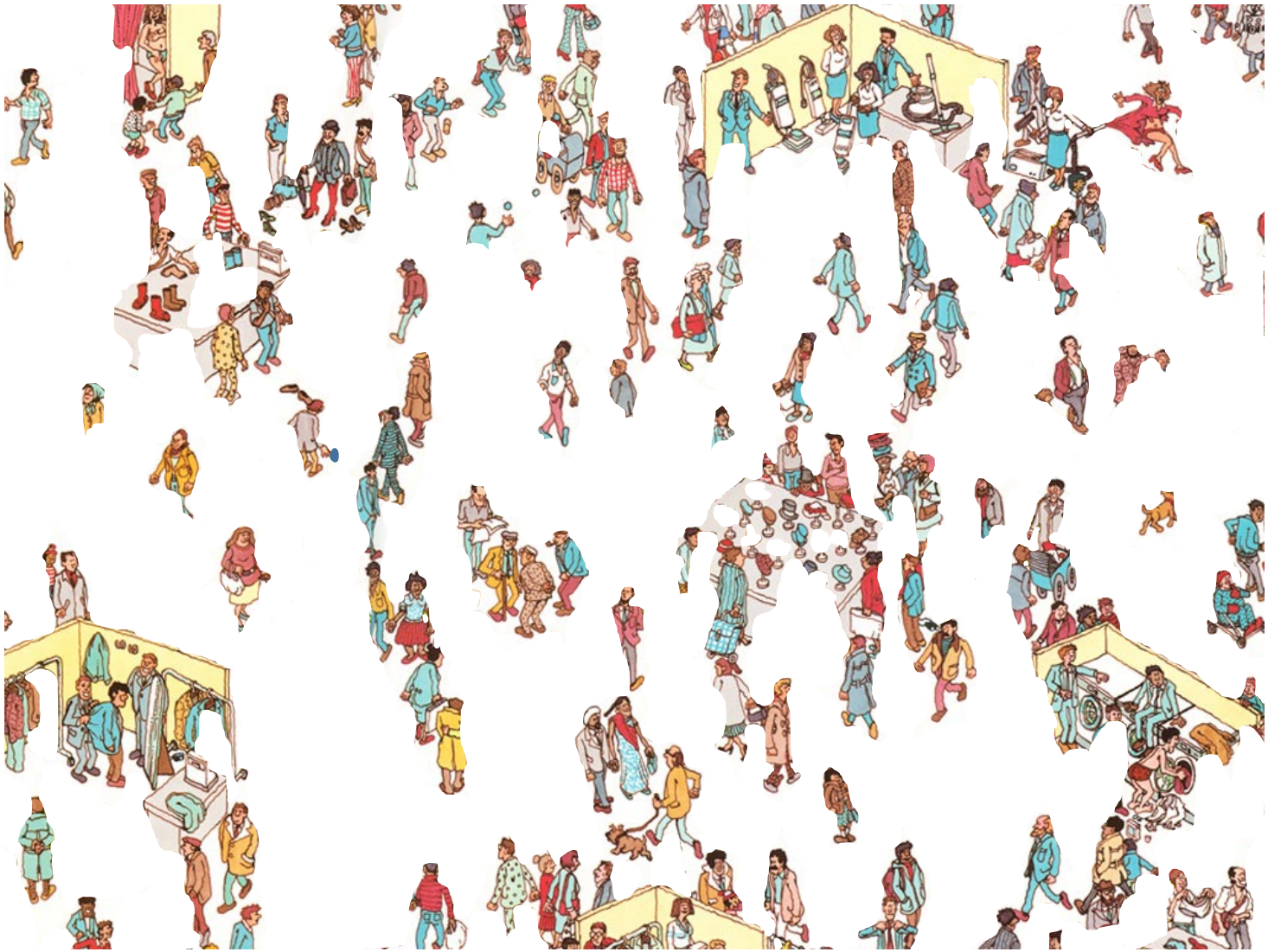

APGC

MS

Where's Waldo?

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UPLC

MS

IMS

HDMS^E

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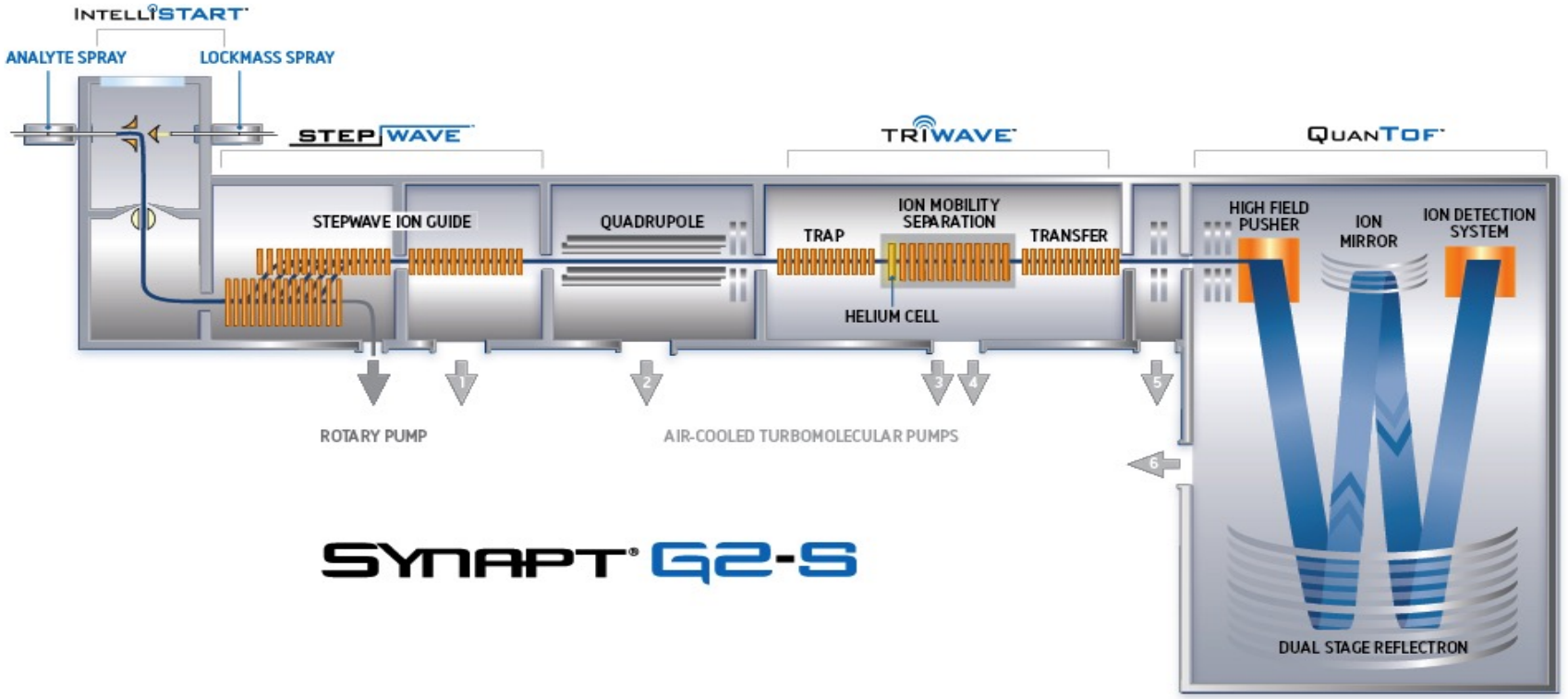
- Provides accurate mass on precursors and product ions by rapidly alternating between high and low energy
  - Clean spectra for intact molecular ion and all fragments
  - For comprehensive structural elucidation



Transfer Fragmentation

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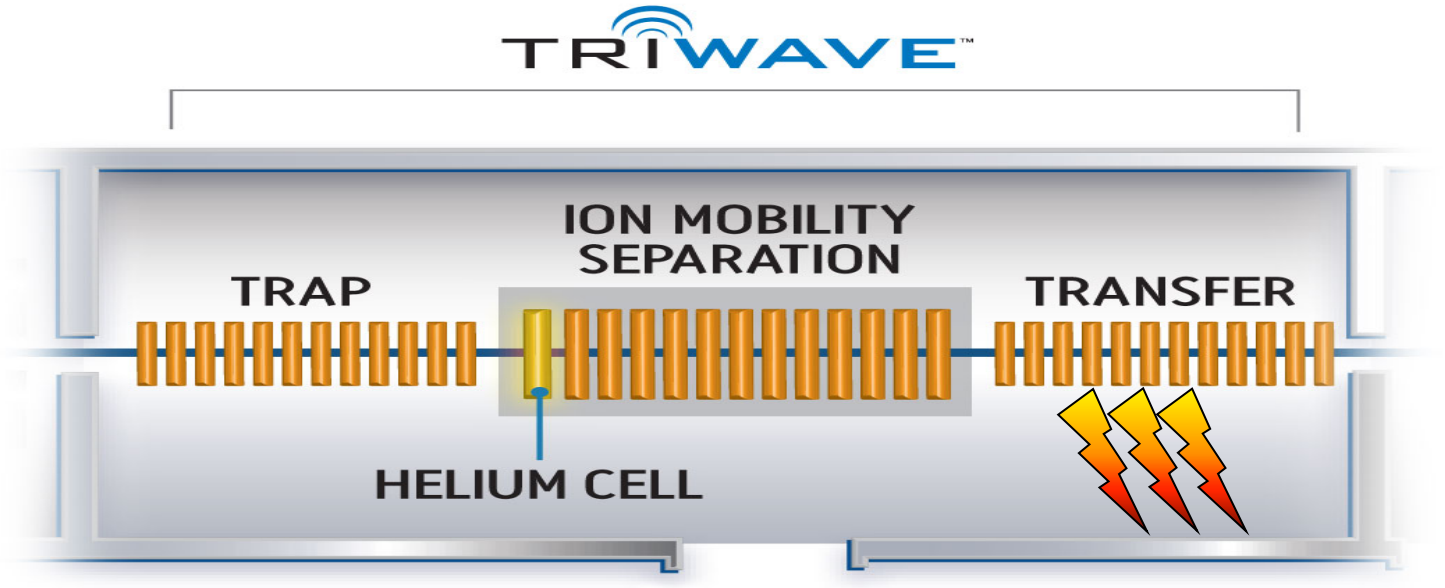

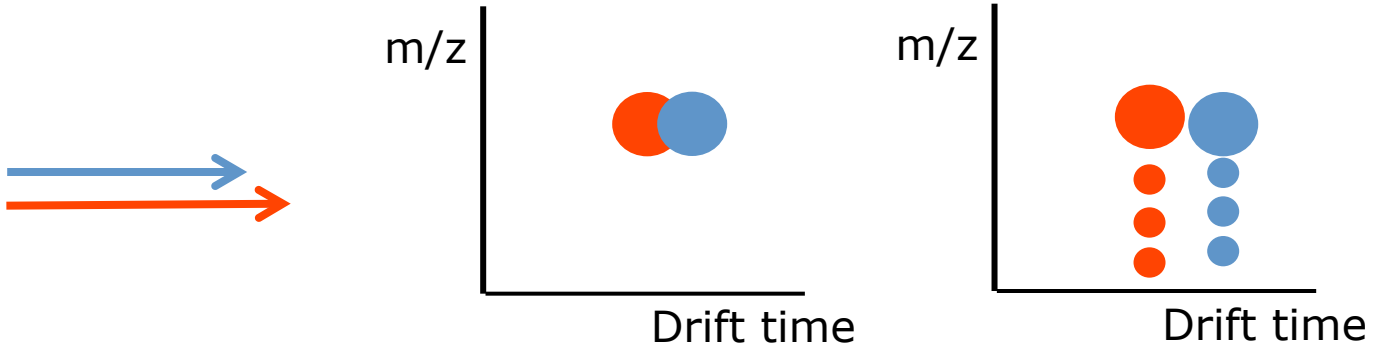

Precursor ions

Precursor ions

Precursor and products align

CCS/RT Comparison for IDs in Samples

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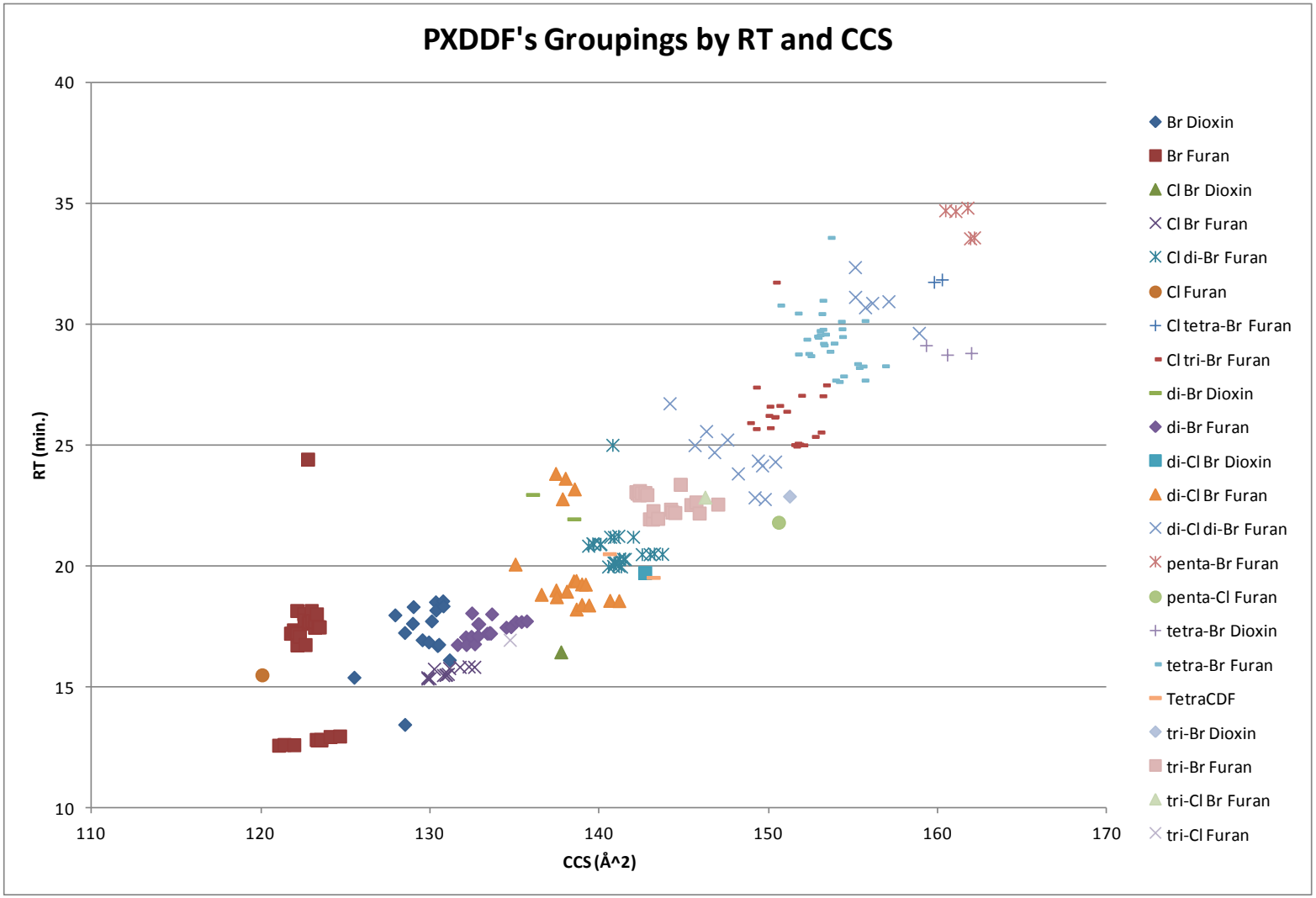

High and Low Energy HDMS^E Spectra

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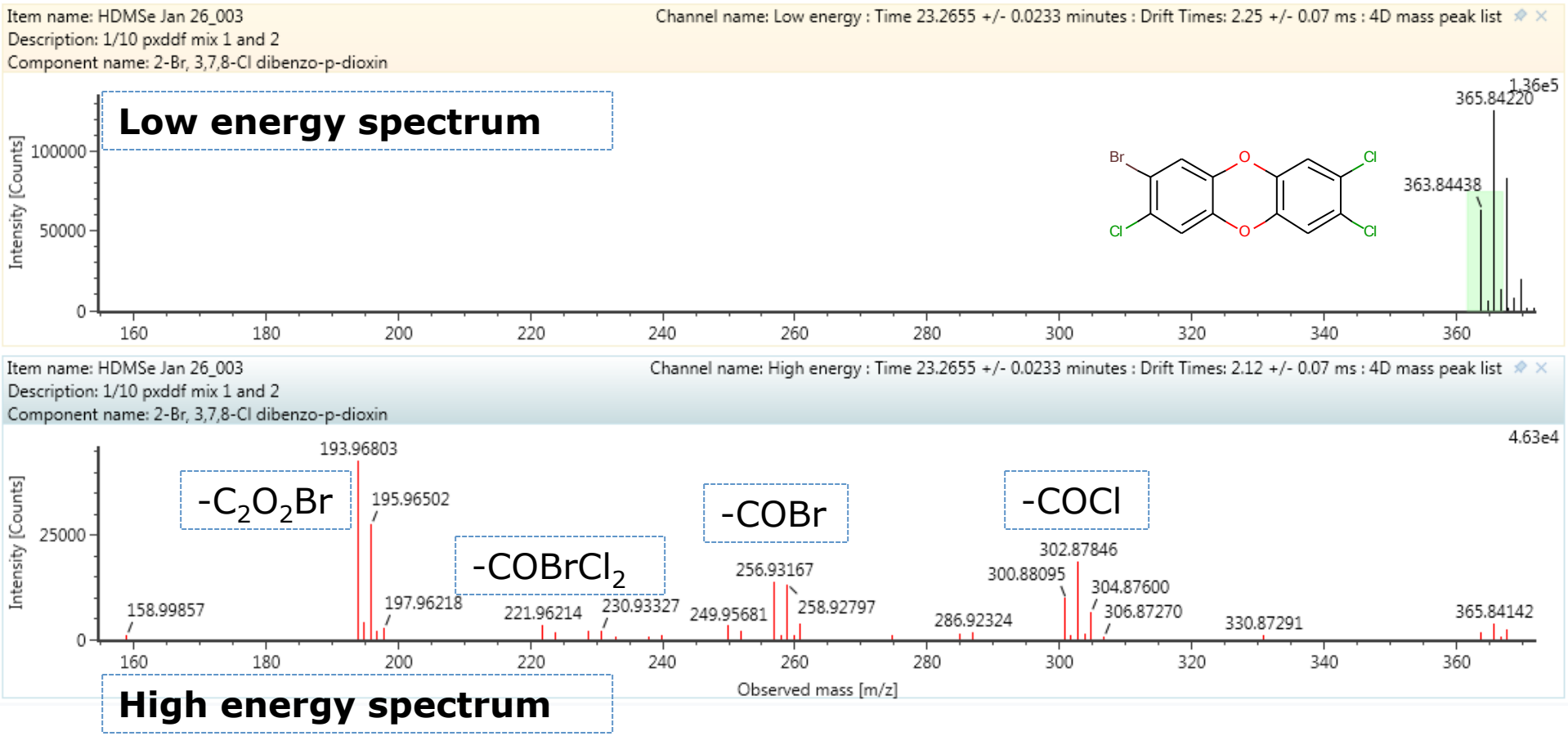

RTs, Fragments and Collisional Cross Section (CCS) for Available Standards

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PXDD	Formulae	RT	Theoretical Monoisotopic Mass (Da)	Mass Error (ppm)	CCS (Å^2)	Fragments (Da)
8-Br, 2,3-Cl dibenzofuran	C12H5OBrCl2	19.21	313.8896	-0.79	138.71	206.9768; 172.0080
3-Br, 2,7,8-Cl dibenzofuran	C12H4OBrCl3	22.74	347.8506	-3.57	145.64	240.9379; 205.9690
4-Br, 2,3,7,8-Cl dibenzofuran	C12H3OBrCl4	27.18	381.8116	-2.1	151.88	318.8484; 274.8989; 239.9293
1,2-Br, 7,8-Cl dibenzofuran	C12H4OBr2Cl2	24.68	391.8001	-2.9	145.68	312.8823; 284.8873; 233.9639
1,3-Br, 2,7,8-Cl dibenzofuran	C12H3OBr2Cl3	29.39	425.7611	-2.59	152.52	346.8433; 267.9250
7-Br, 2,3-Cl dibenzo-p-dioxin	C12H5O2BrCl2	19.72	329.885	1.21	143.18	266.9212; 222.9717; 160.0080
2-Br, 3,7,8-Cl dibenzo-p-dioxin	C12H4O2BrCl3	23.27	363.8455	-3.01	149.97	300.8823; 256.9328; 221.9639; 193.9690
2-Br, 1,3,7,8-Cl dibenzo-p-dioxin	C12H3O2BrCl4	27.61	397.8059	-2.74	156.12	334.8433; 290.8938; 227.9300
2,3-Br, 7,8-Cl dibenzo-p-dioxin	C12H4O2Br2Cl2	25.77	407.7939	-0.14	152.7	344.8318; 300.8823
8-Br, 2,3,4-Cl dibenzofuran	C12H4OBrCl3	22.83	347.8506	1.15	145.31	240.9379; 205.9690; 268.9328
2,3-Br, 7,8-Cl dibenzofuran	C12H4OBr2Cl2	25.19	391.8001	-3.06	147.88	312.8823; 284.8873; 233.9639

***mix 2 run separately as well as in mix analysis to ensure retention times**

Results: QC Injections

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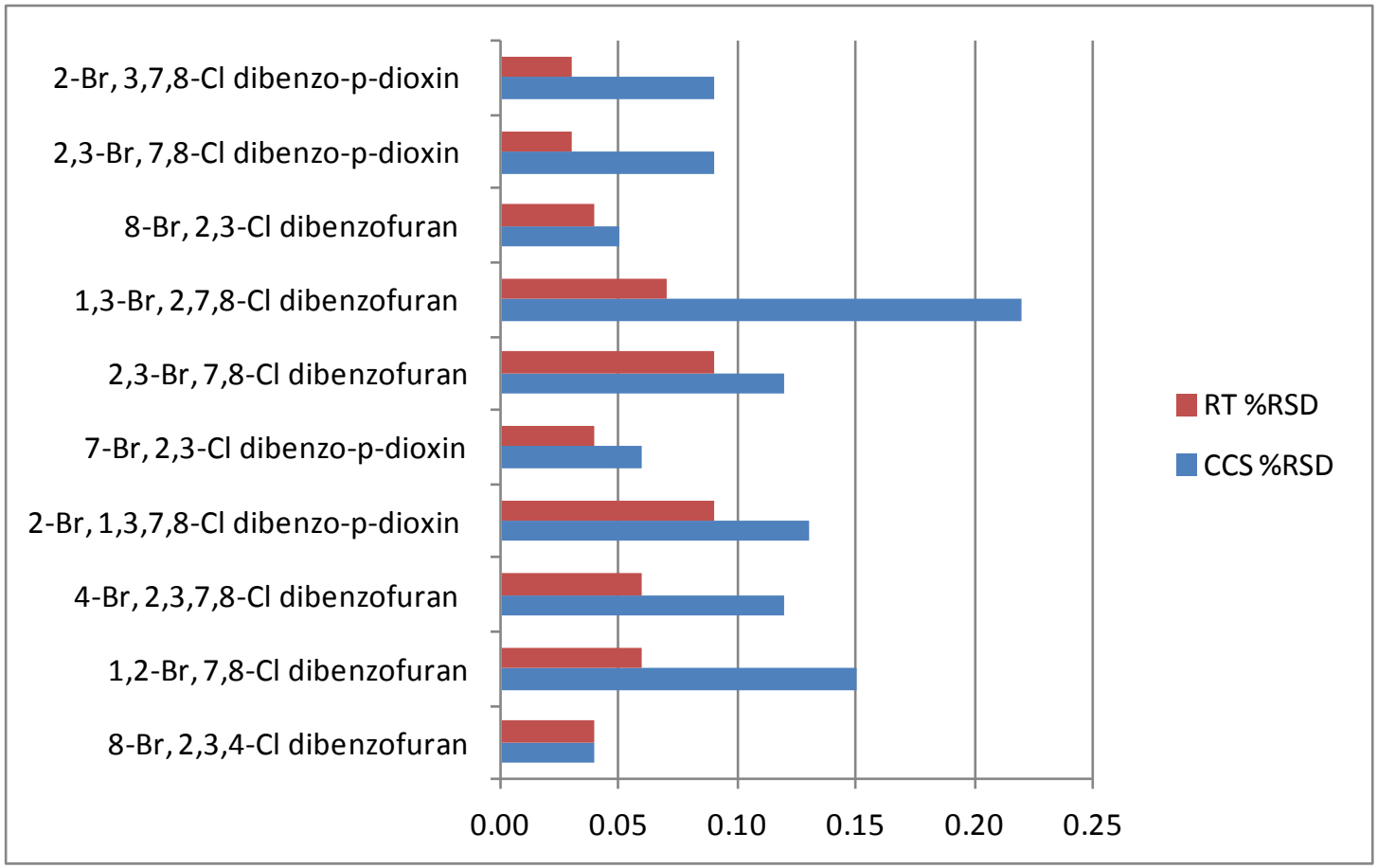

Searching for additional congeners

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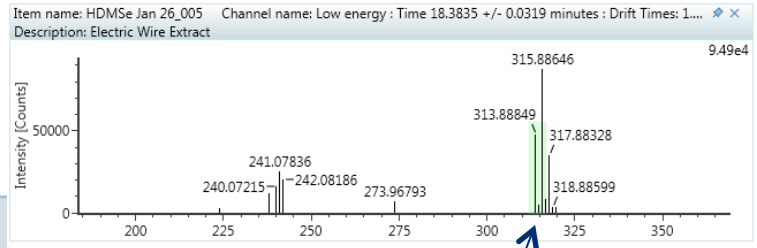

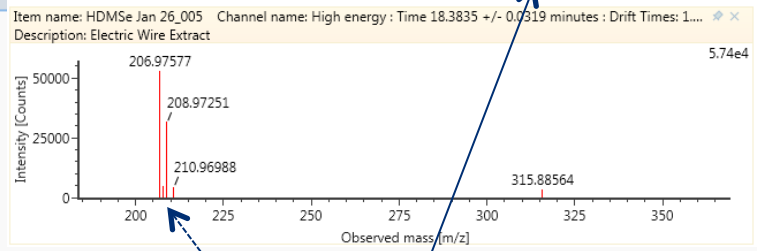

Parameters

m/z:	313.88896	
Retention time:	19.24	min
m/z tolerance:	5	ppm
Retention time tolerance:	10	min

Start

Results (13 found)

	Component name	m/z	Observed neutral mass (Da)	Observed RT (min)	Observed drift time (ms)	Observed collision cross section (Å²)
1	Candidate Mass_12	313.8885	313.8885	18.38	1.98	139.38
2	Candidate Mass_13	313.8888	313.8888	18.56	2.02	141.16
3	Candidate Mass_14	313.8884	313.8884	18.72	1.94	137.47
4	Candidate Mass_15	313.8885	313.8885	18.82	1.92	136.57
5	Candidate Mass_16	313.8884	313.8884	18.95	1.95	138.07
6	8-Br, 2,3-Cl dibenzofuran	313.8890	313.8895	19.24	1.98	139.18
7	Candidate Mass_17	313.8886	313.8886	19.38	1.96	138.48
8	Candidate Mass_18	313.8892	313.8892	20.07	1.88	135.03
9	Candidate Mass_19	313.8884	313.8884	22.77	1.94	137.82

Assign

Other Mixed-halogenated Components

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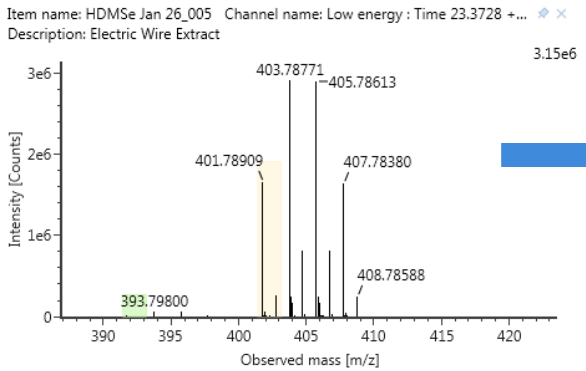
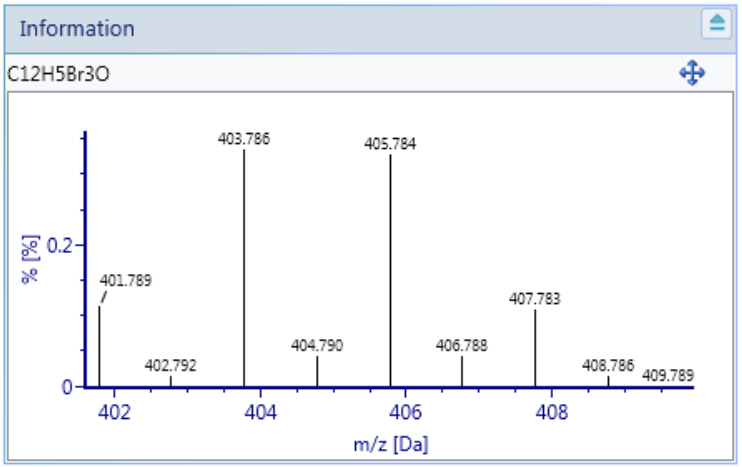
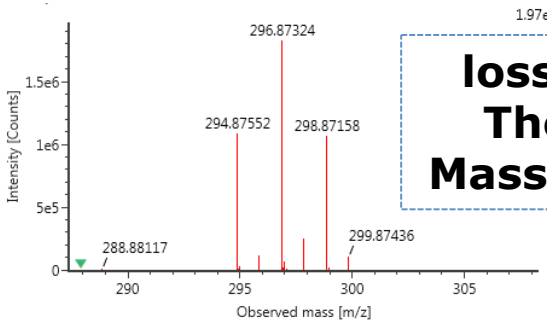
- **In addition to congeners in standards, more halogenated compounds were observed when XIC was searched**



Perform elemental composition



Propose product ion from HE spectrum



loss of -COBr
Theoretical Mass: 294.8753

Proposed PXDD/F's in Wire Extract

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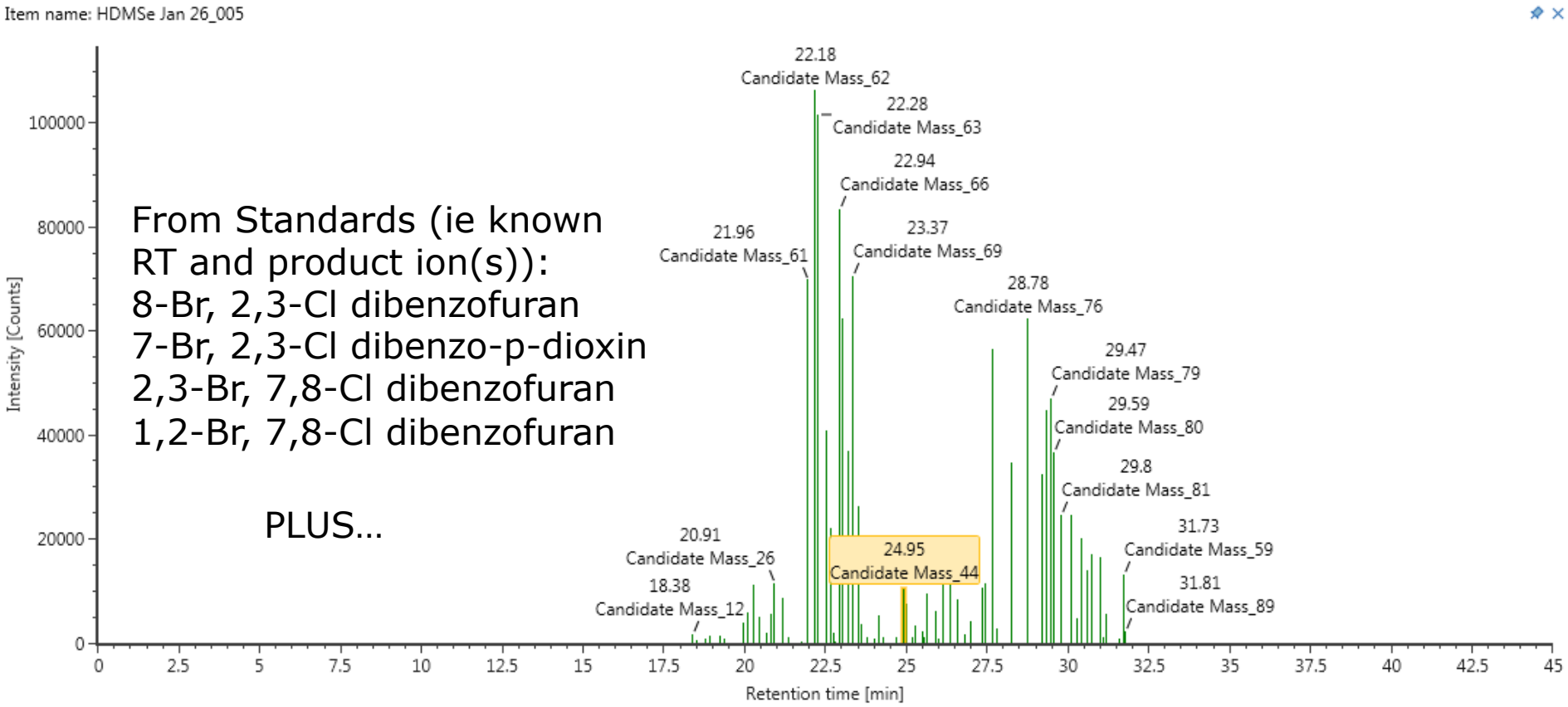
From Standards (ie known RT and product ion(s)):
8-Br, 2,3-Cl dibenzofuran
7-Br, 2,3-Cl dibenzo-p-dioxin
2,3-Br, 7,8-Cl dibenzofuran
1,2-Br, 7,8-Cl dibenzofuran

PLUS…



Sample Identifications

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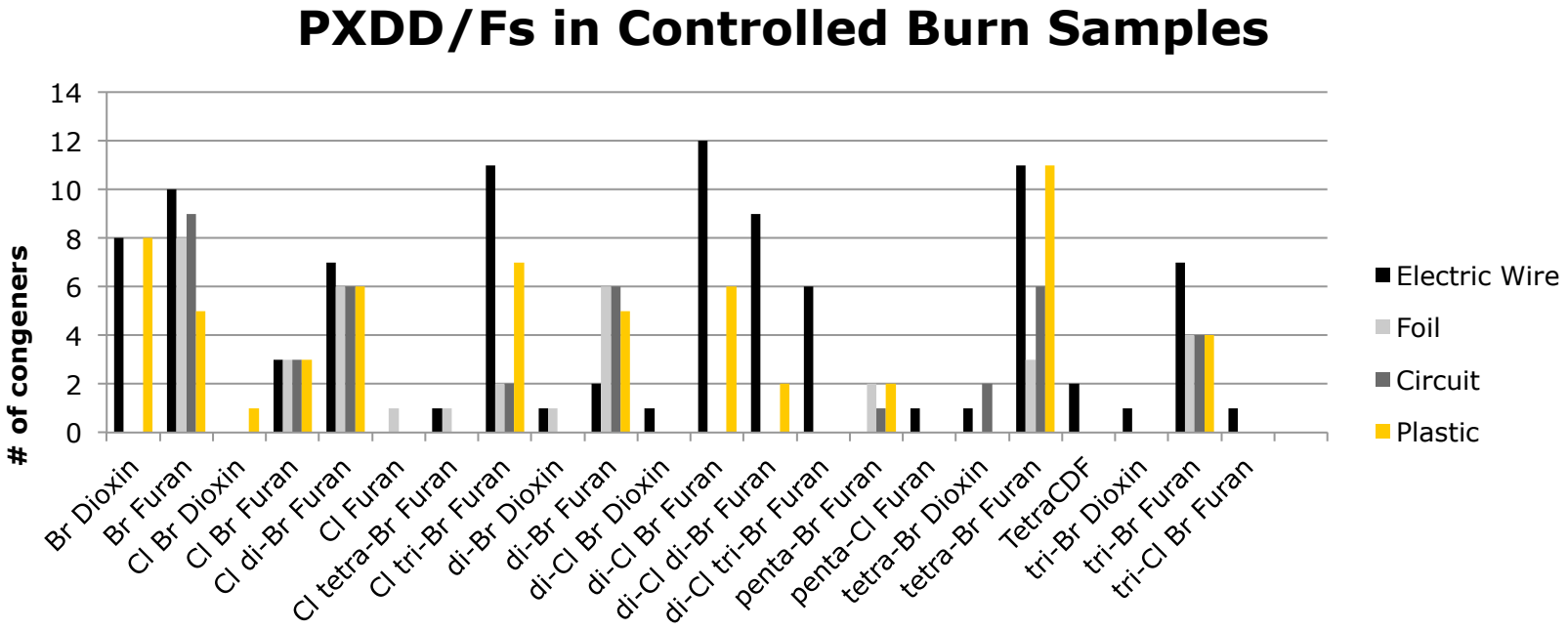
- Screening list updated to include all theoretical PXDD/F's
- All IDs required to have a diagnostic fragment (–COX loss)
- In-source fragments observed and removed accordingly



Conclusions

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- APGC/MS/MS provides improved sensitivity
  - + 20 to 40 X versus magnetic sector
- PXDDs and PXDFs found in nearly all fire debris samples
  - APGC allowed detection of more compounds than previous techniques
- IMS provides additional information for ID of congeners
  - Important for congeners for which no commercial standard exists yet

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Acknowledgements

- Penn State University
  - Biochemistry, Microbiology, and Molecular Biology Department
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  - Brian Ross
- Ontario Ministry of the Environment
  - Eric Reiner
  - Terry Kolic
- Wellington Laboratories
- Restek Corporation

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