

Enhanced performance of 4D wide-scope target screening in environmental (bio)monitoring studies utilizing LC-ESI-TIMS-QTOF-MS and a comprehensive database

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Introduction

Thousands of chemicals are released daily into the environment...



...posing potential threats to human, animals and the environment.



comprehensive and systematic environmental (bio)monitoring

detection of contaminants with potential persistent, bioaccumulative and toxic properties



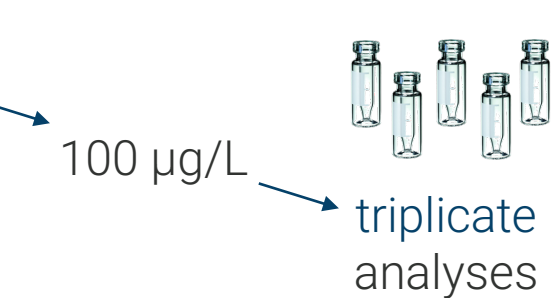
Incorporation of TIMS in LC-HRMS:

- new dimension of separation
- additional identification confidence in wide-scope target screening

Methods

Standard solution mixes

>1,000 environmental contaminants in total



100 µg/L

triplicate analyses

Generic sample preparation protocols

Extraction of a broad range of contaminants from different environmental matrices

Instrumentation: LC-ESI-TIMS-QTOFMS

Acquisition mode: broadband Collision Induced Dissociation (bbCID)

- TIMS off mode &
- TIMS on mode

TargetScreener HR workflows



Results

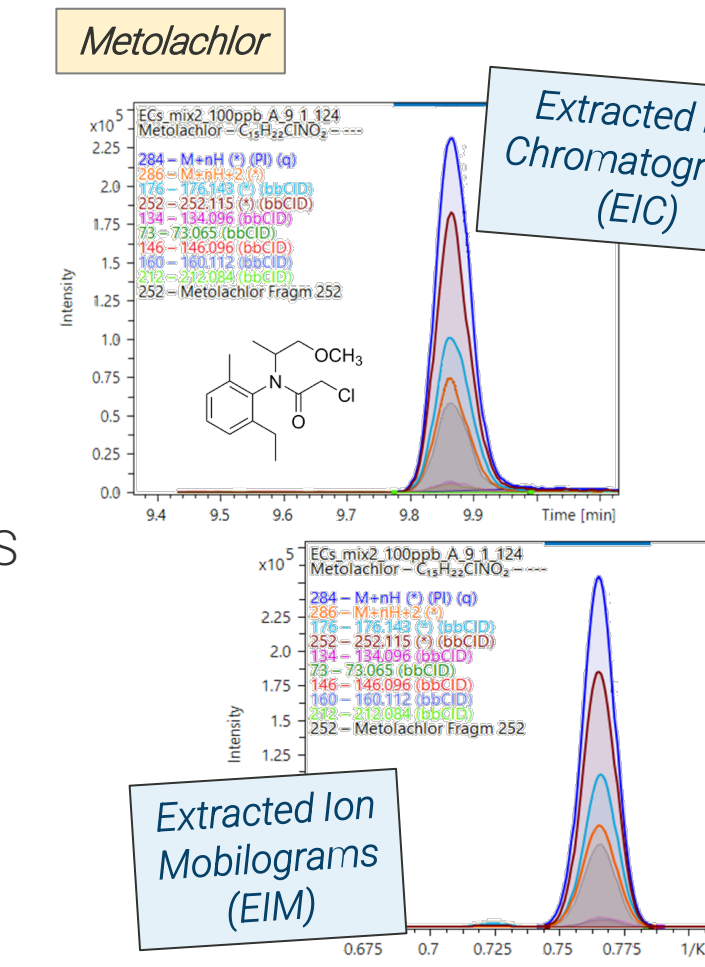
A. Establishment of a CCS-aware database with environmental contaminants

m/z	Rt	Formula	Name	CCS	Qual1	Qual2	Qual3	Qual4	Qual5	Qual6
255.1128	5.13	C15H14N2O2	10-Hydroxycarbamazepine	156.09	194.09643	192.08078	237.10224			
303.2319	8.94	C20H30O2	17-alpha-Methyltestosterone	178.2	97.064791	109.06479	285.22129			
313.0795	6.96	C14H11F3N2O3	5-Hydroxyflunixin	169.2	295.06889					
328.1543	3.79	C19H21NO4	6-O-Monoacetylmorphine (MAM)	176.6	211.07536	268.13321	193.06479	165.06988	229.08592	
284.1194	4.71	C16H14N3O1F1	7-Amino-flunitrazepam	165.03	135.09168	227.0979	256.12445			
337.2122	4.44	C18H28N2O4	Acetabutozol	190.87	116.10699	72.08078	74.06004	98.09626	56.049476	260.12812
170.1176	2.93	C9H15NO2	Acetidine	139.32	82.065126	128.10699	110.09643			
375.2615	5.19	C38H72N2O12H2*2+	Azithromycin (M+2H) ²⁺	304.24	83.049141	116.10699	158.11756	591.42151		
404.1241	7.63	C22H17N3O5	Azoxystrobin	196.54	372.0979	344.103	329.0795	316.1081	301.0846	
309.1822	3.41	C17H20N6	Baquigoprim	179.12	294.15875	277.1322	171.09168	266.14002		
316.008	6.33	C14H10N3O1Br1	Bromazepam	166.4	182.08385	209.09475	288.01309	80.049476		
319.0804	5.73	C16N2H19Br	Brompheniramine	167.66	274.02259	167.07295				
195.0877	4.12	C8H10N4O2	Caffeine	140.26	138.06619	83.060375	110.07127	69.044725	123.04271	163.07401
441.167	6.01	C24H20N6O3	Candesartan	196.75	207.0917	263.1291	235.0978	192.0808	423.1564	395.1503
341.2111	8.24	C22H28O3	Canrenone	186.83	107.08553	97.064791	187.11174	173.09609	283.16926	
306.2064	8.67	C18H27NO3	Capsaicin	184.05	137.05971	122.03623	69.069877			

LC-ESI-TIMS-QTOFMS database

Bruker's TargetScreener HR platform

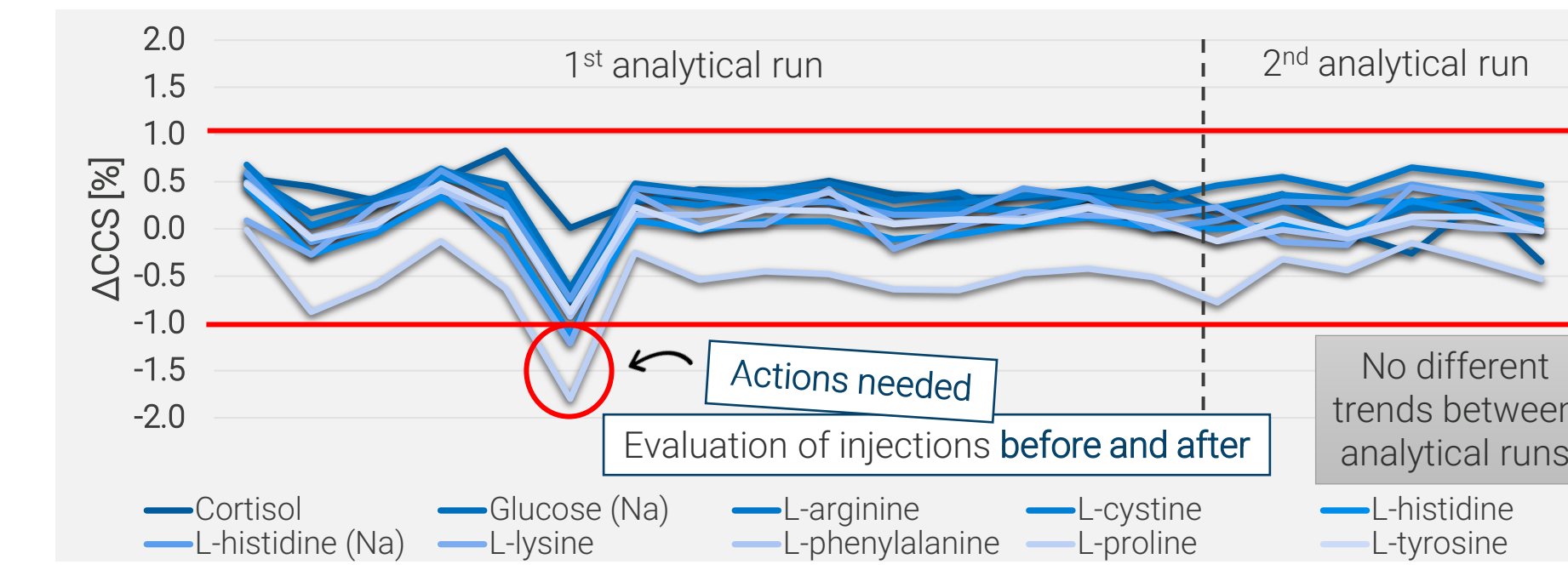
- Retention time (RT)
- Formula and m/z of the precursor ion (the most abundant ion in Full Scan MS)
- Characteristic isotopic peaks
- Qualifier bbCID ions & Full Scan MS ions (ions with > 50% relative intensity as mandatory)
- Ion-mobility derived Collision Cross Section (CCS)



B. Quality Control protocol for CCS measurements

Standard solution mix with reference values → triplicate measurements before, during and after the analyses

- Evaluation of mass accuracy, resolution, RT shift, peak width, sensitivity
- Evaluation of %ΔCCS by comparison of the experimental CCS values with those of the Unified CCS Compendium*

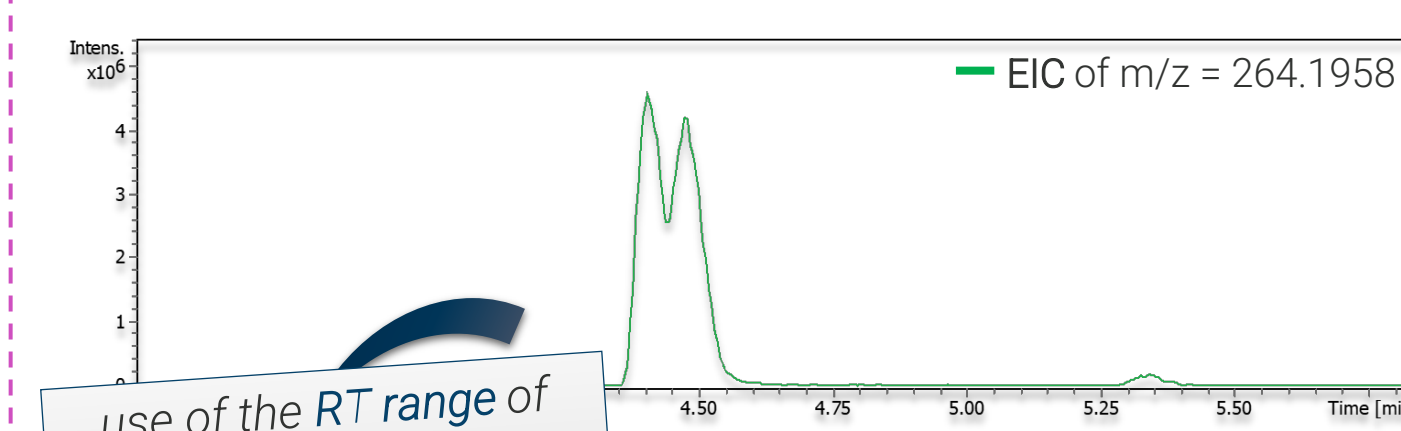
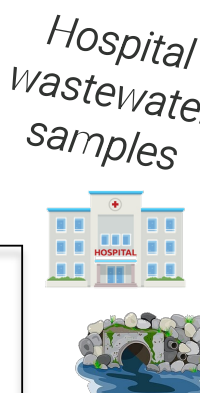


* J. A. Picahe et al., Collision cross section compendium to annotate and predict multi-omic compound identities, Chem. Sci., 2019, 10, 983–993, DOI: 10.1039/C8SC04396E.

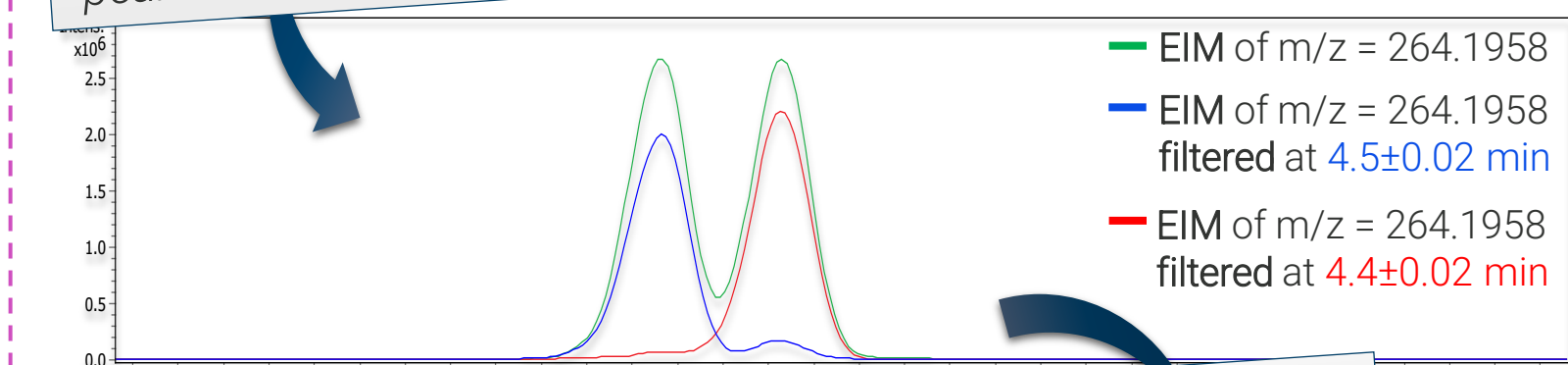
C. Overall analytical performance of the LC-TIMS-HRMS platform

Analyte separation:

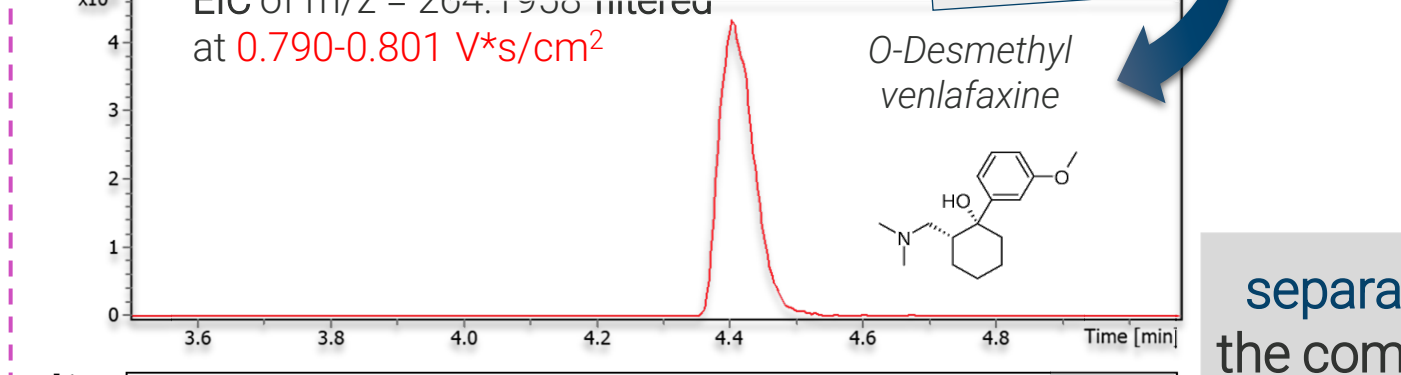
insufficient chromatographic separation of the isomeric compounds O-Desmethylvenlafaxine & Tramadol



use of the RT range of each chromatographic peak for filtering the EIM

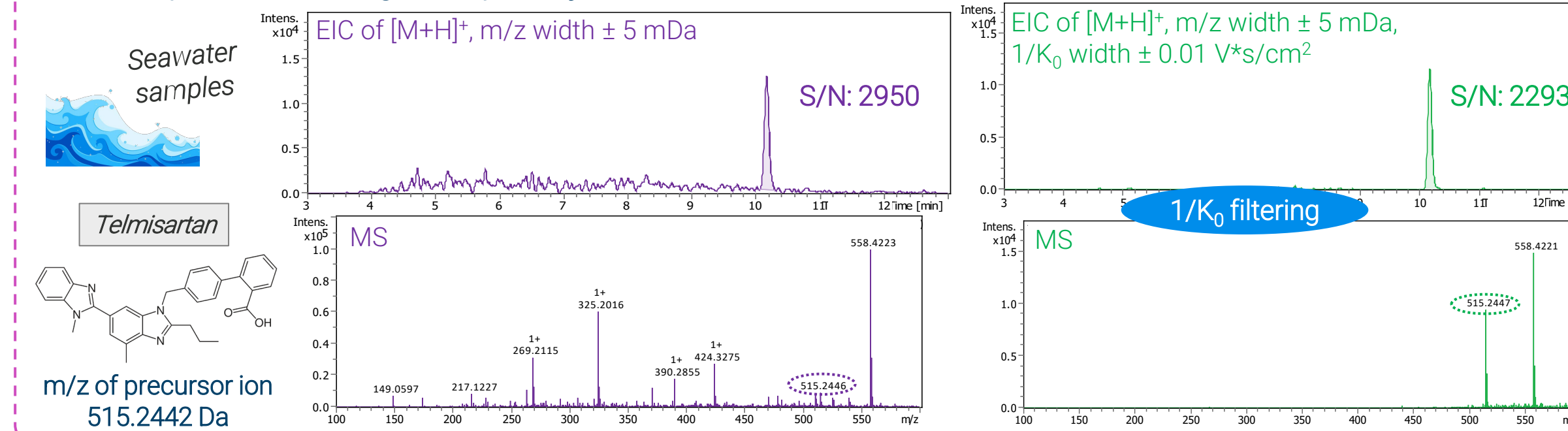


use of the 1/K₀ range of each mobility peak for filtering the EIC



separation of the compounds due to their different ion mobilities

Mass spectra of higher quality:

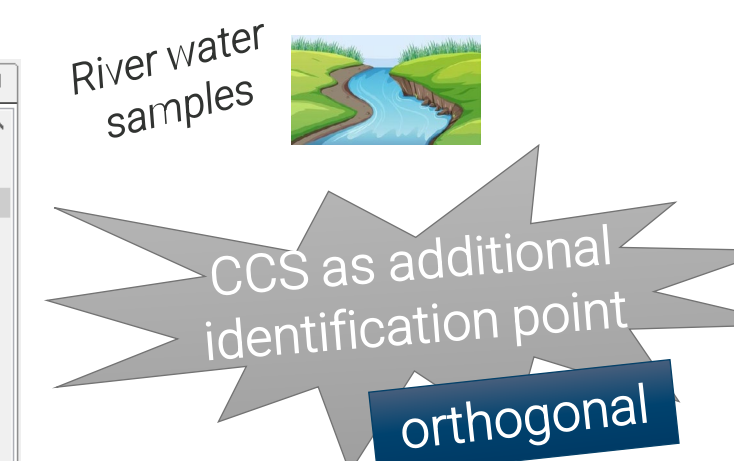
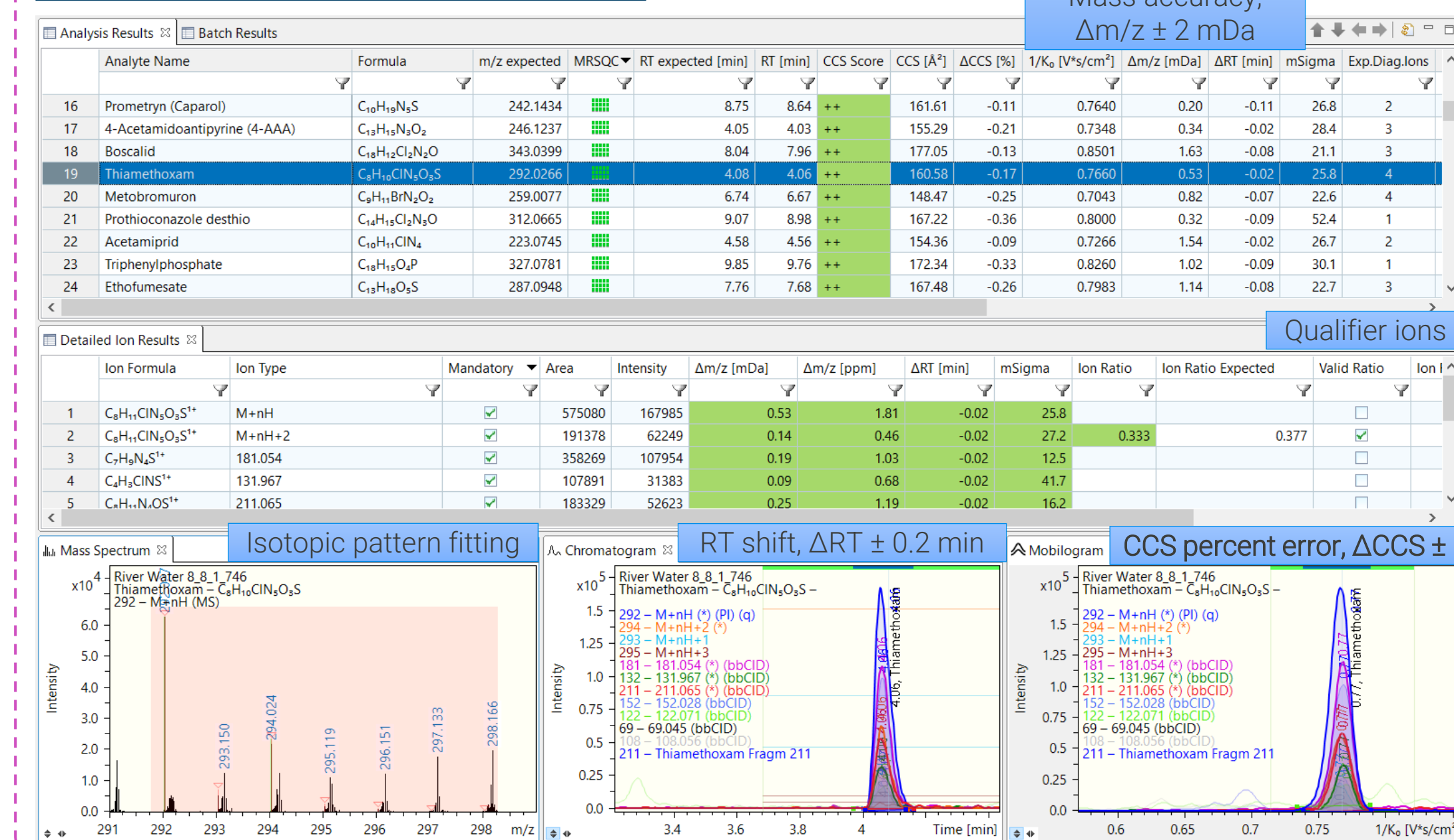


By ion mobility filtration:

- ✓ Improved S/N ratio
- ✓ Clear MS spectrum

Lower method detection limit can be achieved

Additional identification criterion:



CCS as additional identification point

orthogonal

4D wide-scope target screening

Reduction of false positive results

Qualitative and quantitative results of higher confidence

Summary

- ❖ Establishment of a CCS-aware database containing >1,000 environmental contaminants by utilizing LC-ESI-TIMS-QTOFMS data
- ❖ Quality assurance of the CCS measurements
- ❖ 4D wide-scope target screening in environmental samples
- ❖ Demonstration of the benefits of LC-TIMS-HRMS in environmental (bio)monitoring studies

Conclusion

The hyphenation of TIMS with HRMS benefits environmental (bio)monitoring.

- The new dimension of TIMS assists the separation of various isomeric/ isobaric co-eluting compounds.
- The ion mobility filtration suppresses matrix signal and provides higher-quality mass spectra even in highly complex matrices, improving sensitivity and thus analyte detection.
- Ion mobility-derived CCS values are an additional identification criterion and reinforce the established identification point system for wide-scope target screening, leading to 4D-identification.

Ion Mobility: Applications