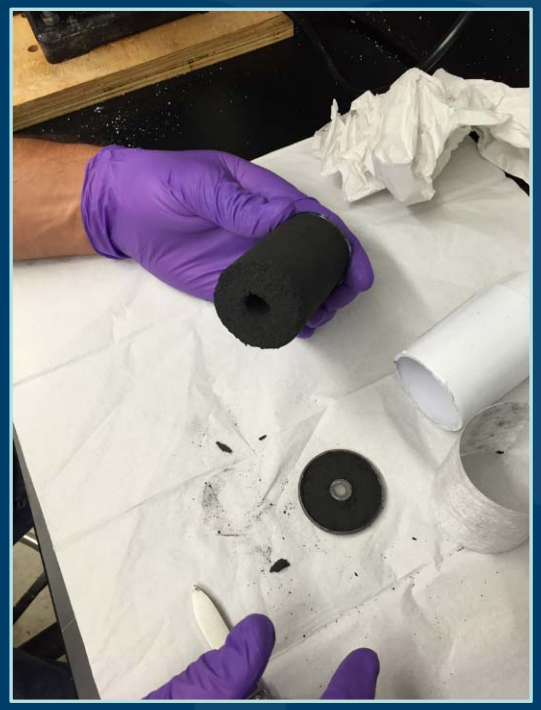
EPA United States Environmental Protection Agency

Using Point of Use Sampling Devices and High Resolution Mass Spectrometry Techniques for Characterizing Drinking Water Exposures



Mark Strynar

Rebecca McMahen, Seth Newton, Jon Sobus

NonTarget 2016,
Ascona, Switzerland
May 29 -June 3,
2016

EPA
United States
Environmental Protection
Agency

Human Exposure Pathways

EPA
United States
Environmental Protection
Agency

Screening Intention?

EPA
United States
Environmental Protection
Agency

Screening Intention?

EPA
United States
Environmental Protection
Agency

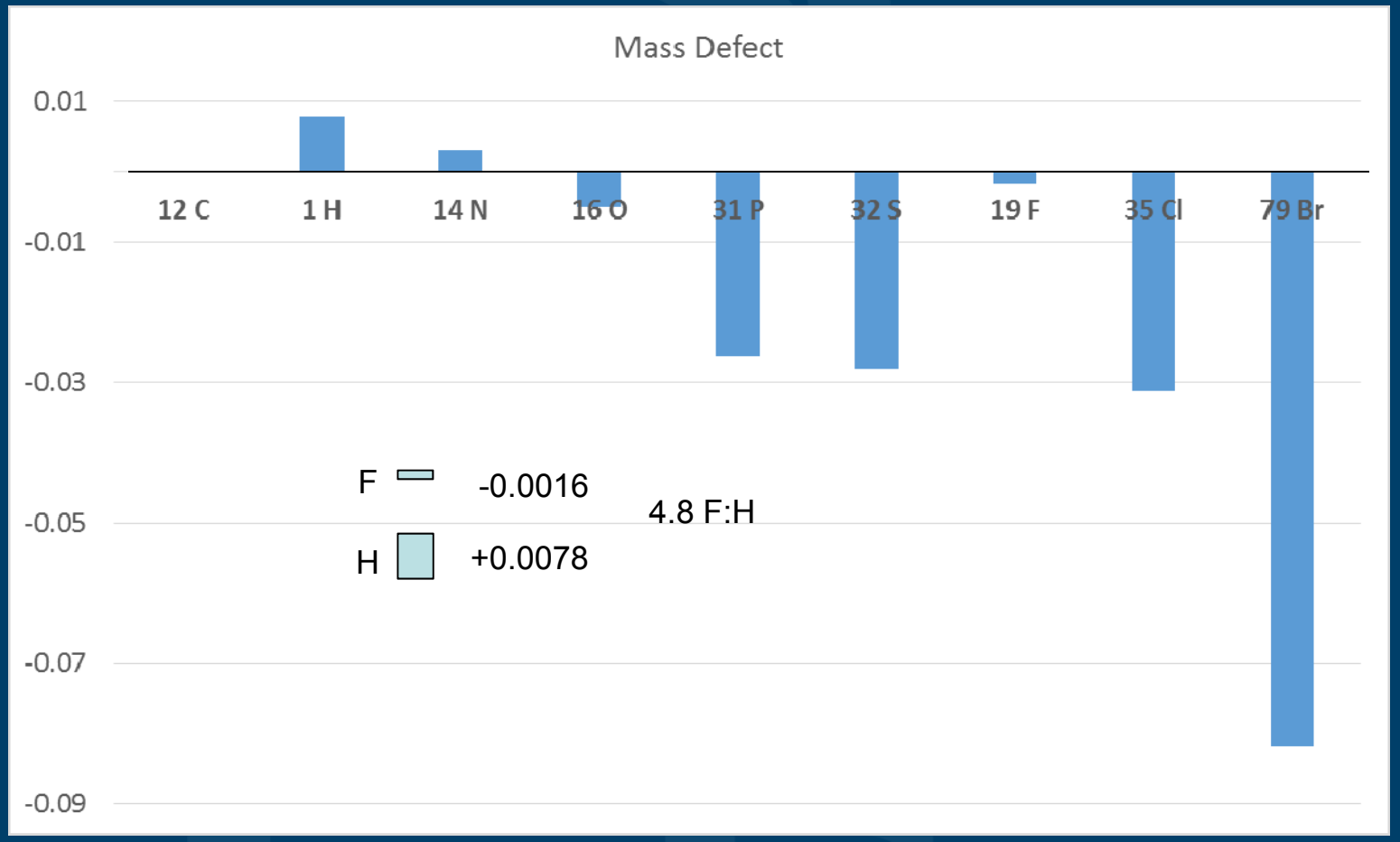
Screening Intention?

EPA United States Environmental Protection Agency

Characteristics for Elevated NTA Scrutiny

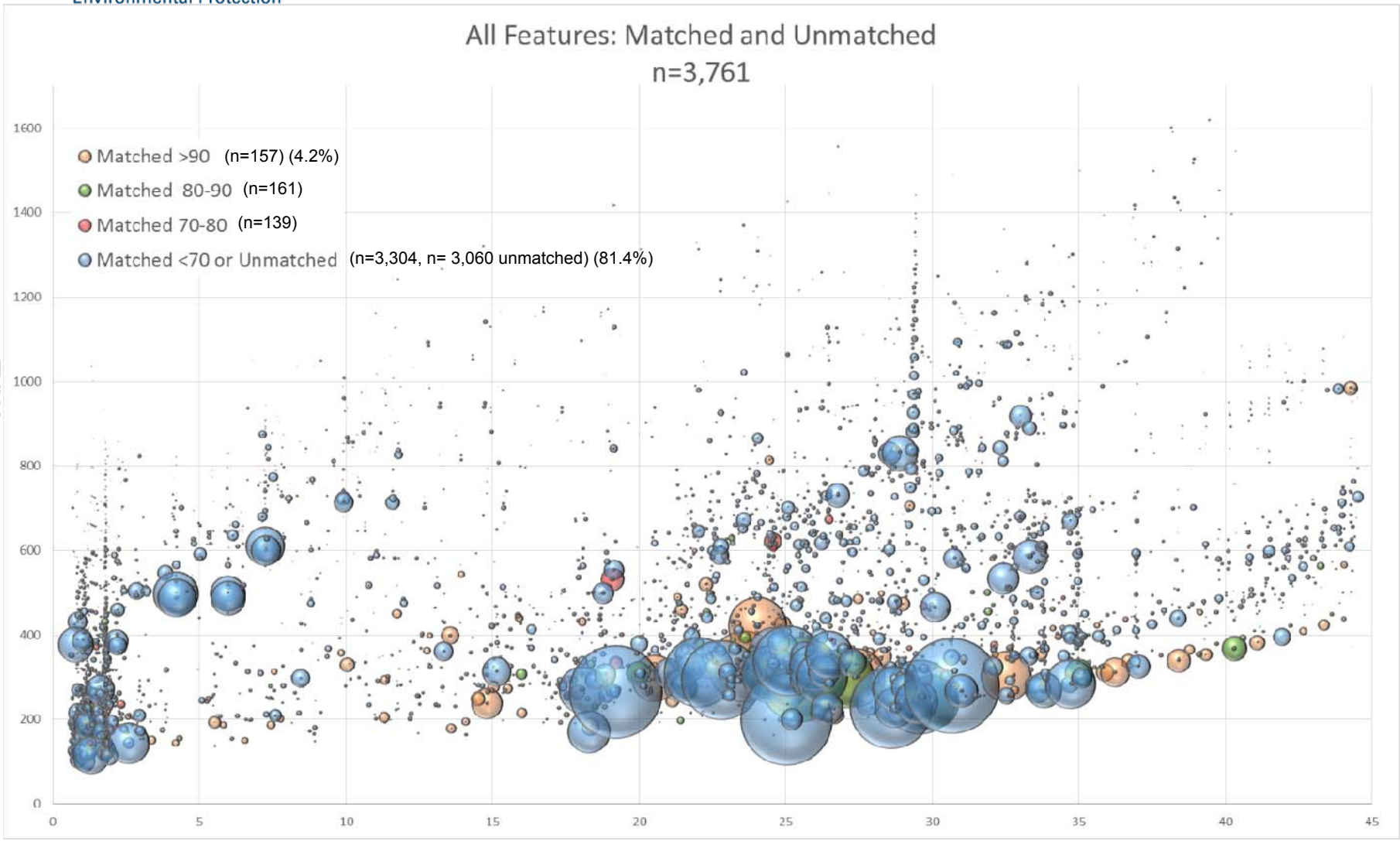
- Large peaks (abundance vs. number; lognormal distribution)
- Detection frequency (found in many samples)
- Contain halogens (Cl, Br) spectral features
- Mass defect (negative vs positive)
- ???

Typical Elements (CHNOPS F Cl Br)



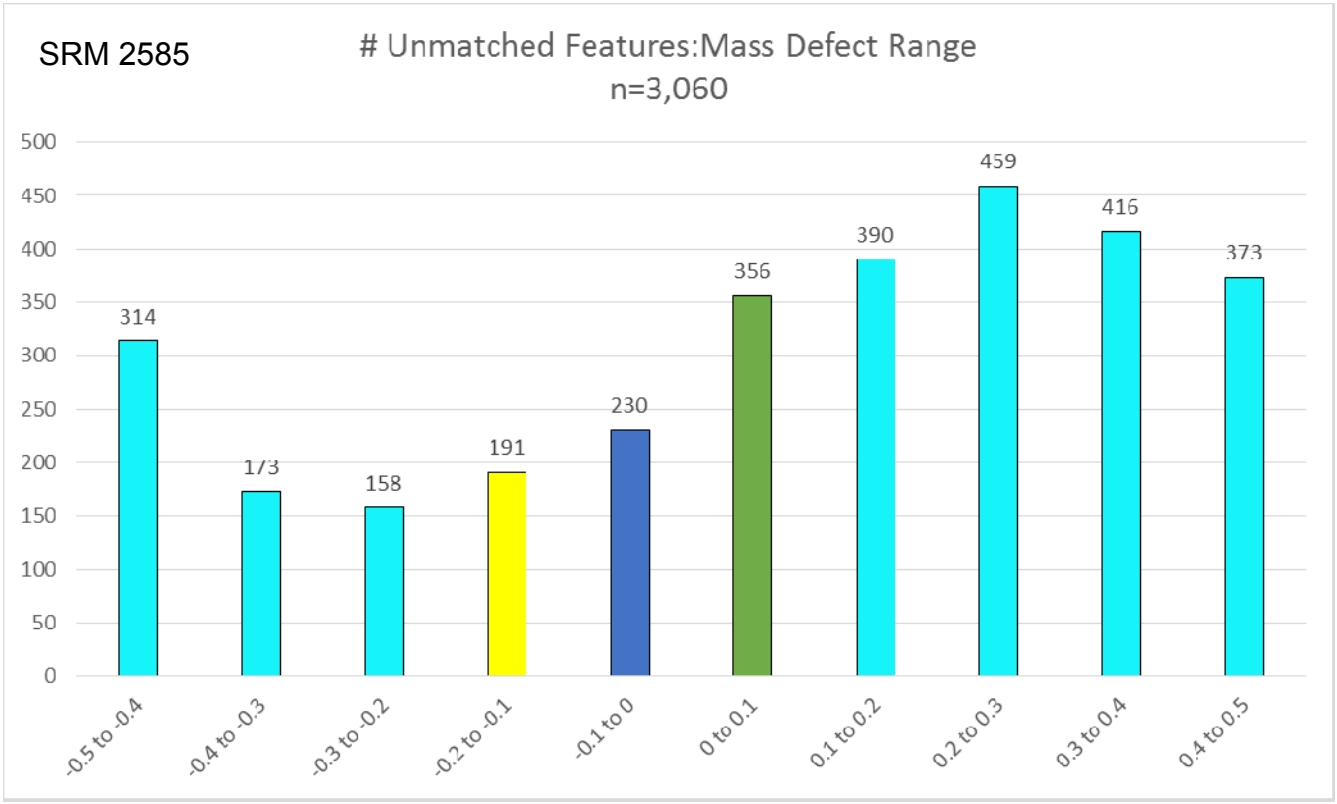
United States Environmental Protection

SRM 2585 dust example

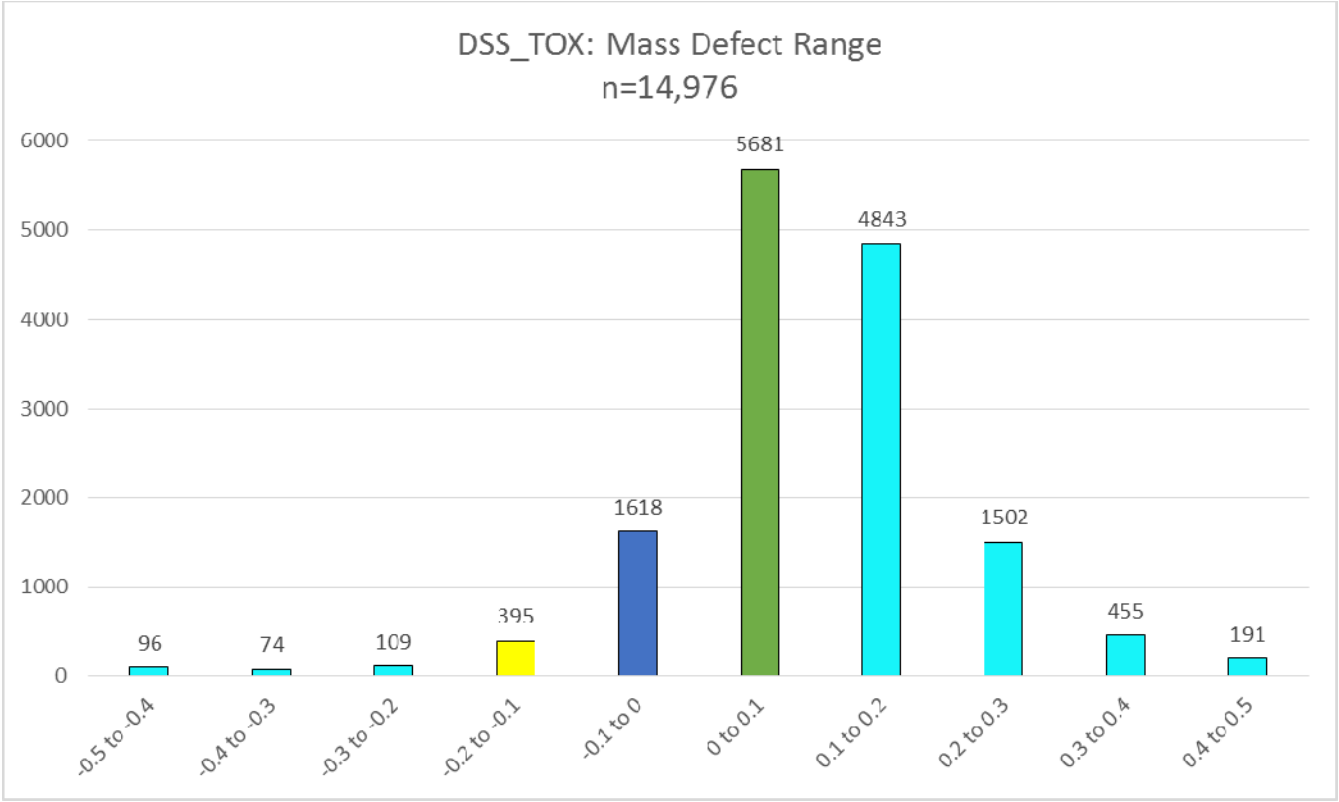


United States Environmental Protection Agency

Database mass defect
Vs.
Sample Mass Defect

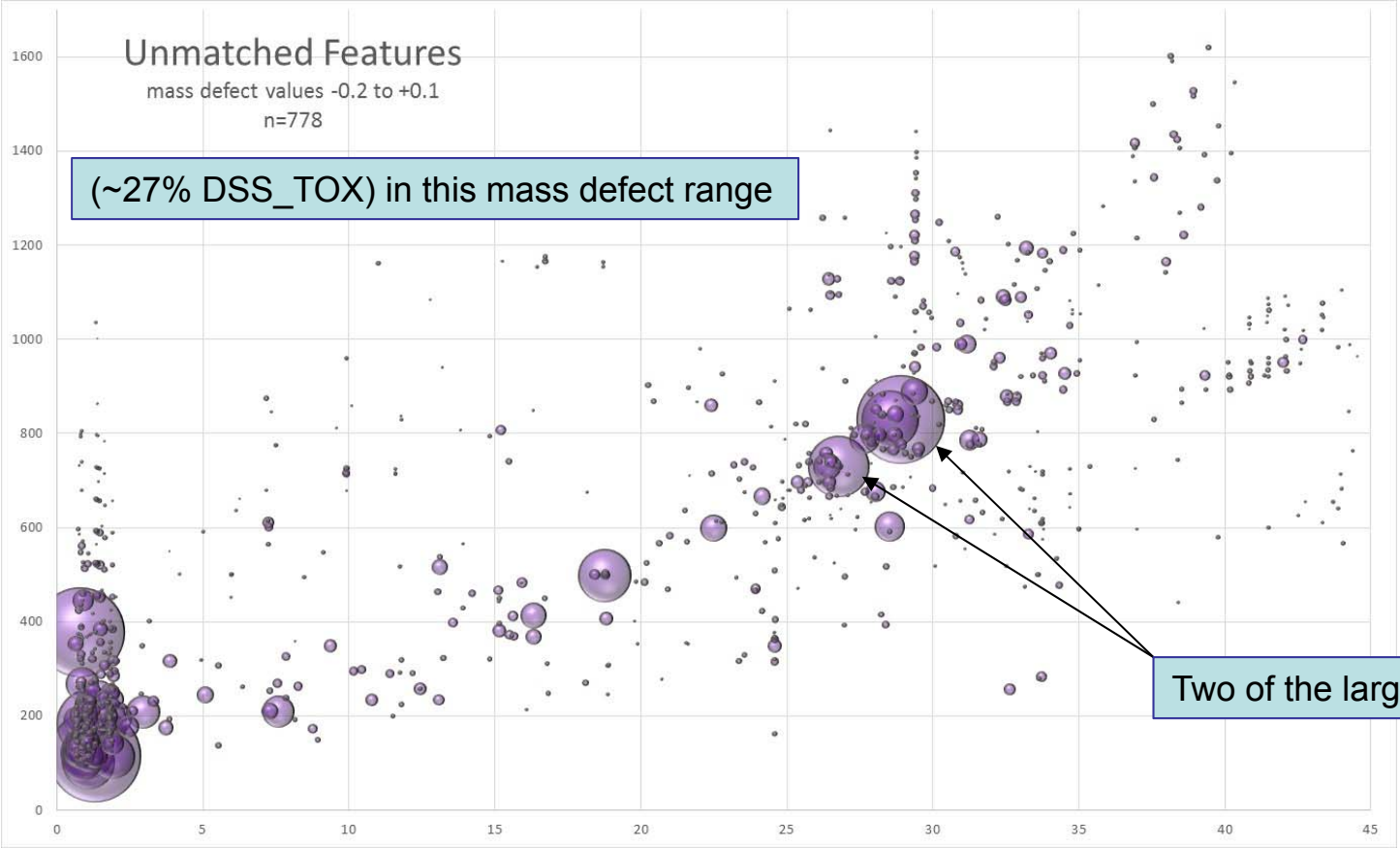


Database mass defect
Vs.
Sample Mass Defect



United States Environmental Protection Agency

NIST SRM 2585 Organic Compounds in Hose Dust



Environment International 88 (2016) 269–280

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

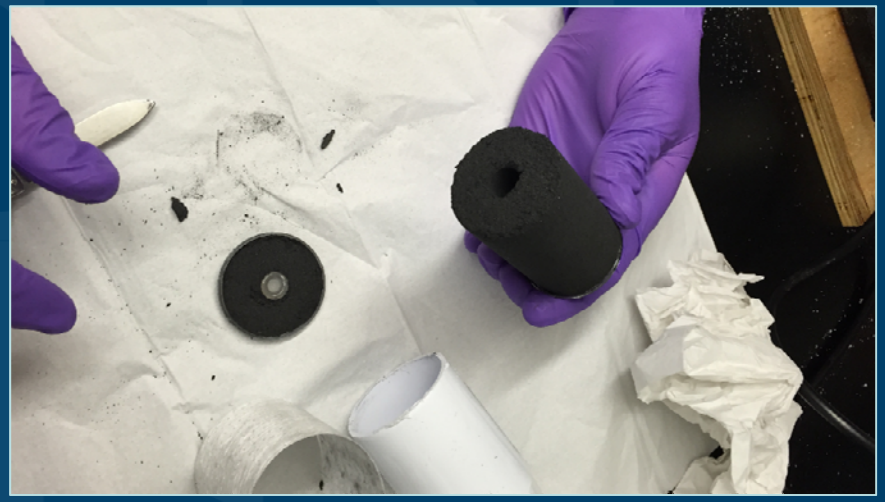
Linking high resolution mass spectrometry data with exposure and toxicity forecasts to advance high-throughput environmental monitoring

Julia E. Rager [a], Mark J. Strynar [b], Shuang Liang [a], Rebecca L. McMahen [a], Ann M. Richard [c], Christopher M. Grulke [d], John F. Wambaugh [c], Kristin K. Isaacs [b], Richard Judson [c], Antony J. Williams [c], Jon R. Sobus [b,*]

EPA
United States
Environmental Protection
Agency

- Pilot scale deployment at 9 homes
  (Research Triangle Park, NC USA)
- Municipal water (7); well water (2)
- Left on tap >1 month
- Cold water filtration
- Extracted (24 hr. soxhlet 80:20 DCM:methanol)
- Suspect and Non-targeted screening

EPA
United States
Environmental Protection
Agency



Office of Research and Development
National Exposure Research Lab/ Human Exposure and Atmospheric Science Division

EPA
United States
Environmental Protection
Agency

Office of Research and Development
National Exposure Research Lab/ Human Exposure and Atmospheric Science Division

EPA United States Environmental Protection Agency

LC/TOFMS Analysis

Agilent 6200 series TOF MSD
+/- Mode
ESI

Agilent 1100 HPLC
45 minute Methanol/Di $_{\text{formate}}$ Gradient
Agilent Poroshell 120 EC-C18, 3 x 50 mm,
2.7 µm column

EPA United States Environmental Protection Agency

Feature Identification

- Molecular Feature Extraction (MFE) criteria:

Feature Peaks	Ion Species	Charge State	Mass Filters	Compound Filters	Quality Filter
≥ 1000 counts	Positive ions: +H, +Na	Isotope peak spacing tolerance: 0.0025 m/z plus 7.0 ppm	Filter mass list using 5.0 ppm tolerance	Relative height ≥ 0.10%	Compound quality score ≥ 80
	Negative ions: -H, $+HCOO^-$	Charge states limit: 2		Absolute height ≥ 1000 counts	

Chemical Database (DSSTox)

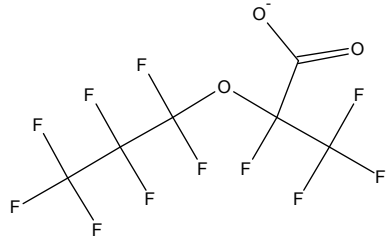
- Carefully curated database of standardized chemical mass, formula, structure, and other information files
- One-to-one mapping of CAS-to-chemical name
- Chemicals include environmental contaminants, pharmaceuticals, and other industrial chemicals

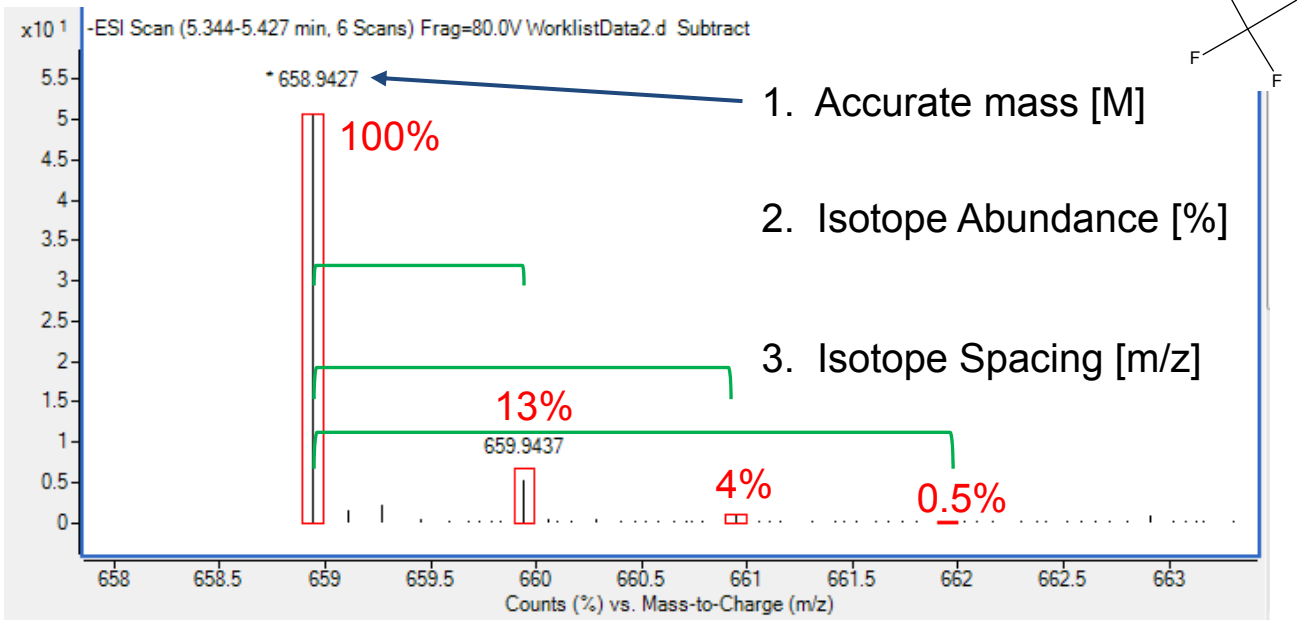
- version of DSSTox used
- ~33,000 chemicals

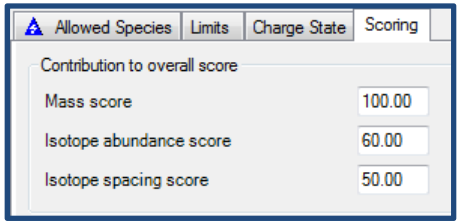
United States Environmental Protection Agency

Isotope Cluster Scoring

Ex. C_{12} H F_{22} O_6



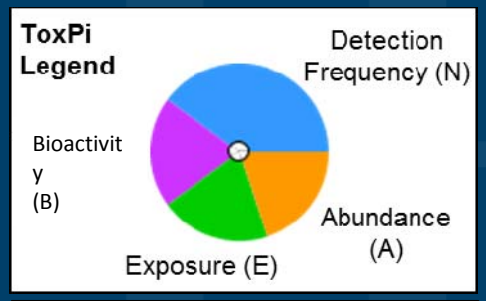




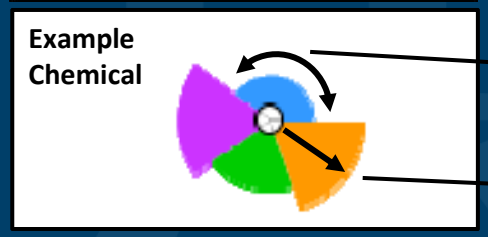
Prioritization Scoring with ToxPi

$$\text{ToxPi Score}_i = w_A \frac{A_i}{A_{max}} + w_N \frac{N_i}{N_{max}} + w_E \frac{E_i}{E_{max}} + w_B \frac{B_i}{B_{max}}$$

$w_A = w_E = w_T = 1;\ w_N = 2$



Individual components of a unit circle are scaled and represented as "slices"



Width indicates the relative weight of the variable

Distance from the origin is proportional to the normalized value of the data

(Reif et al. 2010)

EPA United States Environmental Protection Agency

Suspect screening of BRITA Filters

	LC-Neg	LC-Pos	GC
Total Number of Features:	4320	**10602**	**9609**
Average (standard deviation) number of features per sample:	480 (219)	1178 (575)	**1068 (244)**
Total Number of Features that match to Database:	181	249	**233**
Percent of features that matched to the database:	**4.2%**	**2.3%**	**2.4%**
Number of Unique Formulas:	166	**231**	**93**

Found on both LC and GC

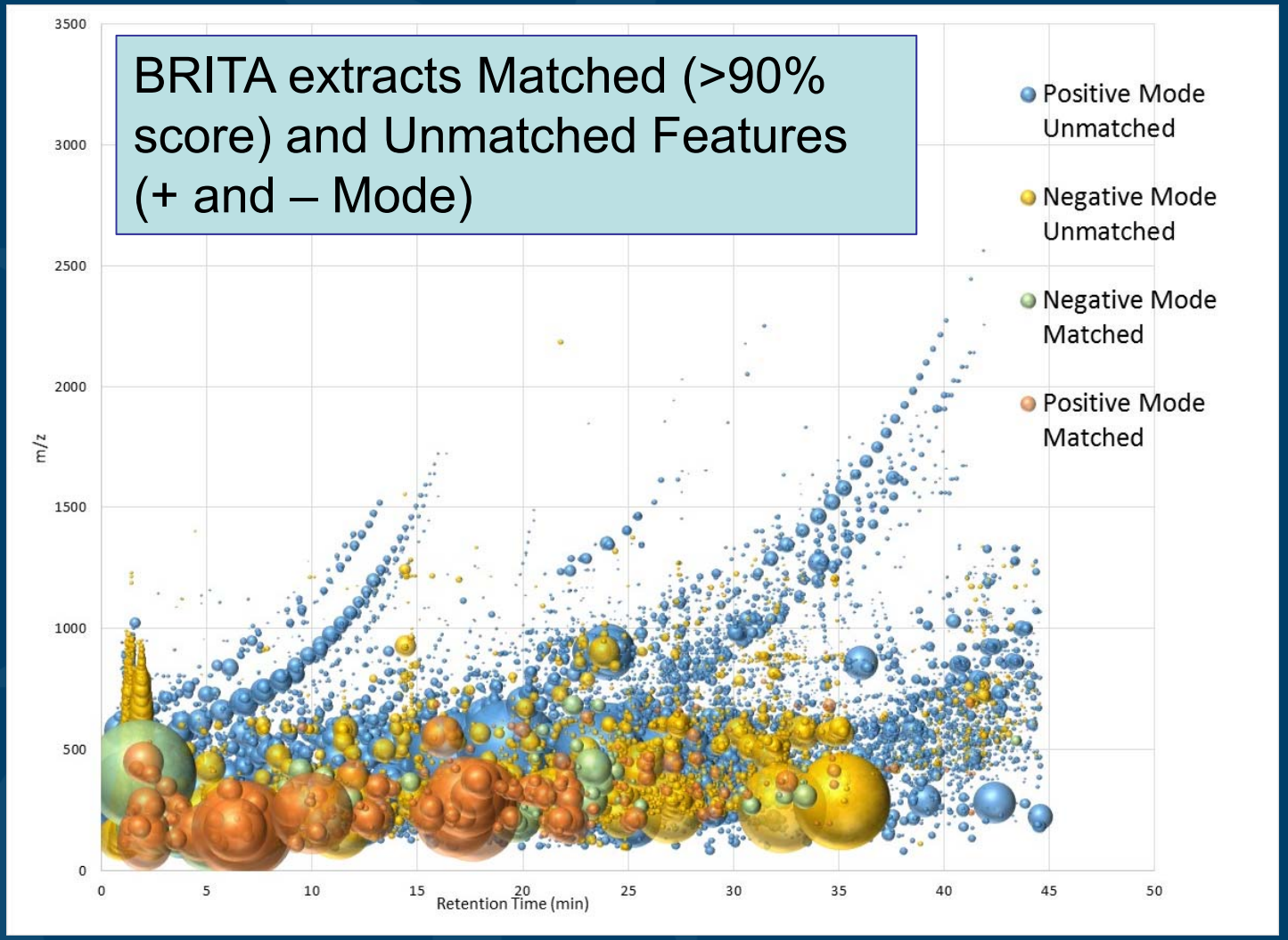
DSSTox Name	NIST name
Methyl decanoate	Methyl ester decanoic acid
2-[2-(2-Butoxyethoxy)ethoxy]ethanol	2-[2-(2-butoxyethoxy)ethoxy]-Ethanol
Tris(2-chloroethyl) phosphate	Tri(2-chloroethyl) phosphate
Triethyl phosphate	Triethyl phosphate
Simazine	6-chloro-N,N'-diethyl-1,3,5-Triazine-2,4-diamine
Atrazine	Atrazine

Chemicals detected that are monitored for in USEPA DW programs

- Atrazine
- Simazine
- PFOS
- PFOA
- PFNA
- PFHxS

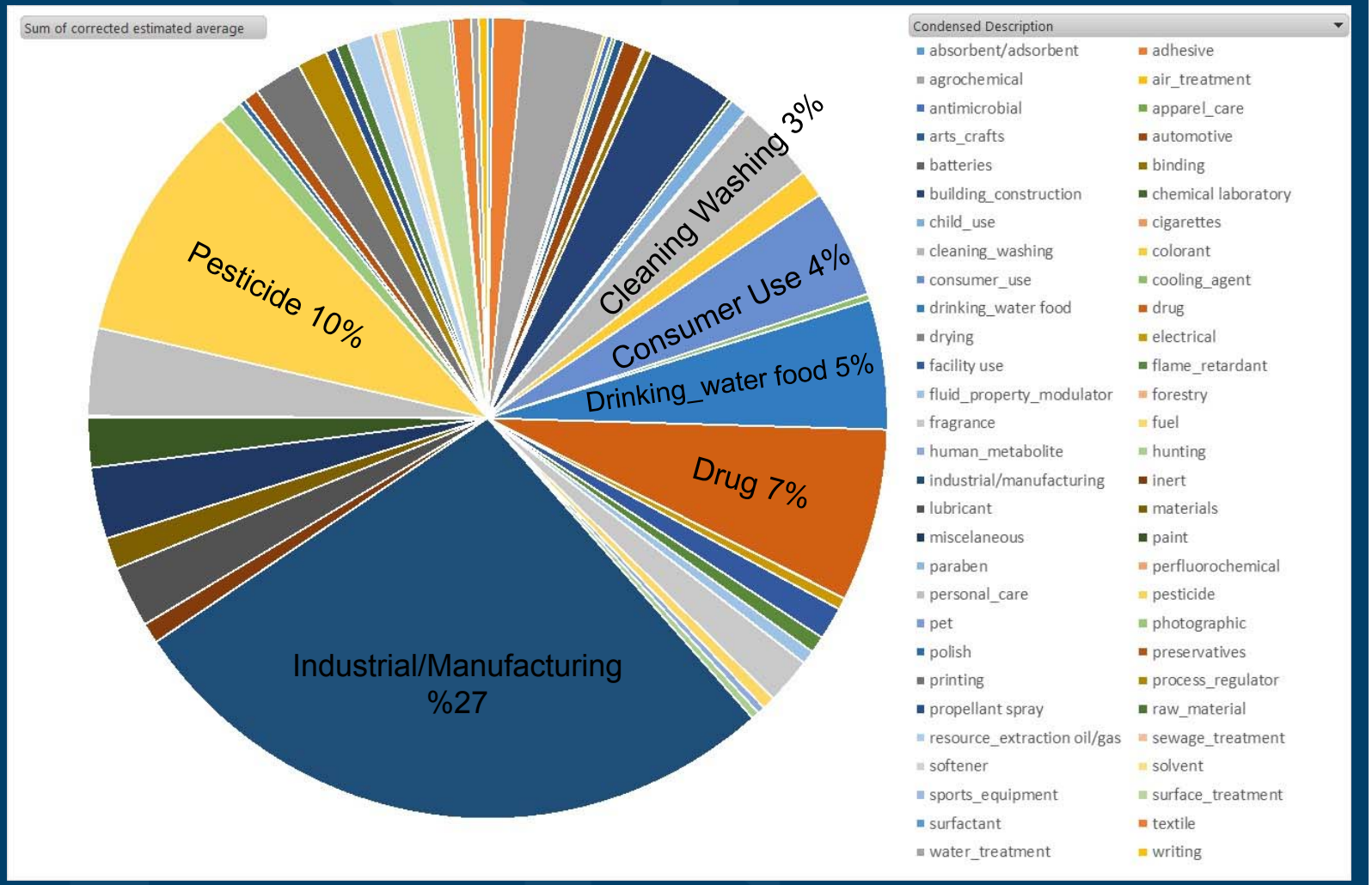
EPA
United States
Environmental Protection
Agency

BRITA extracts Matched (>90% score) and Unmatched Features (+ and – Mode)



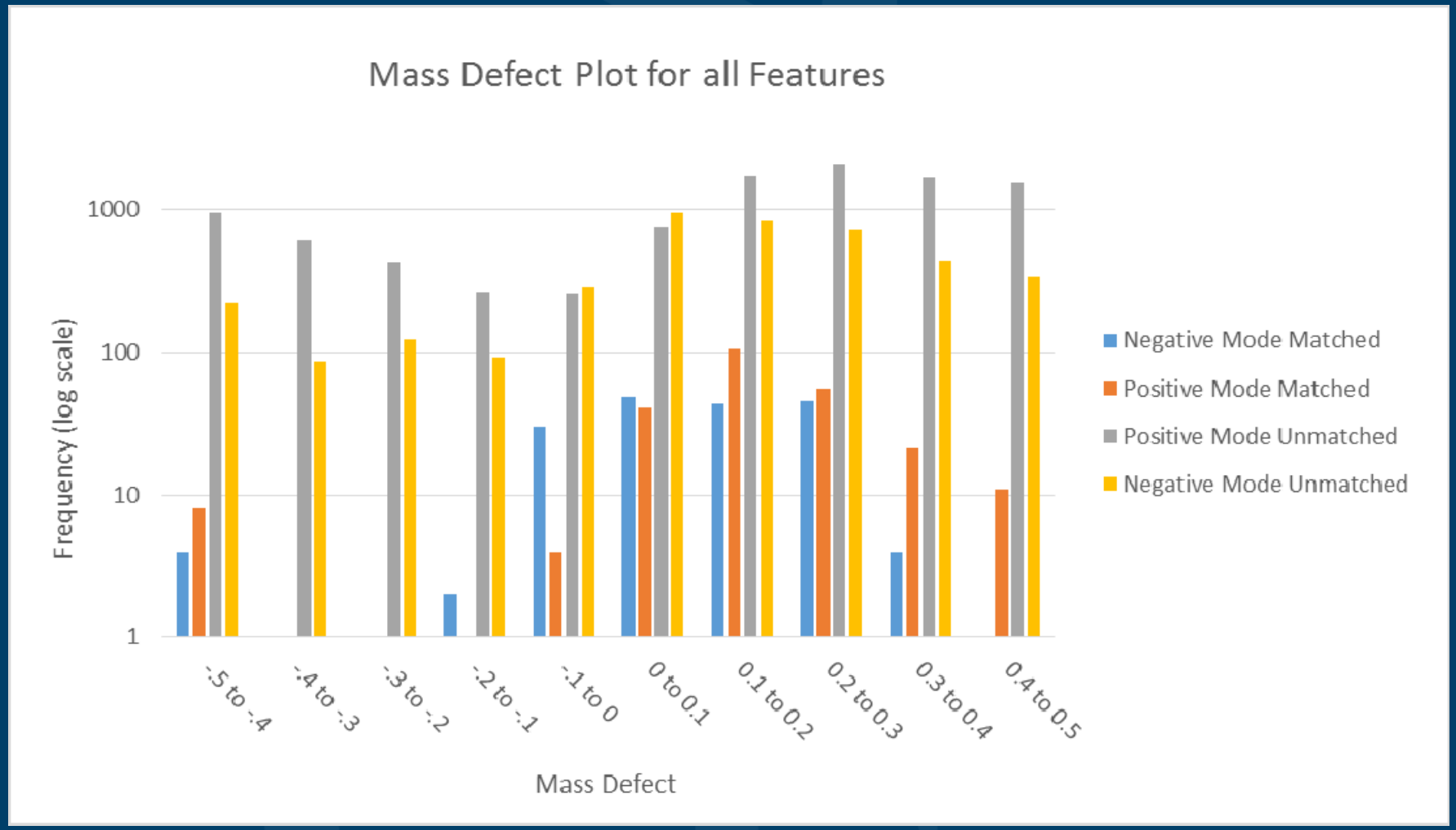
United States Environmental Protection Agency

CPCat: Chemical and Product Categories



EPA United States Environmental Protection Agency

Mass Defect all features Matched and Unmatched



United States Environmental Protection Agency

Top 25 tentative formulas based on ToxPi scores

Chemical Name	Formula	CAS	ToxPi Rank	DF Rank	Abund. Rank
1,2-Benzisothiazolin-3-one	C7H5NOS	2634-33-5	1	4	
Dichexamethylenecarbamide **(2)**	C13H24N2O	25991-86-0	2	1	8
1,1,3,3-Tetrabutylurea	C17H36N2O	4559-86-8	3		
2H-Azepin-2-one, 1-(3-aminopropyl) hexahydro- **(5)**	C9H18N2O	24566-95-8	4	2	4
Tracazolate	C16H24N4O2	41094-88-6	5	3	6
1,4,7,10-Tetraoxacyclododecane **(6)**	C8H16O4	294-93-9	6	4	19
(E,Z)-3,13-Octadecadien-1-ol acetate	C20H36O2	53120-26-6	7		
(2-Benzyl-1,3-dioxolan-4-yl)methanol (1)	C11H14O3	29895-73-6	8		
1,2,4-Butanetriol **(3)**	C4H10O3	3068-00-6	9	6	
TDCPP	C9H15Cl6O4P	13674-87-8	10		14
Triethyl citrate	C12H20O7	77-93-0	11		
PFOA	C8HF15O2	335-67-1	12	21	
1-Dodecanamine, N,N-dimethyl-, benzoate	C14H31N	68473-31-4	13		
1-Nonanone, 1-(2,5-dihydroxyphenyl)- **(1)**	C15H22O3	7337-44-2	14		
1-Phenanthrenecarboxylic acid, 1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-9-oxo-, (1R,4aS,10aR)-	C20H26O3	18684-55-4	15		
1,3-Dioxan-5-ol, 2-(phenylmethyl)-	C11H14O3	4740-79-8	16		
Dodecanoic acid, 2-(2-hydroxyethoxy)ethyl ester	C16H32O4	141-20-8	17	7	
1,3,5-Trioxane, 2,4,6-tripropyl-	C12H24O3	2396-43-2	18		
PFOS	C8HF17O3S	29081-56-9	19	22	
1-[2-(2-Methoxy-1-methylethoxy)-1-methylethoxy]-2-propanol	C10H22O4	20324-33-8	20		
Atrazine	C8H14ClN5	1912-24-9	21	11	18
1-Propanamine, 3-(C11-14-isoalkyloxy) derivs., C13-rich	C16H35NO	151789-06-9	22		
Octadecanoic acid, 26-hydroxy-3,6,9,12,15,18,21,24-octaoxahexacos-1-yl ester	C36H72O11	5349-52-0	23	8	
2-Propenoic acid, 3-(2-furanyl)-, 2-methylpropyl ester	C11H14O3	68480-18-2	24		
2-Ethylhexylparaben	C15H22O3	5153-25-3	25		

Top 25 tentative formulas based on Detection Frequency

Chemical Name	Formula	CAS	ToxPi Rank	DF Rank	Abund. Rank
Dichexamethylenecarbamide (1)	C13H24N2O	25991-86-0	2	1	8
2H-Azepin-2-one, 1-(3-aminopropyl)hexahydro- (5)	C9H18N2O	24566-95-8	4	2	4
Tracazolate	C16H24N4O2	41094-88-6	5	3	6
1,4,7,10-Tetraoxacyclododecane (6)	C8H16O4	294-93-9		4	19
1,2-Benzisothiazolin-3-one	C7H5NOS	2634-33-5	1	5	
1,2,4-Butanetriol (3)	C4H10O3	3068-00-6	8	6	
Dodecanoic acid, 2-(2-hydroxyethoxy)ethyl ester	C16H32O4	141-20-8	16	7	
Octadecanoic acid, 26-hydroxy-3,6,9,12,15,18,21,24-octaoxahexacos-1-yl ester	C36H72O11	5349-52-0	23	8	
Ethanedithioamide, N,N'-bis(2-hydroxyethyl)-	C6H12N2O2S2	120-86-5		9	
Lipoxin A4	C21H34O5	89663-86-5		10	
Atrazine	C8H14ClN5	1912-24-9	20	11	18
2,4-Heptadecanedione (2)	C17H32O2	64042-18-8		12	
Adiphenine (2)	C20H25NO2	64-95-9		13	
Deethylatrazine	C6H10ClN5	6190-65-4		14	
Octanoic acid, 1,3-propanediyl ester	C19H36O4	56519-71-2		15	
Deferiprone (2)	C7H9NO2	6606-66-2		16	
2-[(4-Chloro-o-tolyl)oxy]-N-methoxyacetamide (1)	C10H12ClNO3	1081-53-4		17	
Hexadecanamide, N,N'-1,2-ethanediylbis-	C34H68N2O2	5518-18-3		18	
Hexanedioyl dichloride	C6H8Cl2O2	111-50-2		19	
Sucrose octanoate	C28H50O13	42922-74-7		20	
PFOA	C8HF15O2	335-67-1	11	21	
PFOS	C8HF17O3S	29081-56-9	18	22	
1H-Pyrrole-2-acetic acid, 1-methyl-, ethyl ester (9)	C9H13NO2	49669-45-6		23	12
Piperazinium, 1-cyclopentylidene-4-(ethoxycarbonyl)-, tetrafluoroborate(1-)	C12H21N2O2	99377-81-8		24	22
.beta.-Alanine, N-(2-carboxyethyl)-N-dodecyl-, disodium salt (1)	C18H35NO4	3655-00-3		25	

Top 25 formulas based on Abundance

Chemical Name	Formula	CAS	ToxPi Rank	DF Rank	Abund. Rank
1,1'-Biphenyl, 4-cyclohexyl- (3)	C18H20	3842-58-8			1
2,4,8,10-Tetraoxaspiro[5.5]undecane-3,9-diethanol, .beta.,.beta.,.beta.',.beta.'-tetramethyl-	C15H28O6	1455-42-1			2
1H-Benzotriazole, 5-methyl-, sulfate (2:1) (6)	C7H7N3	67924-12-3			3
2H-Azepin-2-one, 1-(3-aminopropyl)hexahydro- (5)	C9H18N2O	24566-95-8	4	2	4
2,6-Dimethyl morpholine (11)	C6H13NO	141-91-3			5
Tracazolate	C16H24N4O2	41094-88-6	5	3	6
Epoxomicin	C28H50N4O7	134381-21-8			7
Dichexamethylenecarbamide (1)	C13H24N2O	25991-86-0	2	1	8
Phosphonic acid, methyl-, bis[(5-ethyl-2-methyl-2-oxido-1,3,2-dioxaphosphorinan-5-yl)methyl] ester	C15H31O9P3	42595-45-9			9
(E)-beta-Damascone (4)	C14H22	23726-91-2			10
1,1-Methylenebis(4-isocyanatocyclohexane) (1)	C15H22N2O2	5124-30-1			11
1H-Pyrrole-2-acetic acid, 1-methyl-, ethyl ester (9)	C9H13NO2	49669-45-6		23	12
Benzenediazonium, 2,5-diethoxy-4-(4-morpholinyl)-, hexafluorophosphate(1-) (3)	C14H20N3O3	4255-94-1			13
TDCPP	C9H15Cl6O4P	13674-87-8	9		14
1,3-Propanediamine, N-(3-aminopropyl)-N-methyl-N'-(2-nitrophenyl)-	C13H22N4O2	68039-17-8			15
Pentanoic acid, 3-[2,2-dimethyl-1-oxo-3-[(1-oxopentyl)oxy]propoxy]-2,2-dimethylpropyl ester	C20H36O6	71850-74-3			16
Ethyl 2-[[[2,4(or3,5)-dimethyl-3-cyclohexen-1-yl]methyl]amino]benzoate	C18H25NO2	68228-09-1			17
Atrazine	C8H14ClN5	1912-24-9	20	11	18
1,4,7,10-Tetraoxacyclododecane (6)	C8H16O4	294-93-9		4	19
N,N,N',N',N'',N''-Hexakis(methoxymethyl)-1,3,5-triazine-2,4,6-triamine	C15H30N6O6	3089-11-0			20
beta-Zearalanol (1)	C18H26O5	42422-68-4			21
Azabuperone (1)	C12H21N2O2	99377-81-8		24	22
1-Methyl-4-(4-methylpentyl)cyclohex-3-ene-1-carbaldehyde (12)	C14H24O	66327-54-6			23
Triethyl phosphate	C6H15O4P	78-40-0			24
6-Bromo-5-methylimidazo[4,5-b]pyridine	C7H6BrN3	28279-41-6			25

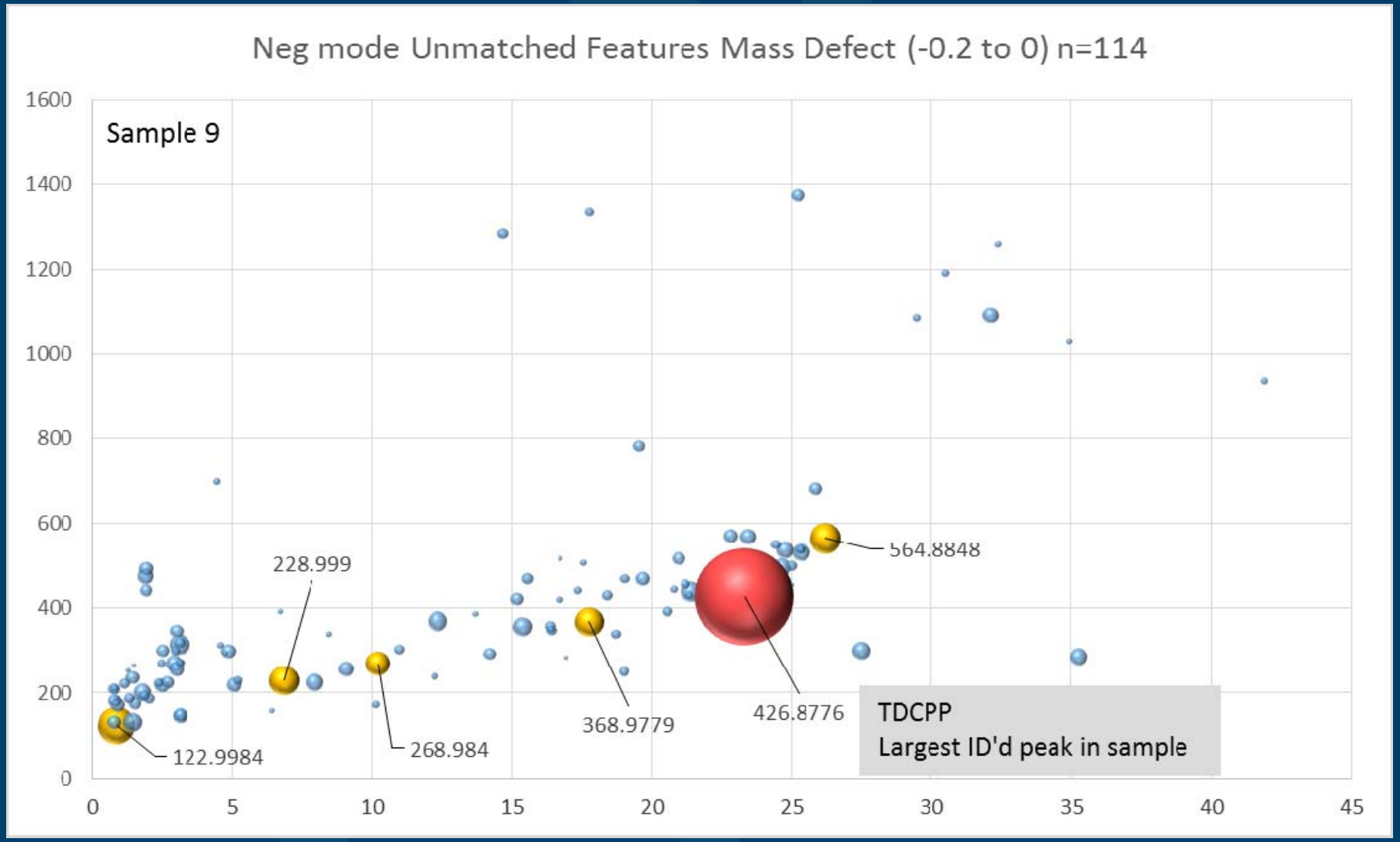
NTA bubble plot mass defect (-0.2 to 0) example

Sample 9
990 features detected MFE
517 some % match score
50 scored >90%

473 features unmatched
114 features mass defect -0.2 to 0

#	RT	m/z	Vol	% volume	Running Total %	33,844,462	total area
1	0.866	122.9984	2471805	7.30	7.3		
2	26.224	564.8848	1667960	4.93	12.2		
3	6.836	228.999	1624823	4.80	17.0		
4	17.777	368.9779	1510733	4.46	21.5		
5	10.199	268.984	1047183	3.09	24.6		

NTA bubble plot mass defect (-0.2 to 0) example



EPA United States Environmental Protection Agency

Summary

- BRITA cartridges appear an inexpensive useful media to retain organic contaminants in DW investigation
- LC/TOFMS suspect screening is able to detect 260 unique formulas (856 potential unique
- chemicals) from DSS-TOX ~33k
- Large majority of the detected features (both numbers and abundance) are unmatched to DSS-TOX
- Additional follow-up investigation of unmatched features and GC/TOFMS are needed to further understar
- Remaining chemical space

EPA United States Environmental Protection Agency

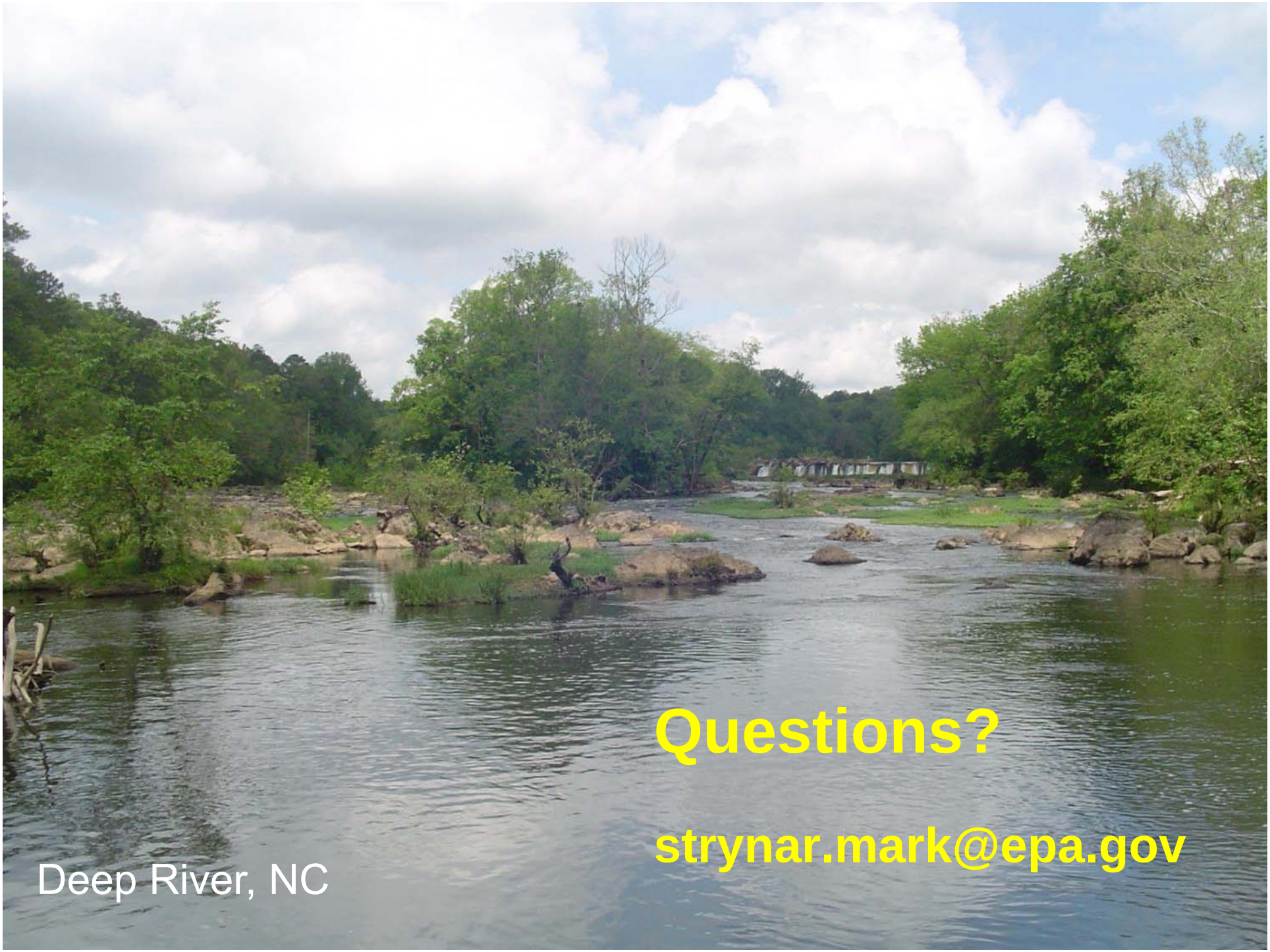
Acknowledgements

Co-authors:
Rebecca McMahen
Seth Newton
Jon Sobus

Help with DSS_TOX :
Ann Richard
Tony Williams
Chris Grulke

Help with ToxPi:
Julia Rager

GC/MS:
Scott Clifton


Questions?
strynar.mark@epa.gov
Deep River, NC