Quantification and Isomer Differentiation of PFAS at ppb/ppt Levels using MALDI-TOF with Trapped Ion Mobility

Aidan Reynolds (reyno569@msu.edu),[1] Abby Smith (smit3178@msu.edu),[1] Tian (Autumn) Qiu (qiutian8@msu.edu)[1]

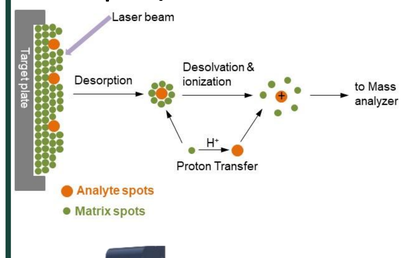
[1]Department of Chemistry, Michigan State University, East Lansing, MI 48824, USA

Introduction

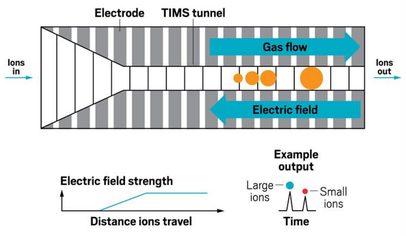
- ❖Poly- and perfluoroalkyl substances (PFAS) are a class of organic compounds that are regarded worldwide as environmental contaminants.[1]
- ❖There is an urgent need to quantify and characterize PFAS in various matrices to understand their adverse health effects.
- ❖Current efforts have been centered around liquid chromatography tandem mass spectrometry, which requires extensive sample preparation, require longer times of analysis and are prone to contamination.[2]
- ❖Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) is a versatile technique capable of analyzing the distribution of PFAS in plant and animal tissues to correlate localization of PFAS to their mechanisms of toxicity, with minimal contamination risks.[3]
- ❖Coupling MALDI-TOF MS with trapped ion mobility spectrometry (TIMS) allows for differentiation of structural isomers present in the environment by separation of chemical shape in addition to size, and charge.[4,5]
- ❖Utilizing MALDI-TOF MS with TIMS, we developed and optimized an alternative mass spectrometry method for PFAS analysis

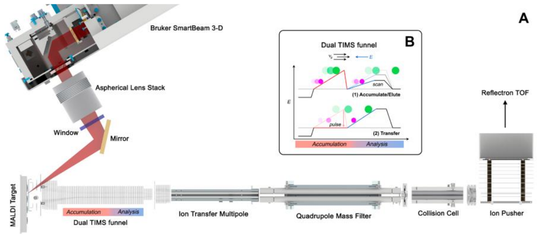
Experimental Methods

Matrix-assisted laser desorption/ionization mechanism



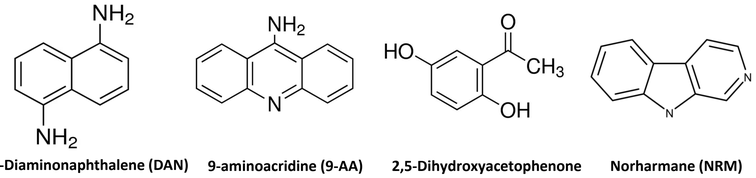
Trapped ion mobility spectrometry





Bruker timsTOF fleX

Bruker timsTOF fleX ion flight path schematic



1,5-Diaminonaphthalene (DAN) **9-aminoacridine (9-AA)** **2,5-Dihydroxyacetophenone** **Norharmane (NRM)**

❖ Names and structures of all chemical matrices used in method development and optimization

Results: Matrix Screening

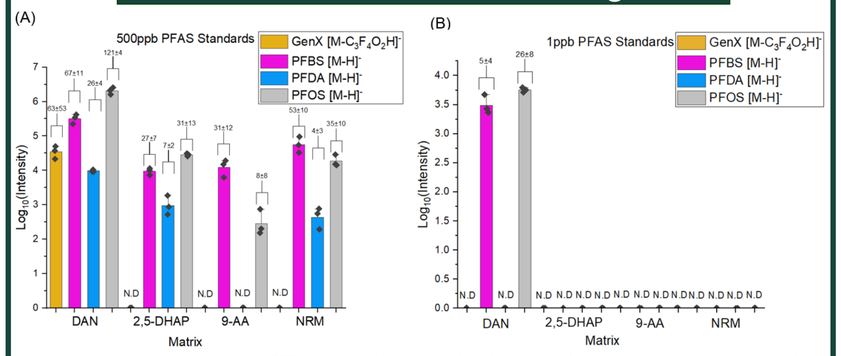
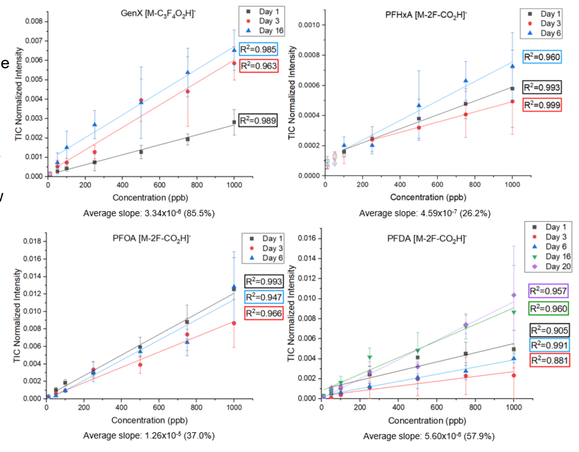


Figure 1. Matrix screening for (A) 500 ppb and (B) 1 ppb of PFAS solution. Different colored bars represent the average signal intensities of ions from a specific PFAS, and solid diamonds indicate individual data points (n=3). Error bars represent standard deviation. Numbers above each bar indicate the S/N ratio of the signal of interest from raw spectra (average ± SD). Regions labeled N.D represent nondetectable signals with S/N<3. The Y-axis is plotted in logarithmic scale.

Results: PFAS Quantitation and Detection

Figure 2. Parts per billion calibration curves for PFCAs. Data points represents average normalized intensity from the five replicates in each experiment, and error bar represents standard deviation. Solid shapes indicate data points with average S/N of raw spectra over 10 and used for linear regression of calibration curves. Hollow shapes represent detectable data points with S/N less than 10 and not included for linear regression. Averages and RSD% for multi-day TIC normalized slopes are presented below each calibration curve.



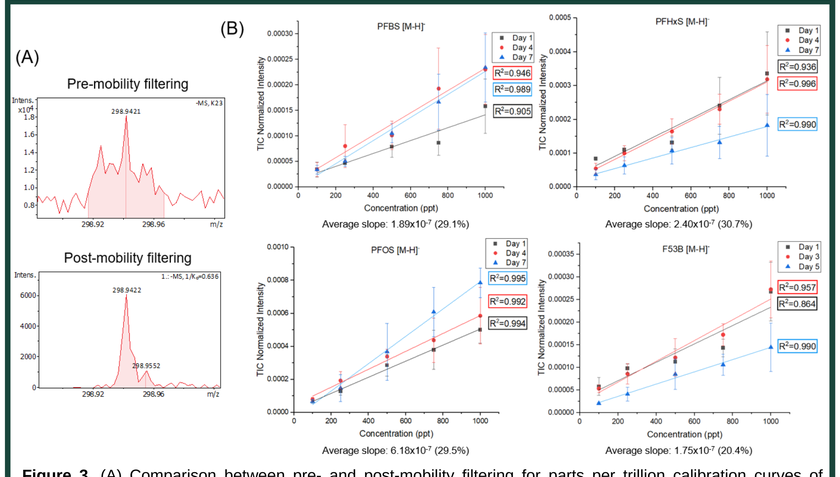


Figure 3. (A) Comparison between pre- and post-mobility filtering for parts per trillion calibration curves of PFSAs. (B) Parts per trillion calibration curves for PFBS, PFHxS, PFOS and F53B. Data points represents average normalized intensity from the five replicates in each experiment, and error bar represents standard deviation. Solid shapes indicate data points with average S/N of raw spectra over 10 and used for linear regression of calibration curves. Hollow shapes represent data points with S/N less than 10 and not included for linear regression. Averages and RSD% for multi-day TIC normalized slopes are presented below each calibration curve.

Results: PFAS Isomer Differentiation

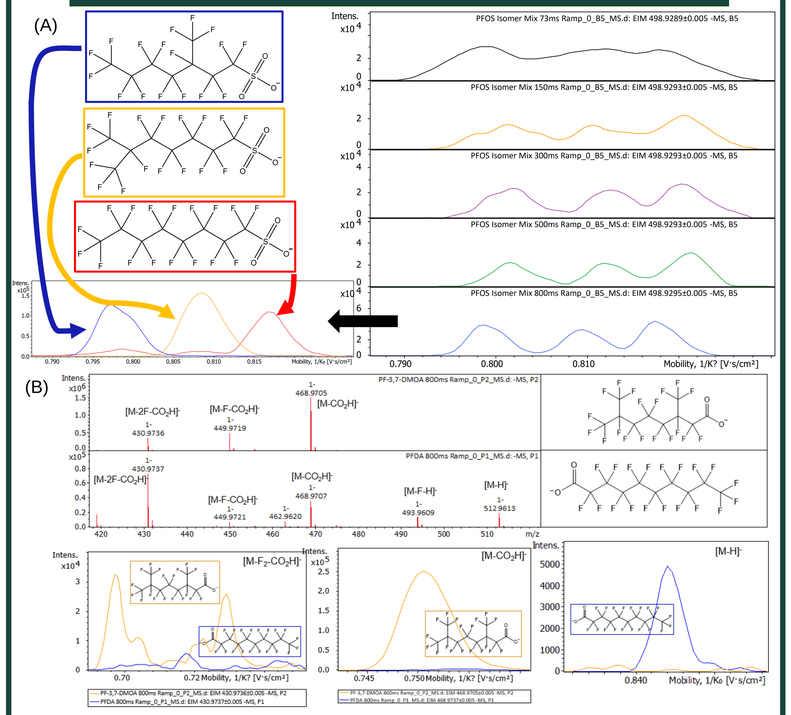


Figure 4: Differentiation of perfluorooctane sulfonic acid structural isomers (A) and perfluorodecanoic acid (B) by trapped ion mobility spectrometry. TIMS was capable of differentiating PFOS isomers, but due to differences in fragmentation pattern and intensity, TIMS was not applicable for PFDA isomers.

Conclusions

- ❖ We present a high-throughput alternative method of PFAS analysis capable of parts per billion quantitation and detection of PFCAs and parts per trillion detection and quantitation of PFSAs in fluid matrices.
- ❖ We firstly demonstrated isomer differentiation utilizing TIMS for perfluorooctane sulfonic acid structural isomers
- ❖ Differences in fragmentation patterns of PFCAs prevents usage of TIMS for isomer differentiation. These fragmentation patterns should be used as “diagnostic fragment” intensities for isomer differentiation
- ❖ These results demonstrate a significant advancement for mass spectrometry imaging applications for mapping the accumulation and distribution of PFAS in biological tissues

Acknowledgements

This work was supported by startup funding from Michigan State University and a Starter Grant from the Society of Analytical Chemists of Pittsburgh awarded to Dr. Tian (Autumn) Qiu

References

1. Fenton, S. E., *et al.,* Per- and Polyfluoroalkyl Substance Toxicity and Human Health Review: Current State of Knowledge and Strategies for Informing Future Research. *Environ Toxicol Chem* **2021**, *40* (3), 606–630.
2. Dodds, J. N., *et al.,* Rapid Characterization of Per- and Polyfluoroalkyl Substances (PFAS) by Ion Mobility Spectrometry–Mass Spectrometry (IMS-MS). *Anal. Chem.* **2020**, *92* (6), 4427–4435.
3. Yang, C., *et al.,* In Situ Detection and Imaging of PFOS in Mouse Kidney by Matrix-Assisted Laser Desorption/Ionization Imaging Mass Spectrometry. *Anal. Chem.* **2019**, *91* (14), 8783–8788.
4. Arnaud, C. H. Resolving Power for the people: Ion mobility-mass spectrometry expands its offerings. C&EN 2022, Volume 98 Issue 20.
5. Spraggins, J. M.; Djambazova, et al. High-Performance Molecular Imaging with MALDI Trapped Ion-Mobility Time-of-Flight (TimsTOF) Mass Spectrometry. *Anal. Chem.* **2019**, *91* (22), 14552–14560.