ThermoFisher SCIENTIFIC

Orbitrap Exploris™ Isotope Solutions

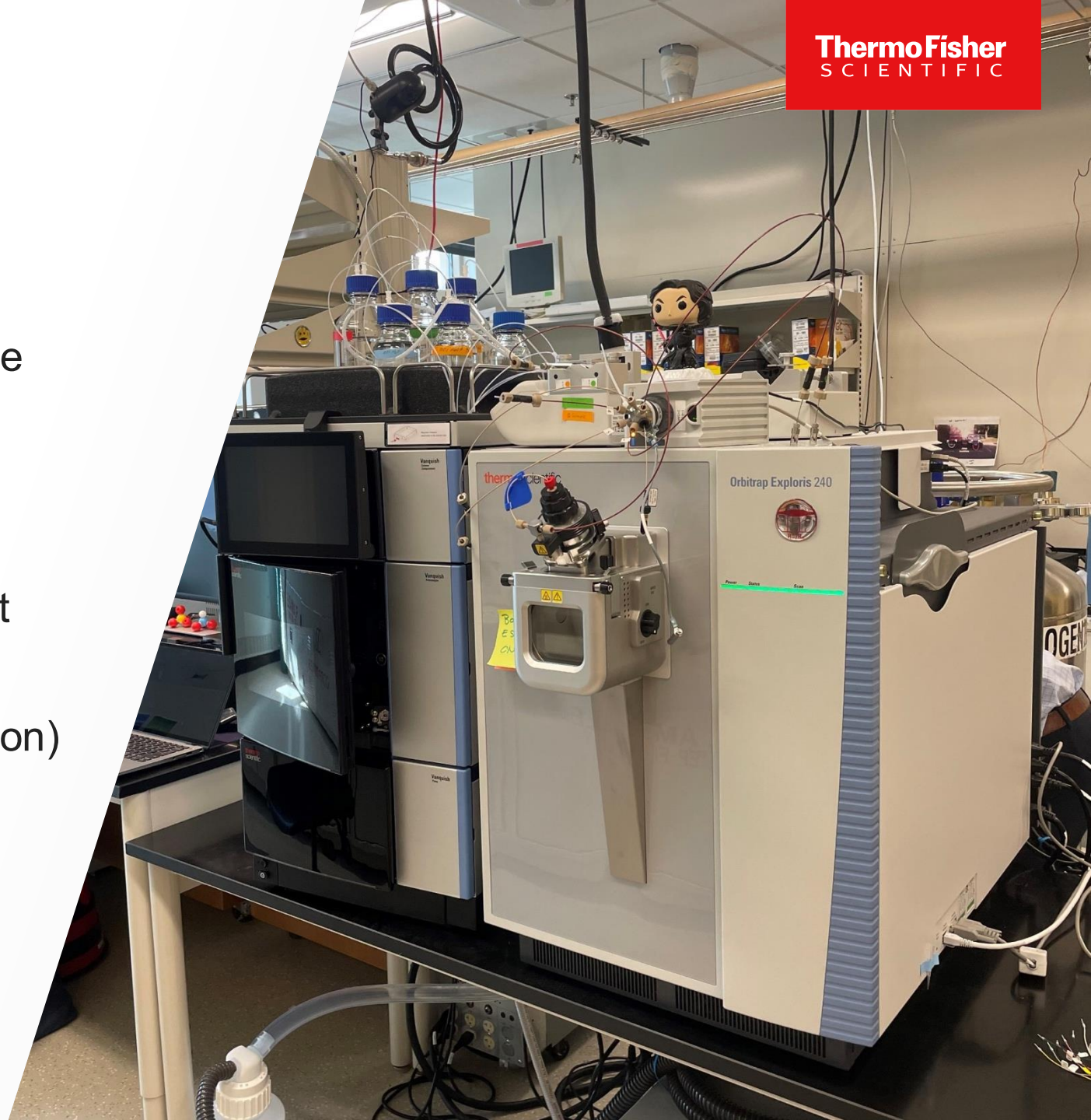
Taylor Graham, Brett Davidheiser, Nils Kuhlbusch, Andreas Hilkert, Dieter Juchelka

June 7, 2026

The world leader in serving science

Outline

- Magnetic sector portfolio
- Ideal molecule to benchmark orbitrap isotope ratios
- Measurement technique
- Review of established compounds
- Current labs with orbitrap isotope equipment
- Thermo demo lab
- Questions (feel free to ask during presentation)



The current Thermo Scientific™ IRMS portfolio

We currently offer a scaled portfolio of MS and sample introduction solutions

- **Thermo Scientific™ DELTA Q™ IRMS**
- Sensitivity up to 800 M/I
- Mass range up to *m*/*z* 96
- Accommodates up to 10 collectors

- **Thermo Scientific™ 253 Plus™ 10 kV IRMS**
- High-precision isotope analysis
- Long term stability and robustness
- Complete automation for ease-of-use

- **Thermo Scientific™ Orbitrap Exploris™ 120/240/480 MS**
- ESI source
- Variable resolution for multiple isotopologue collection
- Complete automation for ease-of-use

Oxyanions: refine understanding of element cycling

Atmosphere ⟷ Soil ⟷ Water

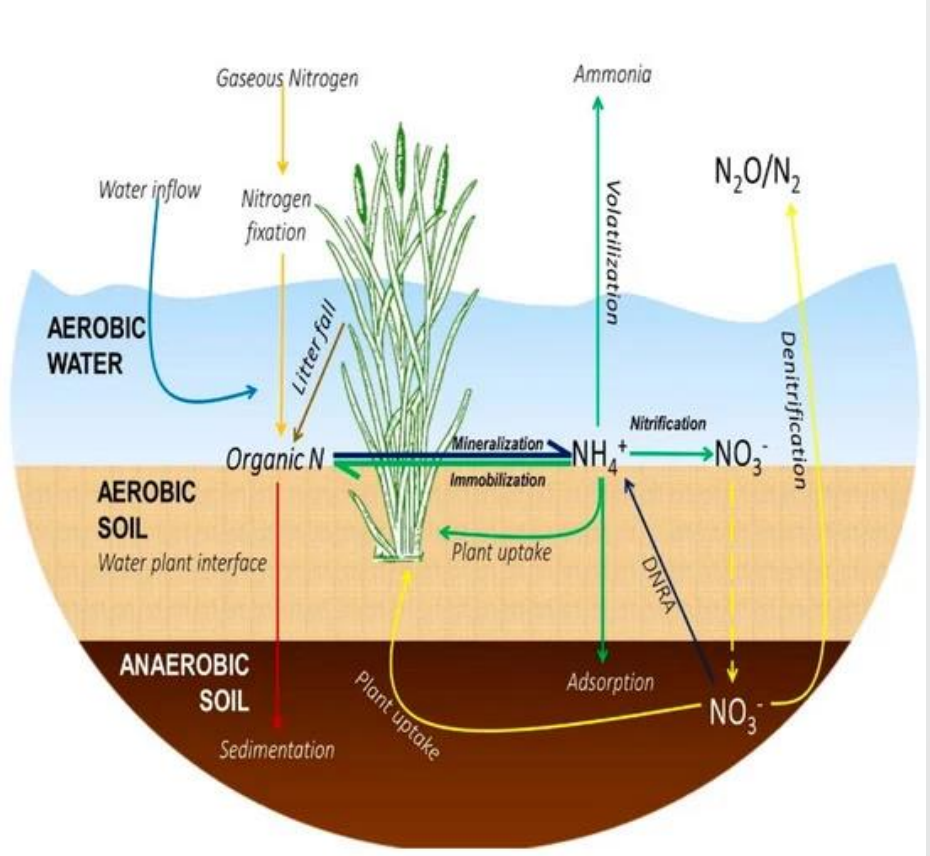
NO_3^- SO_4^{-2} PO_4^{-3}

Oxyanions are important chemical constituents of virtually every environment on Earth.

What are current isotope ratio techniques missing?

A wish list

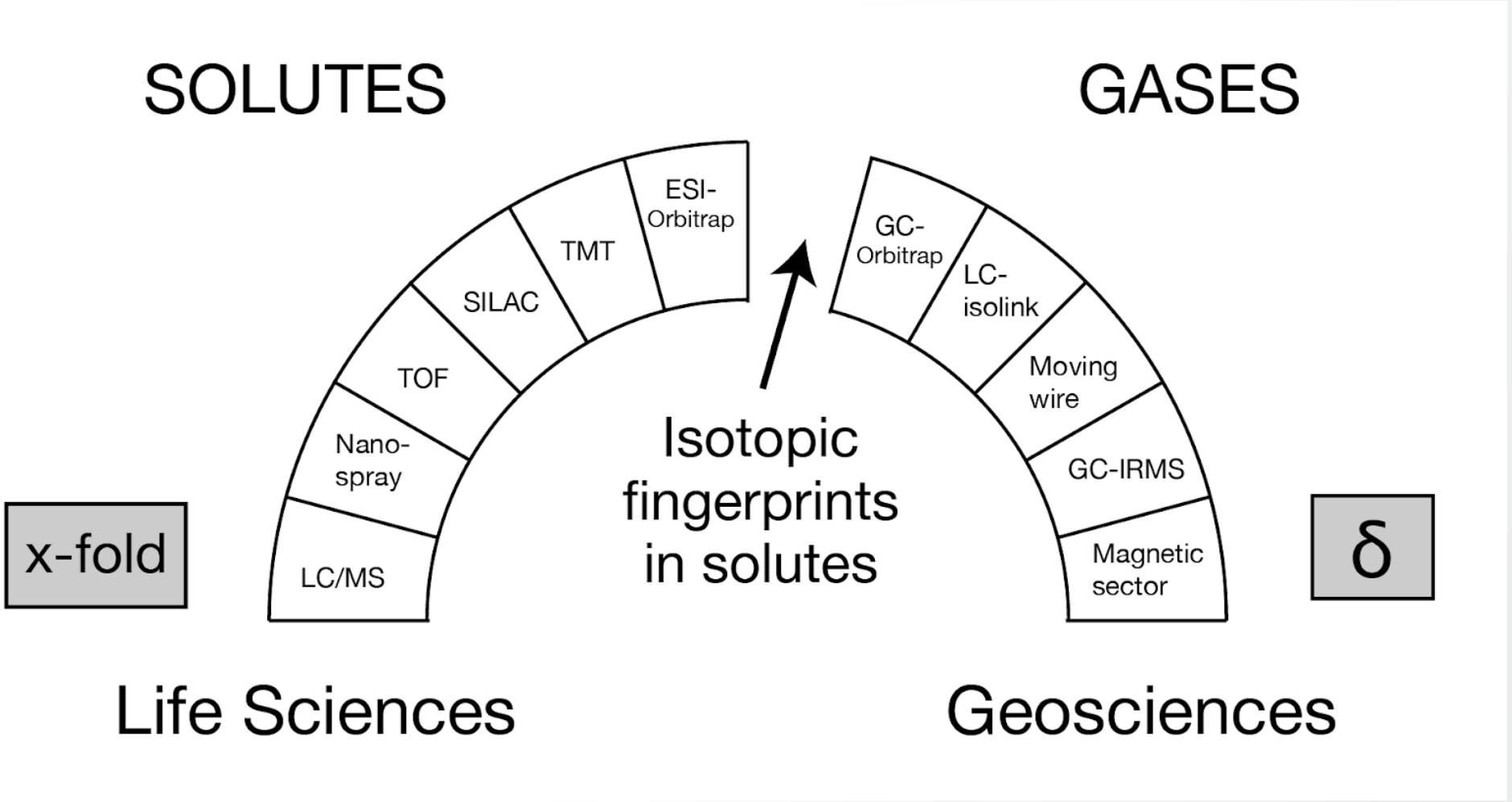
- Direct measurement of intact molecules
- Access to liquid, polar samples
- Higher sensitivity
- Less sample preparation, eliminate solid → gas process
- Position specific isotope analysis



Nitrogen **2021**, 2, 196–217. https://doi.org/10.3390/nitrogen2020013

An opportunity to bridge a gap exists

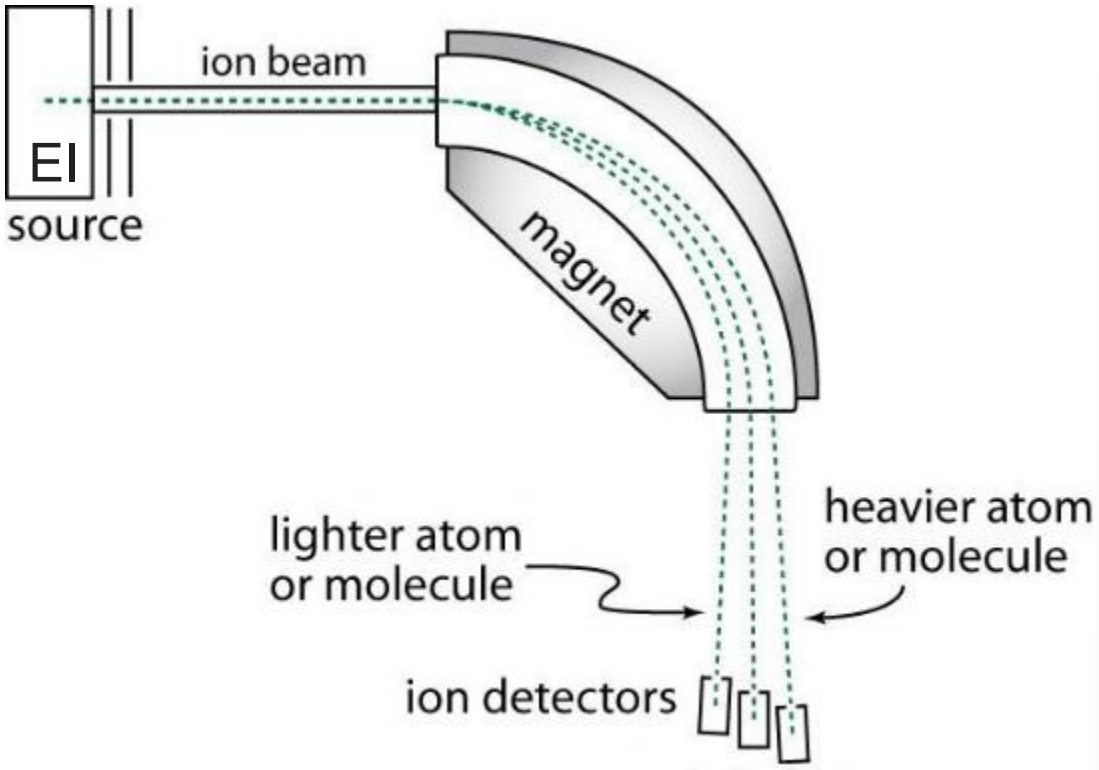
Combine technology developed for Life Science with approaches from stable isotope geochemistry



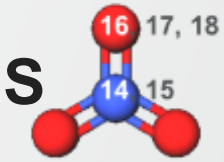
Mass spectrometers for isotope ratio analysis

Classic isotope-ratio MS N_2, O_2, N_2O

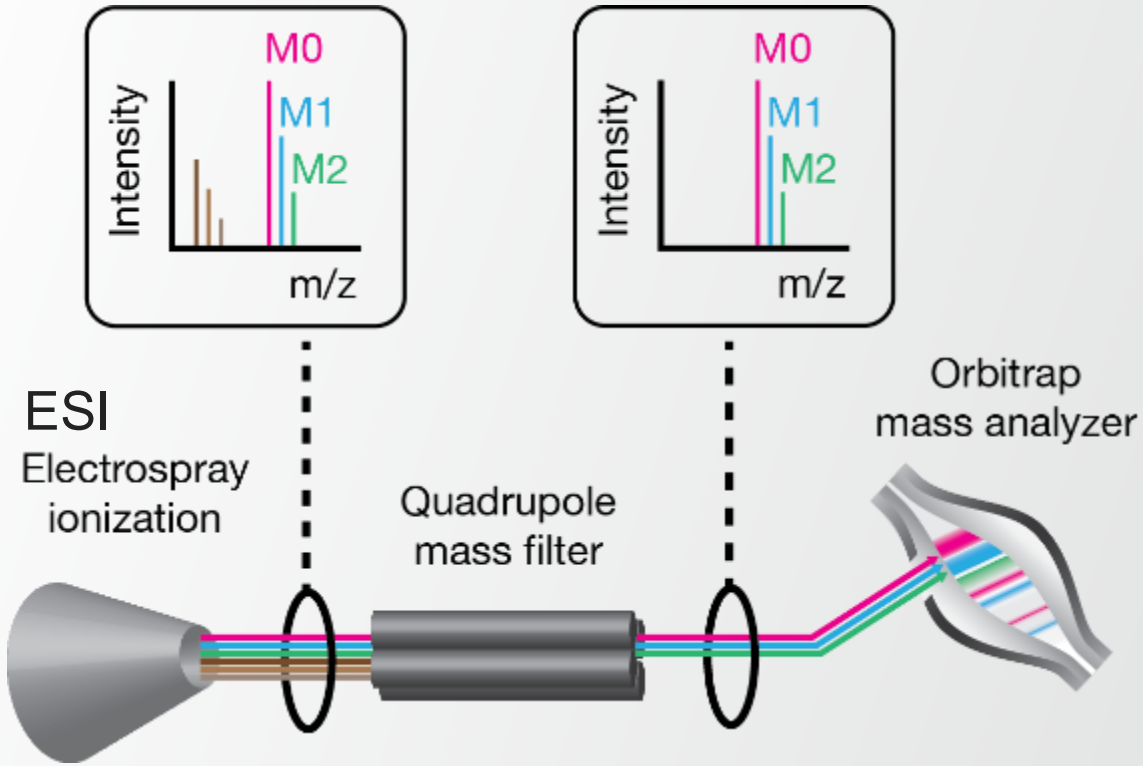
- **Indirect**: Conversion into **simple gases**
- Combining isotopologues on **few signals**



Thermo Scientific Orbitrap™ MS



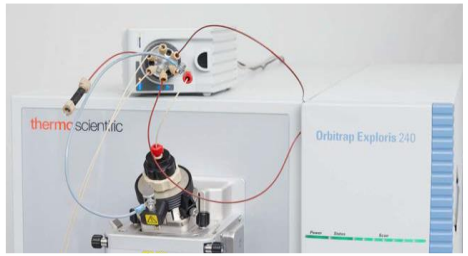
- **Direct**: Intact isotopologues
- Separation of **all species** by HRMS



Orbitrap Exploris Isotope Solutions

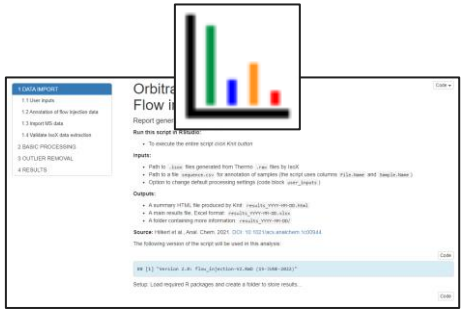
Thermo Scientific™ Orbitrap Exploris™ Isotope Solutions includes:

Thermo Scientific™
Orbitrap Exploris™
120/240/480 MS



Dual Syringe Inlet

Data evaluation Package
for Isotope Ratio MS



Optional Thermo Scientific™ Vanquish™ Neo UHPLC System

What's inside the Orbitrap Exploris MS

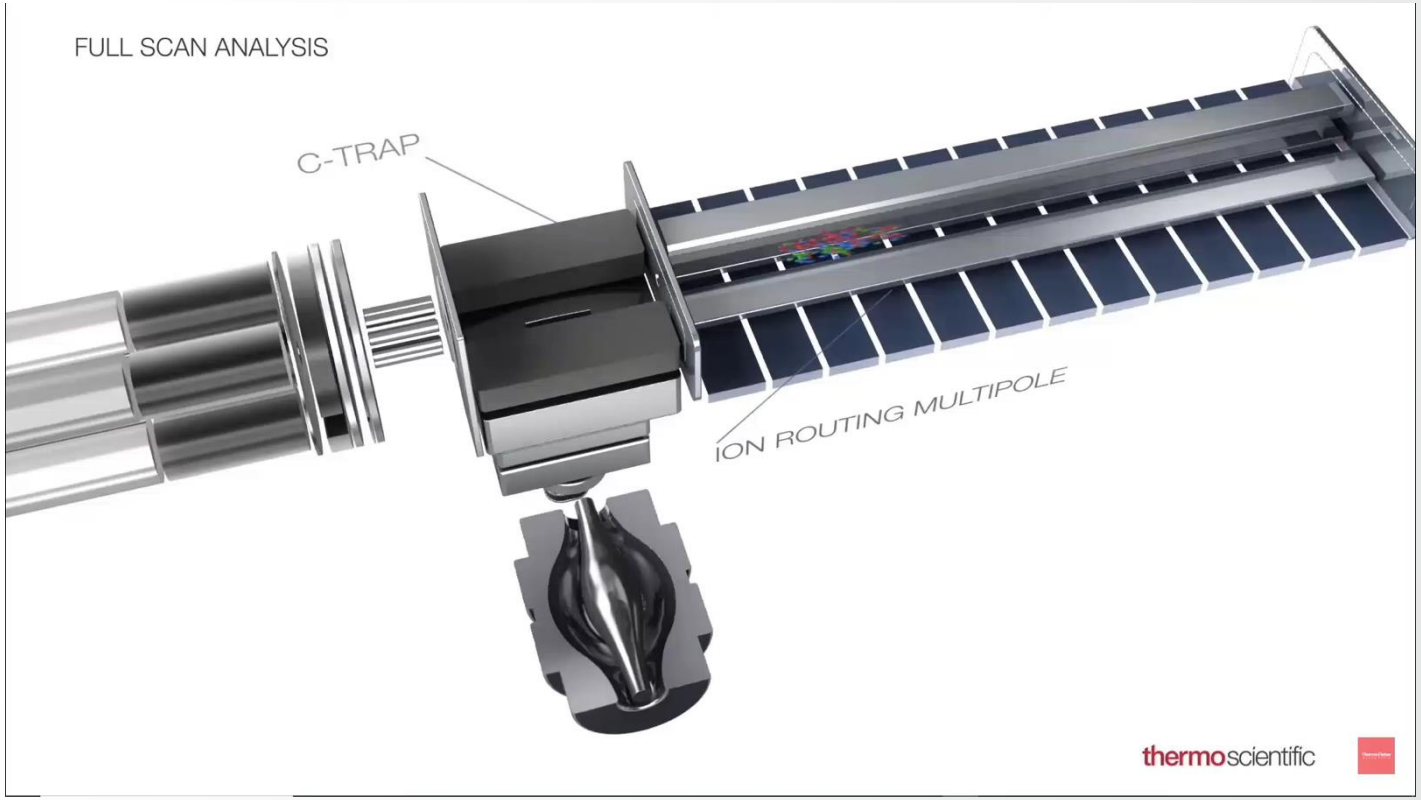
Essential components for isotope ratio analysis

Important parameters for Orbital analyzer

Isotope ratio analysis

- Resolution:
  - Orbitrap analyzes a specific number of ions (ion package) per scan
  - Every scan results in a mass spectrum
  - Higher resolution requires longer scan time:

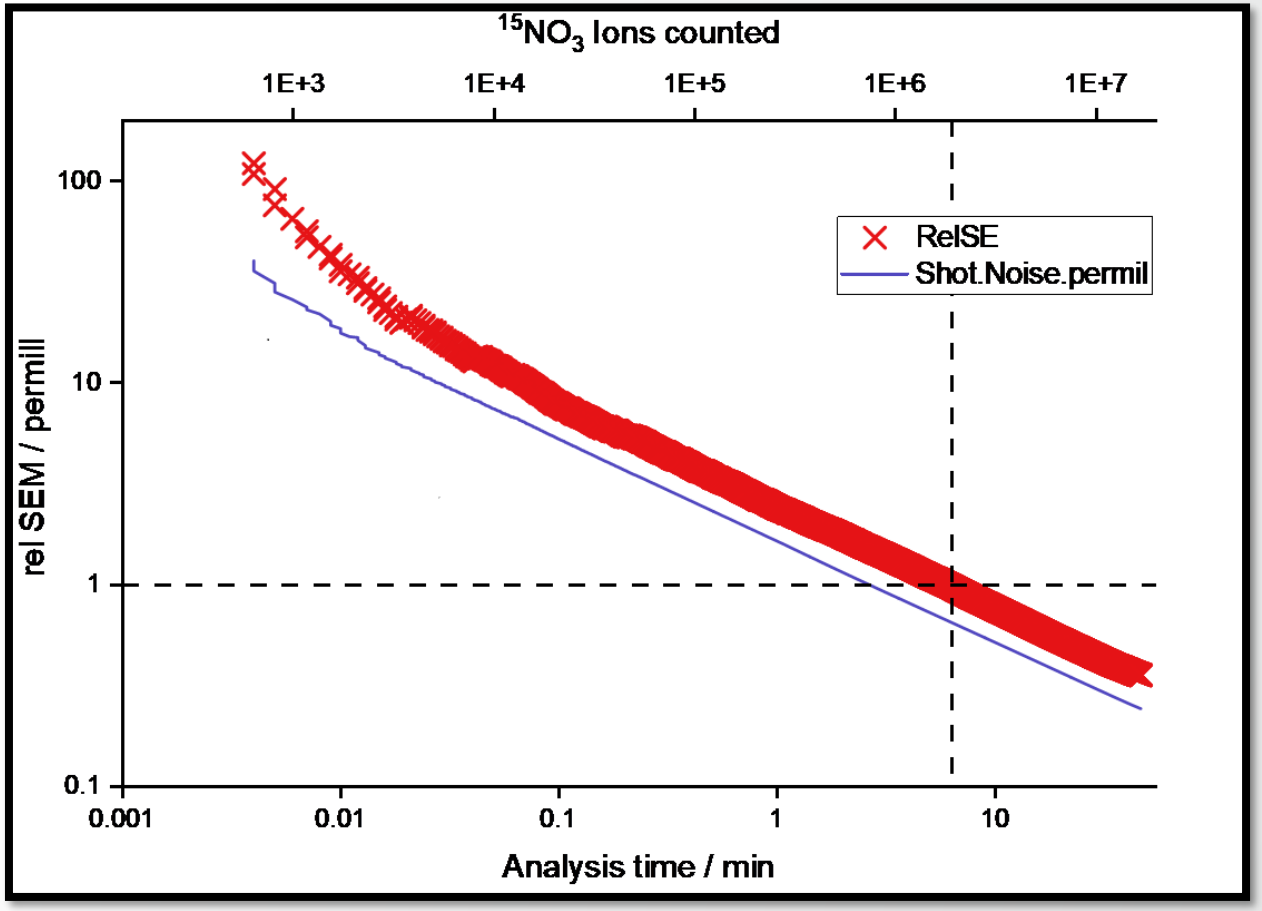
	Resolution at *m/z* 200	Scans per second
NO_3^-	15,000	22
	30,000	12
HSO_4^-	45,000	10
	60,000	7
Organics	120,000	3
	240,000	1.5



Isotope ratio methodology for Orbitrap MS

- **Precision: maximizing ion counts**
  - Longer analysis times achieve greater precision.
  - Lower resolution setting requires less time for scanning.
  - Optimize mass range maximize the number of target ions.

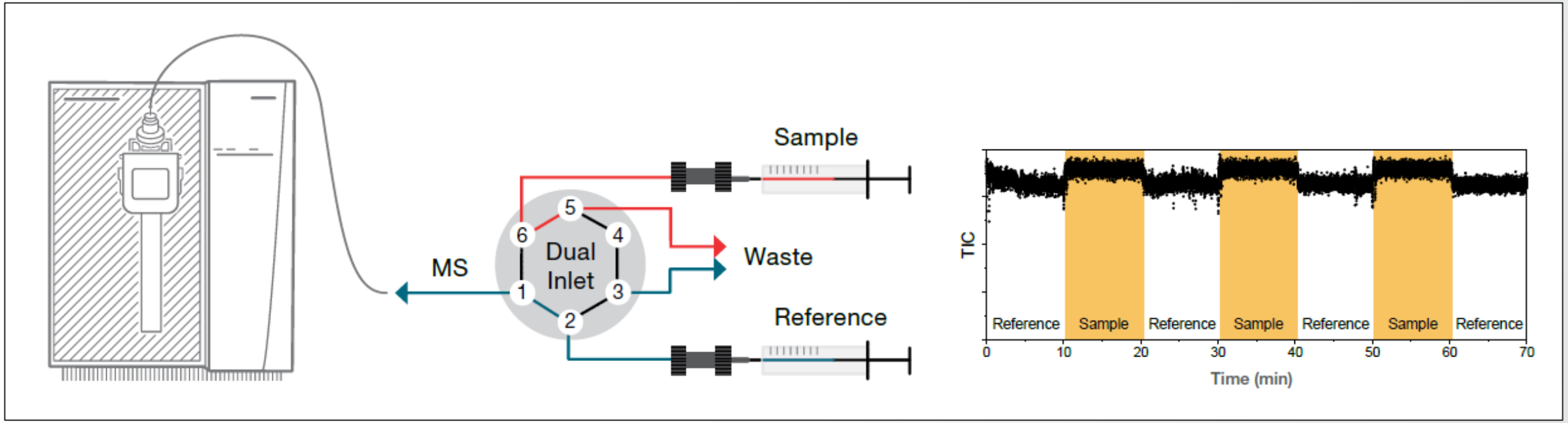
- **Accuracy: Sample/Standard comparison**
  - NO_3^- Analysis of signals (reference/sample) for 6–9 mins



Dual Syringe Inlet

Sample introduction technique

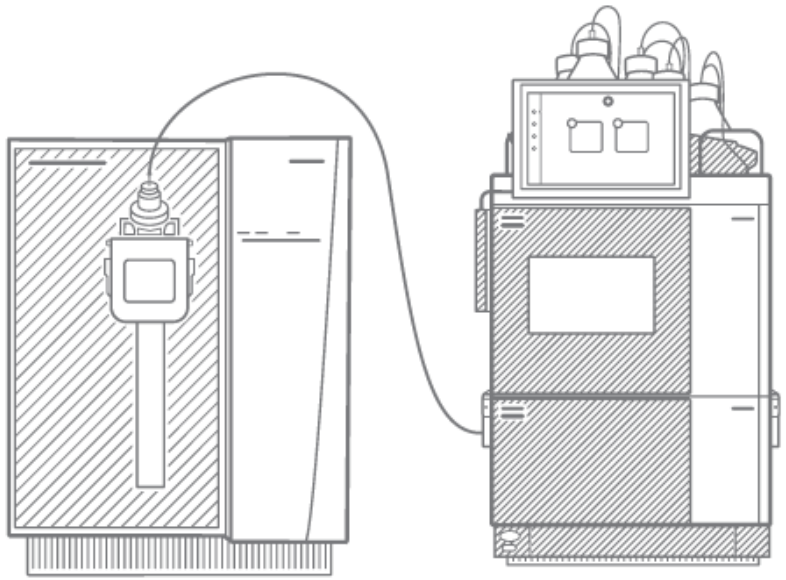
- **Dual Syringe Inlet System** utilizing the diverter valve option of the Orbitrap Exploris MS
- Direct infusion of sample (**50 µM** in MeOH) with a flow rate of **4 µl/min** via a syringe pump; sample reference comparison by switching of a diverter valve.

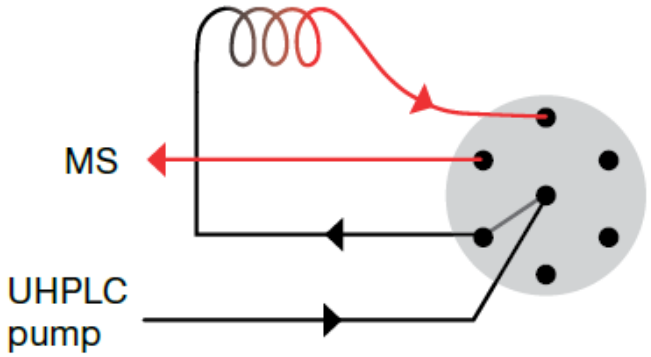


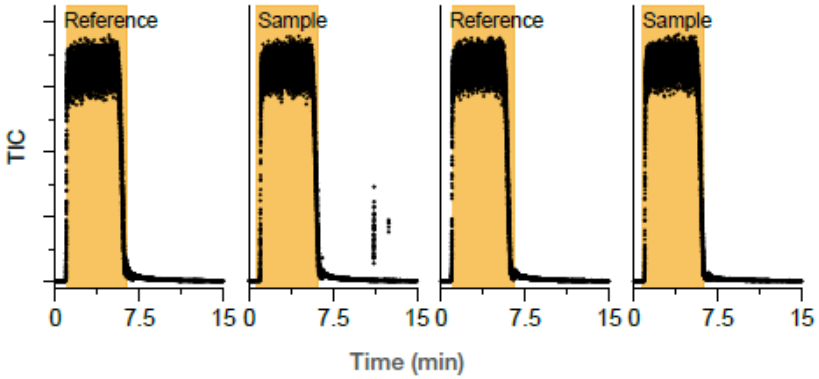
Automated In-Flow Injection

Sample introduction technique

- **In-flow Injection** - Vanquish Neo UHPLC System
- Loop-injection of **20-30 µL** sample (**50 µM** in MeOH) by the Autosampler into a flow of **4 µL/min** of MeOH.



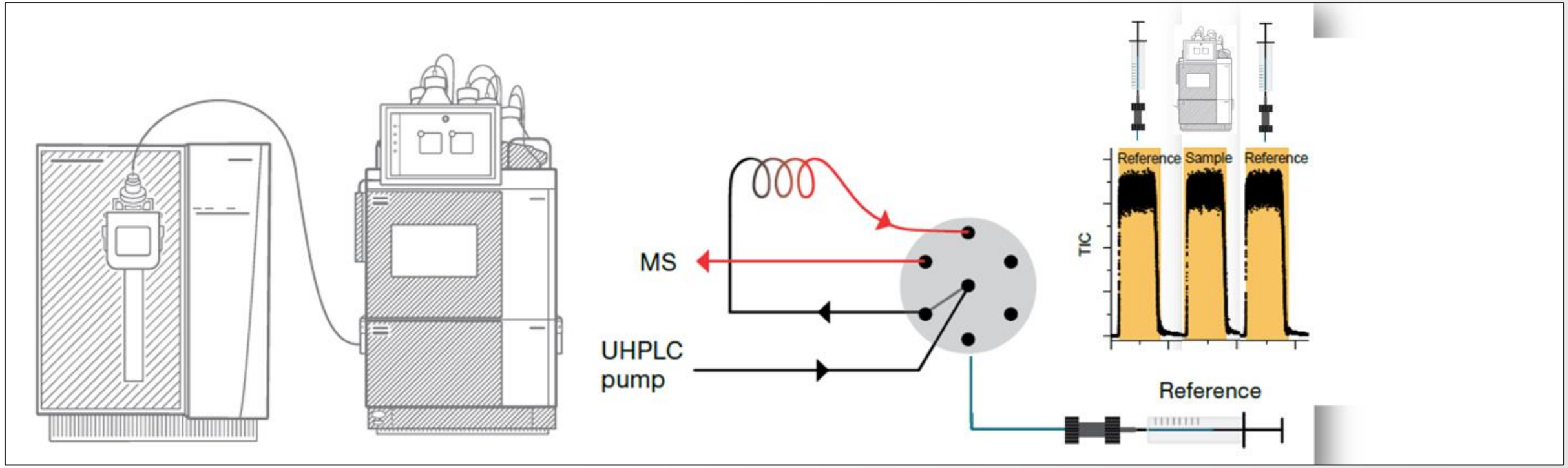




Automated In-Flow Injection with Syringe Reference

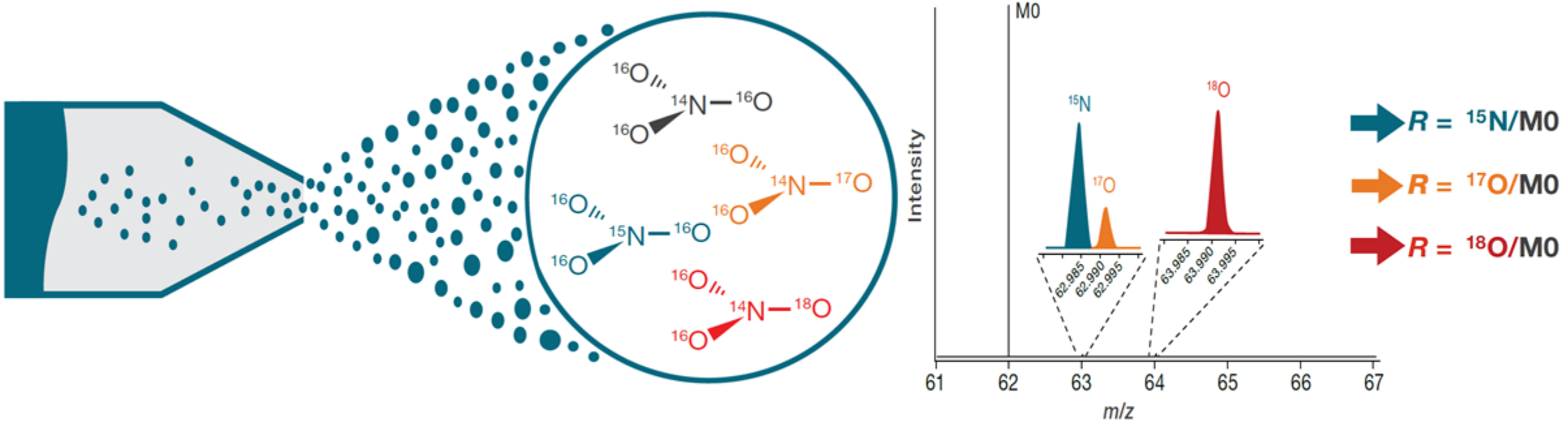
Sample introduction technique

- **In-flow Injection** - Vanquish Neo UHPLC System
- Syringe injected reference material to control for ESI instrument drift. Increases orbitrap uptime while loop is washed out.



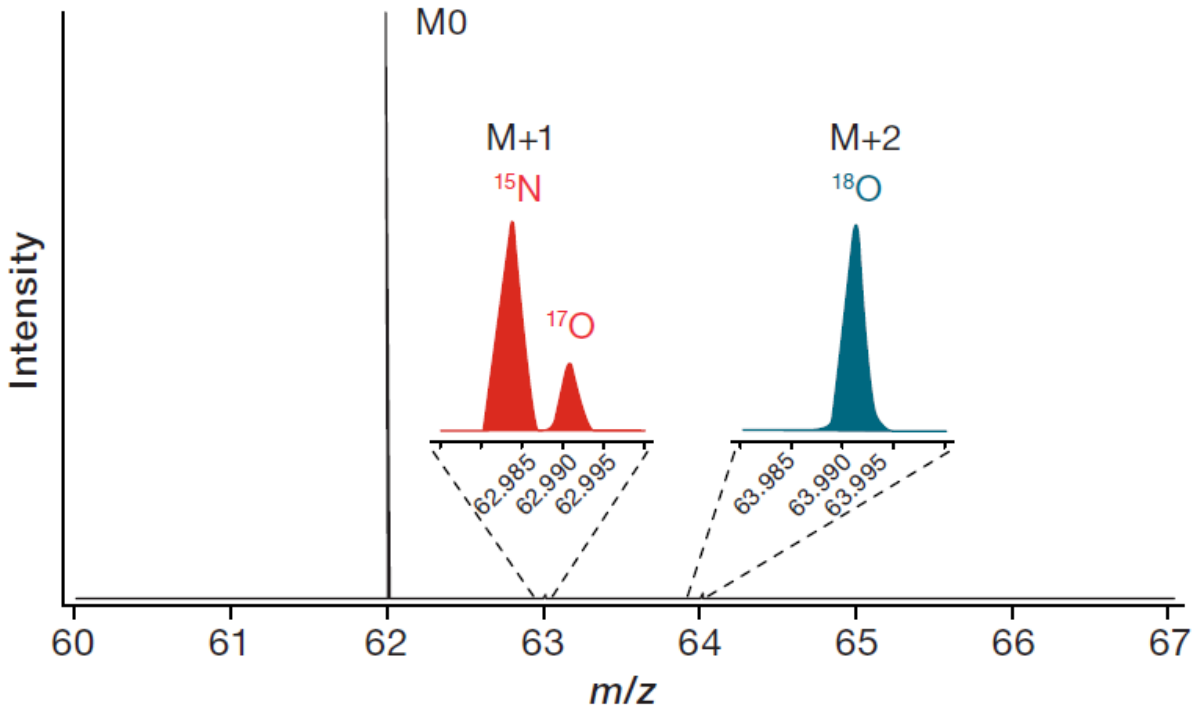
Orbitrap for isotopes: workflow for nitrate

Nitrate simplest model (4 atoms with isotope species: ^{14}N, ^{15}N, ^{16}O, ^{17}O, ^{18}O)



ESI-Orbitrap for isotopes – methodology

‘M0’ experiment

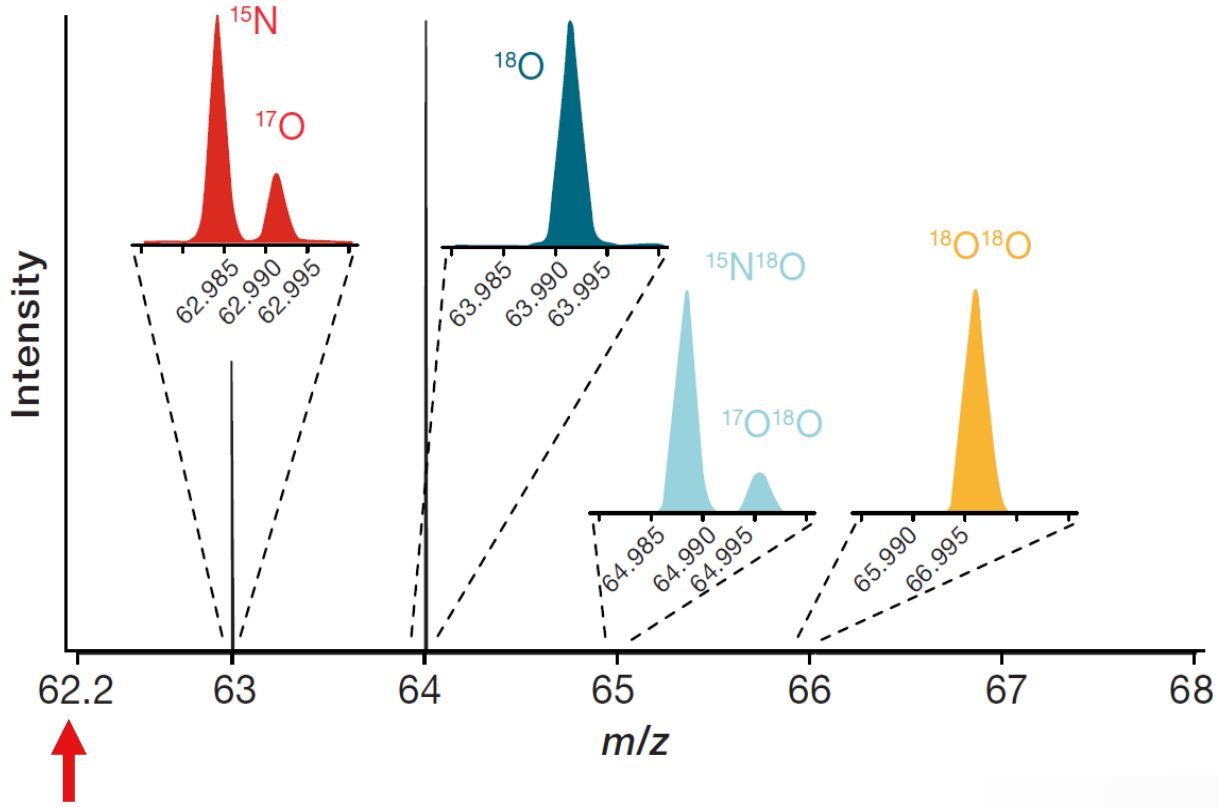


	m/z	Isotopologue	Abundance	Percentage
M0	**61.9884**	$^{14}N^{16}O_3$	**989242**	**98.9**
M+1	**62.9854**	$^{15}N^{16}O_3$	**3637**	**0.36**
	62.9926	$^{14}N^{17}O^{16}O_2$	**1127**	**0.11**
M+2	63.9896	$^{15}N^{17}O^{16}O_2$	4.1	
	63.9926	$^{14}N^{18}O^{16}O_2$	**5951**	**0.60**
	63.9968	$^{14}N^{17}O_2{}^{16}O$	0.4	
M+3	64.9897	$^{14}N^{18}O^{16}O_2$	21.9	
	64.9938	$^{15}N^{17}O_2{}^{16}O$	< 0.1	
	64.9968	$^{15}N^{17}O^{18}O^{16}O$	4.5	
	65.0010	$^{14}N^{17}O_3$	< 0.1	
M+4	65.9939	$^{15}N^{18}O^{16}O_2$	< 0.1	
	65.9969	$^{15}N^{18}O_2{}^{16}O$	11.9	
	65.9981	$^{15}N^{17}O_3$	< 0.1	
	66.0011	$^{15}N^{17}O_2{}^{18}O$	< 0.1	

- M0 peak as basepeak

ESI-Orbitrap for isotopes – methodology

‘noM0’ experiment



Mass Range!

- ^{15}N or ^{18}O peak as base peak

	m/z	Isotopologue	Abundance	Percentage
~~**M0**~~	~~61.9884~~	~~$^{14}N^{16}O_3$~~	~~989242~~	~~**98.9**~~
M+1	**62.9854**	**$^{15}N^{16}O_3$**	**3637**	**33.81**
	62.9926	**$^{14}N^{17}O^{16}O_2$**	**1127**	**10.48**
M+2	63.9896	$^{15}N^{17}O^{16}O_2$	4.1	
	63.9926	**$^{14}N^{18}O^{16}O_2$**	**5951**	**55.32**
	63.9968	$^{14}N^{17}O_2{}^{16}O$	0.4	
M+3	**64.9897**	**$^{15}N^{18}O^{16}O_2$**	**21.9**	**0.20**
	64.9938	$^{15}N^{17}O_2{}^{16}O$	< 0.1	
	64.9968	**$^{14}N^{17}O^{18}O^{16}O$**	**4.5**	**0.04**
	65.0010	$^{14}N^{17}O_3$	< 0.1	
M+4	65.9939	$^{15}N^{18}O^{16}O_2$	< 0.1	
	65.9969	**$^{14}N^{18}O_2{}^{16}O$**	**11.9**	**0.11**
	65.9981	$^{15}N^{17}O_3$	< 0.1	
	66.0011	$^{14}N^{17}O_2{}^{18}O$	< 0.1	

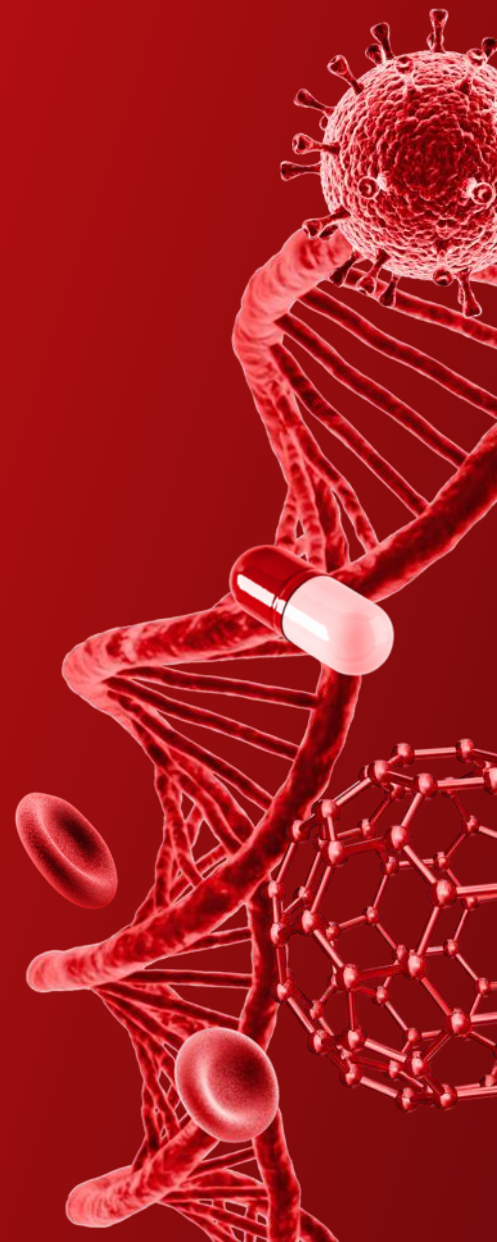
Applications

Published or application notes available for:

- Nitrate
- Sulfate
- Phosphate
- MSA
- Acetate
- Amino Acids – glutamic acid and alanine
- Caffeine
- Vanillin
- Methyl Phosphonic acid (chemical weapon forensics)
- DDT
- PFAS
- SMX
- Glucose
- FAME
- Neonicotinoids
- Perchlorate

Questions

1. What is the ionization method for the Orbitrap?
2. Where can we fragment our molecule?



Dual Inlet measurements of nitrate

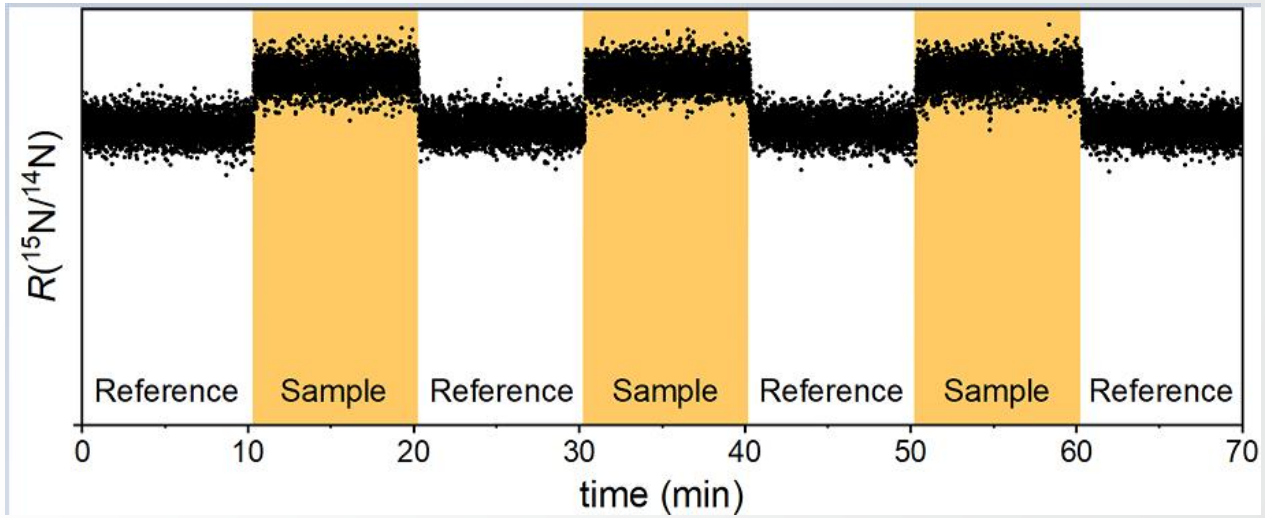
‘M0’ experiment:

- Three nitrate reference materials available from USGS:[1]

	$\delta^{15}N_{AIR}$	$\delta^{18}O_{VSMOW}$	$^{17}O_{VSMOW}$
USGS32	+ 180 ‰	+ 25.7 ‰	-
USGS34	- 1.8 ‰	- 27.9 ‰	- 14.8 ‰
USGS35	+2.7 ‰	+ 57.5 ‰	+ 51.5 ‰

Quality control: $^{15}N/^{14}N$ isotope ratio analysis

Block	Description	Ratio ($^{15}N/^{14}N$)	$\delta^{15}N_{USGS32/Air}$ [‰]	$\delta^{15}N_{USGS32/Air}$ [‰]	Std. Dev.
1	Reference (USGS35)	0.00430			
2	Sample (USGS32)	0.00506	179.5		
3	Reference (USGS35)	0.00430			
4	Sample (USGS32)	0.00506	179.3	179.6	0.4
5	Reference (USGS35)	0.00430			
6	Sample (USGS32)	0.00506	180.1		
7	Reference (USGS35)	0.00430			



[1] Böhlke, J.K .; et al. Rapid Commun. Mass Spectrom., 2003, 17, p. 1835−1846.

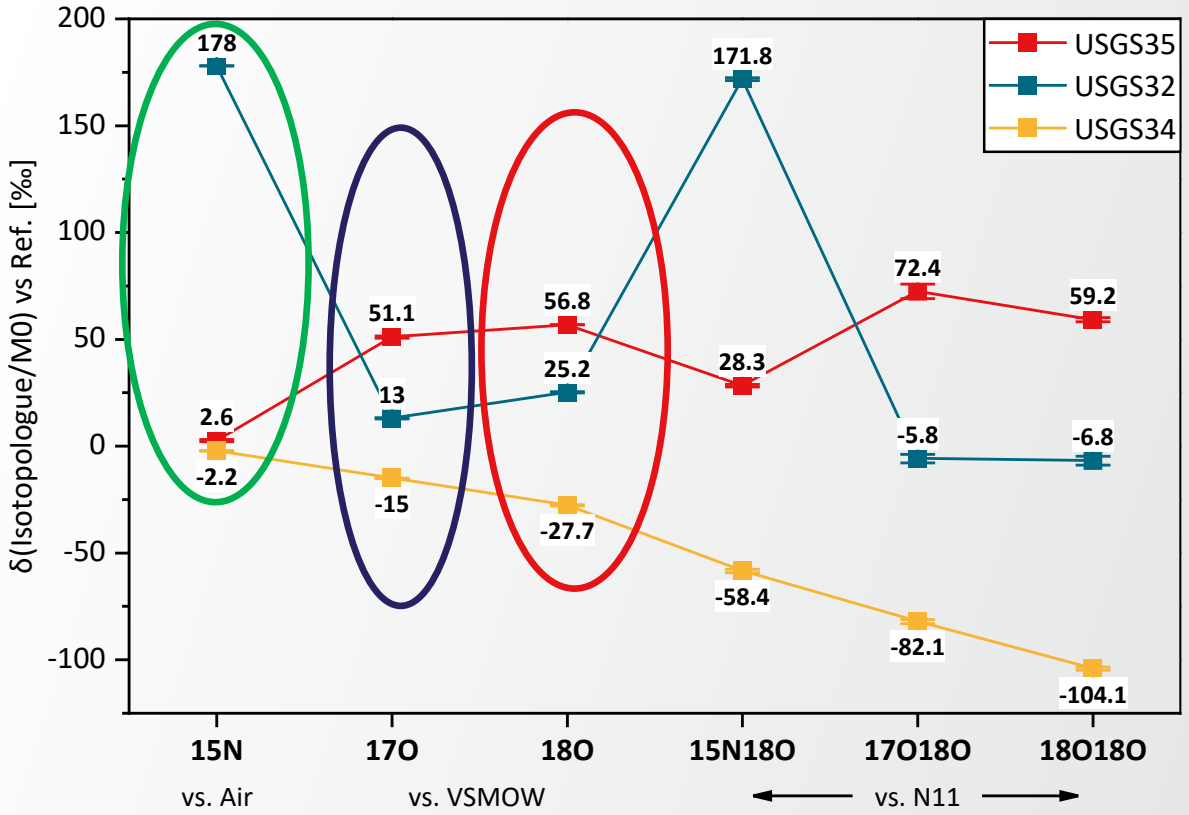
Referencing scheme for nitrate

Analysis of international standards for nitrate

- Isotope ratio data of ‘M0’ and ‘noM0’ experiments using N11 as a working standard:[1]

	$\delta^{15}N_{AIR}$	$\delta^{18}O_{VSMOW}$	$^{17}O_{VSMOW}$
USGS32	+ 180 ‰	+ 25.7 ‰	-
USGS34	- 1.8 ‰	- 27.9 ‰	- 14.8 ‰
USGS35	+2.7 ‰	+ 57.5 ‰	+ 51.5 ‰

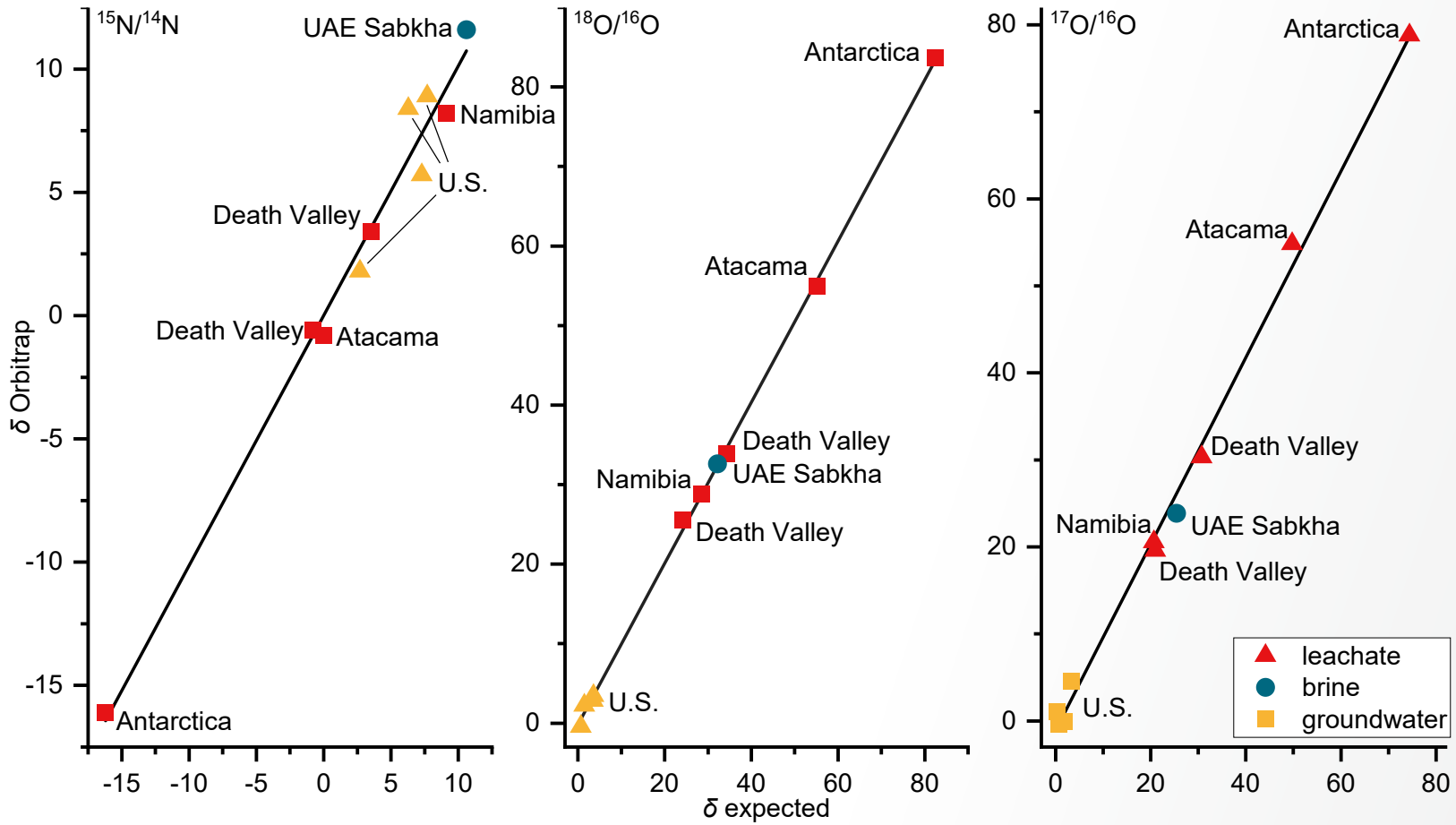
Isotope ratio data of six of nitrate`s most abundant isotopologues using the In-Flow Injection setup.



[1] Böhlke, J.K .; et al. Rapid Commun. Mass Spectrom., 2003, 17, p. 1835−1846.

Nitrate analysis of environmental samples

‘M0’ experiment



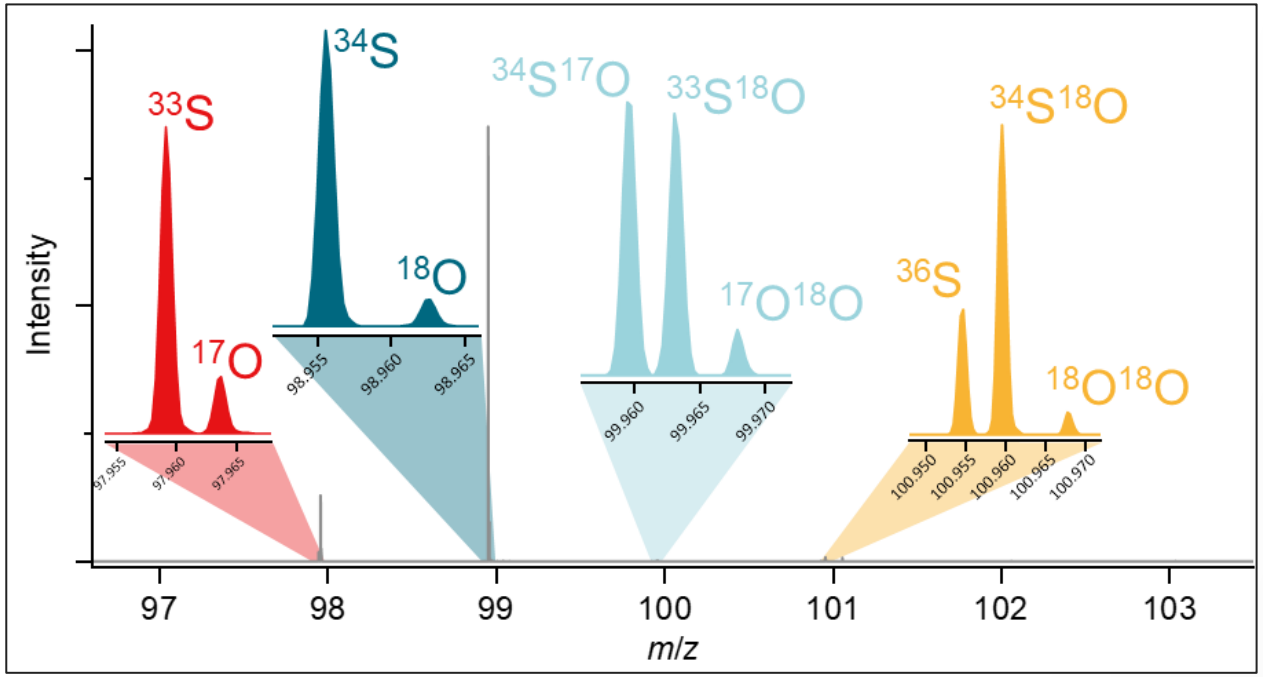
Dual Syringe Inlet methodology

- Sample prep: “Dilute and Shoot”
  - Dilution to **1µM** (**62 pg** NO_3^-/µL) for high salinity samples
- Results $\delta^{15}N$ and $\delta^{18}O$
  - Precision: < 1‰
  - Difference Orbitrap – Expected: < 1‰
- Takeaway
  - ESI tolerates up to **100-fold Cl^-** load
  - Ground waters diluted up to **1/500**

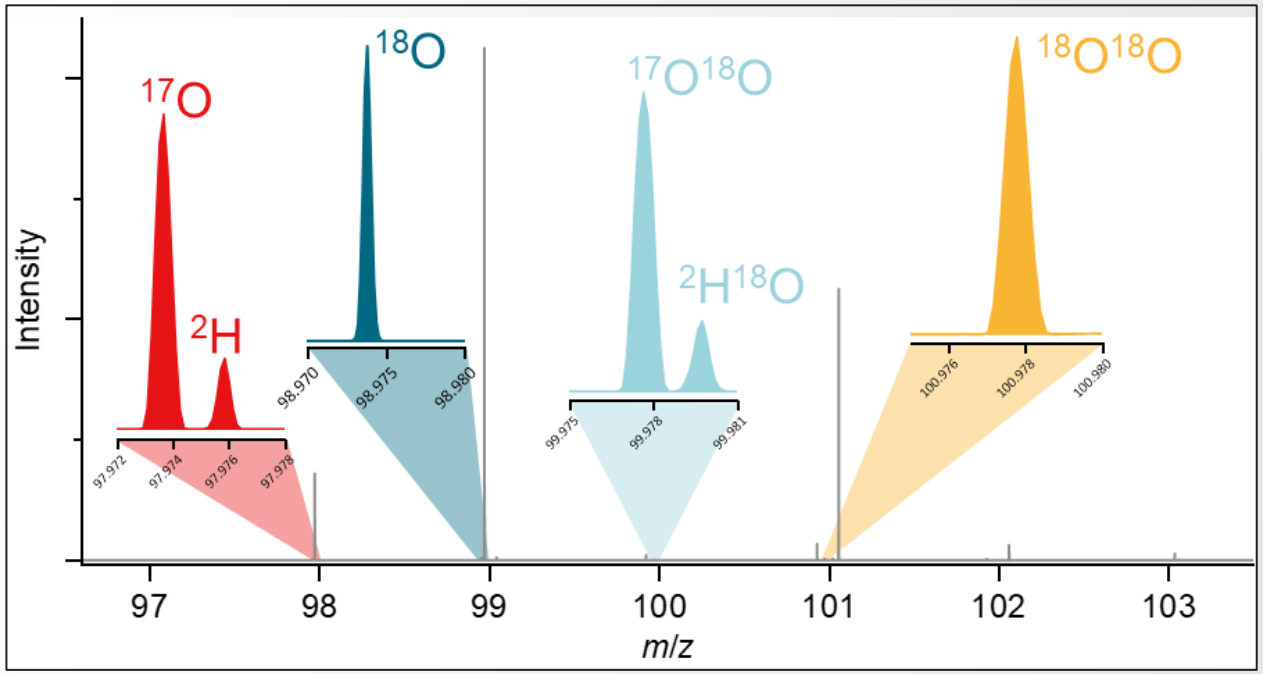
[2] Hilkert, A.; et al. Anal. Chem. 2021, 93, 9139−9148.

Other oxyanions – sulfate and phosphate

Sulfate ionized as HSO_4^-



Phosphate ionized as $H_2PO_4^-$



Stable Isotope Analysis of Intact Oxyanions Using Electrospray Quadrupole-Orbitrap Mass Spectrometry

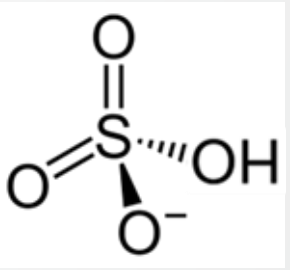
Cajetan Neubauer,* Antoine Crémière, Xingchen T. Wang, Nivedita Thiagarajan, Alex L. Sessions, Jess F. Adkins, Nathan F. Dalleska, Alexandra V. Turchyn, Josephine A. Clegg, Annie Moradian, Michael J. Sweredoski, Spiros D. Garbis, and John M. Eiler

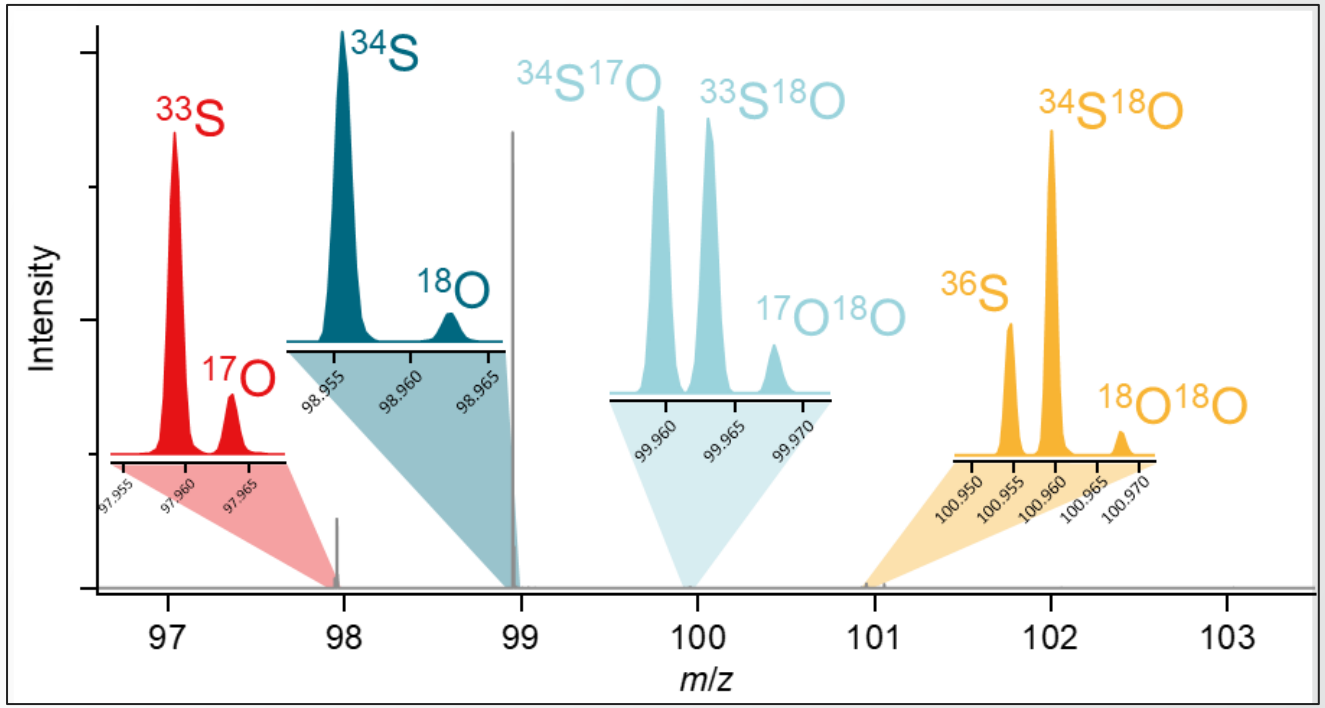
Cite This: *Anal. Chem.* 2020, 92, 3077−3085 Read Online

Isotope mapping of sulfates

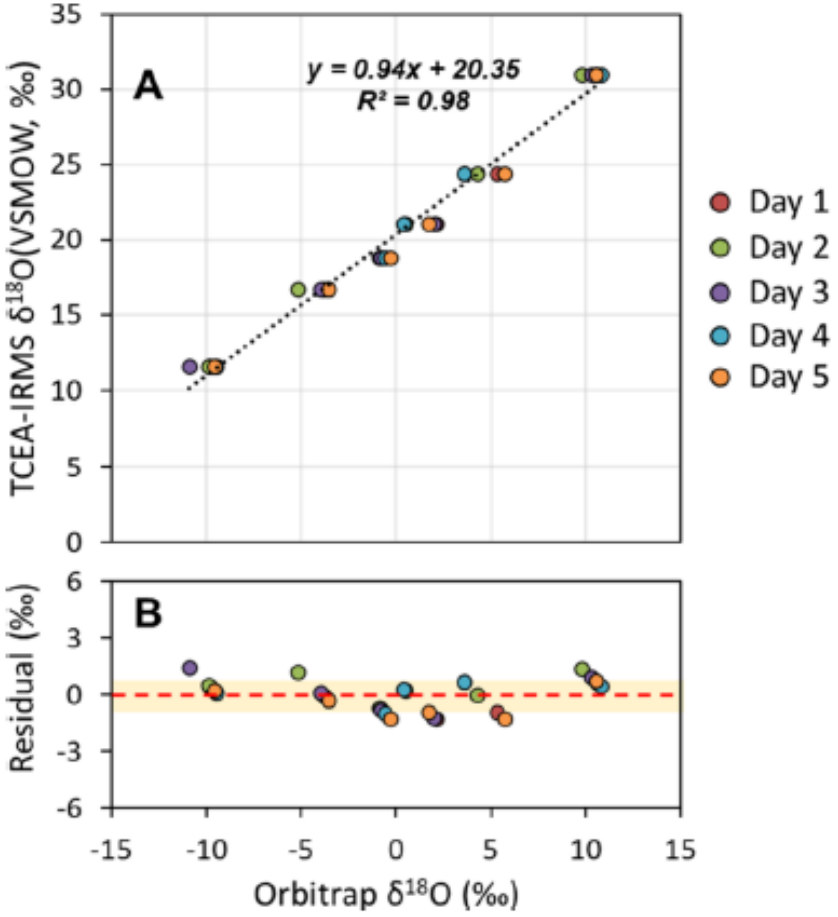
	m/z	Isotopologue	Abundance
M0	**96.9596**	$^{1}H^{32}S^{16}O_4$	9408592
M+1	**97.9590**	$^{1}H^{33}S^{16}O_4$	7427
	97.9638	$^{1}H^{32}S^{17}O^{16}O_3$	1433
M+2	**98.9554**	$^{1}H^{34}S^{16}O_4$	42084
	98.9638	$^{1}H^{32}S^{18}O^{16}O_3$	7632
M+3	**99.9596**	$^{1}H^{34}S^{17}O^{16}O_3$	63
	99.9632	$^{1}H^{33}S^{18}O^{16}O_3$	59
	99.9680	$^{1}H^{32}S^{17}O^{18}O^{16}O_2$	9
M+4	**100.9546**	$^{1}H^{36}S^{16}O_4$	145
	100.9596	$^{1}H^{34}S^{18}O^{16}O_3$	333
	100.9680	$^{1}H^{32}S^{18}O_2{}^{16}O_2$	44

^{32}S ^{33}S ^{34}S ^{36}S x ^{16}O ^{17}O ^{18}O





Isotopes of Phosphate



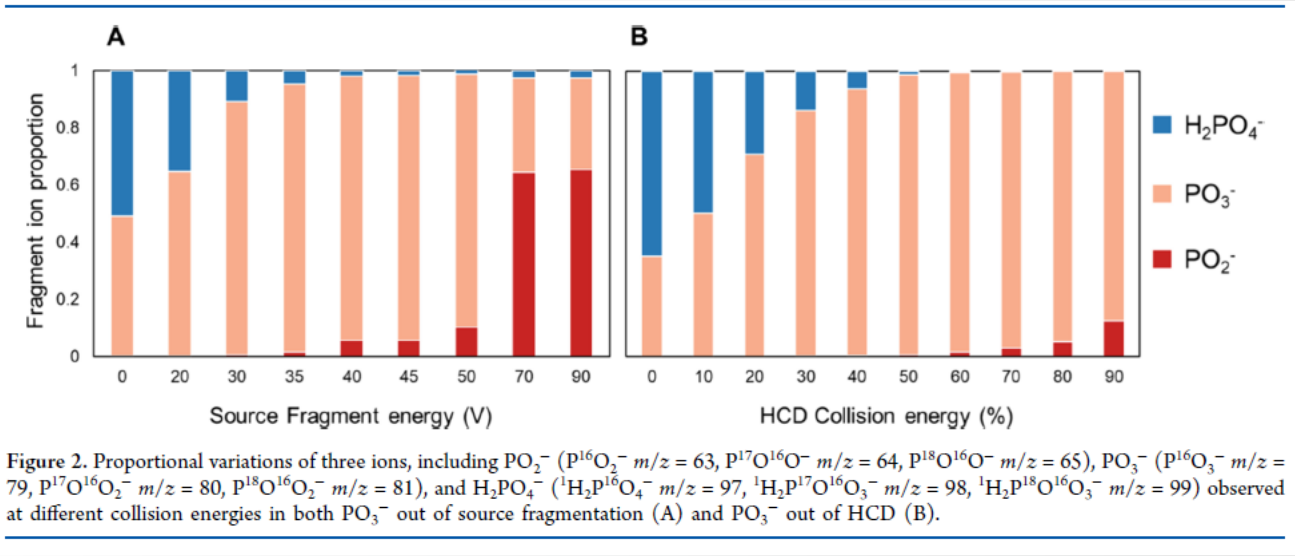


Figure 2. Proportional variations of three ions, including PO_2^- ($P^{16}O_2^-$ m/z = 63, $P^{17}O^{16}O^-$ m/z = 64, $P^{18}O^{16}O^-$ m/z = 65), PO_3^- ($P^{16}O_3^-$ m/z = 79, $P^{17}O^{16}O_2^-$ m/z = 80, $P^{18}O^{16}O_2^-$ m/z = 81), and $H_2PO_4^-$ ($^1H_2P^{16}O_4^-$ m/z = 97, $^1H_2P^{17}O^{16}O_3^-$ m/z = 98, $^1H_2P^{18}O^{16}O_3^-$ m/z = 99) observed at different collision energies in both PO_3^- out of source fragmentation (A) and PO_3^- out of HCD (B).

analytical chemistry

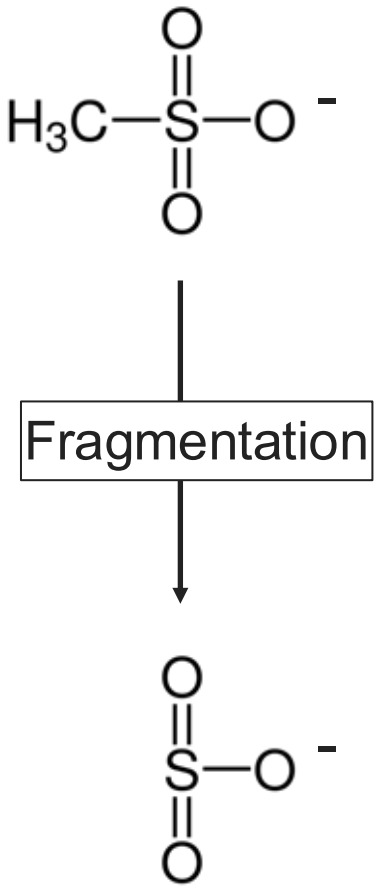
pubs.acs.org/ac Article

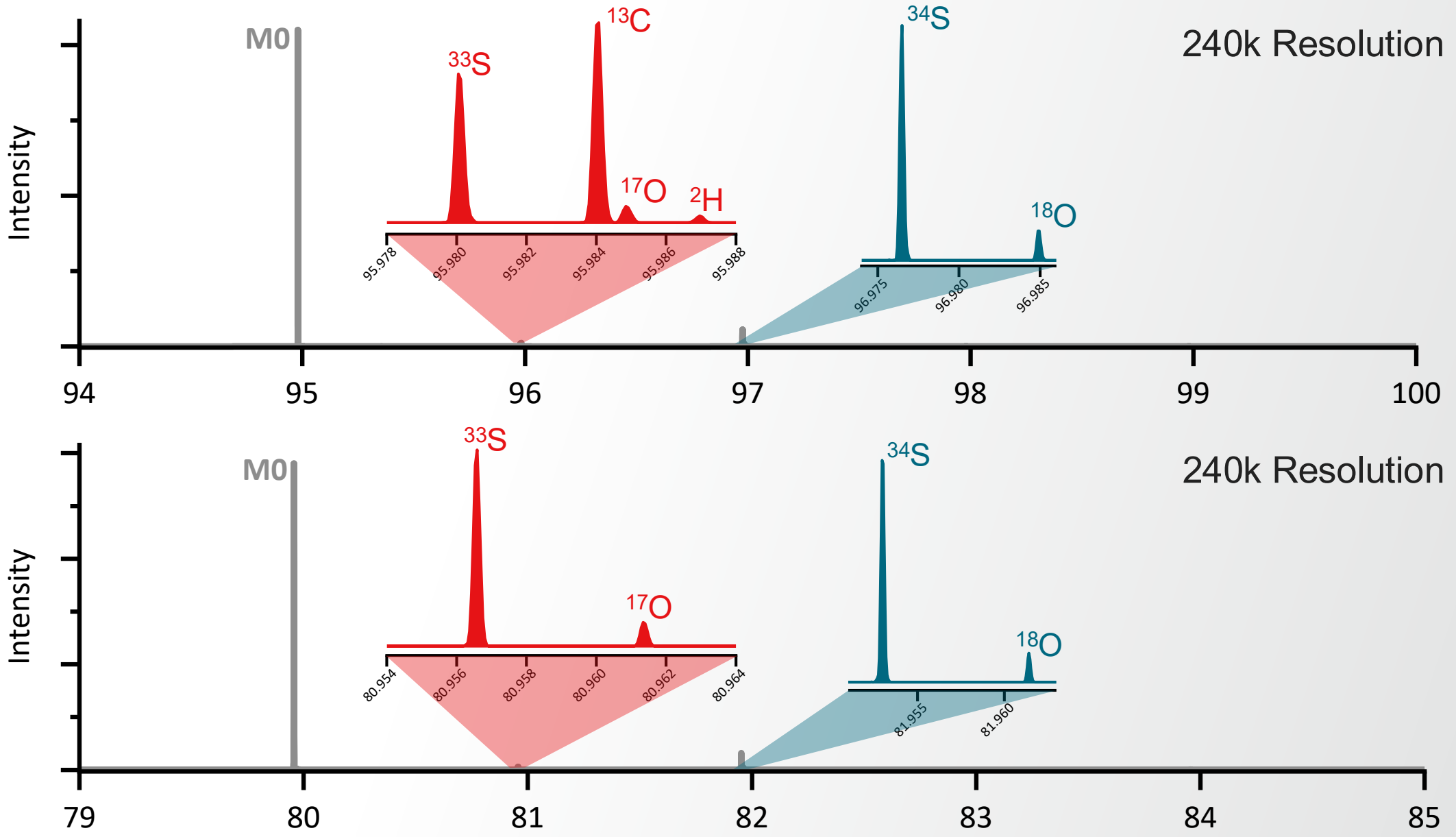
Oxygen Isotope Analysis of Nanomole Phosphate Using PO_3^- Fragment in ESI-Orbitrap-MS

Zhenfei Wang, Shohei Hattori, Yongbo Peng,* Longchen Zhu, Zhao Wei, and Huiming Bao

Cite This: https://doi.org/10.1021/acs.analchem.3c03070 Read Online

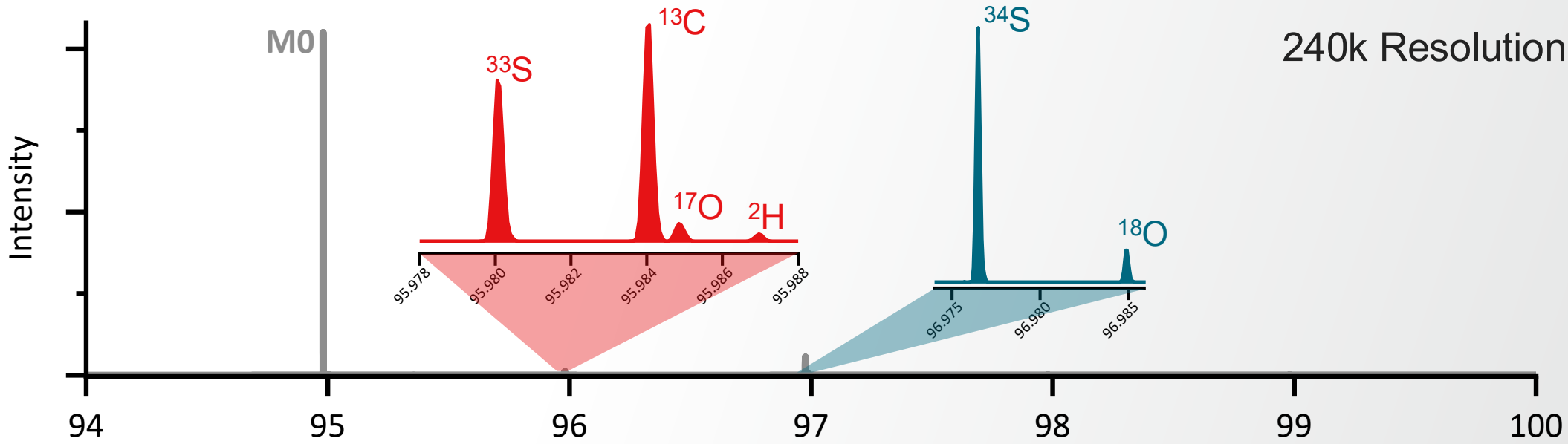
First results of methanesulfonic acid (MSA)



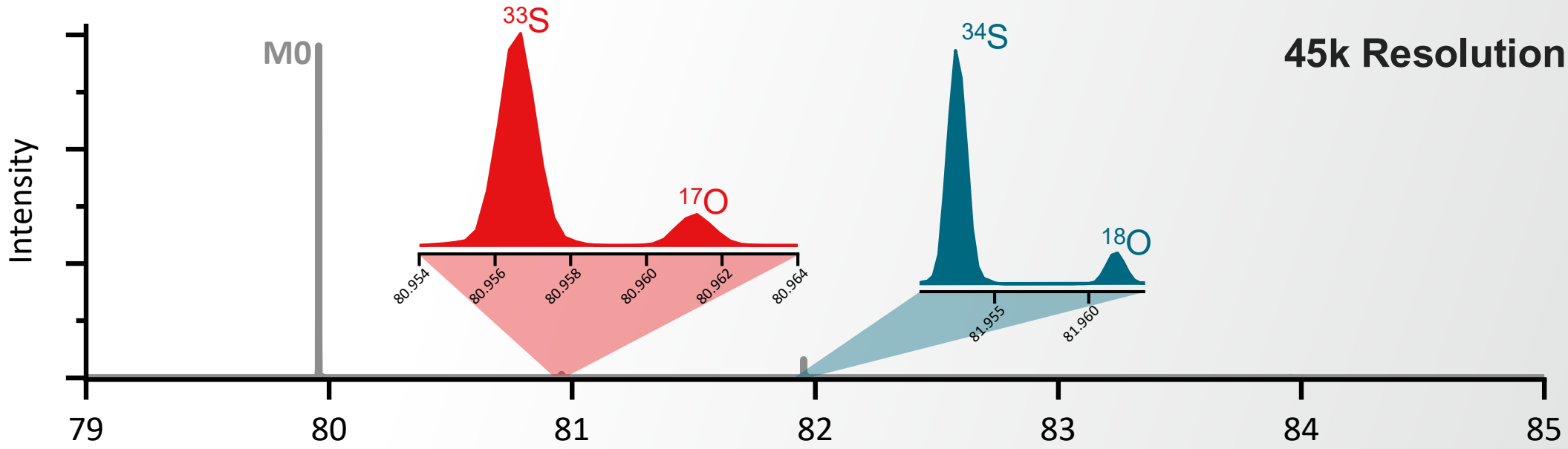


Fragmentation of methanesulfonic acid (MSA)

~ 1 scan/s



~ 10 scan/s



MSA using SO_3^- Fragment Paper

pubs.acs.org/ac Article

Triple Oxygen Isotope Analysis of Methanesulfonate Using the SO_3^- Fragment in ESI-Orbitrap-MS

Yihang Hong, Longchen Zhu, Daniel R. Crocker, Tengyu Liu, Zhenfei Wang, Zhao Wei, Chen Yu, Yu Wei, Hao Yan, David T. Johnston, Issaku E. Kohl, Yongbo Peng, Andreas Hilkert, Cajetan Neubauer, and Shohei Hattori*

Cite This: *Anal. Chem.* 2025, 97, 14339–14348 Read Online

- HCD Collision Energy ~60% (compared to 50% for PO_3^-)
- Offline purification and separation to remove SO_3^- contribution to MSA SO_3^-
- Murchison meteorite contains distinctly extraterrestrial isotope signatures for δ13C, δD and Δ33S

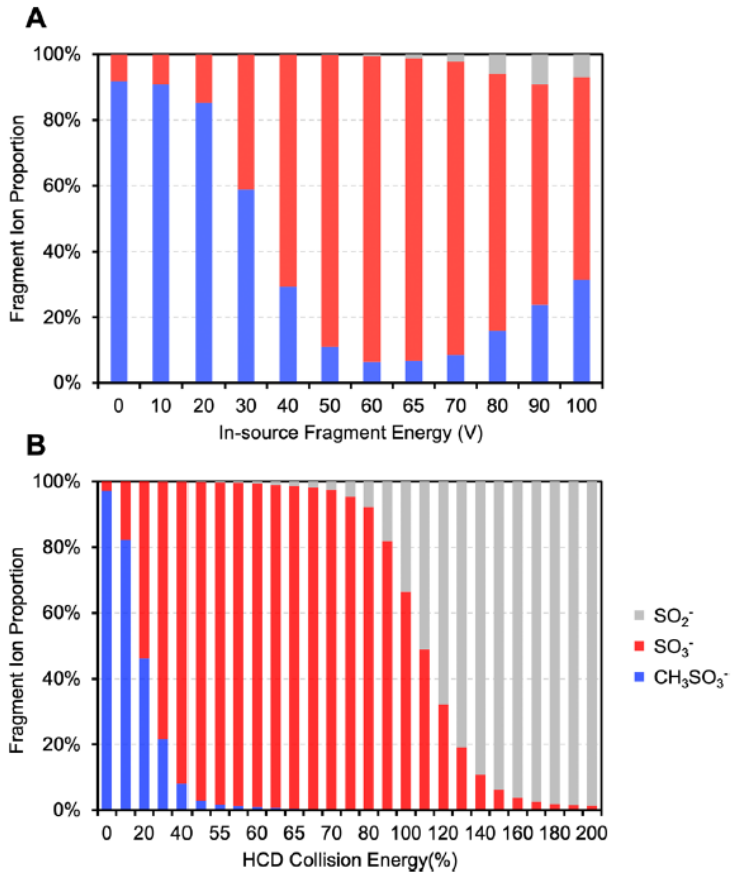
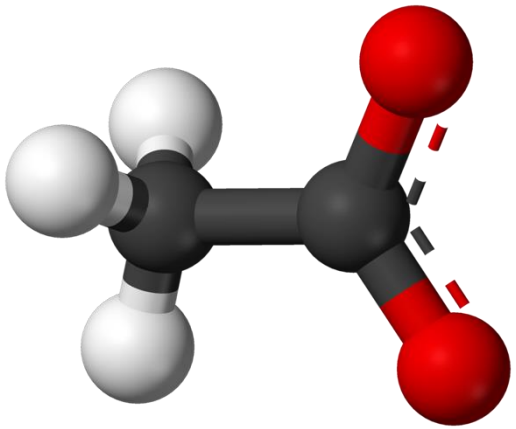
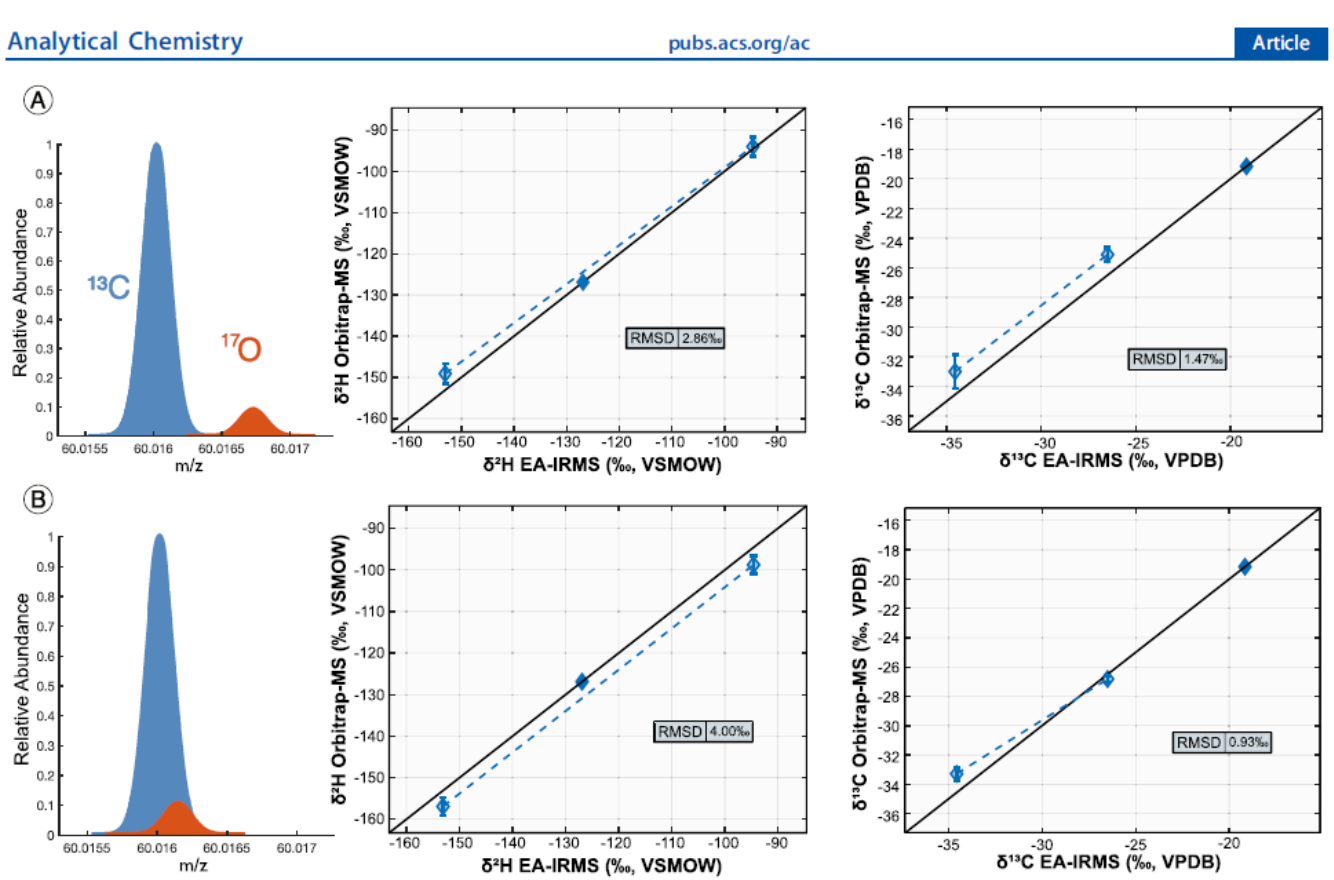


Figure 2. Proportion variations of three ions of SO_2^- [$^{32}S^{16}O_2^-$ (m/z = 63.96245)], SO_3^- [$^{32}S^{16}O_3^-$ (m/z = 79.95736)], and $CH_3SO_3^-$ [$^{12}C^1H_3{}^{32}S^{16}O_3^-$ (m/z = 94.98084)] under the different (A) in-source fragmentation energy and (B) HCD collision energy conditions.

Acetate Isotopes on the Orbitrap





Article

Simultaneous, High-Precision Measurements of δ^2H and $\delta^{13}C$ in Nanomole Quantities of Acetate Using Electrospray Ionization-Quadrupole-Orbitrap Mass Spectrometry

Elliott P. Mueller,* Alex L. Sessions, Peter E. Sauer, Gabriella M. Weiss, and John M. Eiler

Cite This: *Anal. Chem.* 2022, 94, 1092−1100 Read Online

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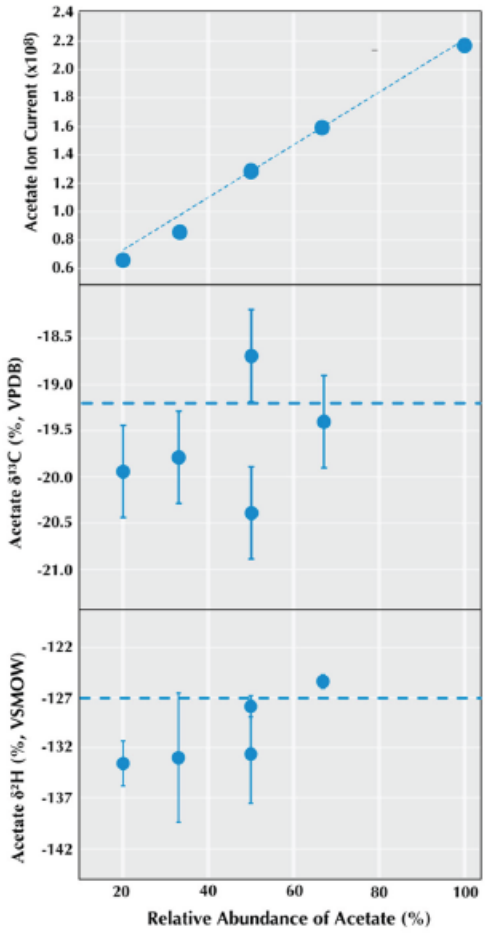
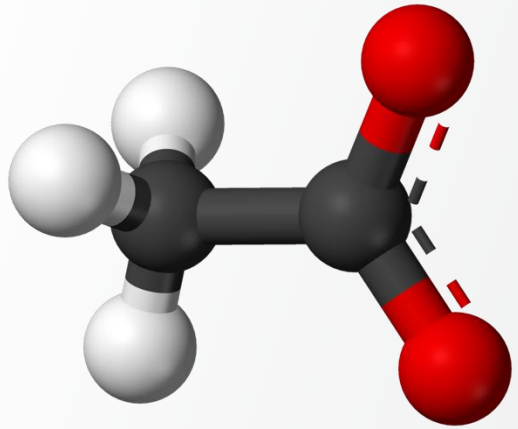


Figure 3: Five mixtures of organic acids containing different proportions of acetate, propionate, and butyrate with known $\delta^{13}C$ and $\delta^{2}H$ values were measured against a pure acetate standard. All mixtures had an absolute acetate concentration of 50 µM, yet acetate's SIC changed dramatically.



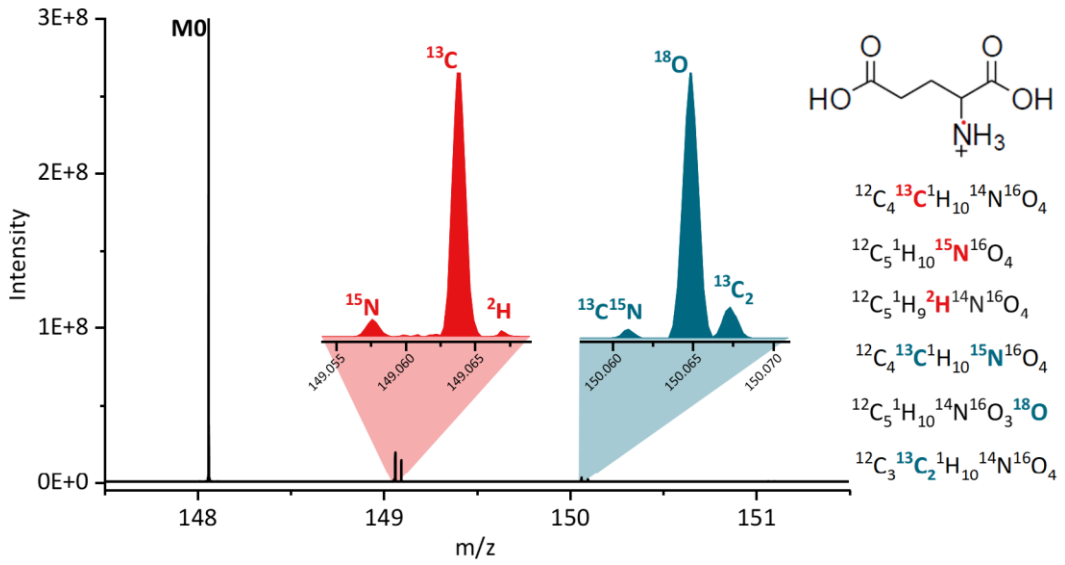
pubs.acs.org/ac Article

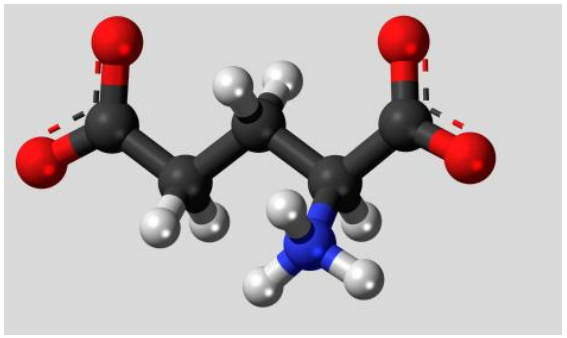
Simultaneous, High-Precision Measurements of $\delta^{2}H$ and $\delta^{13}C$ in Nanomole Quantities of Acetate Using Electrospray Ionization-Quadrupole-Orbitrap Mass Spectrometry

Elliott P. Mueller,* Alex L. Sessions, Peter E. Sauer, Gabriella M. Weiss, and John M. Eiler

Cite This: *Anal. Chem.* 2022, 94, 1092–1100 Read Online

Glutamic Acid Isotopes





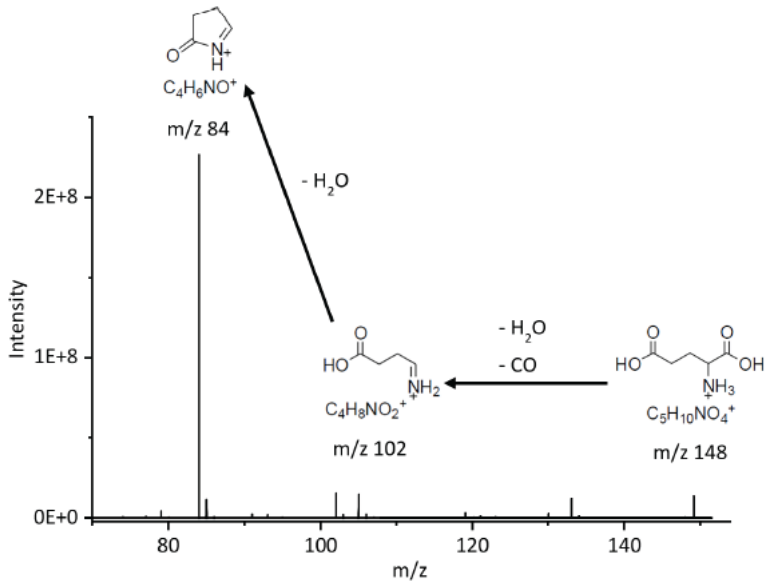


Figure 2. MS2 mass spectrum with 70% NCE acquired with glutamic acid.

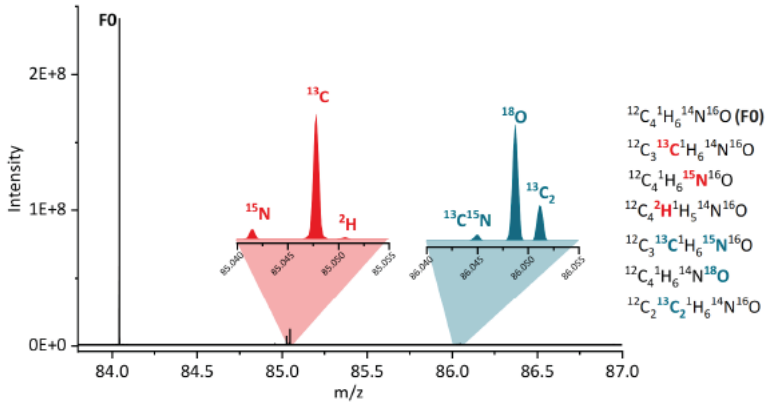
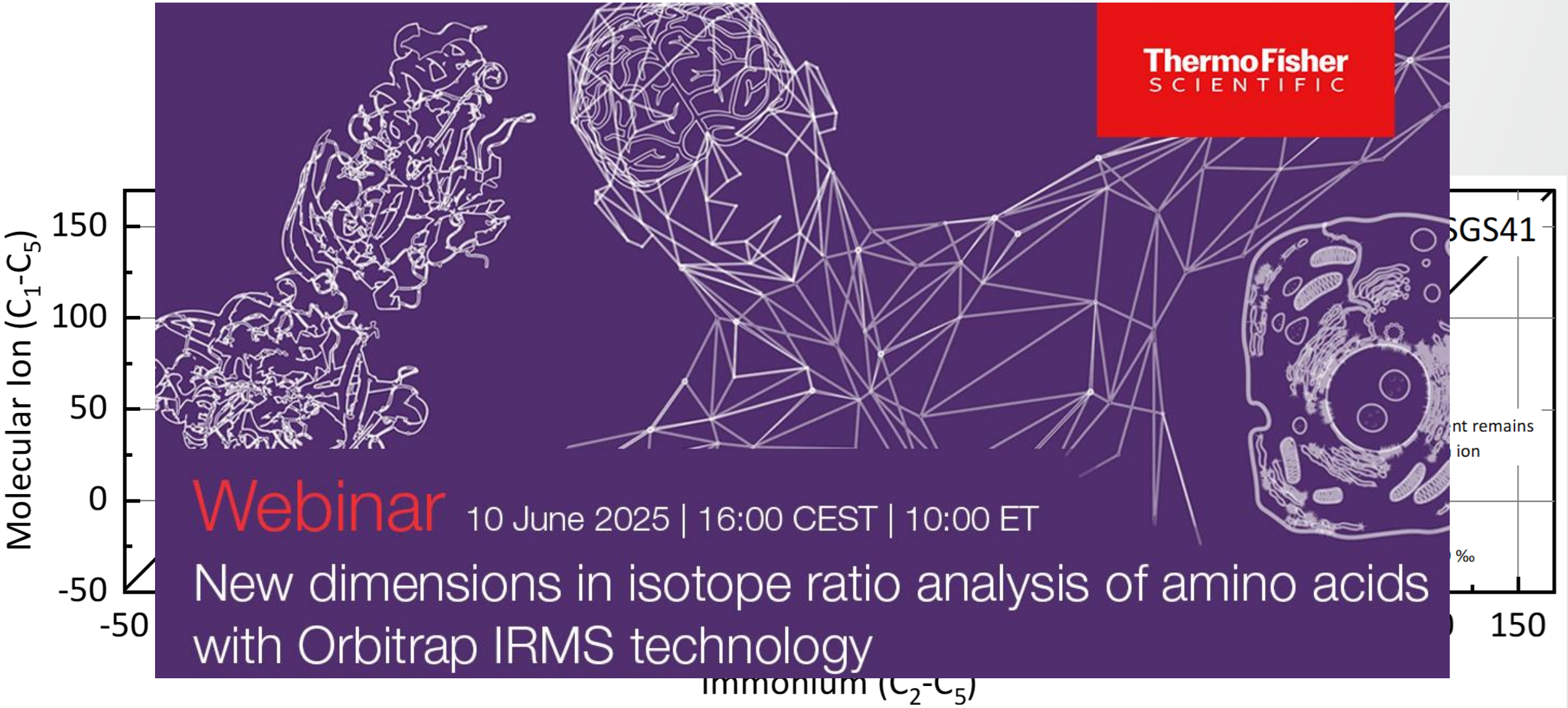


Figure 3. Isotopic pattern of fragment at m/z 84 at 90,000 resolution.

Thermo Fisher Scientific TN003099

Glutamic Acid Isotopes



Thermo Fisher Scientific TN003099

Alanine Isotopes

Table 1
Details about different methods of position-specific isotope analysis (PSIA). Strengths and weaknesses of each type of PSIA are presented. It is important to note that individual analytical goals and available resources are the overall determining factor for which method is best for a given project.

Method	Measured species	Sensitivity (nmol)	Strengths	Weaknesses	Select References
Chemical or enzymatic degradation + IRMS	Conversion of analyte to CO2	100s	Uses established IRMS methods, ability to constrain all positions	Many steps, requires derivatization, large sample size, long analysis times	[2–4]
Pyrolysis + IRMS	Conversion of analyte to CO2	100s	Uses established IRMS methods, ability to constrain all positions	Many steps, requires derivatization, large sample size, long analysis times	[5–7]; Dias et al. (2022)
NMR	Intact molecule	50,000–300,000	Ability to constrain all positions, non-destructive, derivatization not required	large sample size (100s of mmol)	[9,10]; Rasmussen and Hoffman (2020)
Orbitrap-MS	Molecular ion, fragment ions	1–10	Measures intact molecule, small sample size, short analysis time, derivatization not required	Currently no on-line separation for ESI-Orbitrap, need for internationally recognized standards, cannot access all positions without chemical preparation	[13,14]; this study

Contents lists available at ScienceDirect

International Journal of Mass Spectrometry

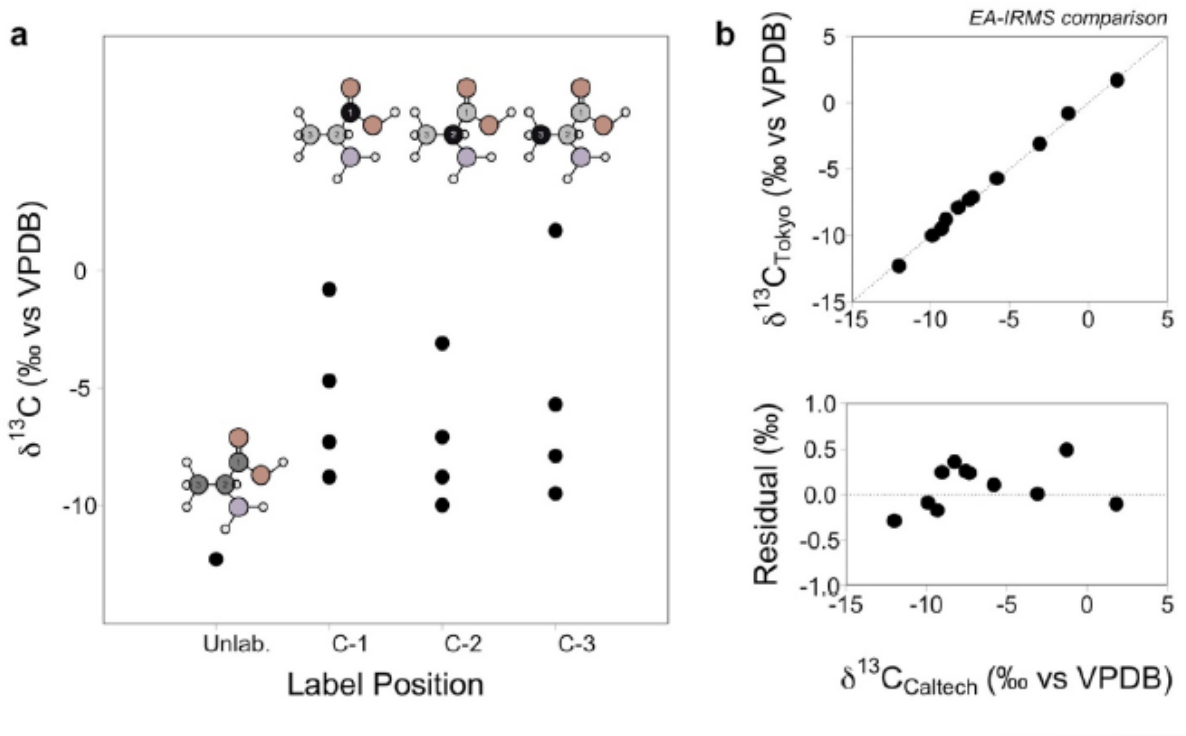
journal homepage: www.elsevier.com/locate/ijms

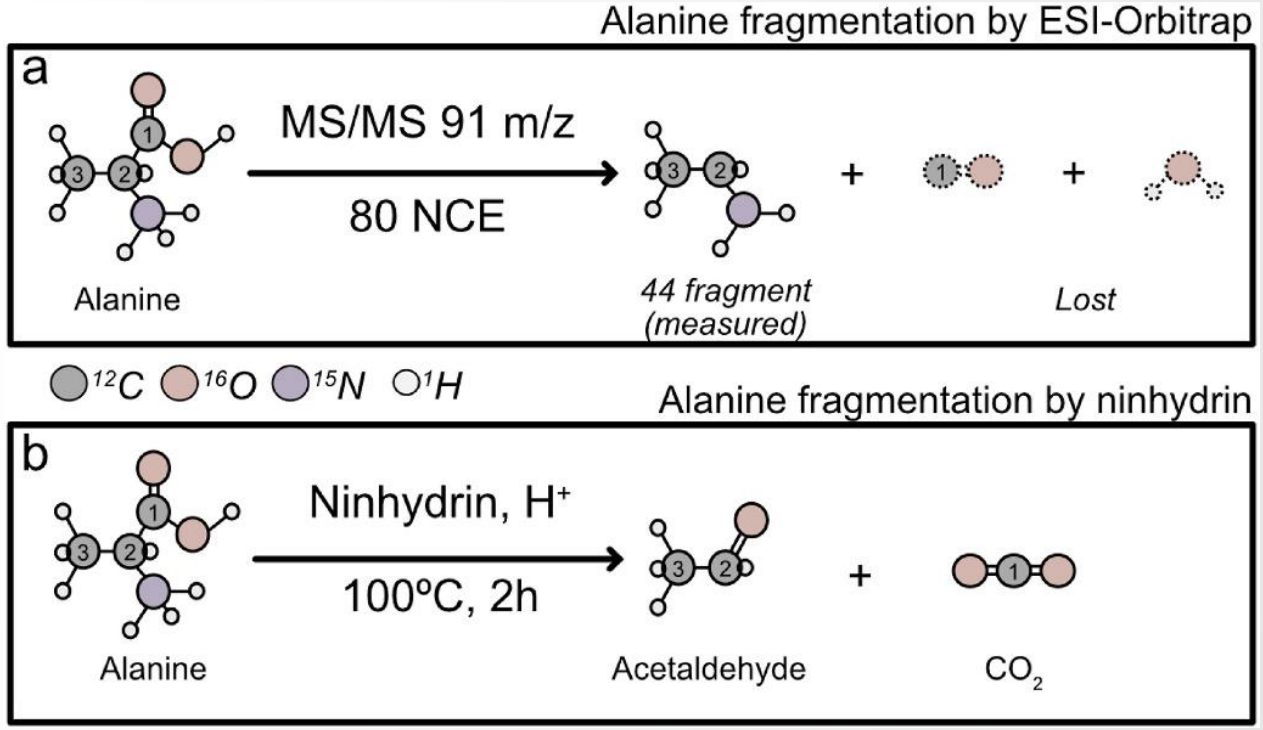
Analysis of intramolecular carbon isotope distributions in alanine by electrospray ionization Orbitrap mass spectrometry

Gabriella M. Weiss[a,b,*,1], Alex L. Sessions[a], Maxime Julien[c,d], Timothy Csernica[e], Keita Yamada[d], Alexis Gilbert[d,f], Katherine H. Freeman[b], John M. Eiler[a]

[a] Division of Geological and Planetary Sciences, California Institute of Technology, Pasadena, CA, 91125, USA
[b] Department of Geosciences, The Pennsylvania State University, University Park, PA, 16803, USA
[c] GFZ German Research Centre for Geosciences - Helmholtz Centre Potsdam, Organic Geochemistry, Potsdam, Germany
[d] Department of Chemical Science and Engineering, Tokyo Institute of Technology, Yokohama, 226-8503, Kanagawa, Japan
[e] Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA
[f] Earth-Life Science Institute, Tokyo Institute of Technology, Meguro, 152-8550, Tokyo, Japan

Alanine Isotopes





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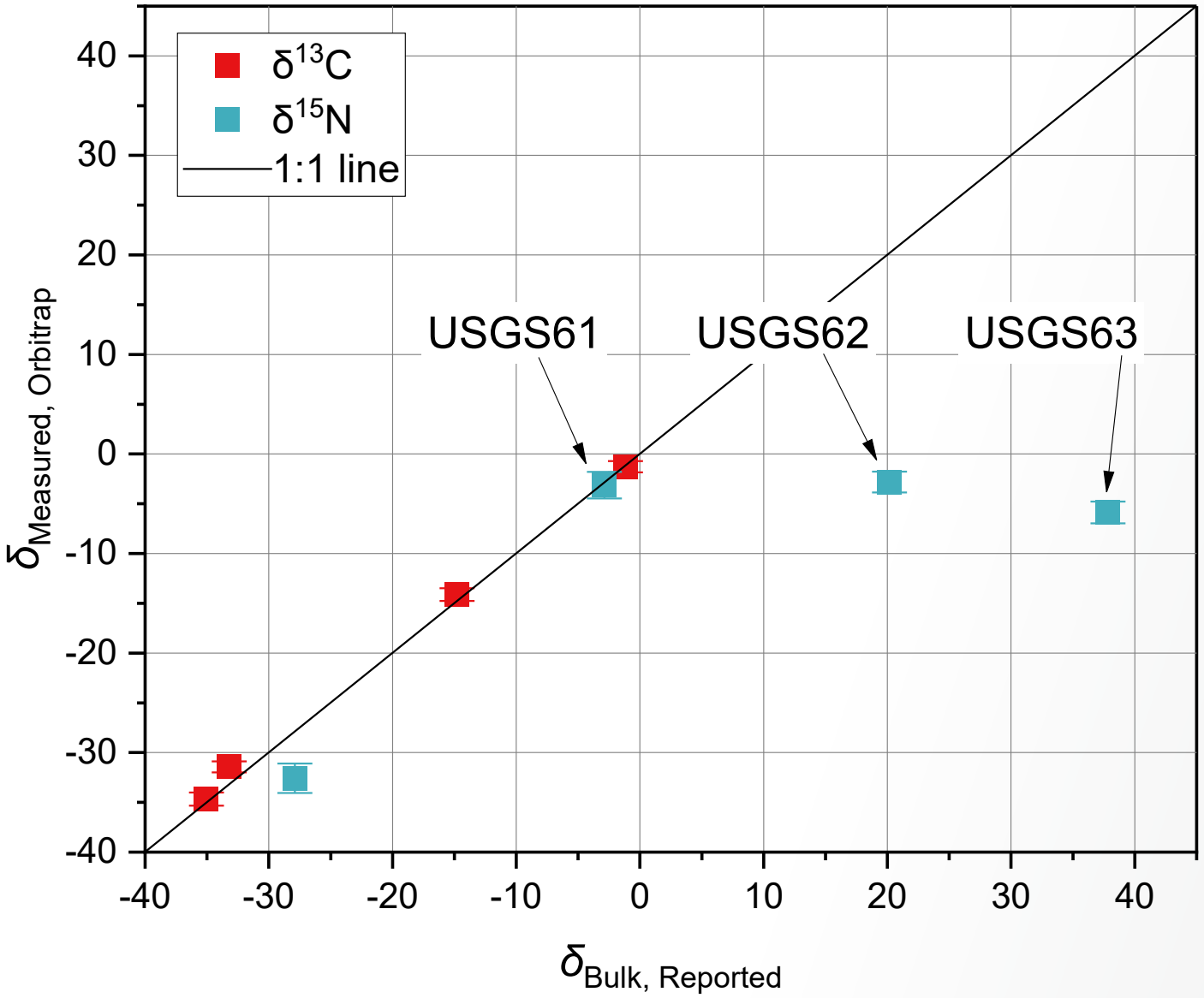
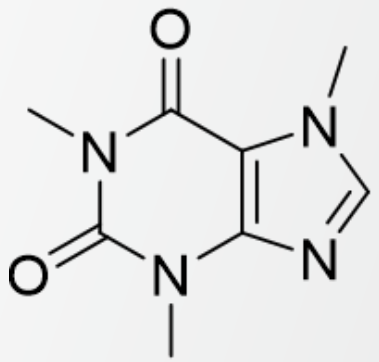
[f] Earth-Life Science Institute, Tokyo Institute of Technology, Meguro, 152-8550, Tokyo, Japan

Accuracy - Caffeine reference materials



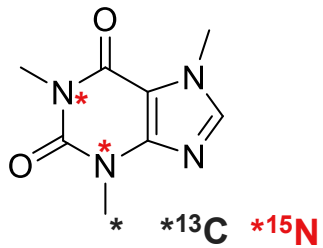


	$\delta^{13}C_{VPDB,reported}$	$\delta^{13}C_{VPDB,measured}$
IAEA600*	-27.8	-27.8
USGS61	-35.1	-34.7 ± 0.7
USGS62	-14.8	-14.1 ± 0.6
USGS63	-1.2	-1.3 ± 0.6
Lab_Std.	-33.2	-31.4 ± 0.6

*Used as calibration point

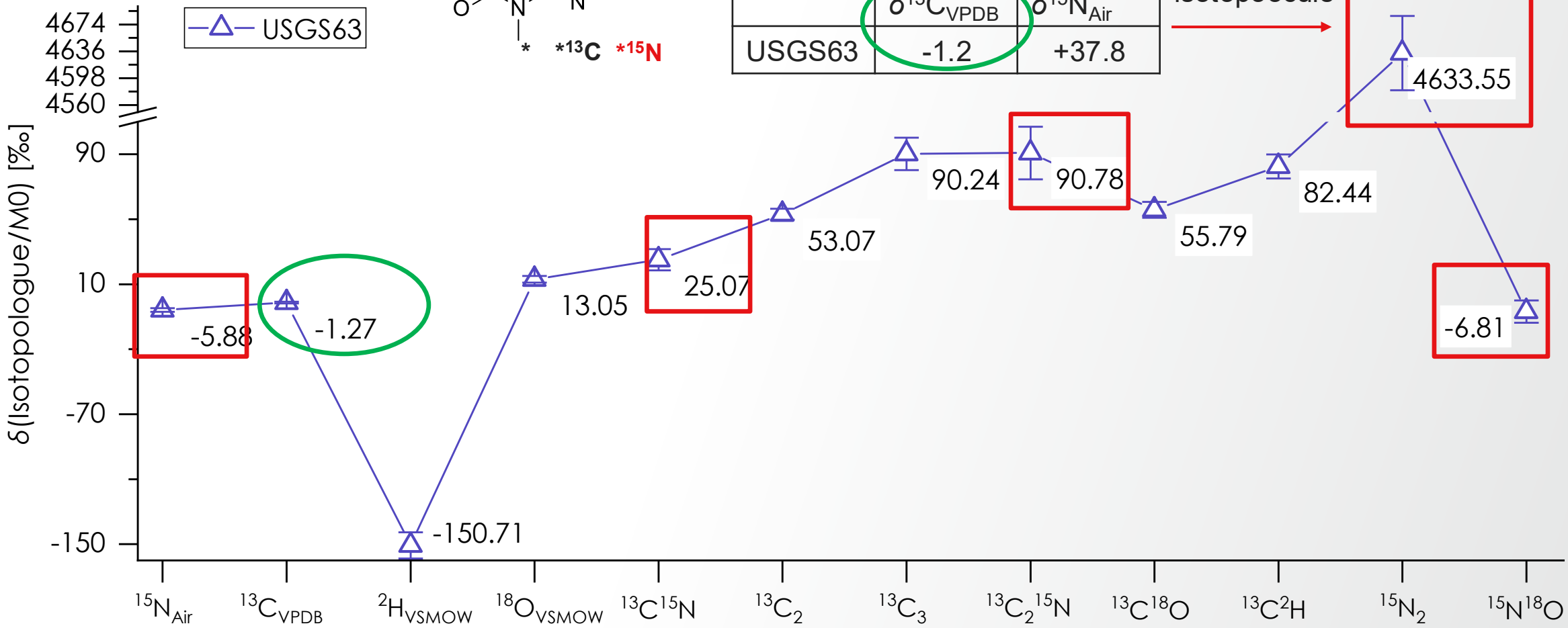
- Work in press by Nils Kuhlbusch

Position specific labels in reference materials



	$\delta^{13}C_{VPDB}$	$\delta^{15}N_{Air}$
USGS63	-1.2	+37.8

Label in $^{15}N^{15}N$-doubly substituted isotopoocule



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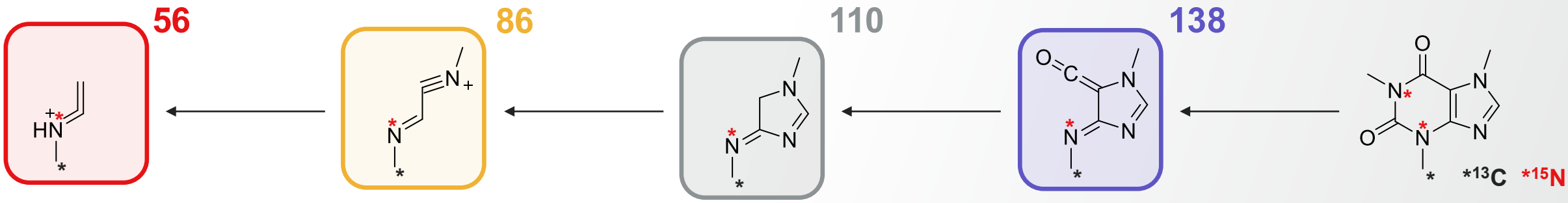
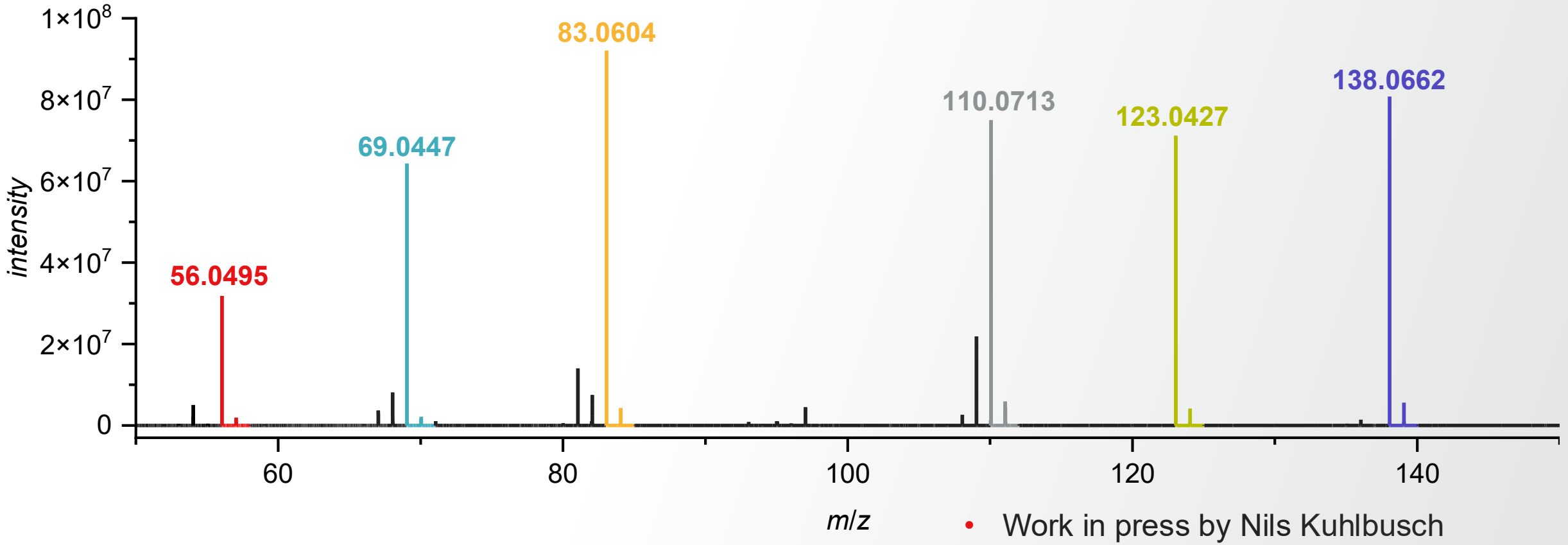
Position specific isotope analysis (PSIA)





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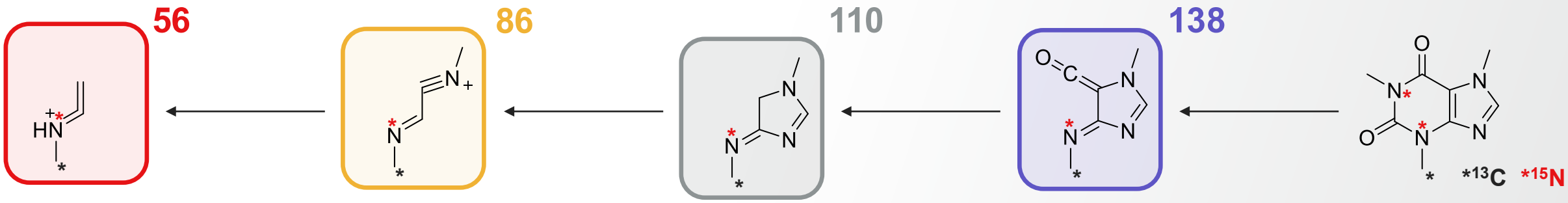
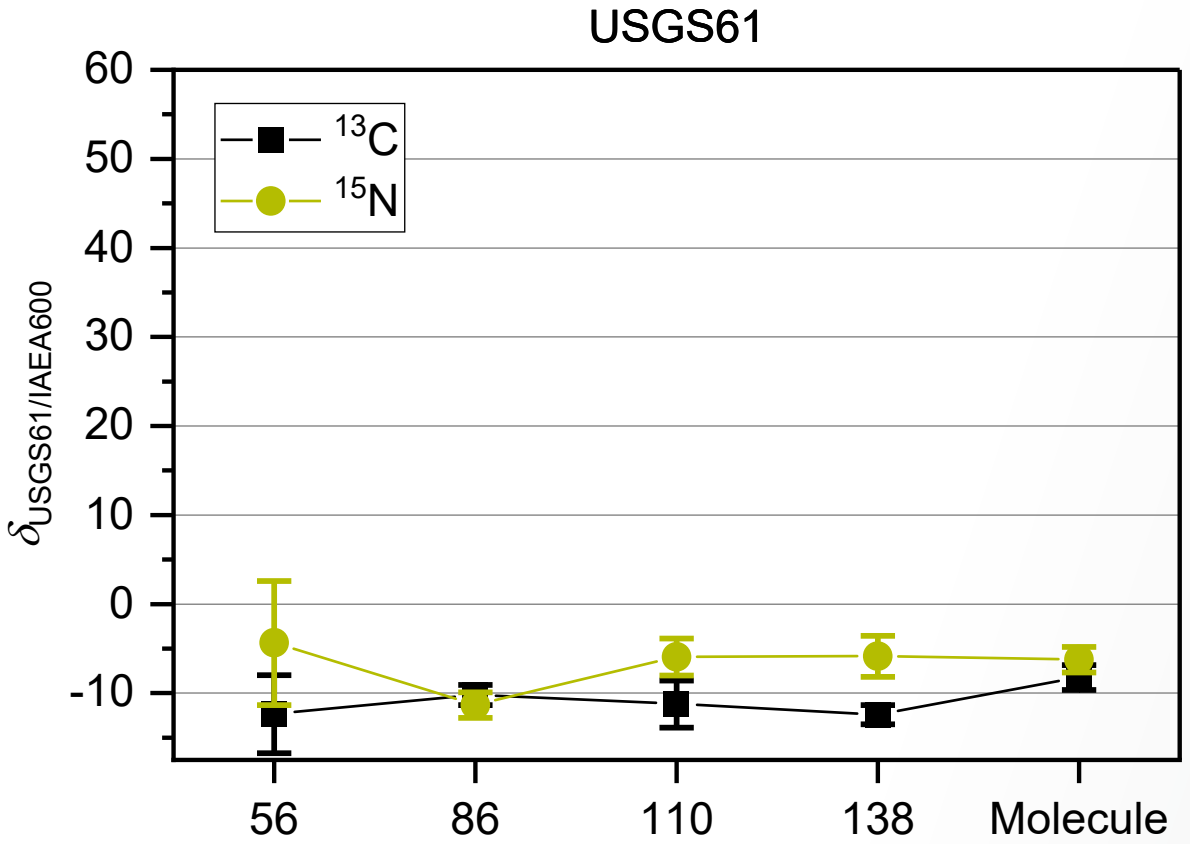
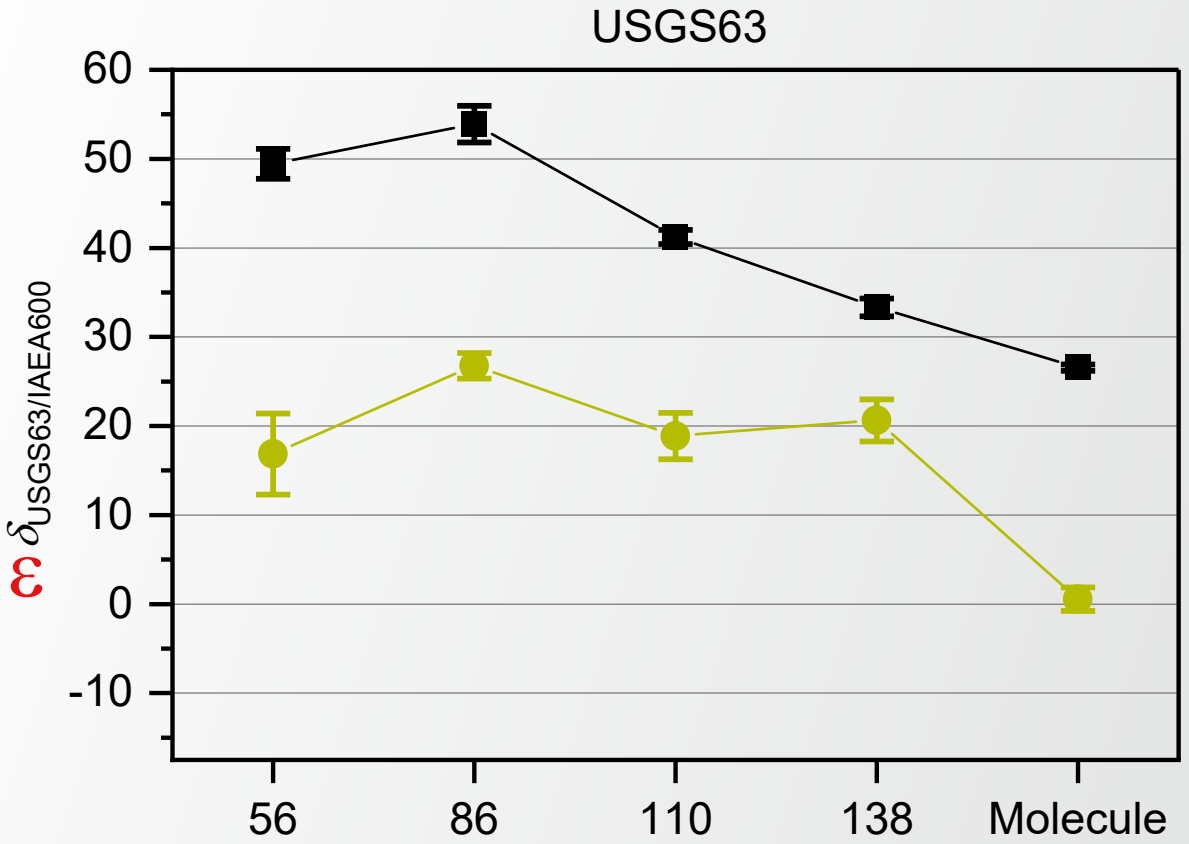
PSIA of caffeine reference materials







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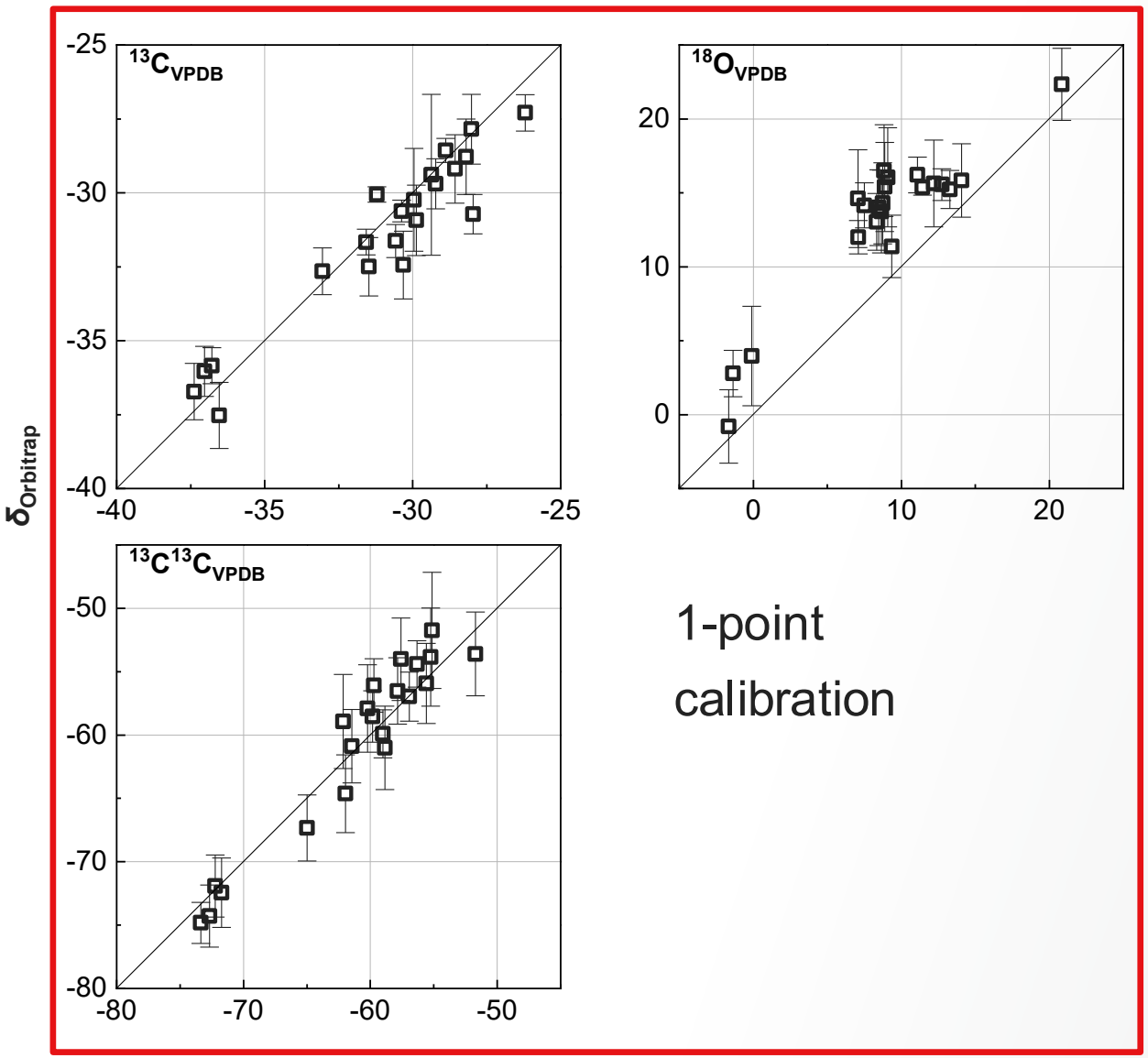
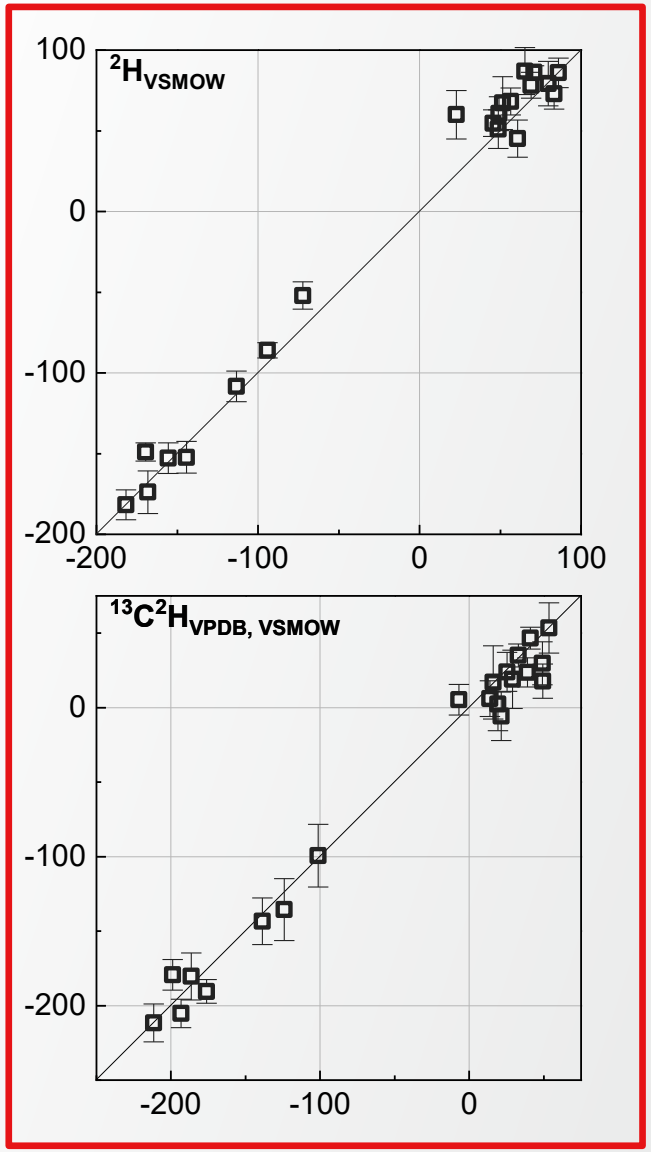
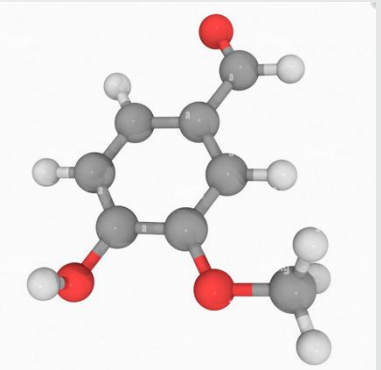
Vanillin data







Acknowledgement: samples courtesy and GC-IRMS data provided by David Psomiadis and Balazs Horvath, Imprint Analytics GmbH, Austria

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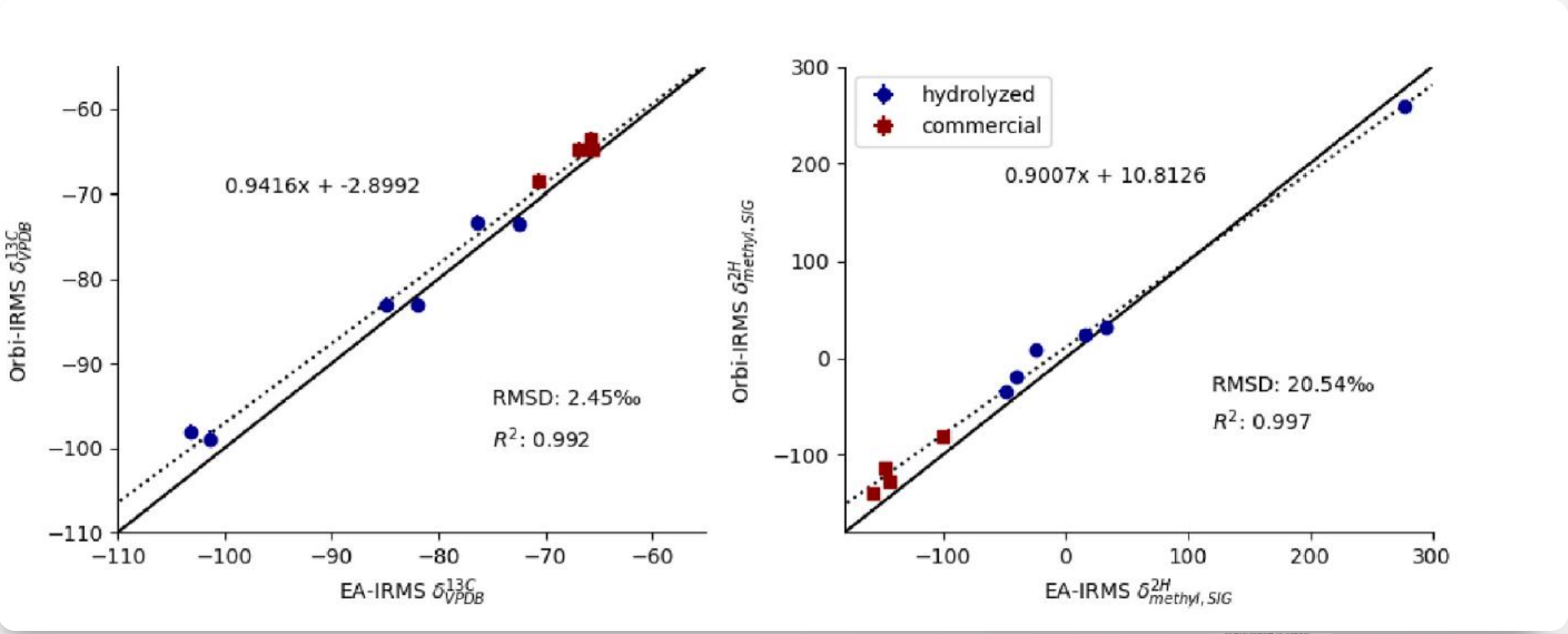
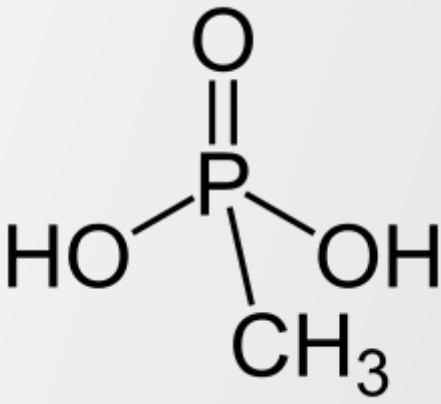
Methyl Phosphonic Acid





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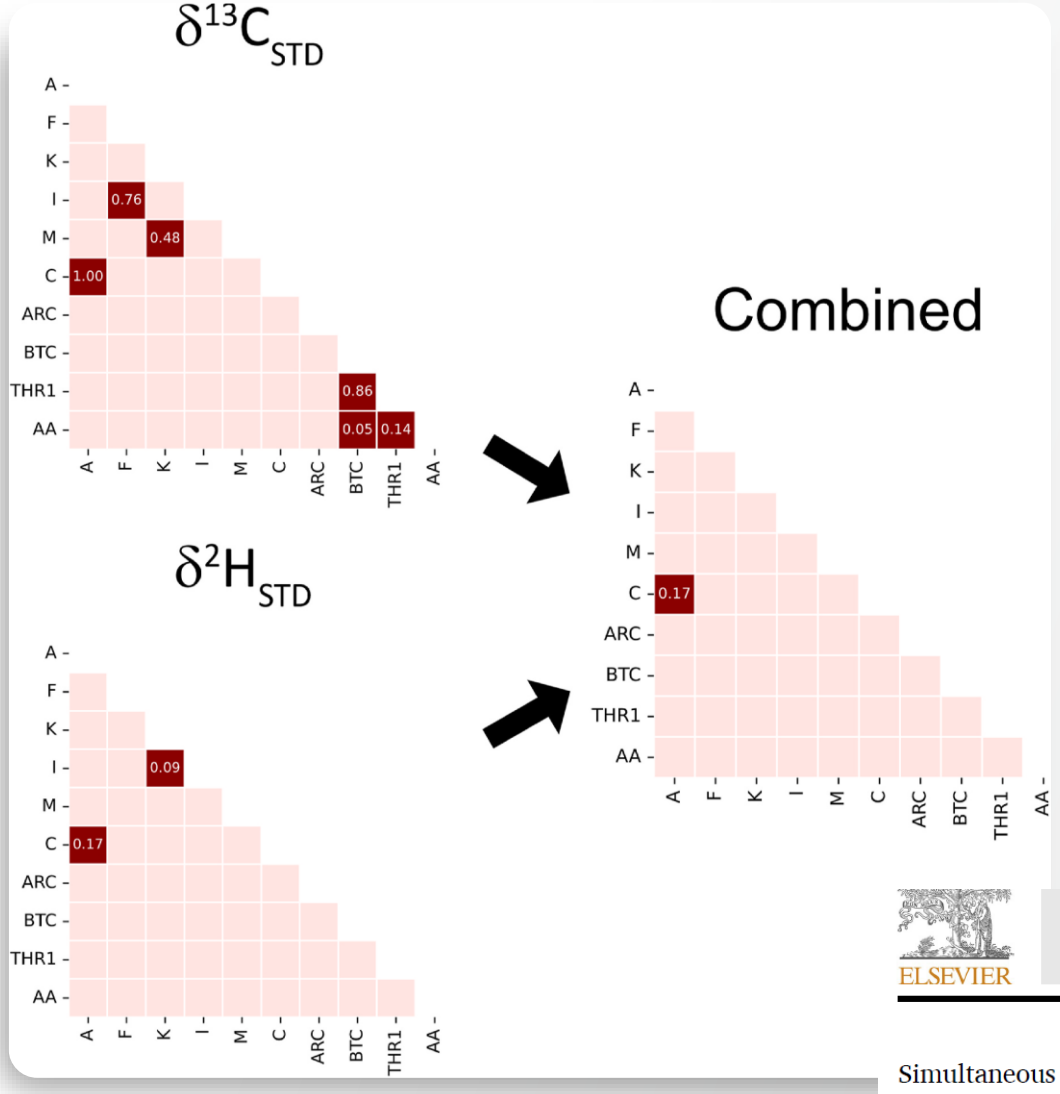
Simultaneous observation of ^{2}H and ^{13}C enrichment of methyl phosphonic acid via Orbitrap-IRMS with applications to nerve agent forensics

Timothy Csernica[a,*], James J. Moran[b,c], Carlos G. Fraga[d], John M. Eiler[a]

[a] Division of Geological and Planetary Sciences, California Institute of Technology, Pasadena, CA, 91125, USA
[b] Department of Integrative Biology and Department of Plant, Soil, and Microbial Sciences, Michigan State University, East Lansing, MI, USA
[c] Pacific Northwest National Laboratory, Richland, WA, USA
[d] Air Force Research Laboratory, 10 E. Saturn Blvd, Edwards Air Force Base, CA, 93524, USA

Methyl Phosphonic Acid



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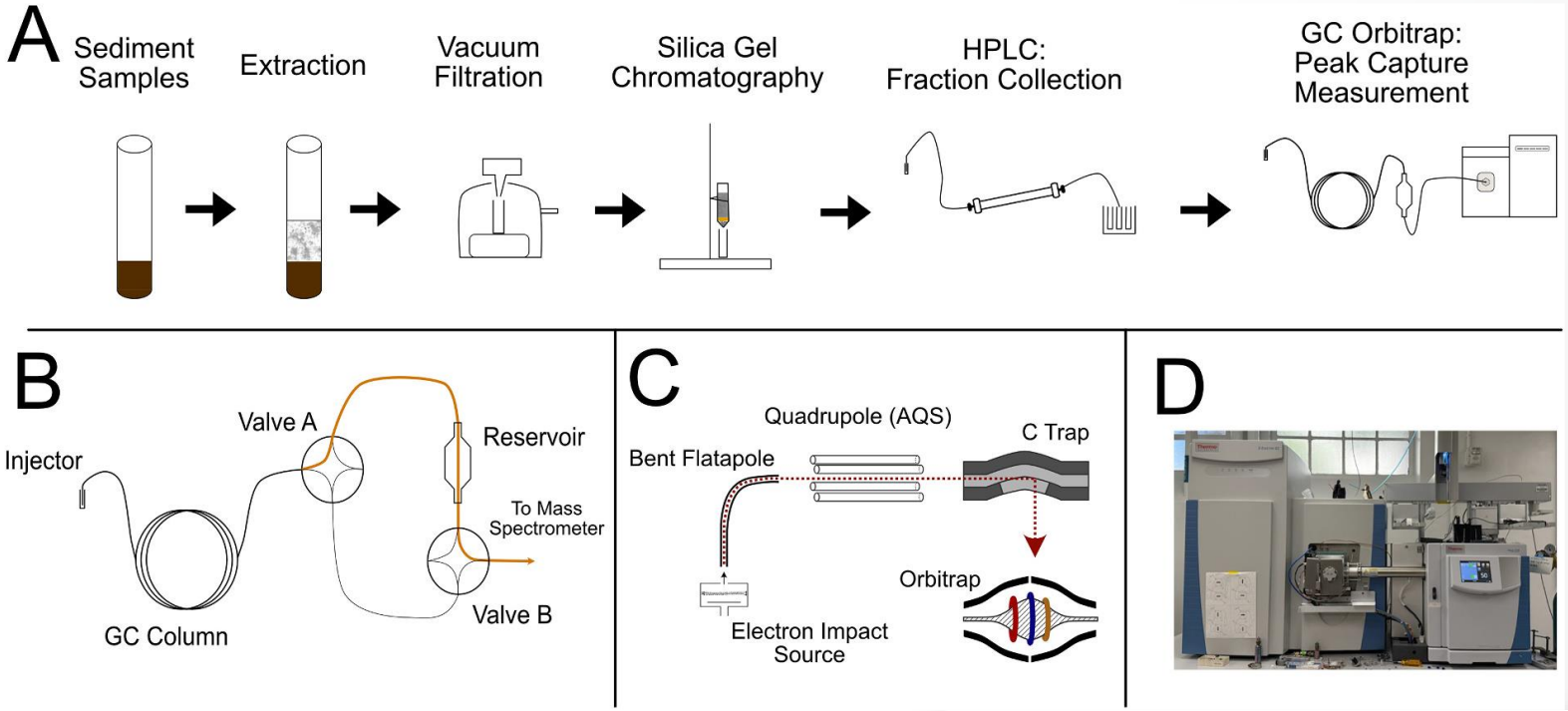
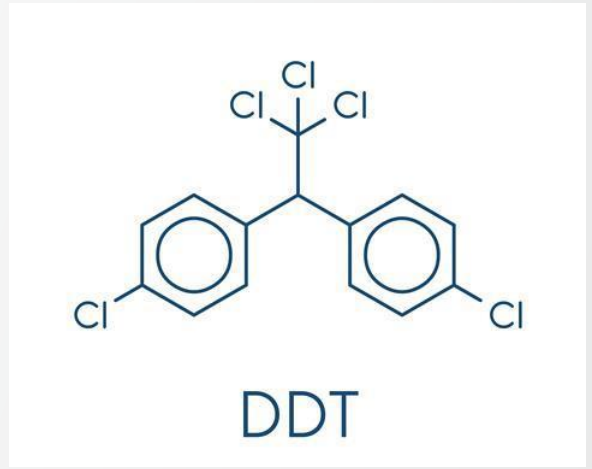
[d] Air Force Research Laboratory, 10 E. Saturn Blvd, Edwards Air Force Base, CA, 93524, USA

DDT





Contents lists available at ScienceDirect

Marine Pollution Bulletin

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

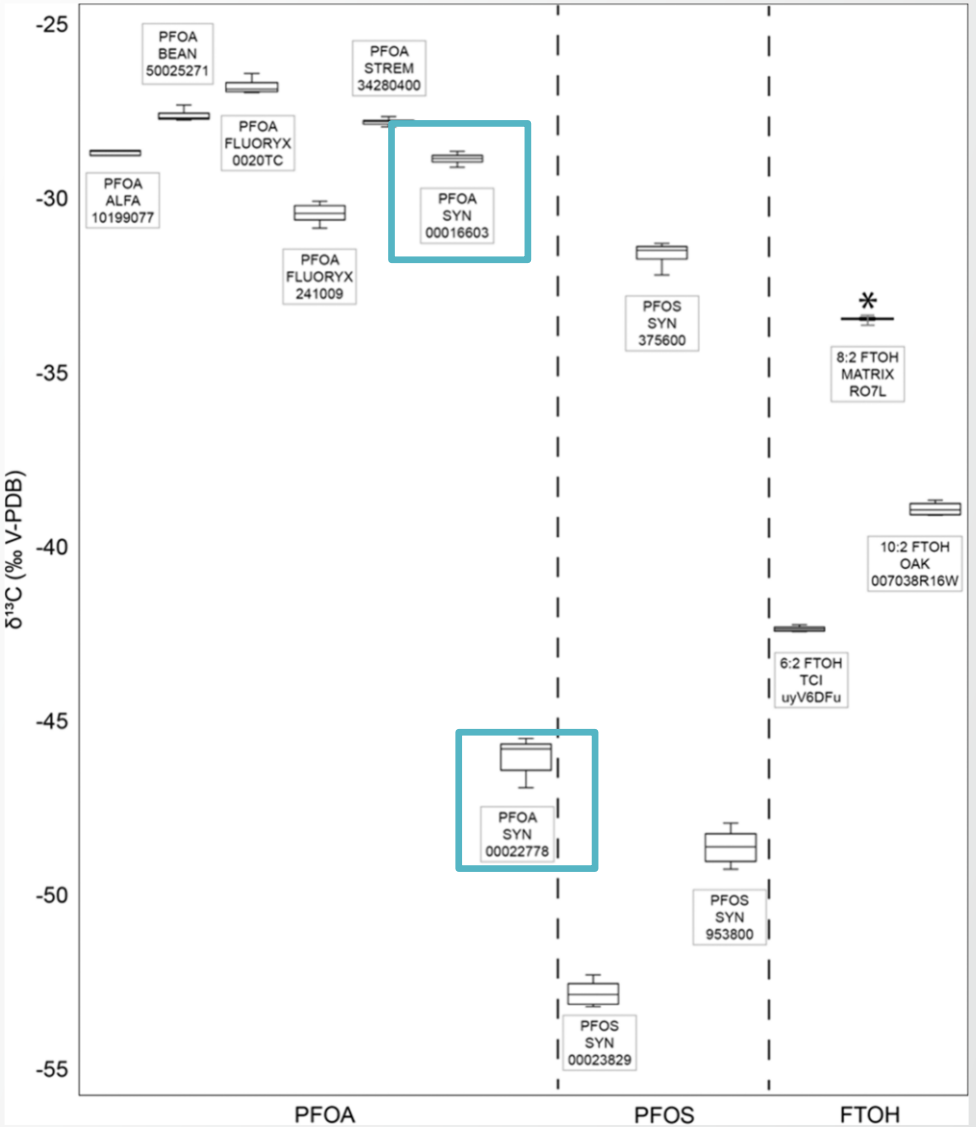
Multi-isotope characterization of 4,4'-DDT isolated from sediment samples via Orbitrap-IRMS

Timothy A. Csernica [a,*], John M. Eiler [a], Alex L. Sessions [a]

[a] Division of Geological and Planetary Sciences, California Institute of Technology, Pasadena, CA, 91125, United States of America

Carbon stable isotope analysis of PFAS sources

- Carbon isotope analysis of PFAS, PFOA and FTOH were acquired from multiple vendors and where possible, from multiple lots.
- There was variation in the carbon isotope values among different compounds, manufacturers, and batches.
  - Ex. PFOA Syn $\delta^{13}C$ lots differed (−28.9 ± 0.3‰, and, −46.1 ± 0.7‰).
- Variability among mean carbon isotope values makes EA-IRMS a potentially powerful tracking tool for PFAS contaminants.



- Dombrowski et al (2025). *Environmental Science & Technology Letters* https://doi.org/10.1021/acs.estlett.5c00021

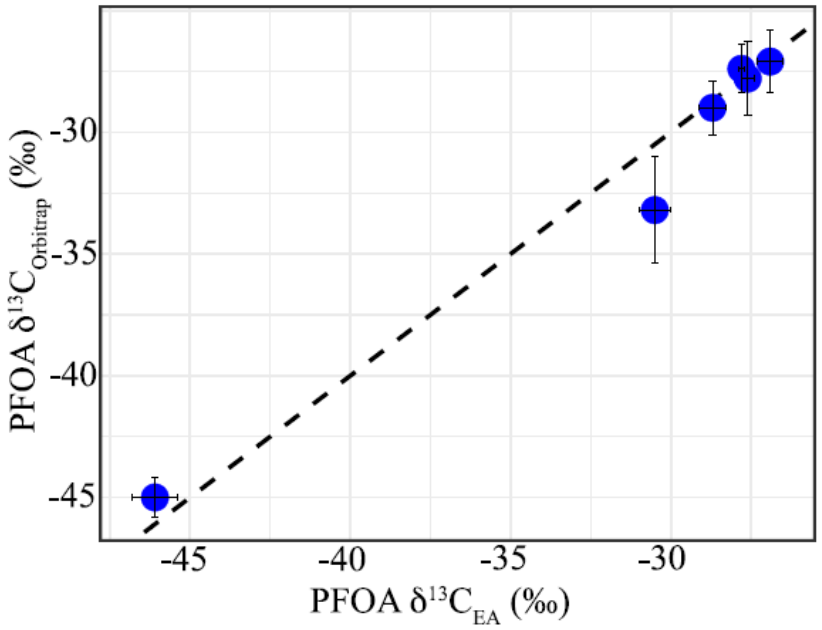
PFOA Carbon Isotope "Fingerprinting"

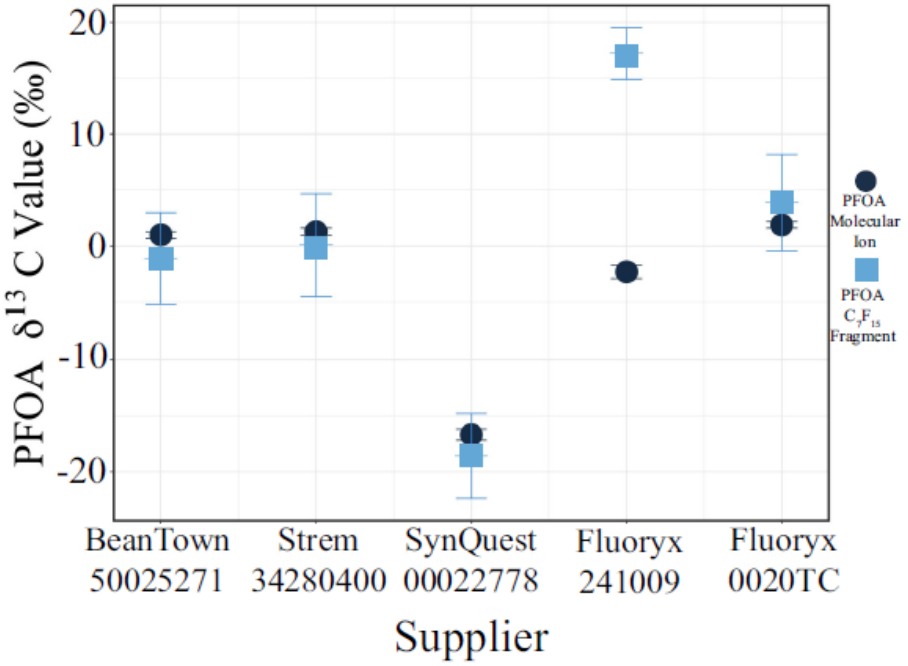
RESEARCH ARTICLE OPEN ACCESS

Stable Carbon Isotope Analysis of Perfluorooctanoic Acid (PFOA) by Microflow-High Pressure Liquid Chromatography-Orbitrap Mass Spectrometry

Paul K. Wojtal[1,2] | Brett Davidheiser-Kroll[3] | Chad S. Lane[1,2] | Ralph N. Mead[1,2]

[1]Center for Marine Science, University of North Carolina Wilmington, Wilmington, North Carolina, USA | [2]Department of Earth and Ocean Sciences, University of North Carolina Wilmington, Wilmington, North Carolina, USA | [3]Thermo Fisher Scientific, Bremen, Germany





PFOS Fingerprinting

Environmental Science & Technology Letters

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Letter

Stable Carbon Isotope Analysis of PFOA and PFOS Using Orbitrap Mass Spectrometry

Hiroto Kawashima,* Tomoha Iezumi, Momoka Suto, and Sachi Taniyasu

Cite This: *Environ. Sci. Technol. Lett.* 2026, 13, 574–579

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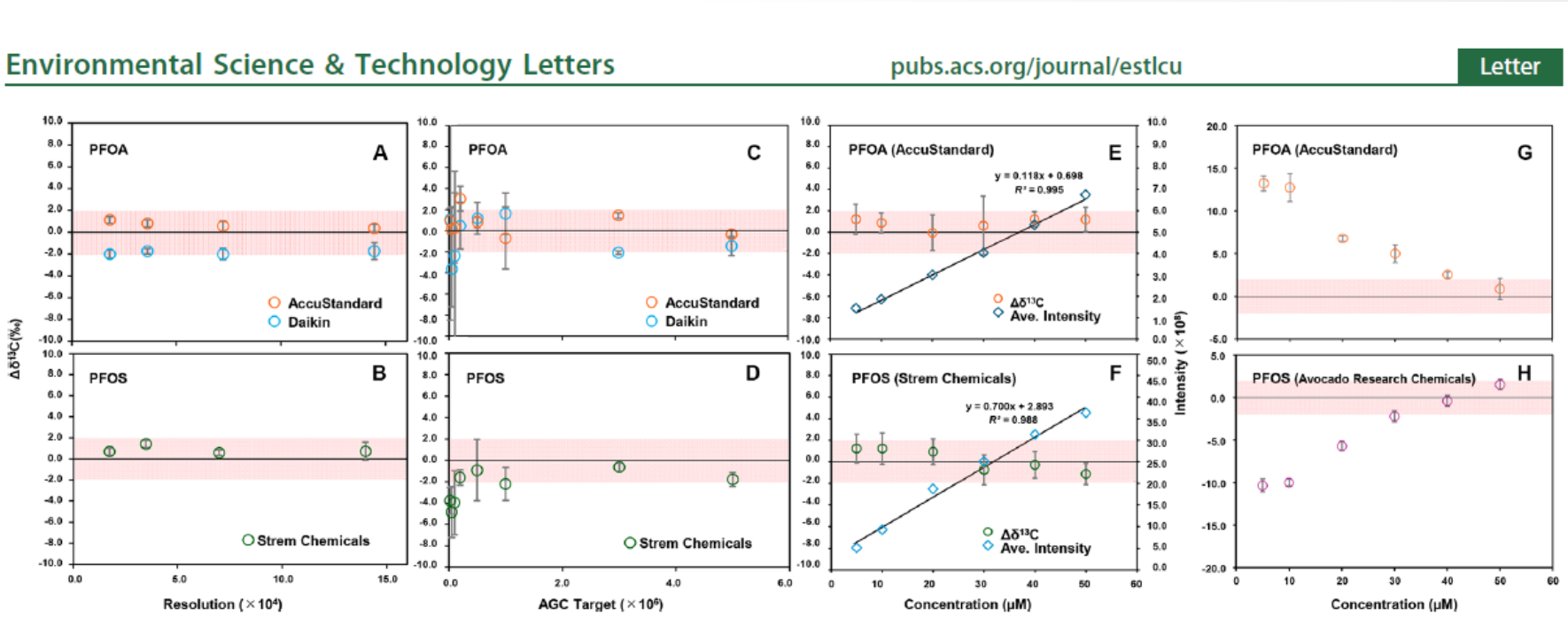
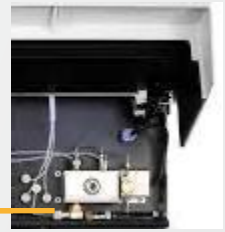
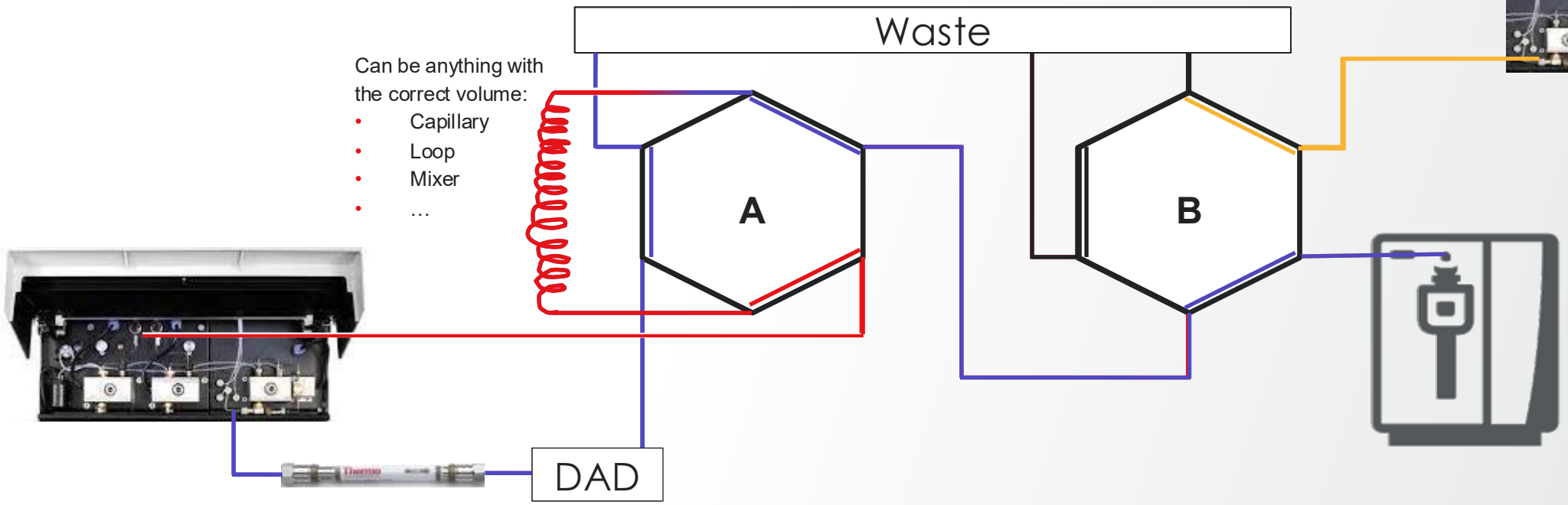


Peak broadening with heart-cut setup

- Caffeine reference in MeOH + 0.1 % FA
- Sample injected onto RPLC column
- MeOH + 0.1 % FA flushing the heart-cut loop

Can be:
- Syringe
- Additional pump
- Autosampler



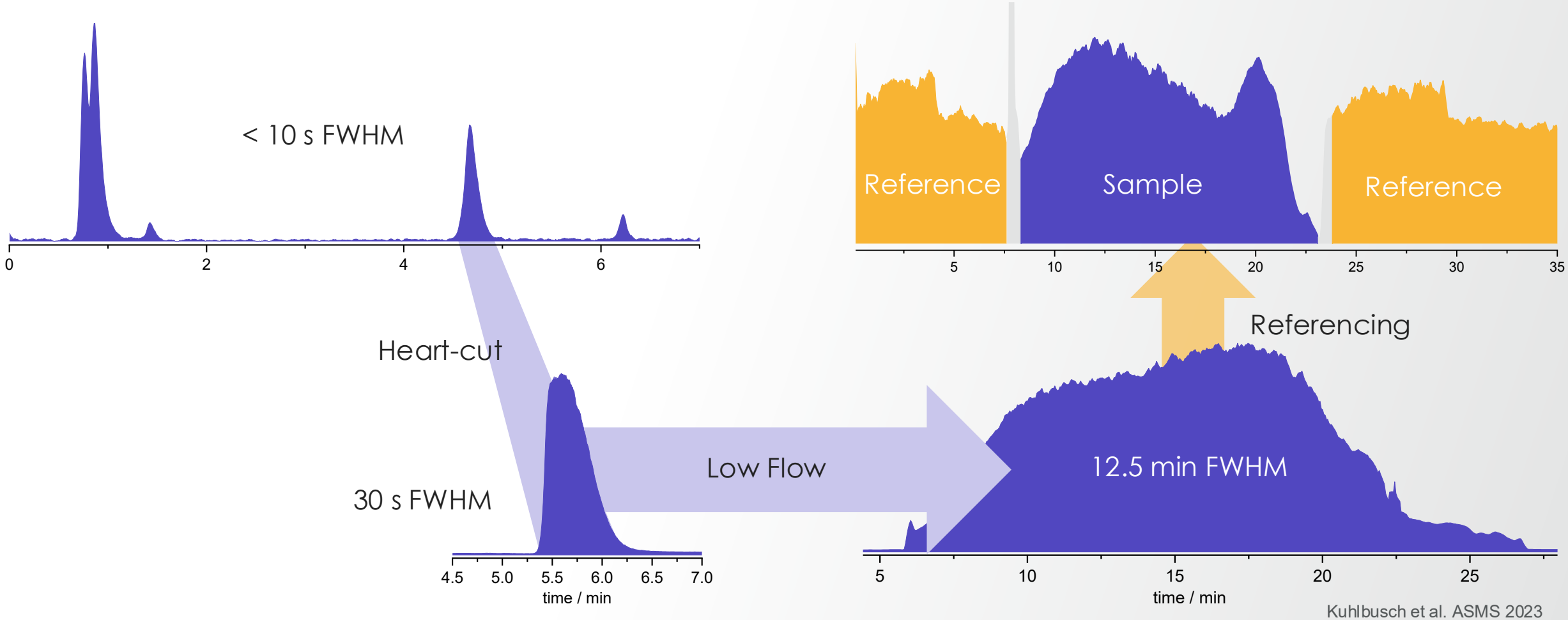


Tested so far:
- RPLC
- HILIC

Kuhlbusch et al. ASMS 2023

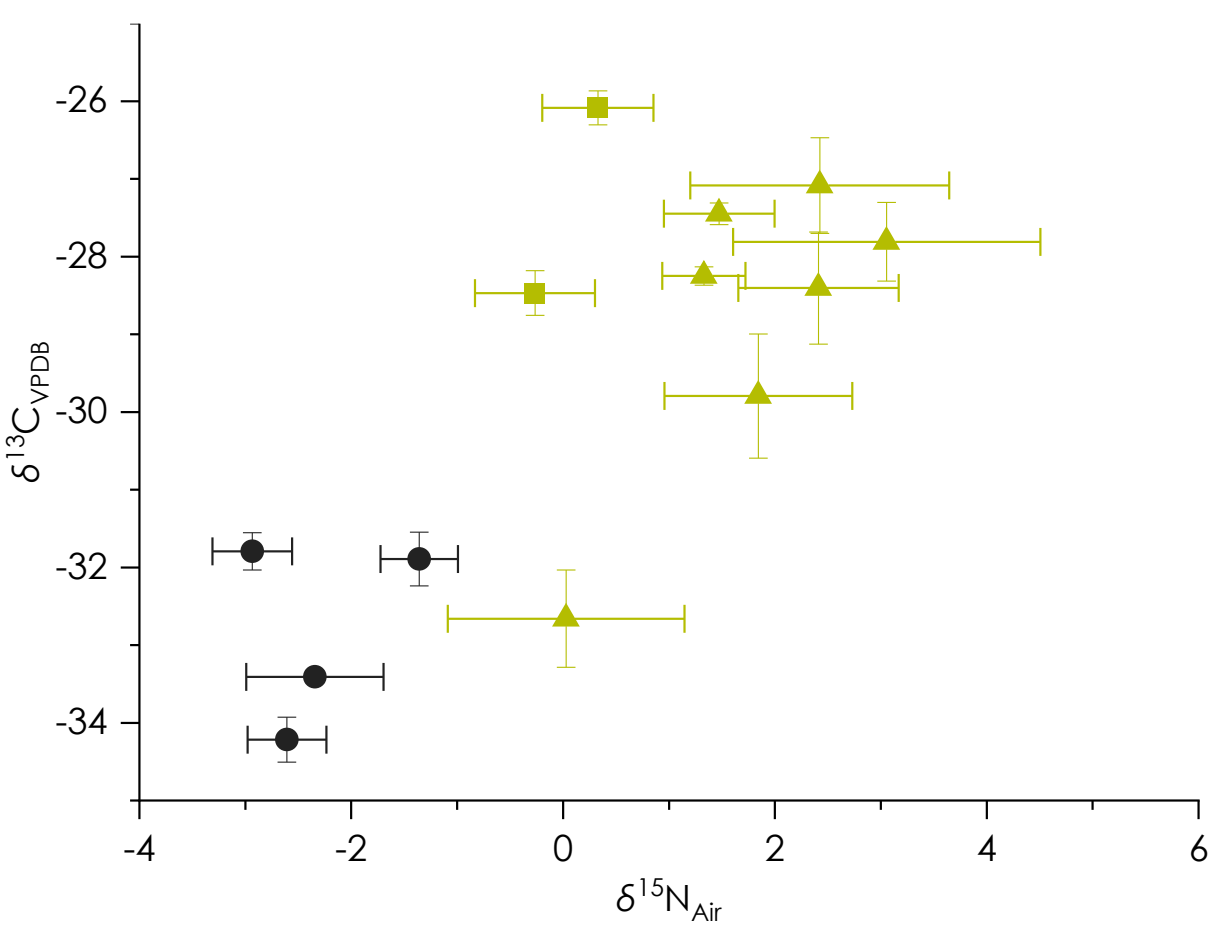
Peak broadening with heart-cut setup

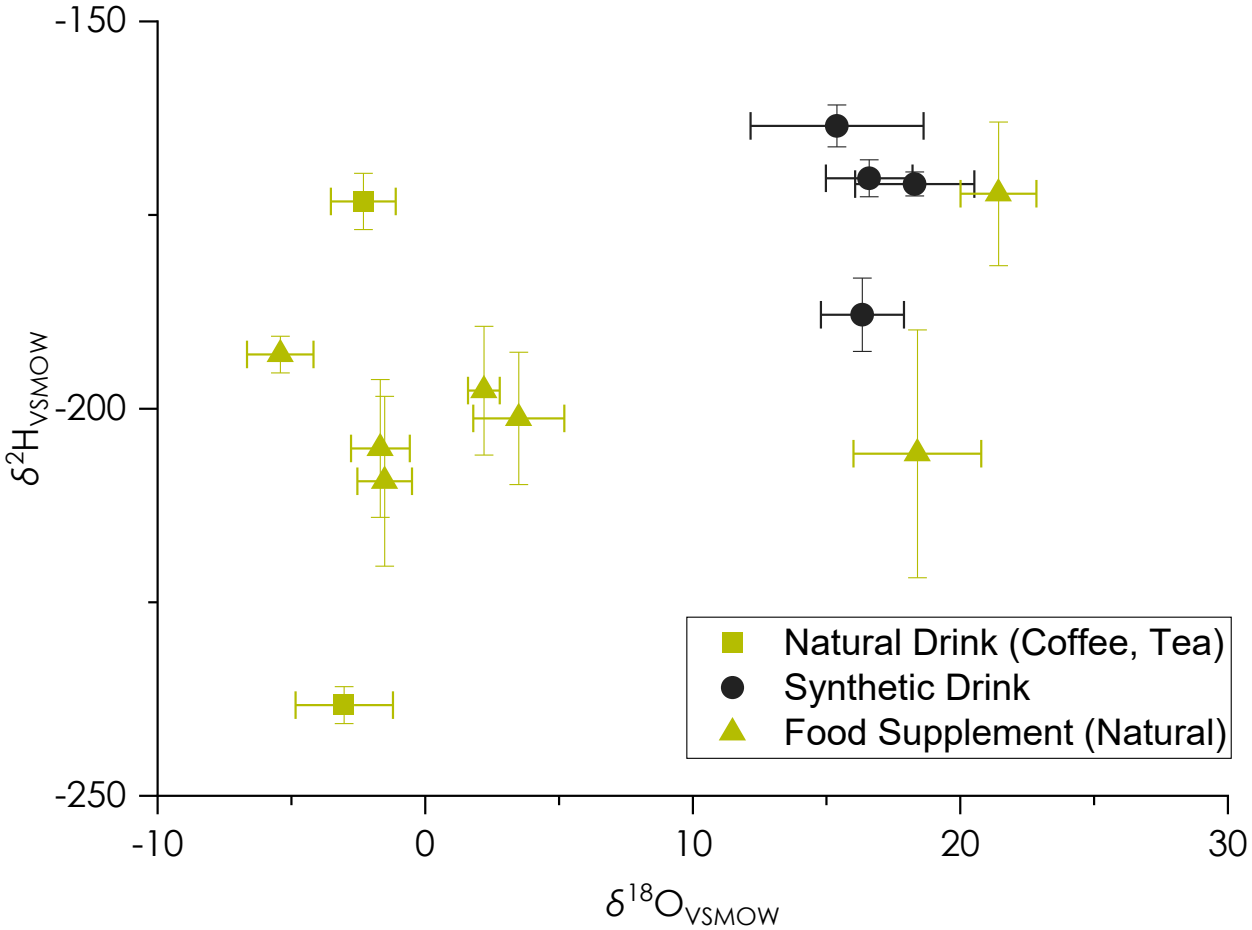
- Broadening of peaks via heart-cut to maximize the number of ions counted



Kuhlbusch et al. ASMS 2023

Caffeine in beverages and food





Kuhlbusch et al. ASMS 2023

HPLC Isotope Orbitrap Coupling

analytical chemistry

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Article

Coupling Liquid Chromatography to Orbitrap Isotope Ratio Mass Spectrometry: Overcoming Isotope Effects of Chromatography and Amount-Dependency by Peak Homogenization

Aoife Canavan, Leonhard Prechtl, Habib Al-Ghoul, Nils Kuhlbusch, Andrea M. Erhardt, and Martin Elsner*

Cite This: *Anal. Chem.* 2026, 98, 590–600

Read Online

- Sulfamethoxazole as target compound
- 4 nmol of sample
- Reproducible compared to GC-IRMS within 1.5 and 0.9 of $\delta^{13}C$ and $\delta^{34}S$, respectively.

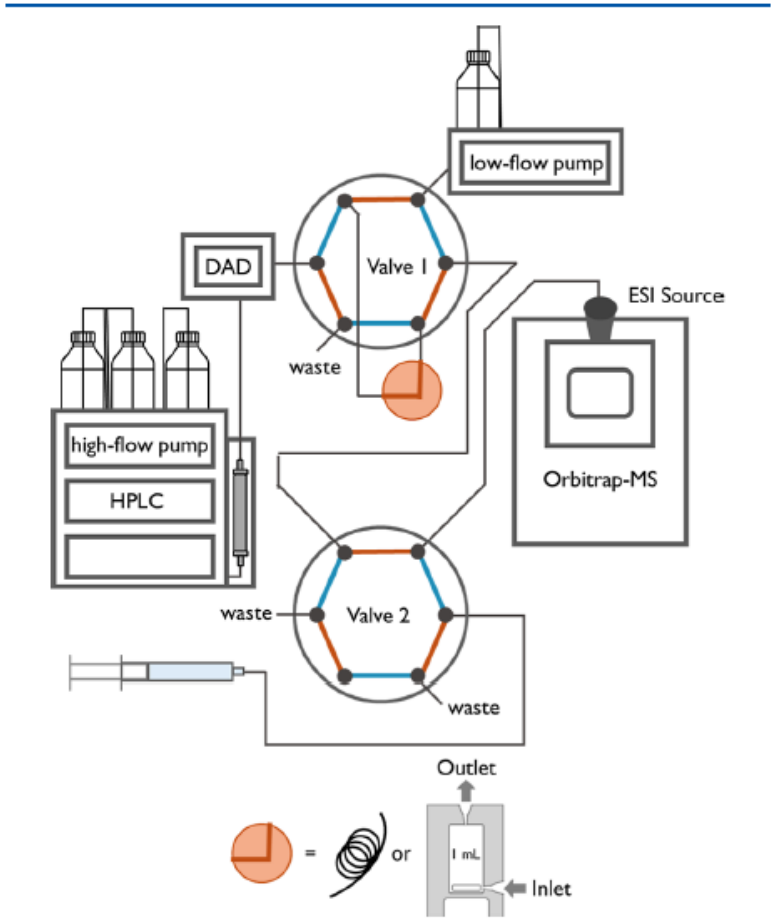

Figure 1. Schematic overview of the coupled HPLC-ESI-Orbitrap-MS system for stable isotope analysis.

HPLC Isotope Orbitrap Coupling

analytical chemistry

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Article

Coupling Liquid Chromatography to Orbitrap Isotope Ratio Mass Spectrometry: Overcoming Isotope Effects of Chromatography and Amount-Dependency by Peak Homogenization

Aoife Canavan, Leonhard Prechtl, Habib Al-Ghoul, Nils Kuhlbusch, Andrea M. Erhardt, and Martin Elsner*

Cite This: *Anal. Chem.* 2026, 98, 590–600

Read Online

- Sulfamethoxazole as target compound
- 4 nmol of sample
- Reproducible compared to GC-IRMS within 1.5 and 0.9 of $\delta^{13}C$ and $\delta^{34}S$, respectively.

Scheme 1. Target Fragments of Sulfamethoxazole after Positive or Negative Electrospray Ionization Using Source Fragmentation or HCD Fragmentation in the IRM

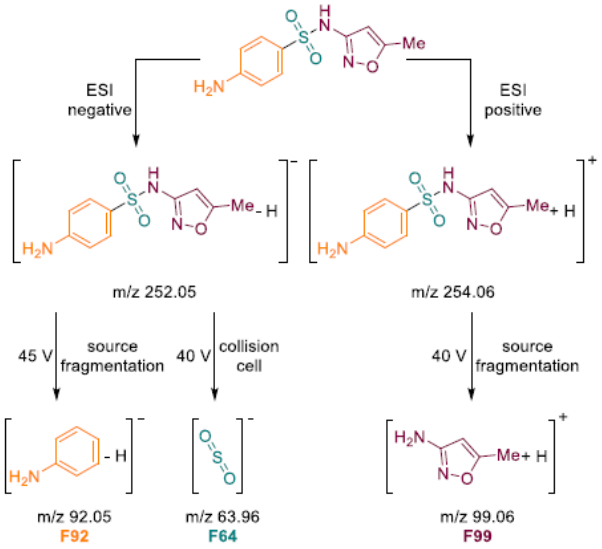
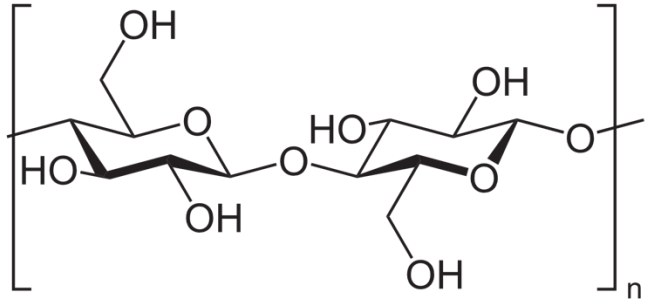


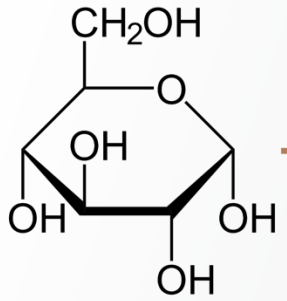
Table 1. Instrument Settings Used for Each Fragment of SMX

	F64	F92	F99
polarity (±)	negative	negative	positive
ion transfer tube temperature (°C)	320	320	320
nominal Orbitrap resolution	30,000	90,000	90,000
AQT isolation window (*m/z*)	249.5–254.5	88.5–95.5	94–104
absolute AGC target (#)	1.5×10^5	1.5×10^5	1.5×10^5
microscans (#)	10	10	10
RF lens (%)	100	100	100
maximum ion injection time (ms)	1000	1000	1000
source fragmentation (yes/no)	no	yes	yes
source fragmentation energy (V)	-	45	40
HCD collison (yes/no)	yes[a]	no	no
absolute HCD collision energy (V)	40	-	-

[a] *m/z* 252 was selected as a precursor ion.

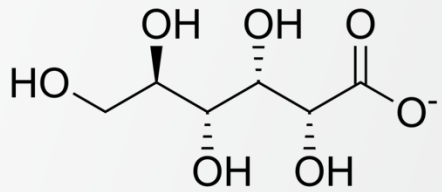
PSIA of cellulose and glucose by Orbitrap Mass Spectrometry



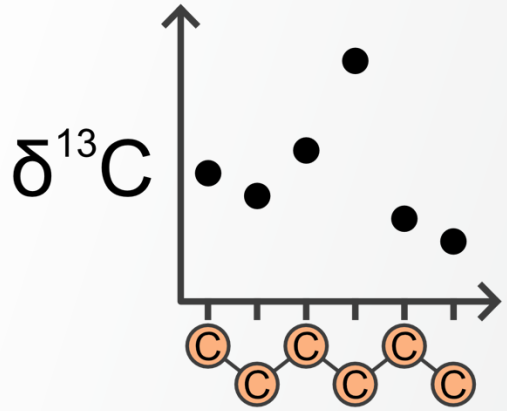


Gluconate:

~5x ionization efficiency vs. glucose, clear fragmentation

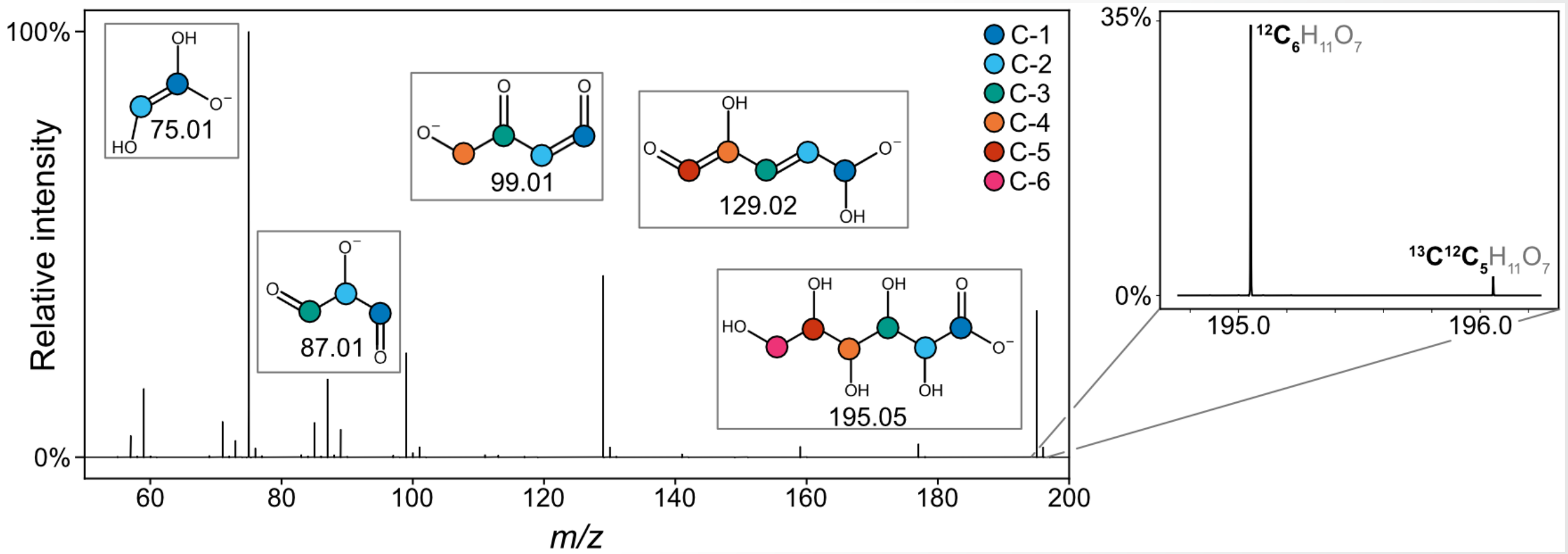


Thermo Q Exactive Orbitrap:
Fragmentation + High-resolution MS

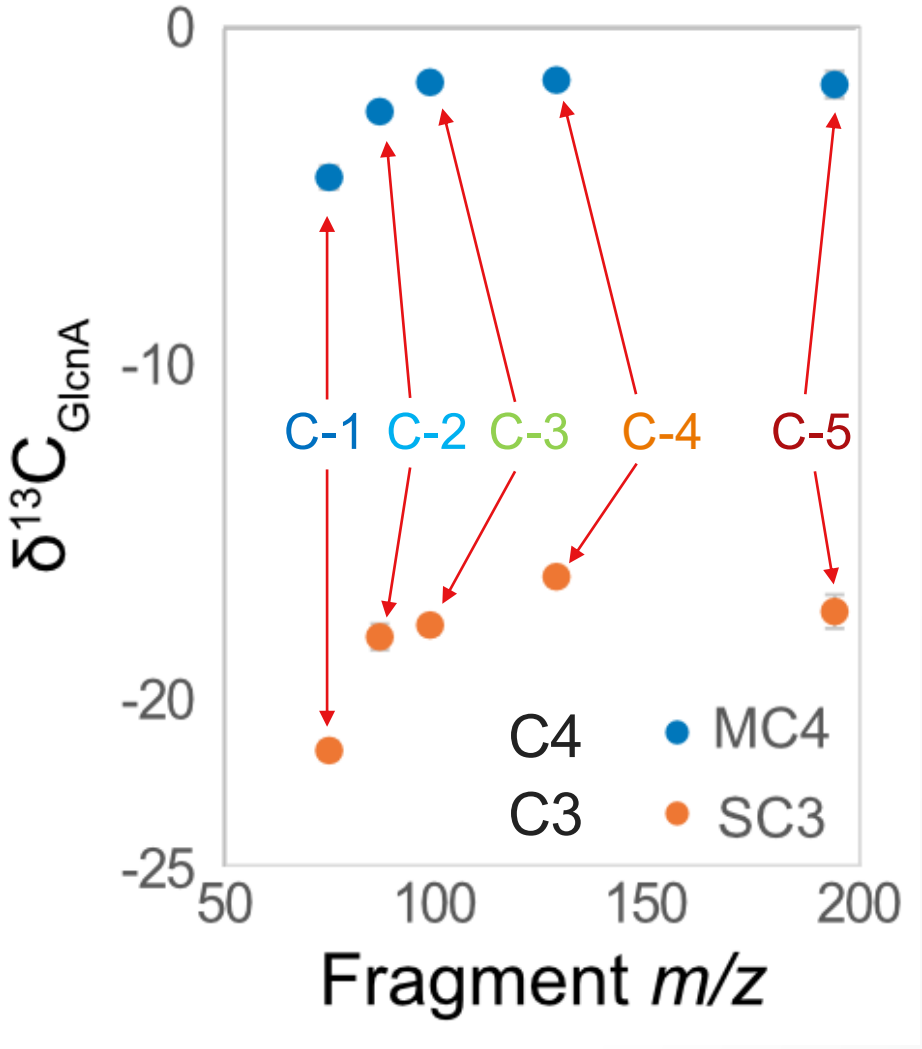


Hannah
PhD Stude
er

Independent observation of $\delta^{13}C$ of 5 atomic positions in glucose



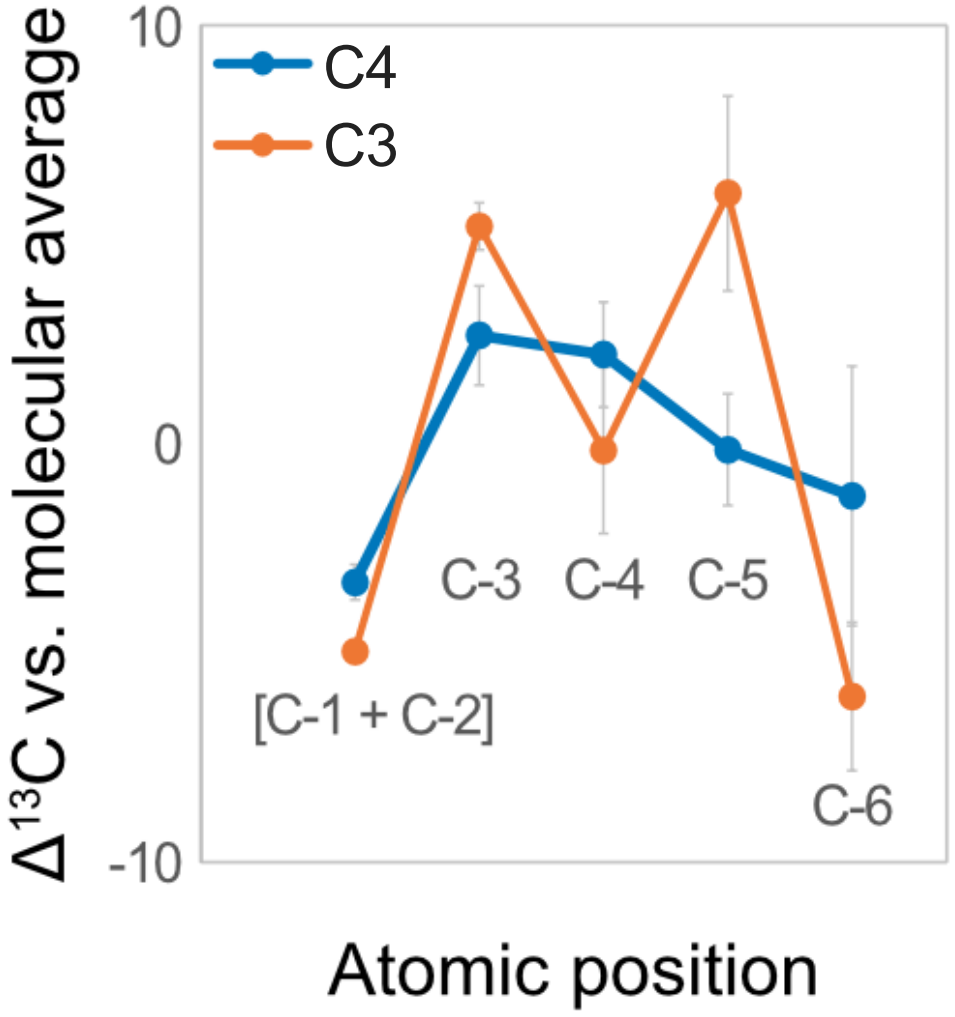
Position-specific $\delta^{13}C$ analysis of C3 and C4 glucose



C4: Corn

C3: Wheat

Position-specific $\delta^{13}C$ analysis of C3 and C4 glucose



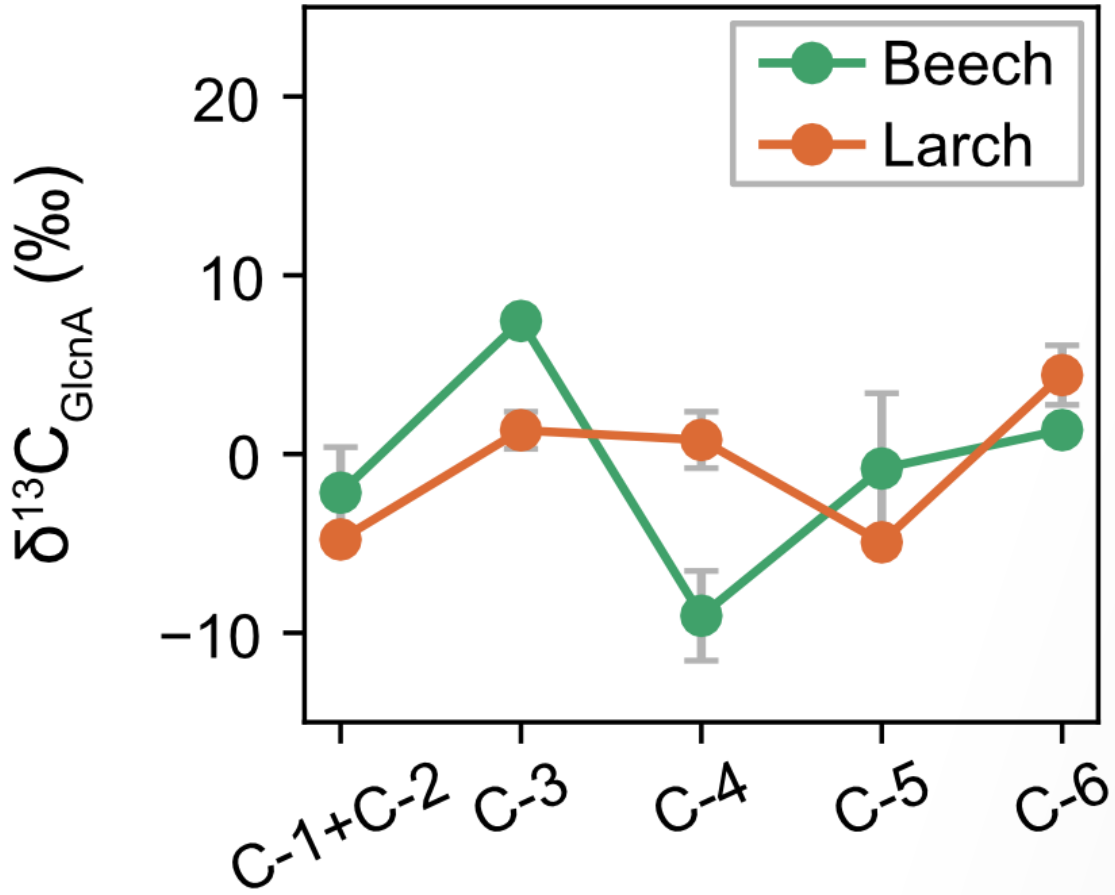
- 0.1 to 0.5‰ precision on fragment measurements of natural glucose
- Average 1.4‰ precision on calculated position-specific values
- Accurate to externally verified values within precision
- Consumes < 50 µg glucose!

Position-Specific Carbon Isotope Analysis of Glucose at Natural Isotope Abundance by Electrospray-Ionization Orbitrap Mass Spectrometry

Hannah Dion-Kirschner,* Celia Kong-Johnson, Kimberly R. Sharp, Nathan Dalleska, John M. Eiler, and Alex L. Sessions

Cite This: *Anal. Chem.* 2026, 98, 915–926 Read Online

Unique intramolecular ^{13}C patterns in gymnosperm and angiosperm cellulose



Larix decidua
(conifer, dry-adapted)

Fagus sylvatica
(angiosperm, humid-adapted)

FAME Analysis

ACS Partner Journal

Journal of the American Society for Mass Spectrometry

pubs.acs.org/jasms

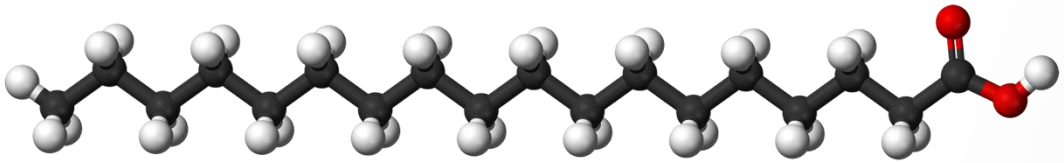
Article

Advancing Stable Isotope Analysis with Orbitrap-MS for Fatty Acid Methyl Esters and Complex Lipid Matrices

Gabriel F. dos Santos,* Giovanni B. Bevilaqua, Alexis Gilbert, Hugo G. Machado, Maxime Julien, Gesiane S. Lima, Nerilson M. Lima, Júlio C. O. Ribeiro, Alexandre A. Ferreira, Ygor S. Rocha, and Boniek Gontijo*

Cite This: https://doi.org/10.1021/jasms.5c00092

Read Online



Stearic acid

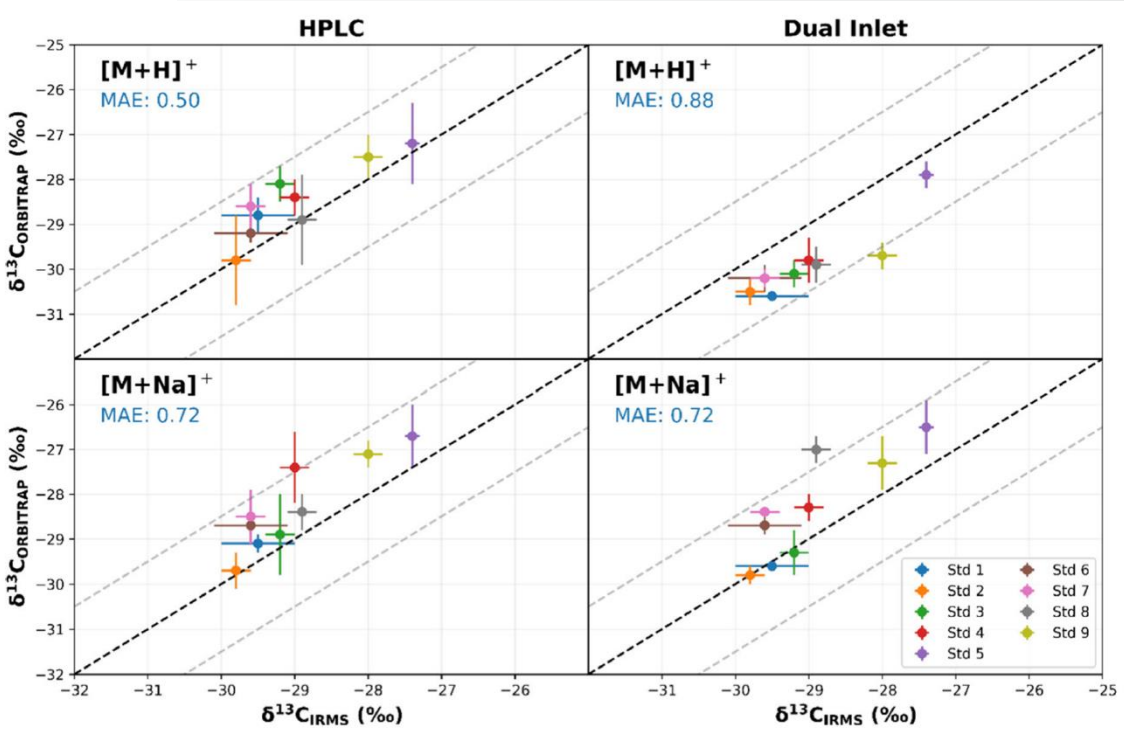


Figure 2. Comparison of $\delta^{13}C$ values for stearic acid methyl ester standards obtained using Dual Inlet and HPLC ESI-Orbitrap MS. $\delta^{13}C$ values for $[M + H]^+$ and $[M + Na]^+$ ions, showing deviations from the GC-C-IRMS measurements. Error bars represent standard deviations across replicates. Additionally, a summary of MAEs and average deviations for each ionization pathway are shown.

Organic Acid Review Paper

analytical chemistry

Open Access

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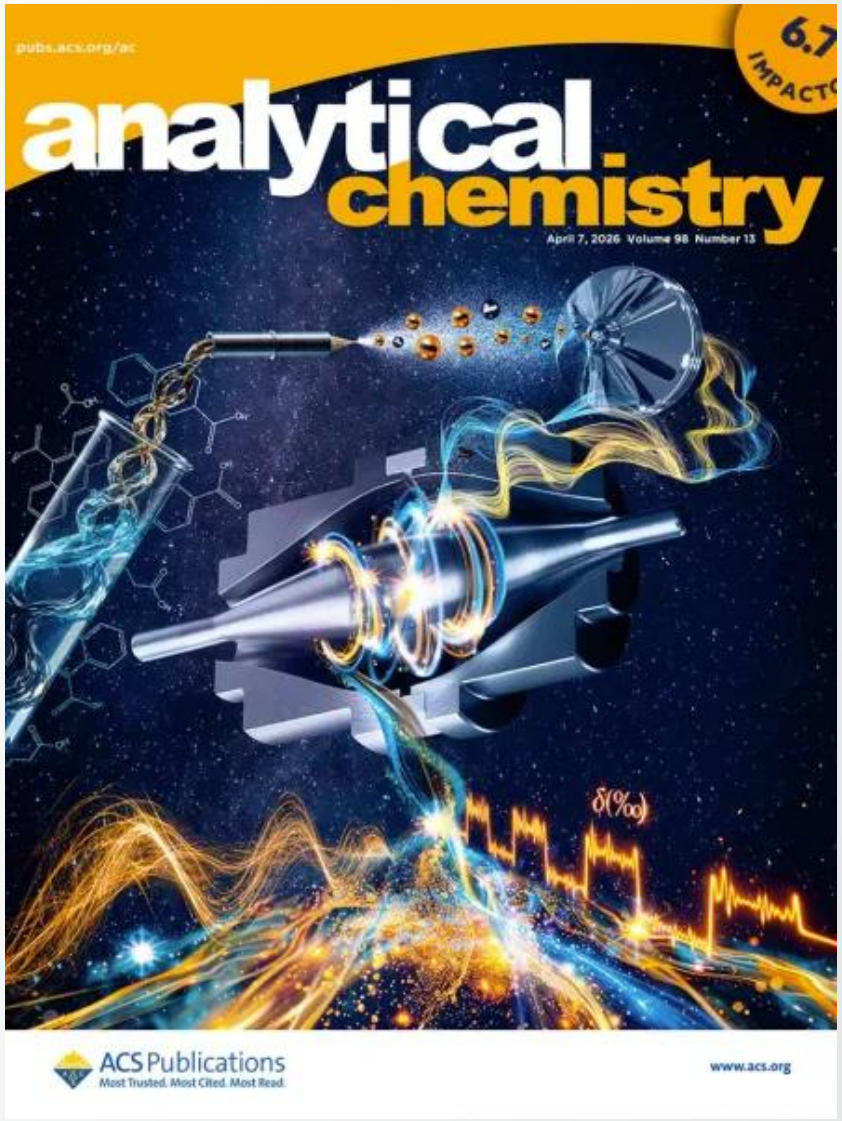
Lessons Learned in Orbitrap MS-Based Isotope Ratio Analysis of Organic Acid Mixtures

Hugo G. Machado,* Elliott P. Mueller, Júlio C. O. Ribeiro, Giovanni B. Bevilaqua, Gabriel F. dos Santos, Alexandre A. Ferreira, Ygor S. Rocha, Surjyendu Bhattacharjee, John M. Eiler, and Boniek Gontijo*

Cite This: *Anal. Chem.* 2026, 98, 9764–9775 Read Online



Neonicotinoids Fingerprinting

Journal of the American Society for Mass Spectrometry

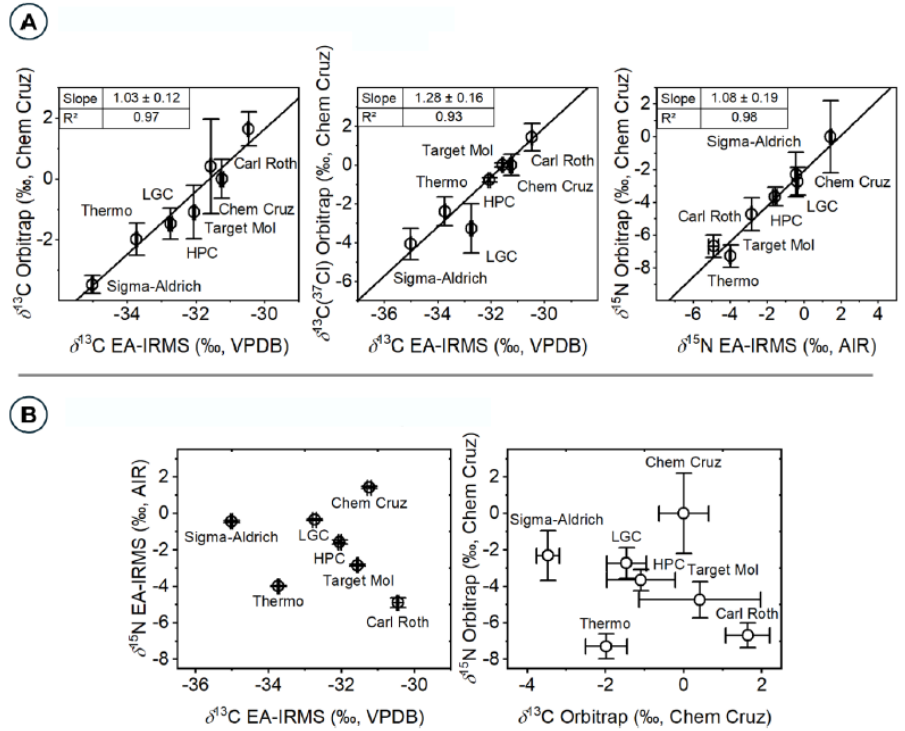
pubs.acs.org/jasms Article

Toward Molecular Forensics of Agrochemicals with Orbitrap IRMS: Isotopic Fingerprints of Imidacloprid Sources and Elucidating Hydrolysis

Felix Niemann, Nils J. Kuhlbusch, Annika Gruhlke, Sarah P. Rockel, Robert G. H. Marks, Klaus Kerpen, Milen Nachev, Maik A. Jochmann,* Andreas Hilkert, and Torsten C. Schmidt

Cite This: https://doi.org/10.1021/jasms.5c00444 Read Online

- Faster than LC-IRMS
- Gives multiple isotope ratios from a single analysis
- LOD is much lower than classical IRMS
- Might be able to build databases for complex molecules to fingerprint these compounds.



Perchlorate

analytical chemistry

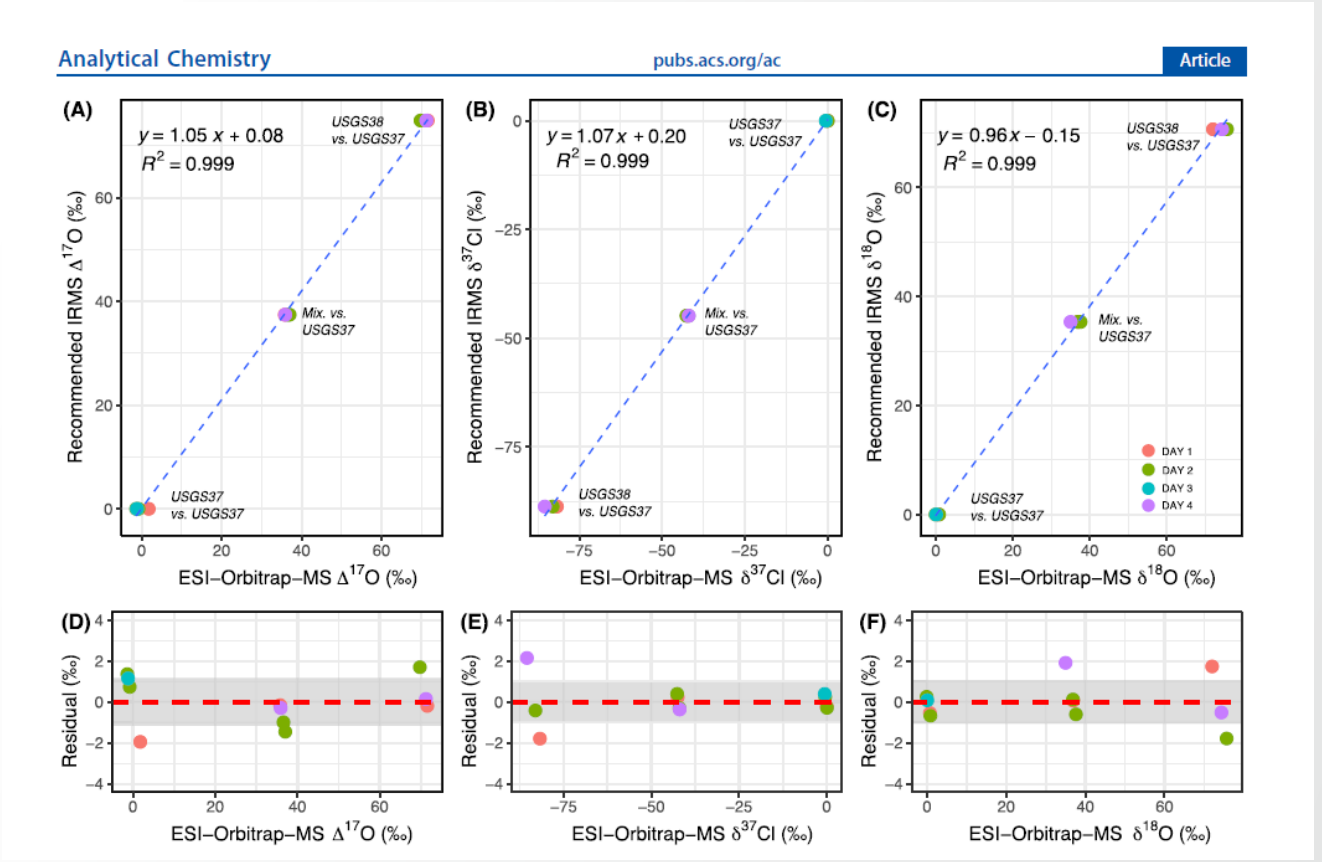
pubs.acs.org/ac Article

Sub-10 Nanomole Perchlorate $\delta^{37}Cl$, $\delta^{18}O$, and $\Delta^{17}O$ Measurements by ESI-Orbitrap-MS

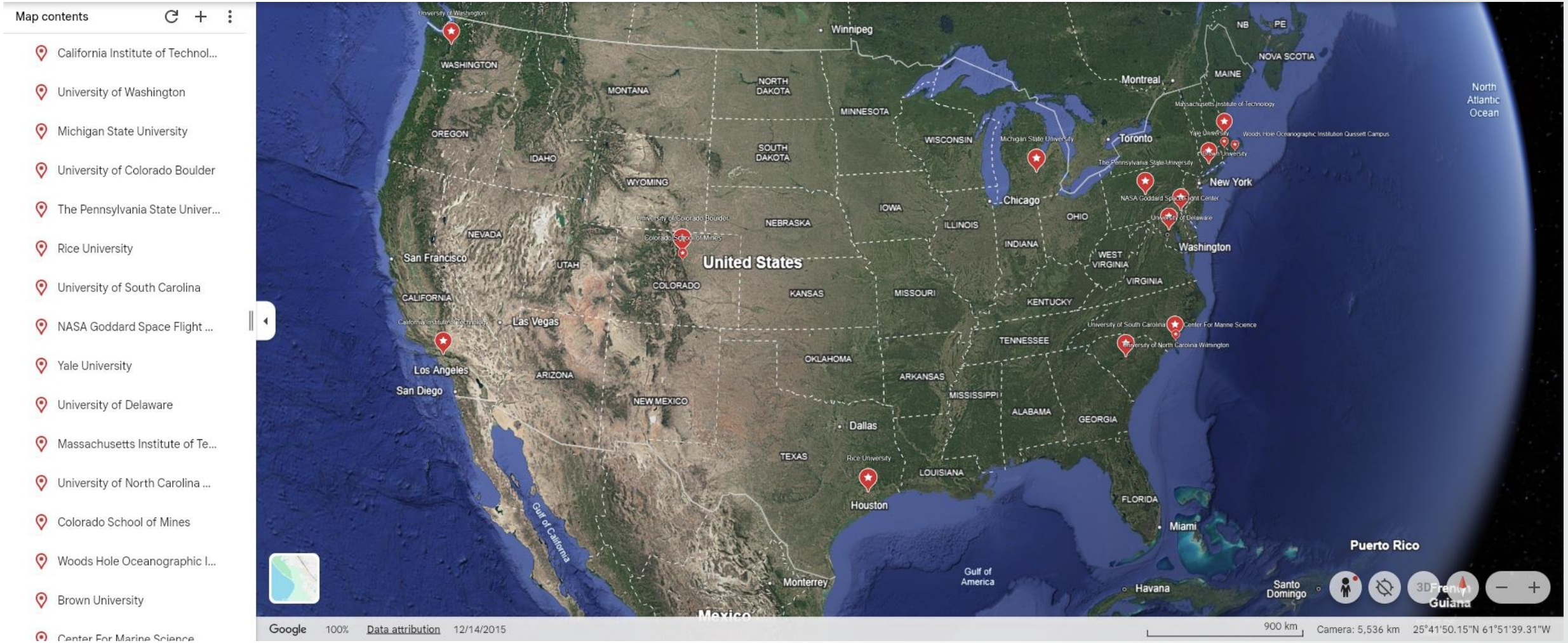
Longchen Zhu, Yihang Hong, Shohei Hattori, Zhenfei Wang, Zhao Wei, Yongbo Peng, Nils Johannes Kuhlbusch, and Huiming Bao*

Cite This: *Anal. Chem.* 2026, 98, 6034–6044 Read Online

- 4 orders of magnitude less sample than conventional IRMS!

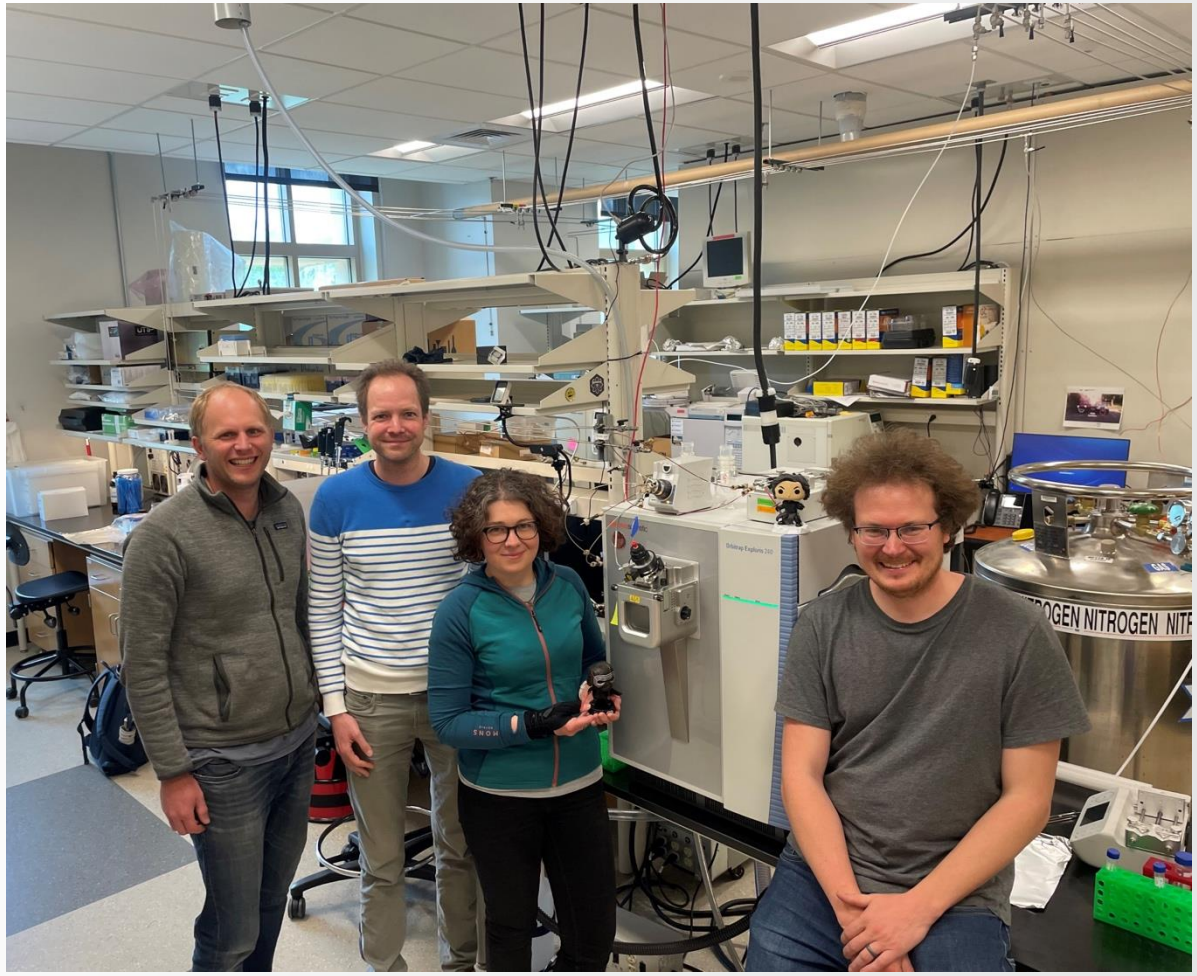


OEIS Systems in the US



Demo Lab at CU Boulder

- Orbitrap 240 with Vanquish Neo UHPLC
- Thermo Fisher: Brett Davidheiser
- PIs: Sebastian Kopf and Cajetan Neubauer
- Post Doc: Kristyna Kantnerova (now Assistant Prof at UCT Prague)



Thank you to our collaborators

Cajetan Neubauer and Kristýna Kantnerová for close collaboration and help

Joel Savarino, John K. Böhlke and Shohei Hattori for providing sample and reference materials

Thermo Fisher Scientific :
Kyle Fort
Konstantin Aizikov
Alexander Makarov
Uwe Rickens
Tabiwang Arrey
Colin Wirth
Christian Klaas
Charles Cartwright

John K. Böhlke
Stan Mroczkowski

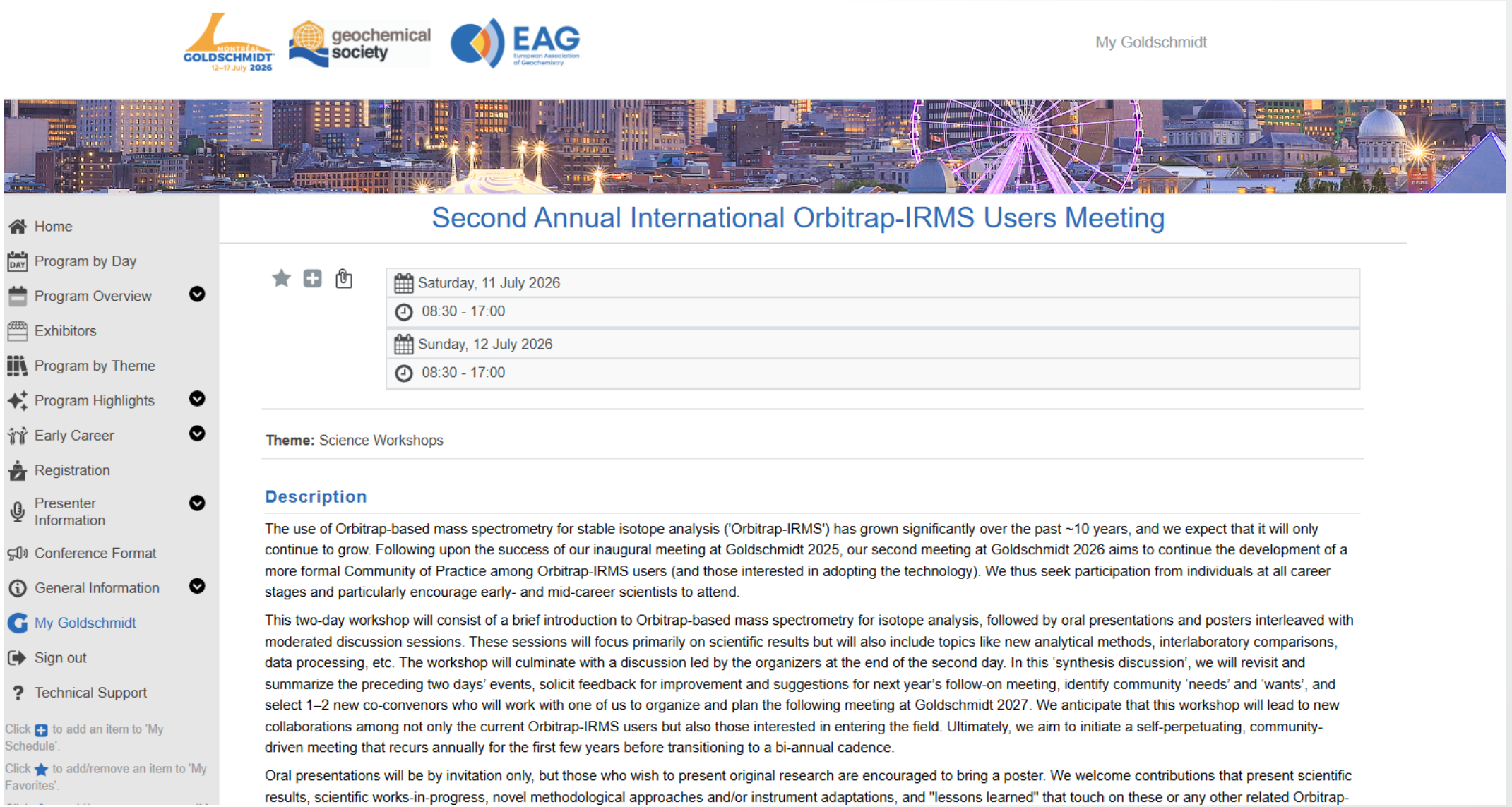
John Eiler
Nathan Dalleska

Sebastian Kopf

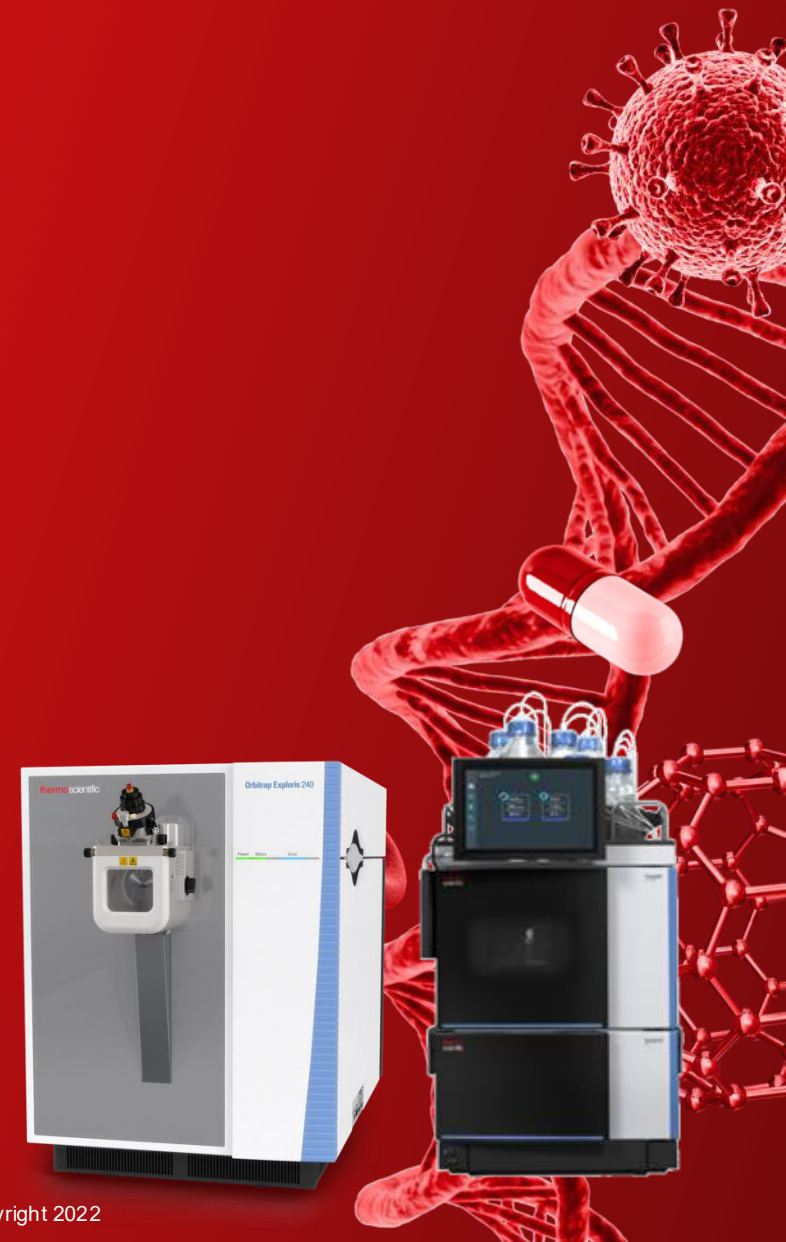
Xingchen Wang

Ralph Mead
Chad Lane
Paul Wojtal

2nd Annual User Meeting July 11th and 12th at Goldschmidt



Thank you



taylor.graham@thermofisher.com | 7 June 2026 | ASITA 2026

Other Things to Watch

ESI-Orbitrap-IRMS Analysis of Free Metabolites for Early Breast Cancer Detection and Insight into Metabolic Mechanisms

POSTER

Presented by Simon Andren

Wednesday, 9 July 2025

10:30 - 12:30

Exhibit and Poster Hall (2nd and 3rd Floors, Prague Congress Centre)

Subsession: 06i-P1 - Technological innovations and methodological advances in isotope geochemistry and isotope ratio mass spectrometry

Session: 06i - Technological innovations and methodological advances in isotope geochemistry and isotope ratio mass spectrometry

Theme: Theme 06: Frontiers in Analytical and Computational Techniques

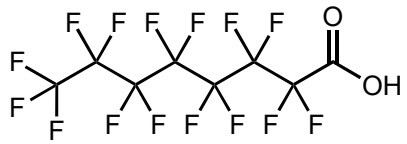
Abstract

Cancer cells rewire their metabolism as they proliferate, altering pathway activities and metabolite quantities. Isotopic analysis of metabolites in blood plasma could thus work as a non-invasive detection method and, in tissue, provide insight into the cancer metabolic network. Studies have shown cancerous cells to be ^{15}N-depleted and ^{13}C-enriched relative to adjacent non-cancerous cells[1]; however, primary isotopic anomalies occur at atomic sites undergoing bond-breaking and are not fully expressed in molecular average or bulk isotope analysis. With the advent of Orbitrap-IRMS, site-specific isotope analysis (SSIA) is now possible, which targets the atomic sites in the individual metabolites that experience the isotopic effect from the metabolically dysregulated reaction.

In this study, we focus on two metabolic hallmarks of breast cancer metabolism: the Warburg effect and glutamine addiction. We aim to determine whether SSIA of ^{13}C in free metabolites of Lactate and Alanine, and ^{15}N in free metabolites of Glutamine, and Arginine can serve as reliable biomarkers for breast cancer and whether specific isotopic patterns are unique for certain subtypes of breast cancer. Our approach involves three distinct stages: sample purification using reverse-phase HPLC and IC fraction collection, ESI-orbitrap-IRMS measurements, and data processing following the mathematical framework for isotomics. Preliminary quantification from the HPLC of these metabolites in the tissue samples reveals significant differences in cancerous versus adjacent healthy tissue, with cancerous tissues showing multi-fold higher concentrations, along with inter-cancer subtype variations. Using ESI-Orbitrap-IRMS, we achieve sub-permille accuracy on the molecular average for glutamine and approximately 1 permille accuracy for lactate on pure standards, verified by EA measurements. Future work will focus on sample purification and verifying the accuracy of SSIA before measuring biological samples. This study continues the work of SSIA on small quantities of polar organic molecules present in complex matrices. Reliable measurements of the intra-molecular isotopic fingerprints of these metabolites can provide valuable insight into the metabolic mechanisms that sustain cancer cell survival and can be used as a novel breast cancer diagnostic tool.

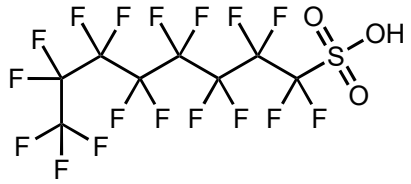
[1] Tea, I. *et al.* 13C and 15N natural isotope abundance reflects breast cancer cell metabolism. *Sci. Rep.* **6**, 34251 (2016)

PFAS



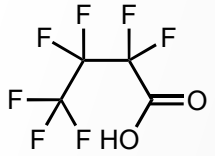
PFOA

Chemical Formula: $C_8HF_{15}O_2$
Exact Mass: 413.97370



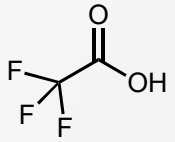
PFOS

1763-23-1
Chemical Formula: $C_8HF_{17}O_3S$
Exact Mass: 499.93749



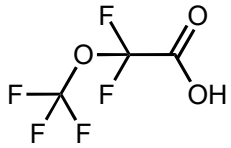
PFBA

Chemical Formula: $C_4HF_7O_2$
Exact Mass: 213.98648



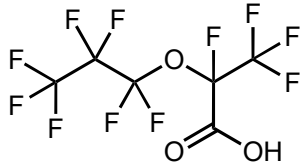
TFA

Chemical Formula: $C_2HF_3O_2$
Exact Mass: 113.99286



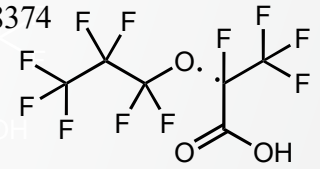
PFMOAA 674-13-5

Chemical Formula:
$C_3HF_5O_3$
Exact Mass: 179.98458

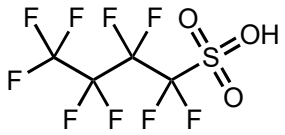


HFPO-DA
13252-13-6

Chemical Formula: $C_3F_7O^{\bullet}$
Exact Mass: 184.98374



Chemical Formula: $C_3HF_4O_2^{\bullet}$
Exact Mass: 144.99127



PFBS

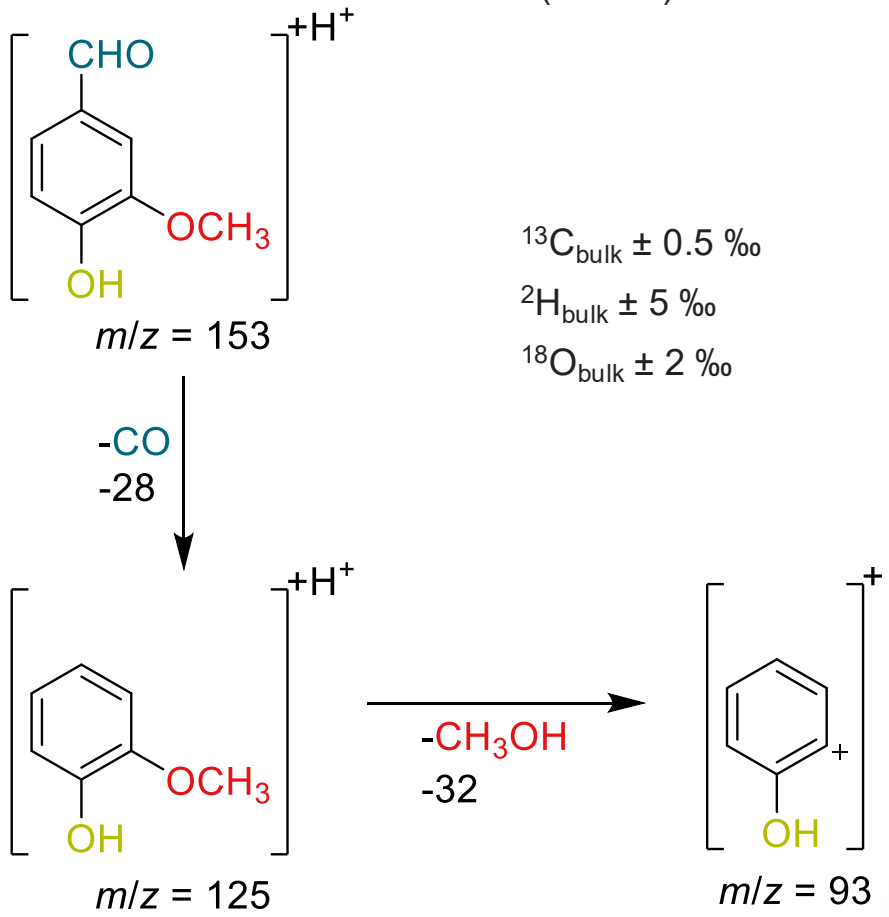
375-73-5
Chemical Formula: $C_4HF_9O_3S$
Exact Mass: 299.95027

HFPO-DA in-source fragmentation very common

Outlook: Position Specific Isotope Analysis (PSIA)

Vanillin

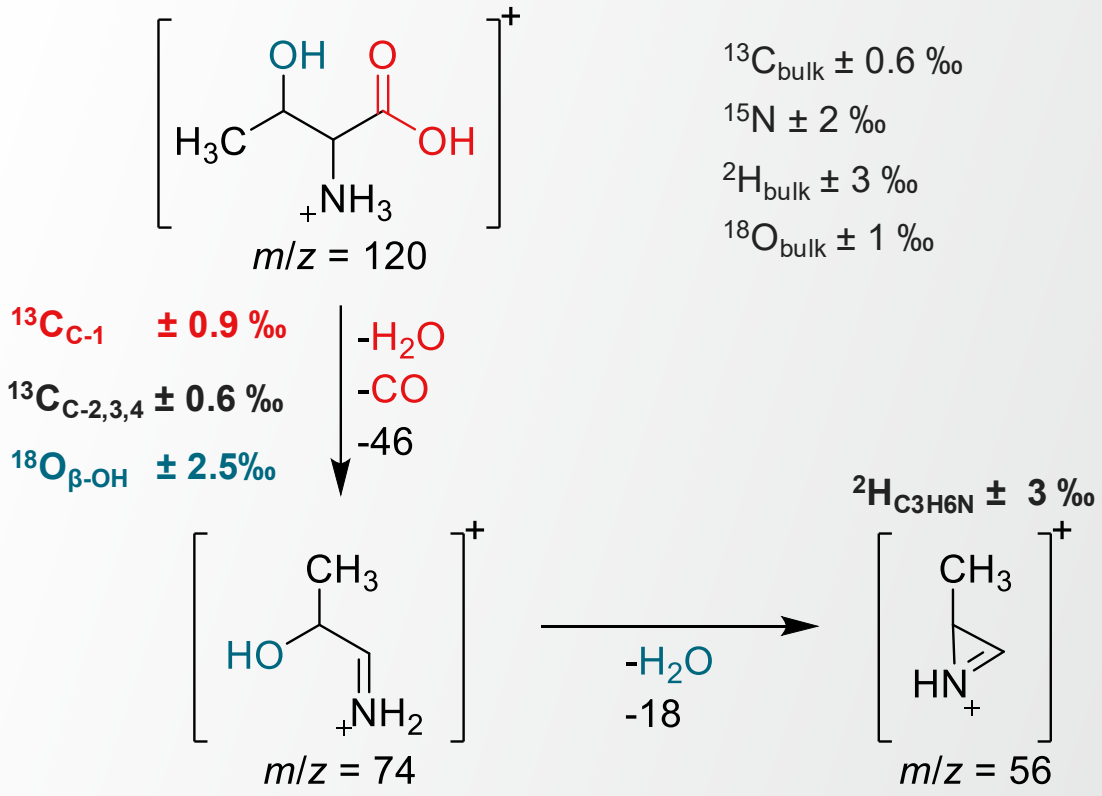
- Fragmentation pattern[6] defines PSIA targets
- Dual Inlet - Zero Enrichment (35 min)



$^{13}C_{bulk}$ ± 0.5 ‰
$^{2}H_{bulk}$ ± 5 ‰
$^{18}O_{bulk}$ ± 2 ‰

Threonine

- Fragmentation pattern [7] defines PSIA targets
- Dual Inlet - Zero Enrichment (24 min)



$^{13}C_{C\text{-}1}$ ± 0.9 ‰
$^{13}C_{C\text{-}2,3,4}$ ± 0.6 ‰
$^{18}O_{\beta\text{-}OH}$ ± 2.5‰

$^{13}C_{bulk}$ ± 0.6 ‰
^{15}N ± 2 ‰
$^{2}H_{bulk}$ ± 3 ‰
$^{18}O_{bulk}$ ± 1 ‰

$^{2}H_{C3H6N}$ ± 3 ‰

[6] Shen Y.; et al. J. Dairy Sci., 2014, 97, 679-686.
[7] Zhang P.; et al. Sci. Rep., 2019, 9, 6453.

Future Frontiers

- PFAS
- Online HPLC methods
- Glucose

Nils Kuhlbusch

Comprehensive IRMS of sulfates

- Dual Inlet experiment: Reference: S-3477 (Working Standard)
  Sample: S-MIF-1, S-MIF-2

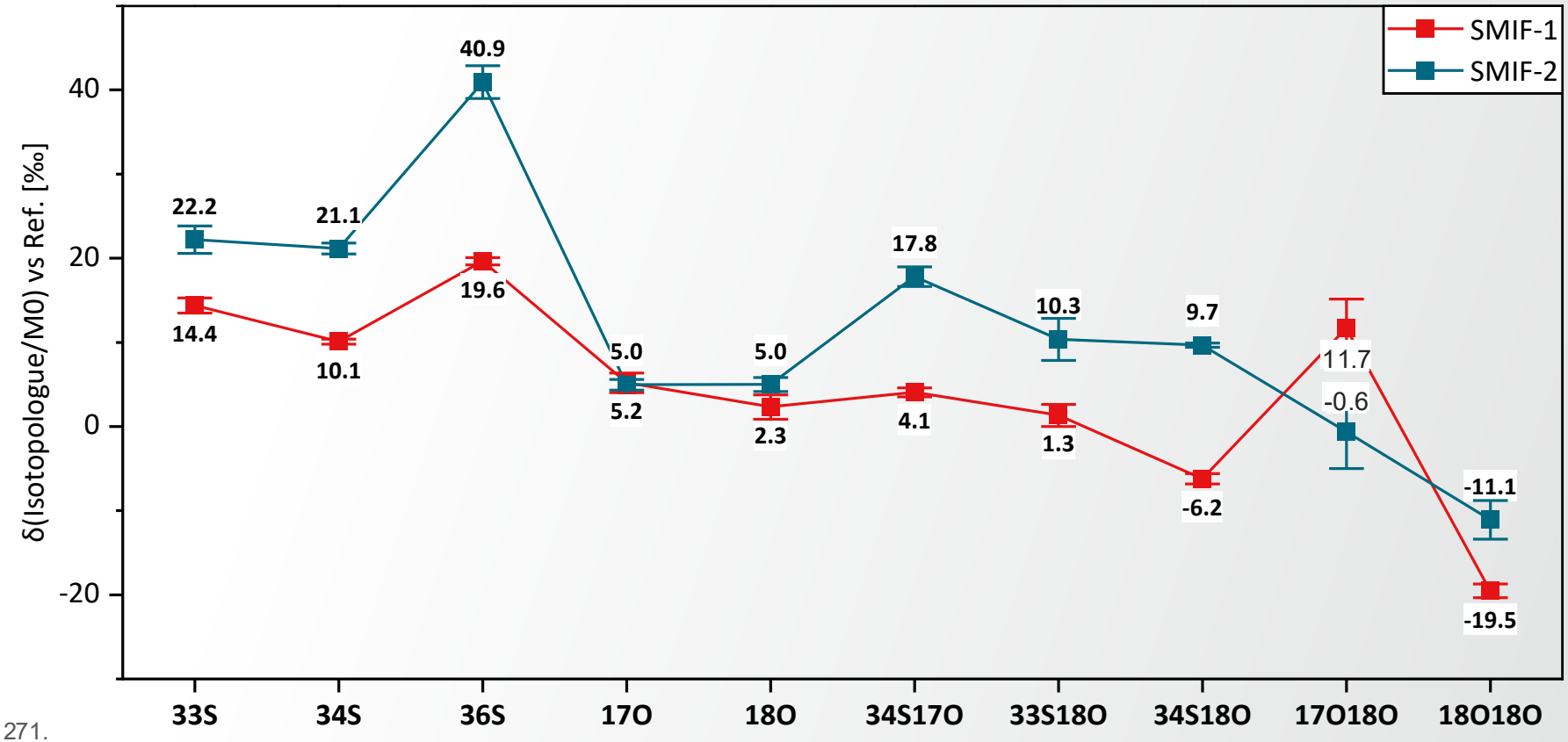
- Reported isotope data:[3]

S-3477 δ^{xx} [‰]		S-MIF1 δ^{xx} [‰]		S-MIF2 δ^{xx} [‰]	
33S	(3.33)	33S	**14.81**	33S	**22.42**
34S	**6.48**	34S	**10.26**	34S	**21.53**
36S	(12.35)	36S	**19.47**	36S	**40.73**
17O	(6.77)	17O	na	17O	na
18O	**13.02**	18O	na	18O	na
Δ33	na (0)	Δ33	**9.54**	Δ33	**11.39**
Δ36	na (0)	Δ36	**-0.14**	Δ36	**--0.33**
Δ17	na (0)	Δ17	**3.3**	Δ17	**3.3**

Böhlke, USGS

Samples provided by Joel Savarino
Institut des Géosciences de l'Environnement/CNRS

- Measured Isotope Data:

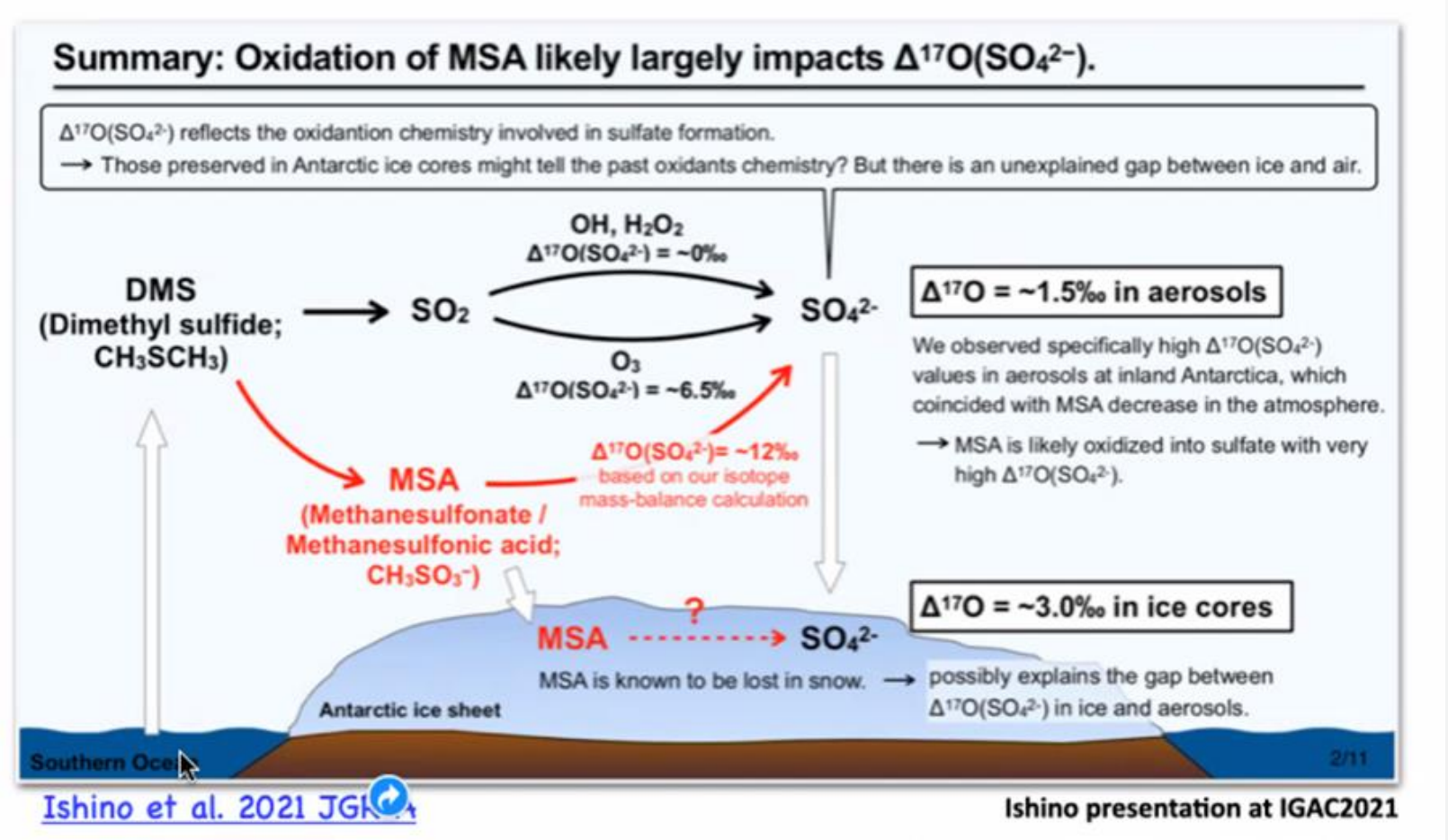


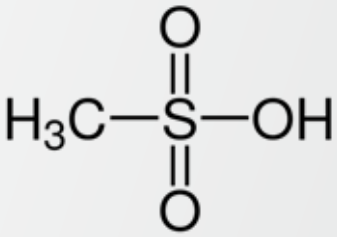
[3] Geng L.; et al. J. Anal. At. Spectrom., 2019, 34, 1263–1271.

Preliminary results - unpublished data

Comprehensive IRMS of methanesulfonic acid (MSA)

- Easy access to test new hypotheses



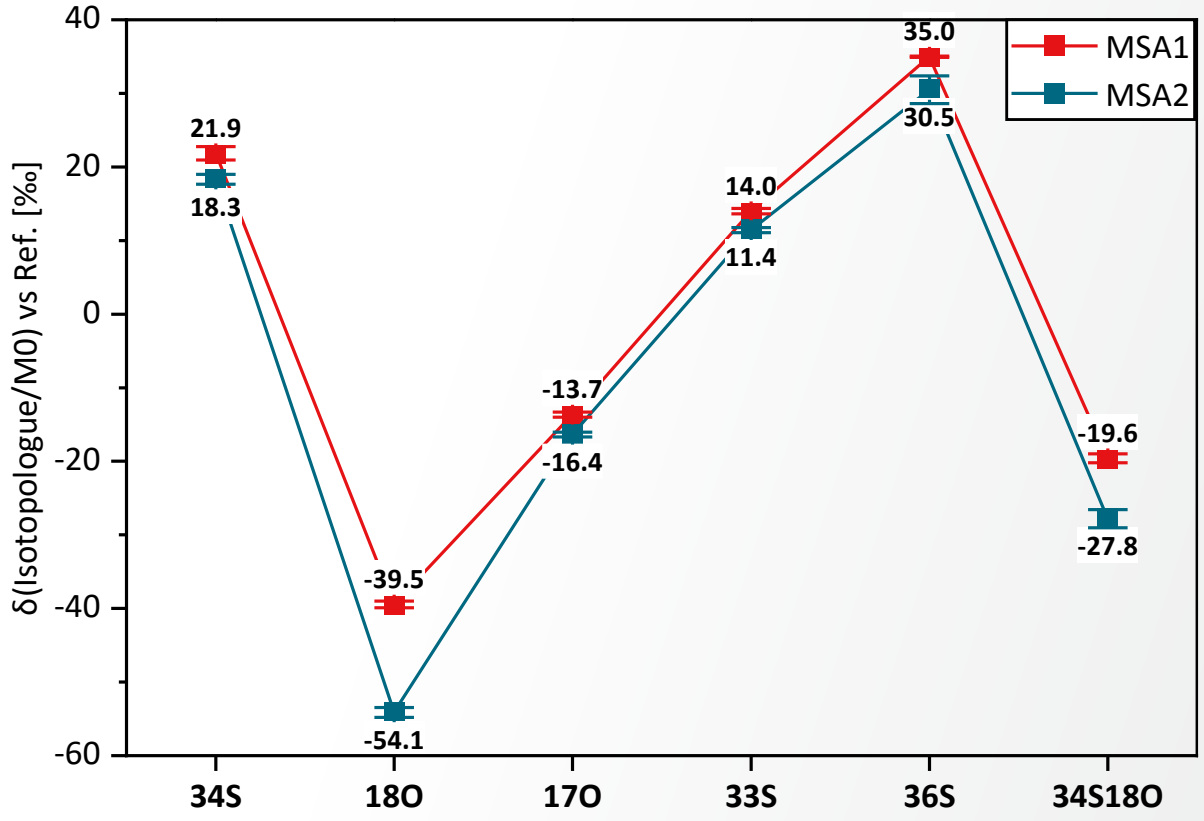


[4] Ishino S.; et al. J. Geophys. Res. Atmos., 2021, 126 (6).
[5] Wang K.; et al. Atmos. Chem. Phys., 2021, 21, 8357–8376.

Analysis of two MSA samples

‘noM0’ experiments:

- **Dual Inlet analysis** of two MSA samples vs a working standard (Sigma-Aldrich)
  - 3x70 min runs → error bars - st. dev. of the 3 runs



Samples provided by Shohei Hattori
Tokyo Tech & Nanjing

Preliminary results - unpublished data

Groundwater Sample Table

Table S2. Sample descriptions and isotopic data (non-Orbitrap).

Lab ID	Sample name	Sample type	NO3- δ15N per mil	NO3- δ18O per mil	NO3- δ17O per mil	NO3- Δ17O per mil	NO3- mM	Cl-/ NO3- M/M	SO4=/ NO3- M/M	Sample description
Reference materials										
USGS32	USGS32	KNO3 ref.	***180.0***	25.3	13.0	-0.2	n/a	n/a	n/a	Bohlke et al. (1993)
USGS34	USGS34	KNO3 ref.	***-1.8***	***-27.8***	-14.8	***-0.3***	n/a	n/a	n/a	Bohlke et al. (2003)
USGS35	USGS35	NaNO3 ref.	2.7	***56.8***	51.1	***21.6***	n/a	n/a	n/a	Bohlke et al. (2003)
N11	N11	KNO3 ref.	3.6	26.3	13.5	***-0.2***	n/a	n/a	n/a	
Desert salts										
N-14362	Atacama	soil leachate	0.0	55.1	49.8	21.2	43.9	1.87	1.53	Jackson et al. (2010)
N-13315	Death Valley	soil leachate	3.5	24.2	20.7	8.1	56.6	n/a	n/a	Jackson et al. (2010)
N-14685	Death Valley	soil leachate	-0.8	34.3	30.8	13.0	23.7	13.9	2.29	Jackson et al. (2010)
N-16854	Namibia	brine	9.1	28.6	21.0	6.1	35.8	103	2.05	Jackson et al. (2015)
N-17499	Antarctica	soil leachate	-16.2	82.5	74.5	31.6	86.4	n/a	n/a	Jackson et al. (2015)
N-13825	UAE sabkha	brine	10.6	32.2	25.5	8.7	173.0	40.3	0.02	Jackson et al. (2015)
Fresh groundwater										
N-13993	New Mexico	groundwater	6.8	0.7	0.4	0.1	0.52	33.1	20.1	Jackson et al. (2010)
N-17008	California	groundwater	7.7	3.6	3.3	1.4	1.04	0.36	0.22	Izbicki et al. (2015)
N-13819	New York	groundwater	7.3	3.5	1.8	0.0	0.50	0.63	0.50	Bohlke et al. (2009)
N-10177	Maryland	groundwater	2.7	1.5	0.8	0.0	1.26	0.30	0.19	Bohlke and Denver (1995)
Reference materials as AgNO3										
N-15038-Ag	USGS34	AgNO3 ref.	-2.0	-27.9	-14.9	-0.3	n/a	n/a	n/a	Bohlke et al. (2003)
N-15039-Ag	USGS35	AgNO3 ref.	2.5	56.0	50.7	21.6	n/a	n/a	n/a	Bohlke et al. (2003)
N-15037-Ag	N11	AgNO3 ref.	3.3	25.6	13.1	-0.2	n/a	n/a	n/a	
Desert salts as AgNO3										
N-14362-Ag	Atacama	AgNO3	-0.2	54.3	49.4	21.2	n/a	n/a	n/a	Jackson et al. (2010)
N-13315-Ag	Death Valley	AgNO3	2.9	23.1	20.1	8.1	n/a	n/a	n/a	Jackson et al. (2010)
N-14685-Ag	Death Valley	AgNO3	-0.6	33.0	30.2	13.0	n/a	n/a	n/a	Jackson et al. (2010)
N-16854-Ag	Namibia	AgNO3	8.8	27.2	20.3	6.1	n/a	n/a	n/a	Jackson et al. (2015)
N-17499-Ag	Antarctica	AgNO3	-16.4	80.8	73.6	31.6	n/a	n/a	n/a	Jackson et al. (2015)
N-13825-Ag	UAE sabkha	AgNO3	10.3	31.3	25.0	8.7	n/a	n/a	n/a	Jackson et al. (2015)
Fresh groundwater as AgNO3										
N-13993-Ag	New Mexico	AgNO3	6.5	0.7	0.5	0.1	n/a	n/a	n/a	Jackson et al. (2010)
N-17008-Ag	California	AgNO3	7.6	3.3	3.1	1.4	n/a	n/a	n/a	Izbicki et al. (2015)

[2] Hilkert, A.; et al. Anal. Chem. 2021, 93, 9139−9148, SI Table.

10 reasons to use Orbitrap Exploris Isotope Solutions

10 reasons to use Orbitrap Exploris Isotope Solutions

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Intramolecular isotopic information is important as it can provide a better understanding of the processes of molecule formation and provide new geochemical proxies for understanding the world around us. Current technology for deriving intramolecular isotopic information is restricted either by large sample sizes, long analysis times or limited applicability across a range of sample types. The powerful, new Thermo Scientific™ Orbitrap Exploris™ Isotope Solutions for natural abundance isotope ratio analysis opens new dimensions for deriving intramolecular isotopic information. Explore why!

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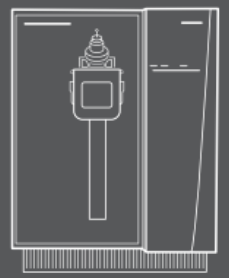
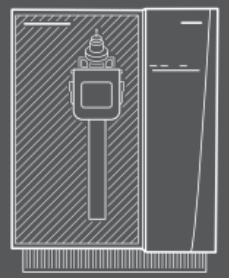
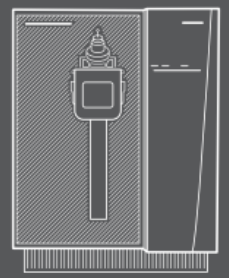


Thermo Scientific™ Orbitrap Exploris™ 120 MS: the ultimate workhorse for isotope ratio analysis of oxyanions and small organic molecules (<100 *m/z*)



Thermo Scientific™ Orbitrap Exploris™ 240 MS: the instrument of choice for isotope ratio analysis of oxyanions and medium sized organic molecules (<200 *m/z*)



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4 **Direct measurements of individual analytes in liquid samples** without chemical derivatization or conversion

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7 **Extraction of accurate isotopic information from singly- and multi-substituted isotopologues** utilizing methodology for amplifying signals from minor isotopologues

8 **Position specific isotope information from functional groups** through controlled fragmentation of molecular ions

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