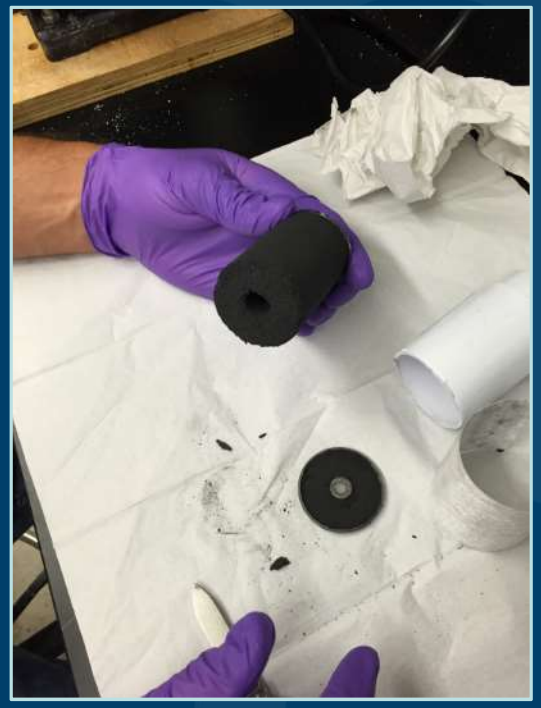
EPA United States Environmental Protection Agency

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

NEMC 2016, Ascona,
August 8-12, 2016

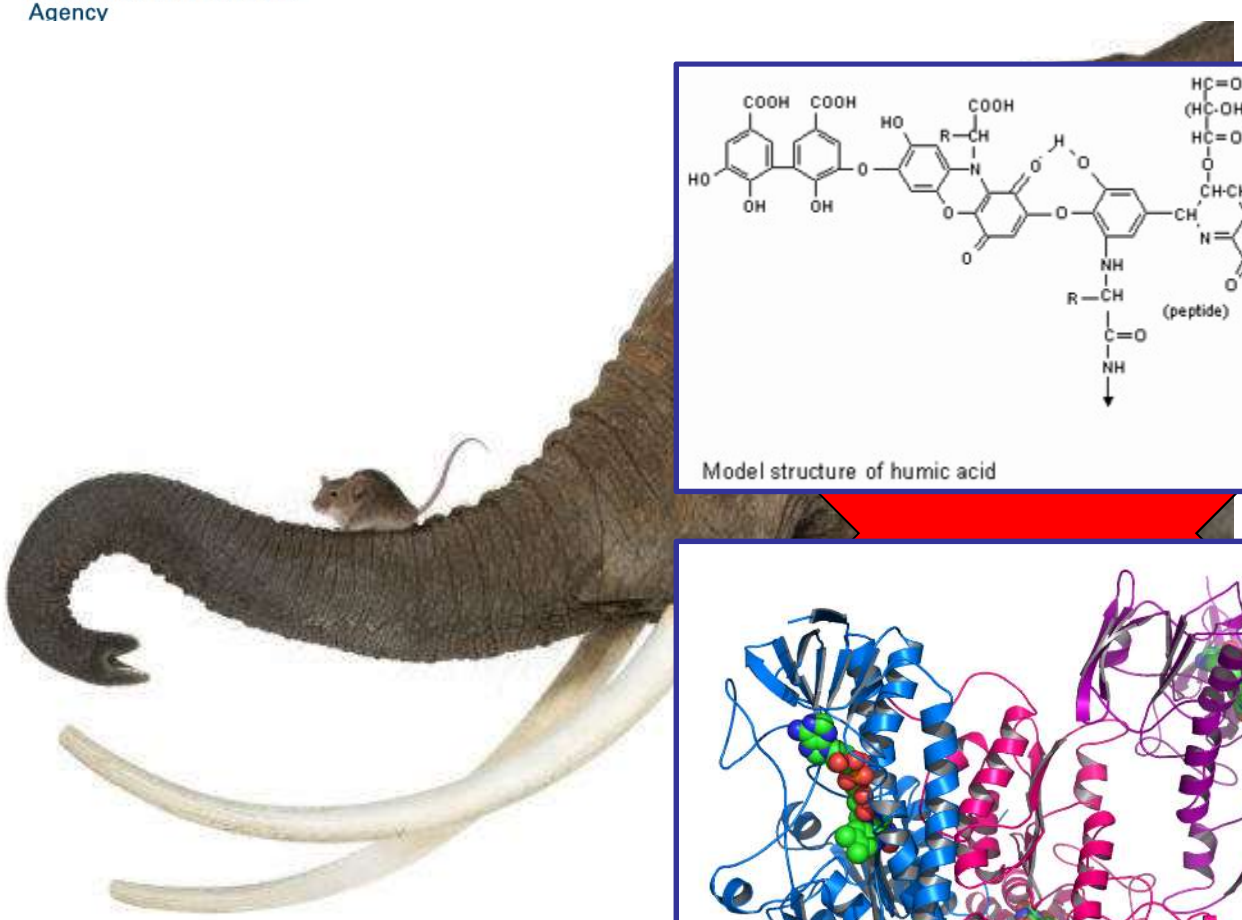
EPA
United States
Environmental Protection
Agency

Human Exposure Pathways

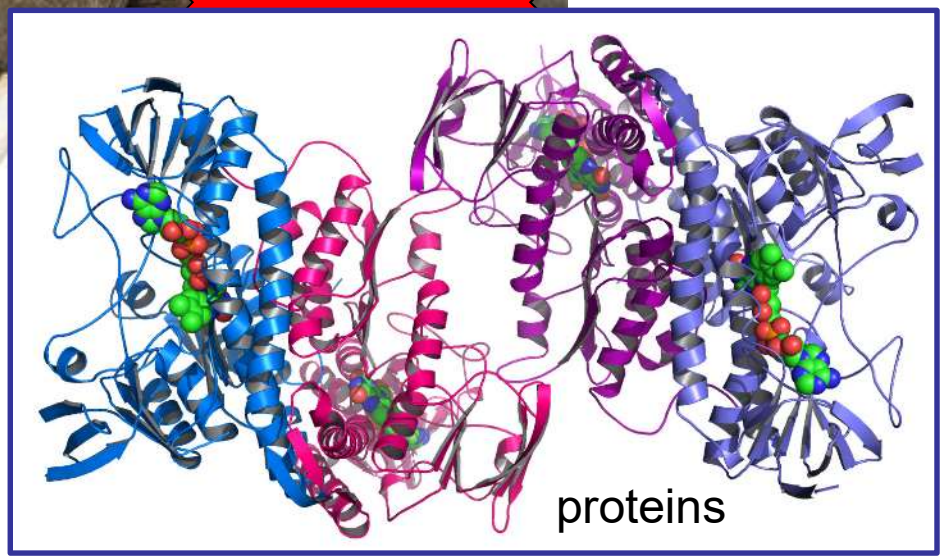
EPA
United States
Environmental Protection
Agency

Screening Intention?

EPA
United States
Environmental Protection
Agency



Model structure of humic acid



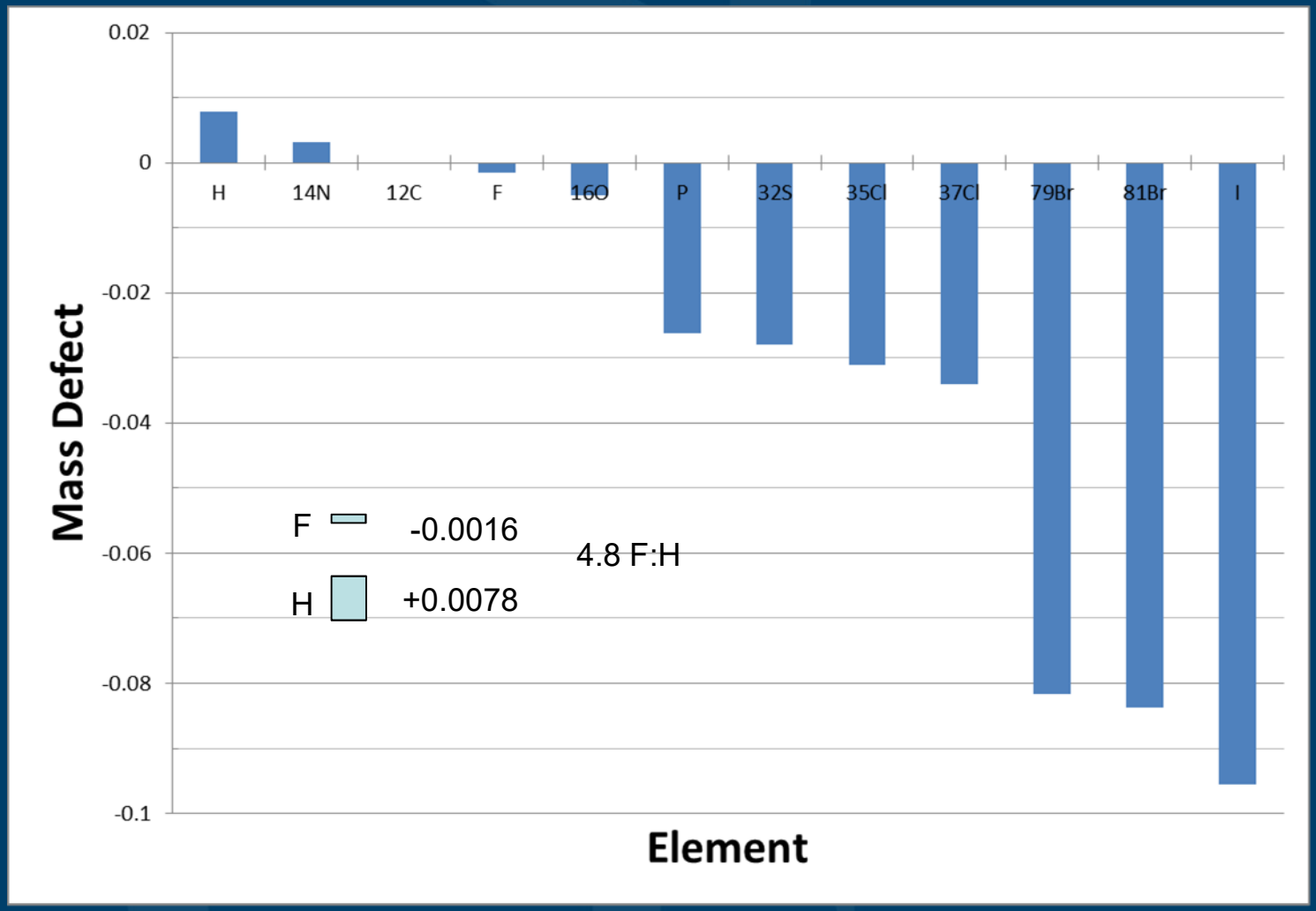
EPA United States Environmental Protection Agency

Usual Suspects 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)
- ???

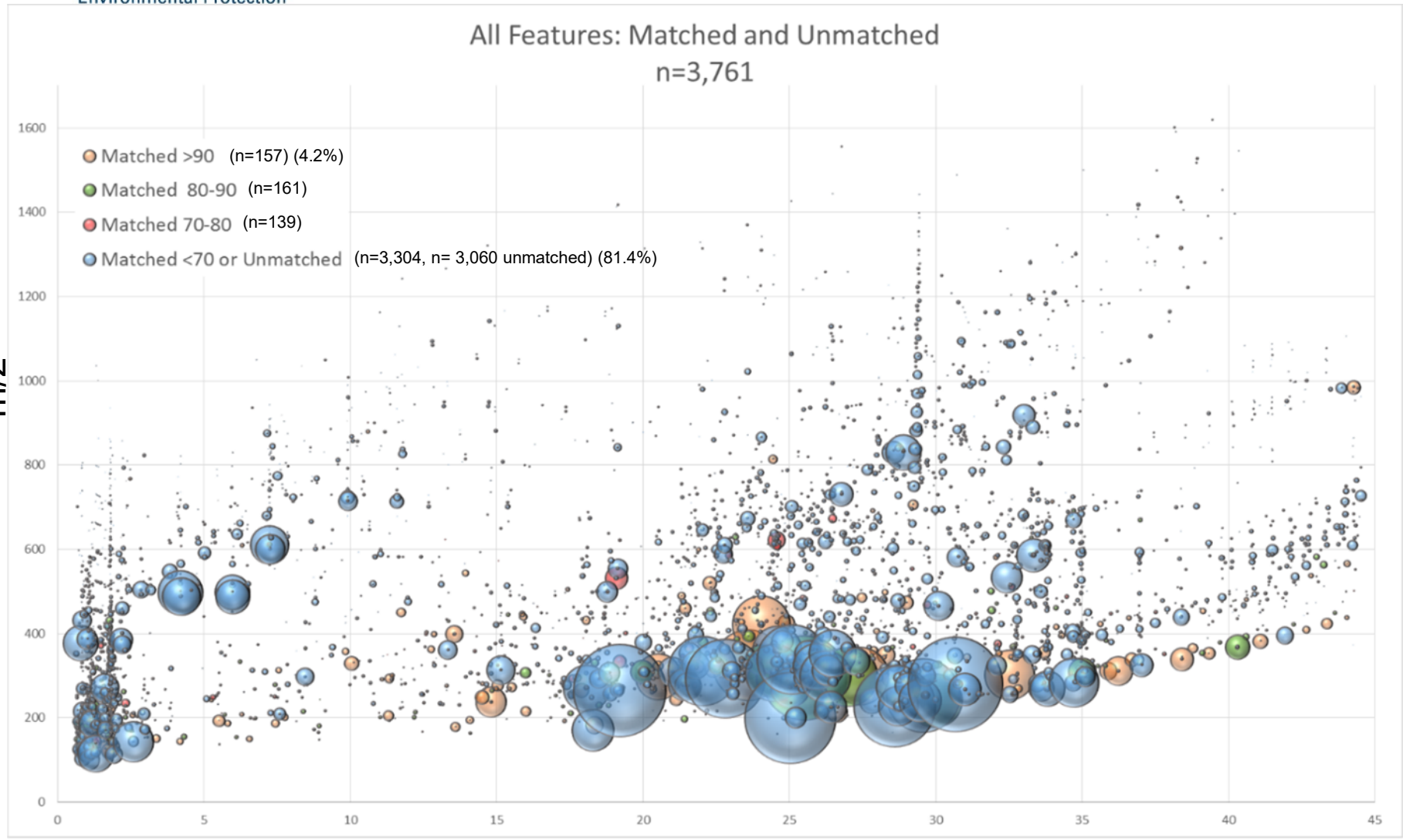
EPA United States Environmental Protection Agency

Typical Elements (C,H,N,O,P,S, F, Cl, Br, I)



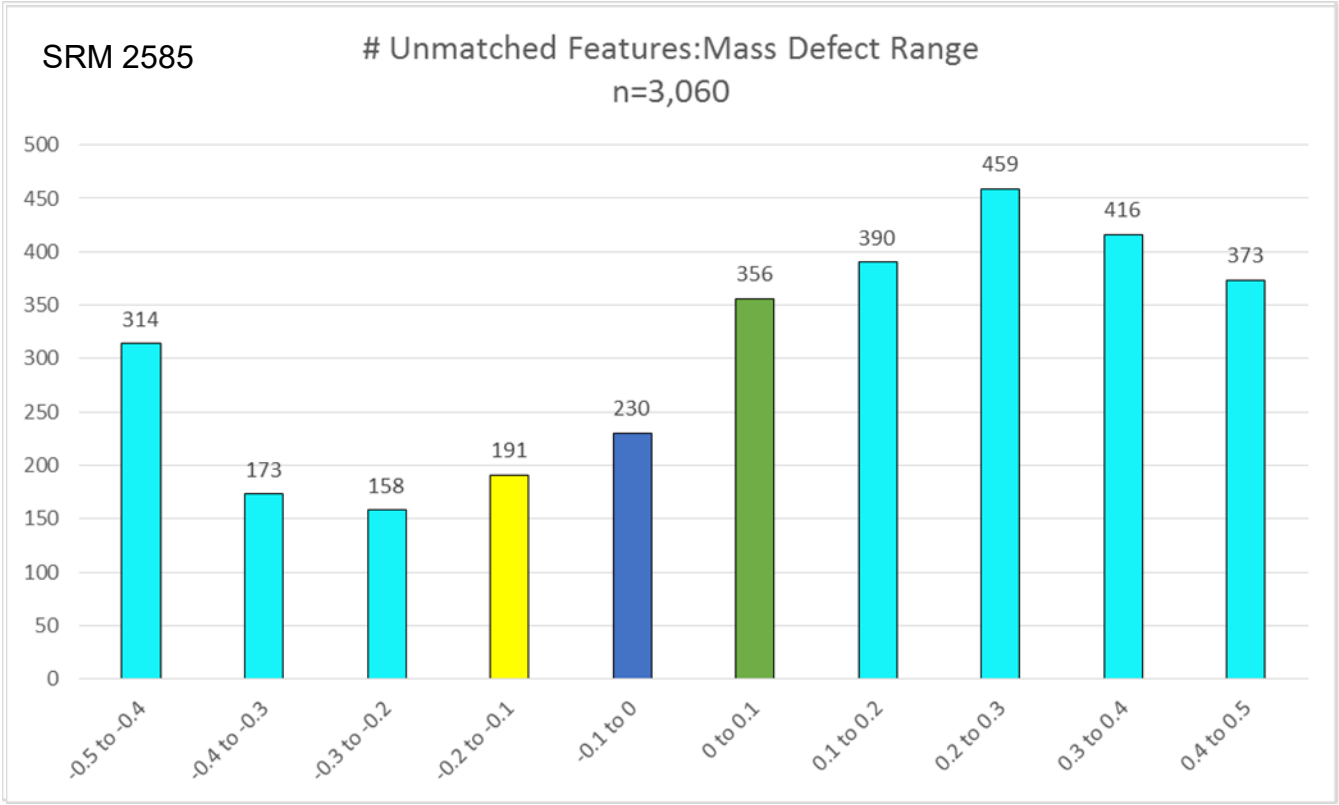
EPA United States Environmental Protection

SRM 2585 dust example



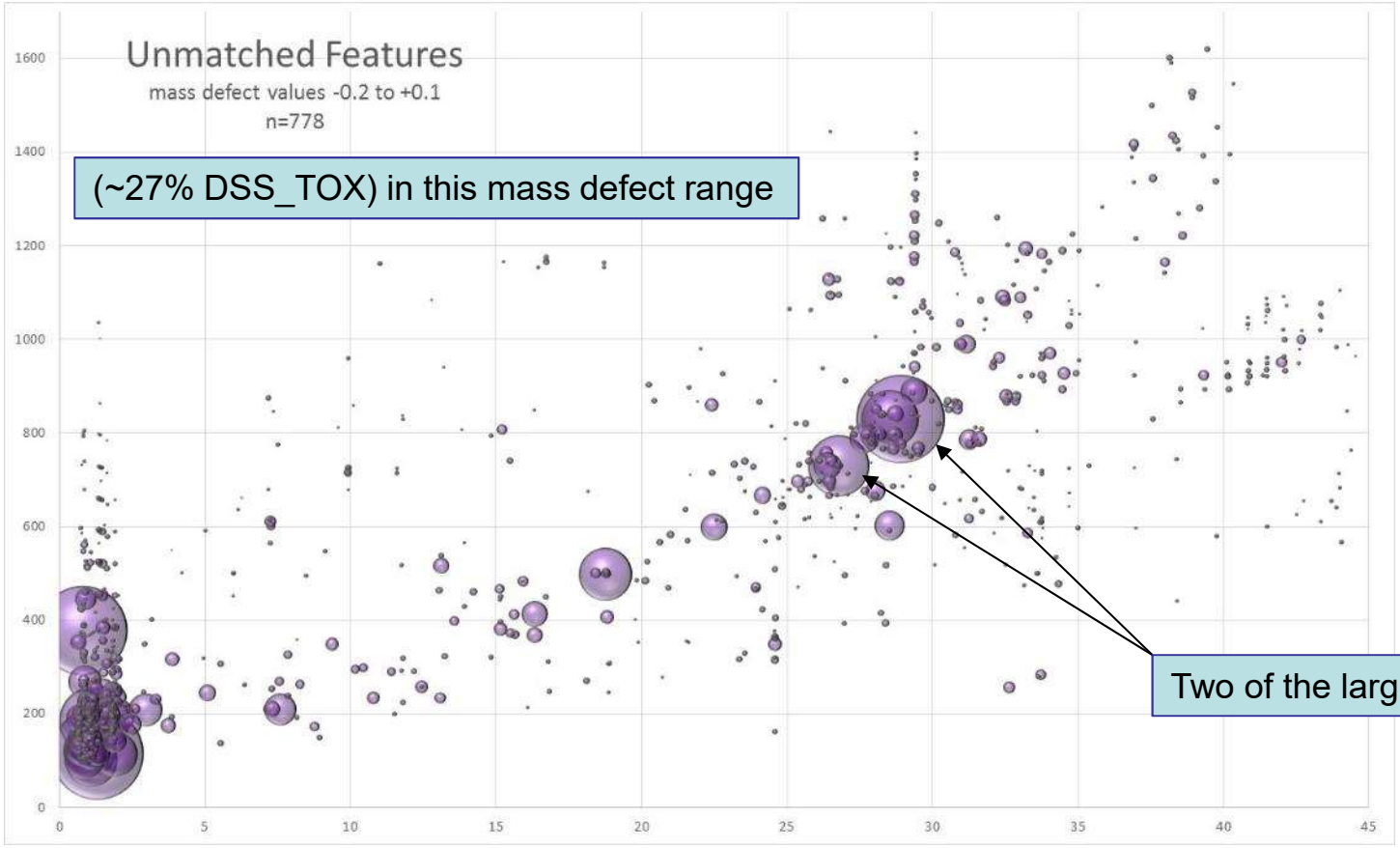
United States Environmental Protection Agency

Database mass defect
Vs.
Sample Mass Defect



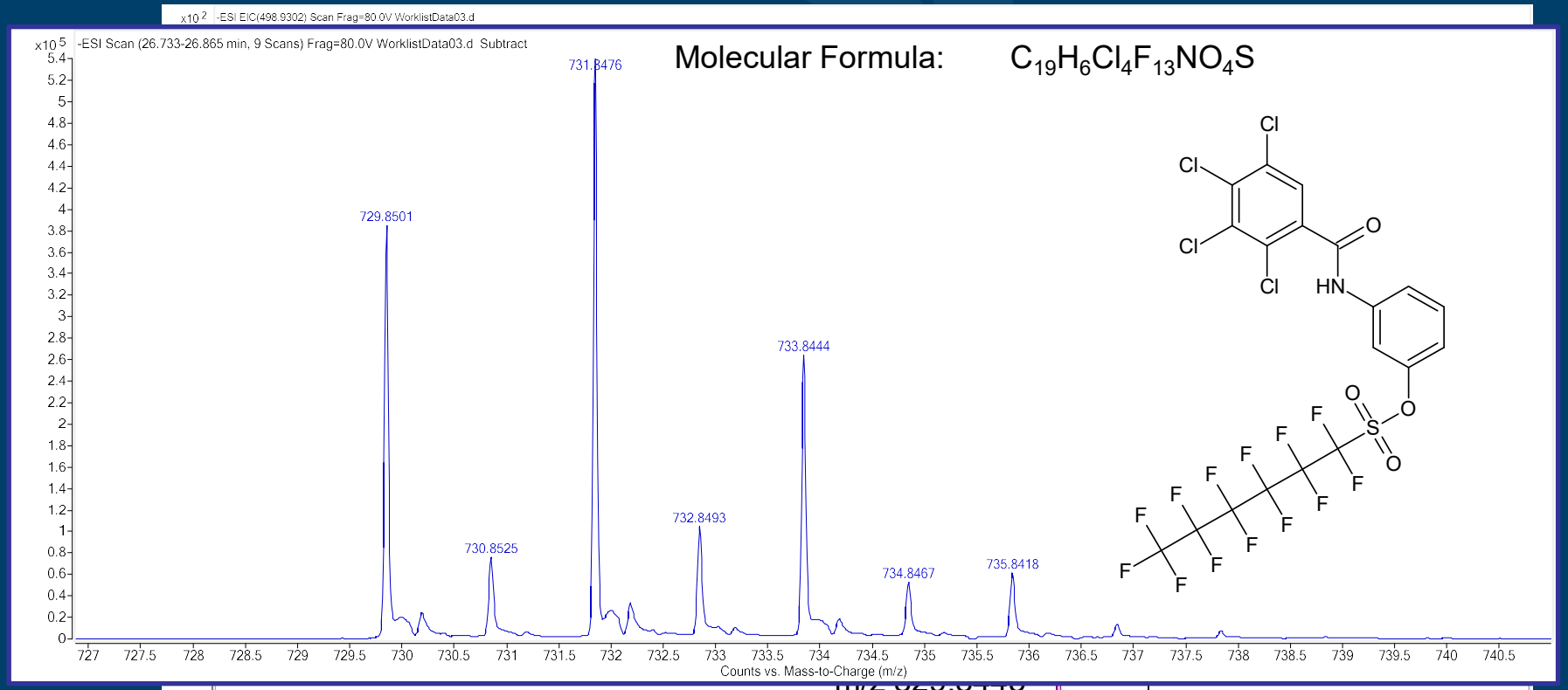
United States Environmental Protection Agency

NIST SRM 2585 Organic Compounds in Hose Dust



United States Environmental Protection Agency

NIST SRM 2585



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

EPA United States Environmental Protection Agency

Fipronil Cl_2
Fipronil Sufone Cl_2
Chlorination (5 ppm)
Removed?

Contents lists available at ScienceDirect

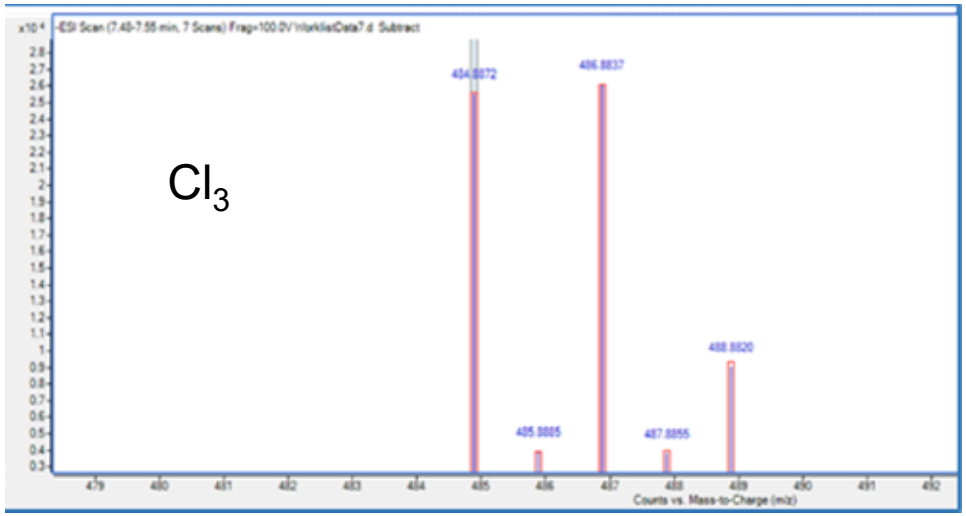
Science of the Total Environment

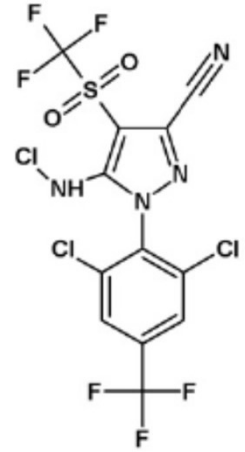
journal homepage: www.elsevier.com/locate/scitotenv

Comparison of fipronil sources in North Carolina surface water and identification of a novel fipronil transformation product in recycled wastewater

Rebecca L. McMahen [a], Mark J. Strynar [b,*], Larry McMillan [c], Eugene DeRose [d], Andrew B. Lindstrom [b]

[a] United States Environmental Protection Agency, National Exposure Research Laboratory, 109 TW Alexander Dr., Durham, North Carolina 27705, United States
[b] United States Environmental Protection Agency, National Exposure Research Laboratory, 109 TW Alexander Dr., Durham, North Carolina 27705, United States
[c] National Caucus and Center on Black Aged Employee, U.S. Environmental Protection Agency, National Exposure Research Laboratory, 109 TW Alexander Dr., Durham, North Carolina 27705, United States
[d] National Institute for Environmental Health Sciences, Nuclear Magnetic Resonance Facility, 111 TW Alexander Dr., Durham, North Carolina 27713, United States





Fipronil Sulfone Chloramine

Molecular Formula: $C_{12}H_3Cl_3F_6N_4O_2S$
Monoisotopic Mass: 485.894648 Da
$[M-H]^-$: 484.887371 Da

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

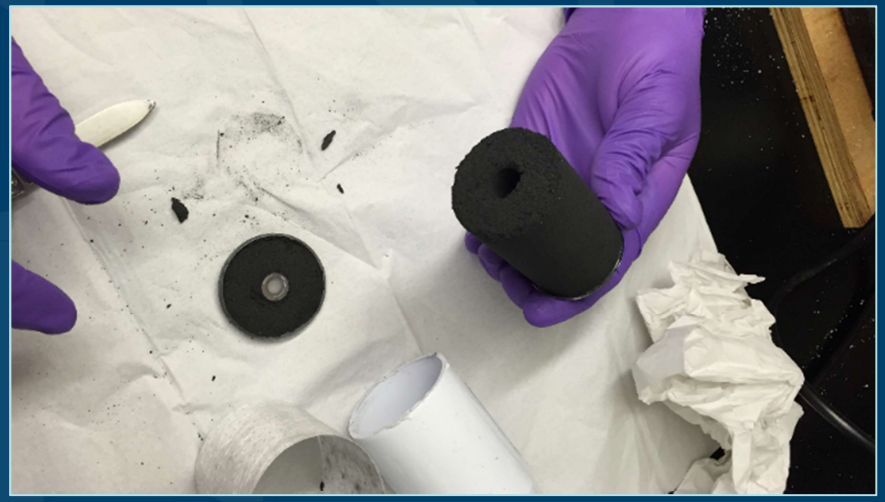
Julia E. Rager [a], Mark J. Strynar [b], Shuang Liang [a], Rebecca L. McMahen [a], Ann M. Richard [c], Christopher M. Grulke [d], John F. Wambaugh [c], Kristin K. Isaacs [b], Richard Judson [c], Antony J. Williams [c], Jon R. Sobus [b,*]

EPA United States Environmental Protection Agency

Point of use BRITA filter

- 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
- ~ $20

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

United States Environmental Protection Agency

LC/TOFMS Analysis

Agilent 6200 series TOF MSD
+/- Mode
ESI

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

Rager et al., 2015 Env. Int'l

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

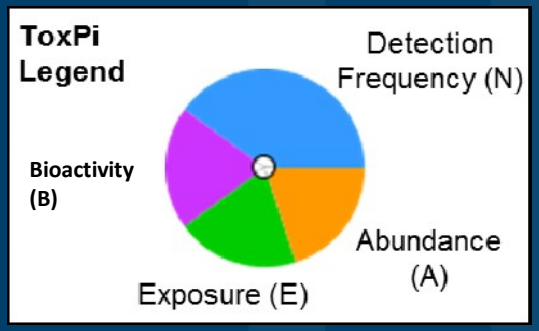
Substance_Name	Substance_CASRN	Substance_Type	Structure_SMILES	Structure_InChI	Structure_InChIKey	Structure_Formula	Structure_MolWt
A-alpha-C	26148-68-5	Single Compound	NC1=NC2=C(C=C1)C1=CC=CC=	InChI=1S/C11H9N3/c12-10-6-	FJTNLJLPLJDTRM-UHFFFAOYS	C11H9N3	183.2093
Acetaldehyde oxime	107-29-9	Single Compound	C\C=N\O	InChI=1S/C2H5NO/c1-2-3-4/h	FZENGILVLUJGJX-NSCUHMNN	C2H5NO	59.0672
Acetamide	60-35-5	Single Compound	CC(N)=O	InChI=1S/C2H5NO/c1-2(3)4/h	DLFVBJFMPXGRIB-UHFFFAOY	C2H5NO	59.0672
Acetaminophen	103-90-2	Single Compound	CC(=O)NC1=CC=C(O)C=C1	InChI=1S/C8H9NO2/c1-6(10)5	RZVAJINKPMORJF-UHFFFAOY	C8H9NO2	151.1626
Acetohexamide	968-81-0	Single Compound	CC(=O)C1=CC=C(C=C1)S(=O)(=	InChI=1S/C15H20N2O4S/c1-1	VGZSUPCWNCWDAN-UHFFFA	C15H20N2O4S	324.3953
Acetone[4-(5-nitro-2-furyl)-2	18523-69-8	Single Compound	CC(C)=NNC1=NC=C(S1)C1=CC	InChI=1S/C10H10N4O3S/c1-6	CUWVNOSSZYUJAE-UHFFFAC	C10H10N4O3S	266.2764
Acetonitrile	75-05-8	Single Compound	CC#N	InChI=1S/C2H3N/c1-2-3/h1H3	WEVYAHXRMPXWCK-UHFFFA	C2H3N	41.0519
Acetoxime	127-06-0	Single Compound	CC(C)=NO	InChI=1S/C3H7NO/c1-3(2)4-5	PXAJQJMDEXJWFB-UHFFFAO	C3H7NO	73.0938
N'-Acetyl-4-(hydroxymethyl)	65734-38-5	Single Compound	CC(=O)NNC1=CC=C(CO)C=C1	InChI=1S/C9H12N2O2/c1-7(13	UFFJUAYKLIGSJF-UHFFFAOYS	C9H12N2O2	180.2038
1-Acetyl-2-isonicotinoylhydr	1078-38-2	Single Compound	CC(=O)NNC(=O)C1=CC=NC=C	InChI=1S/C8H9N3O2/c1-6(12)	CVBGNAKQQUWBQV-UHFFFA	C8H9N3O2	179.176
Dehydroacetic acid	520-45-6	Single Compound	CC(=O)C1C(=O)OC(C)=CC1=O	InChI=1/C8H8O4/c1-4-3-6(10)	PGRHXDWITVMQBC-UHFFFA	C8H8O4	168.1467
1-Acetyl-2-phenylhydrazine	114-83-0	Single Compound	CC(=O)NNC1=CC=CC=C1	InChI=1S/C8H10N2O/c1-7(11)	UICBCXONCUFSOI-UHFFFAOY	C8H10N2O	150.1778
1-Acetylaminofluorene	28314-03-6	Single Compound	CC(=O)NC1=C2CC3=CC=CC=C3	InChI=1S/C15H13NO/c1-10(17	POECHIXSIXBYKI-UHFFFAOYS	C15H13NO	223.2698
4-Acetylaminofluorene	28322-02-3	Single Compound	CC(=O)NC1=C2C(CC3=C2C=CC	InChI=1S/C15H13NO/c1-10(17	PHPWISAFHNEMSR-UHFFFAC	C15H13NO	223.2698
4-Acetylaminophenylacetic a	18699-02-0	Single Compound	CC(=O)NC1=CC=C(CC(O)=O)C	InChI=1S/C10H11NO3/c1-7(12	MROJXXOCABQVEF-UHFFFAC	C10H11NO3	193.1992
N-Acetyl-L-cysteine	616-91-1	Single Compound	CC(=O)N[C@@H](CS)C(O)=O	InChI=1S/C5H9NO3S/c1-3(7)6	PWKSKIMOESPYIA-BYPYZUCN	C5H9NO3S	163.1949
Acifluorfen	50594-66-6	Single Compound	OC(=O)C1=C(C=CC(OC2=CC=C	InChI=1S/C14H7ClF3NO5/c15	NUFNQYOELLVIPL-UHFFFAOY	C14H7ClF3NO5	361.6573
Acrolein	107-02-8	Single Compound	C=CC=O	InChI=1S/C3H4O/c1-2-3-4/h2	HGINCPLSRVDWNT-UHFFFAC	C3H4O	56.0633
Acrolein diethylacetal	3054-95-3	Single Compound	CCOC(OCC)C=C	InChI=1S/C7H14O2/c1-4-7(8-5	MCIPQLOKVXSHTD-UHFFFAO	C7H14O2	130.1849
Acrolein oxime	5314-33-0	Single Compound	O\N=C\C=C	InChI=1S/C3H5NO/c1-2-3-4-5	KMNIXISXZFPRDC-ONEGZZNK	C3H5NO	71.0779
Acronycine	7008-42-6	Single Compound	COC1=CC2=C(C=CC(C)(C)O2)C	InChI=1S/C20H19NO3/c1-20(2	SMPZPKRDRQOOHT-UHFFFAC	C20H19NO3	321.3698
Acrylamide	79-06-1	Single Compound	NC(=O)C=C	InChI=1S/C3H5NO/c1-2-3(4)5	HRPVXLWXLXDGHG-UHFFFAC	C3H5NO	71.0779
Acrylonitrile	107-13-1	Single Compound	C=CC#N	InChI=1S/C3H3N/c1-2-3-4/h2	NLHHRLWOUZZQLW-UHFFFA	C3H3N	53.0626

https://www.epa.gov/chemical-research/distributed-structure-searchable-toxicity-dsstox-database

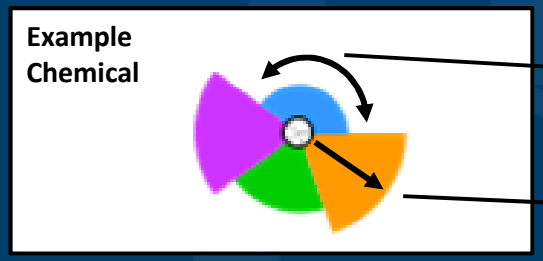
Prioritization Scoring with ToxPi

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

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



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)

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

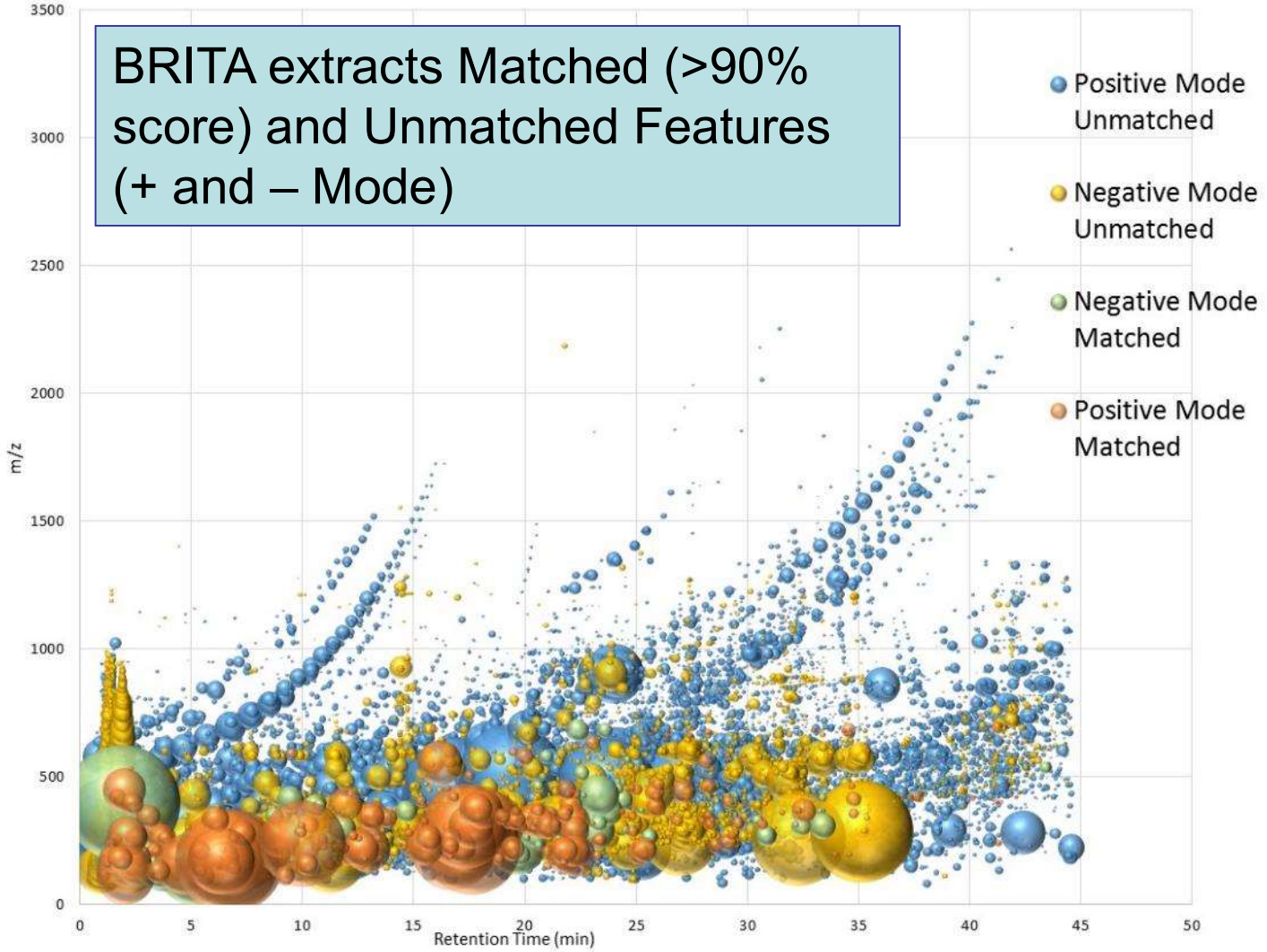
DSSTox Name	NIST name
Methyl decanoate	Methyl ester decanoic acid
2-[2-(2-Butoxyethoxy)ethoxy]ethanol	2-[2-(2-butoxyethoxy)ethoxy]-Ethanol
Tris(2-chloroethyl) phosphate	Tri(2-chloroethyl) phosphate
Triethyl phosphate	Triethyl phosphate
Simazine	6-chloro-N,N'-diethyl-1,3,5-Triazine-2,4-diamine
Atrazine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

Chemicals detected that are monitored for in USEPA DW programs

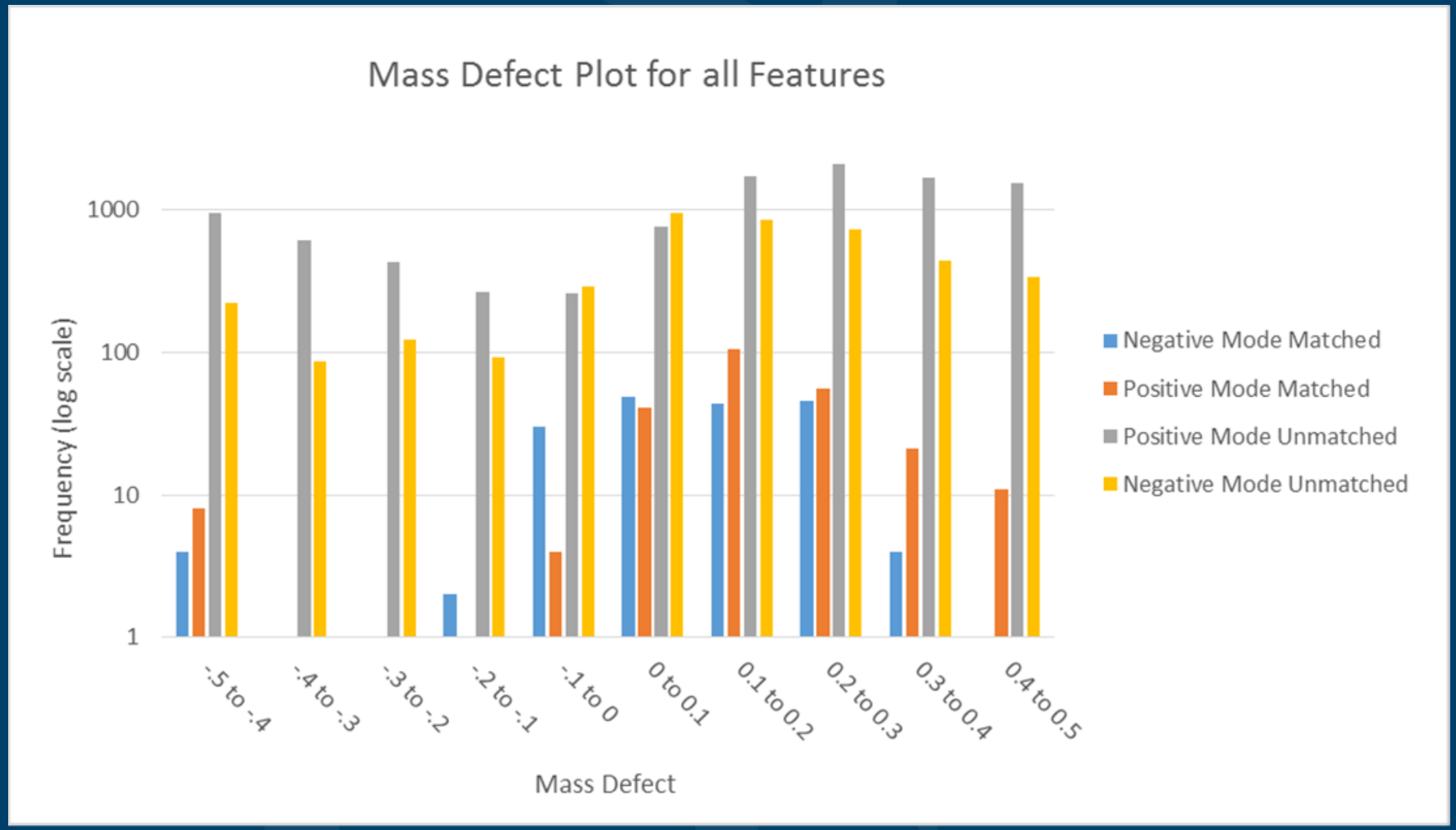
- Atrazine
- Simazine
- PFOS
- PFOA
- PFNA
- PFHxS

EPA
United States
Environmental Protection
Agency

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

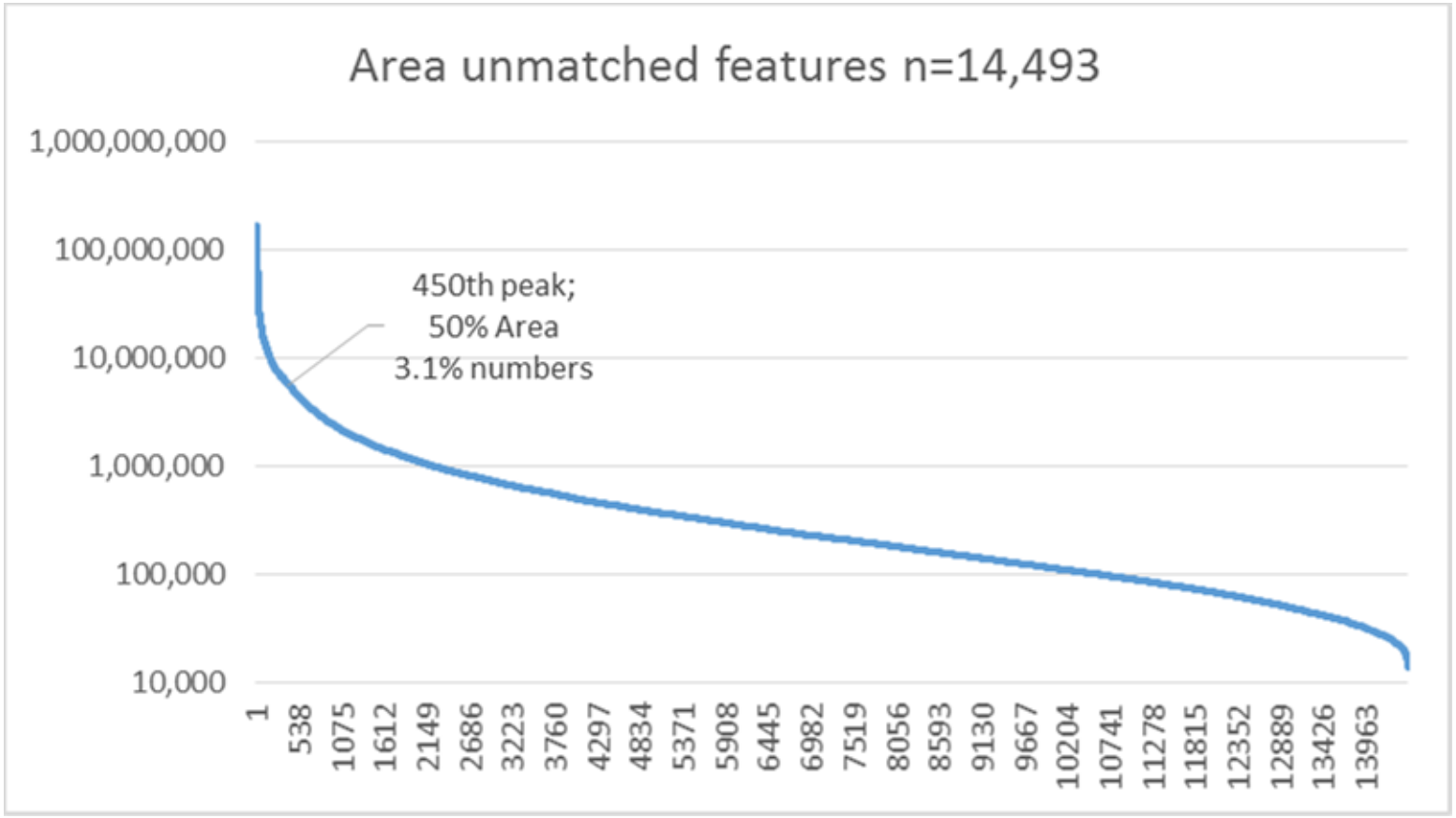


Mass Defect all features Matched and Unmatched



United States Environmental Protection Agency

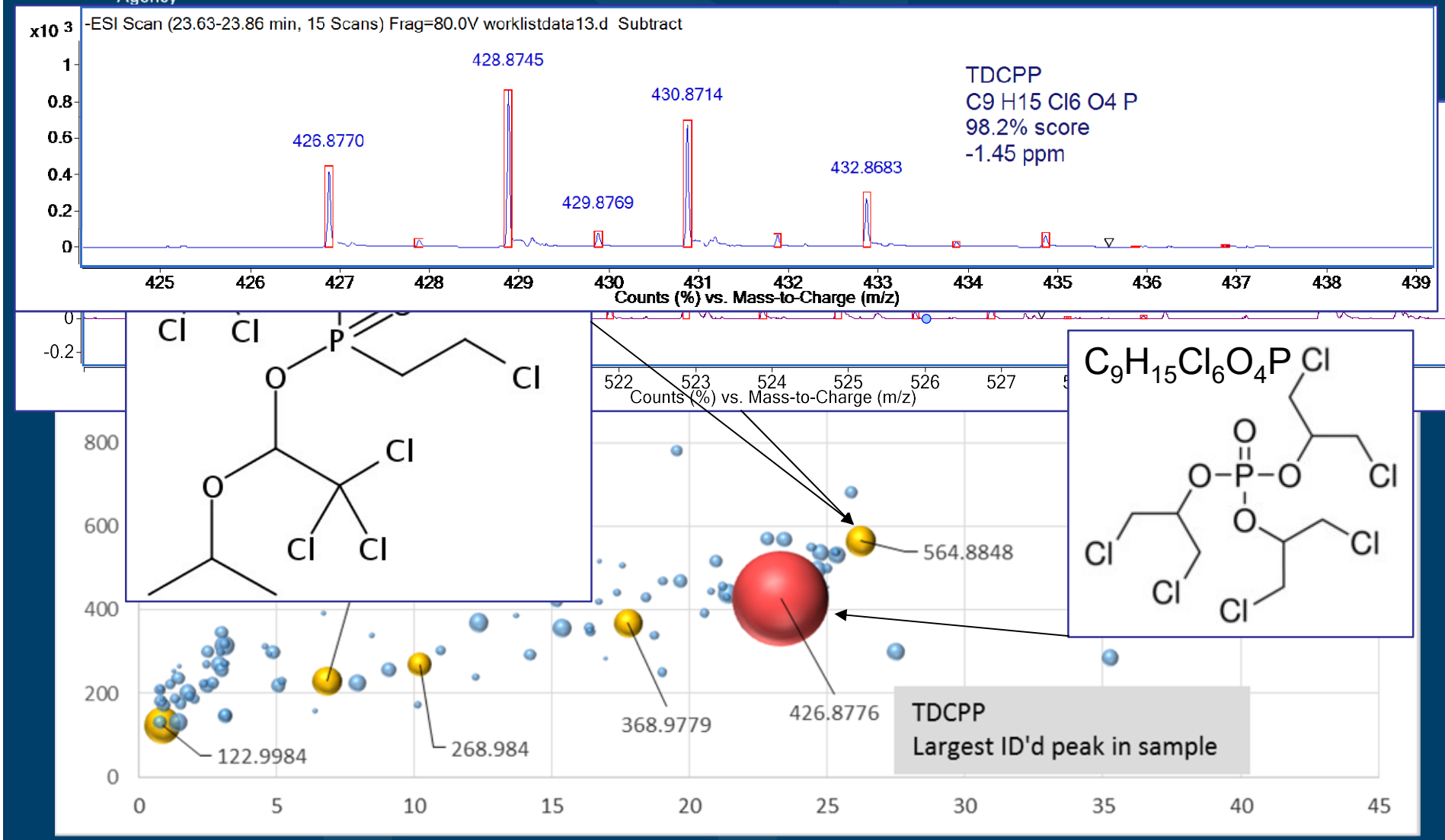
Number of Features vs Area of Features



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		

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 investigations
- 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 understand remaining chemical space

EPA United States Environmental Protection Agency

Acknowledgements

Co-authors:
Rebecca McMahen
Seth Newton
Jon Sobus



Help with ToxPi:
Julia Rager

Help with DSS_TOX :
Ann Richard
Tony Williams


Chris Grulke

GC/MS:
Scott Clifton


Looking for a post-doc
Summer/Fall 2016
EPA RTP, NC USA
Thank You.
strynar.mark@epa.gov
Deep River, NC