Novel approaches for rapid and informative exposure analyses of environmental samples and mixtures

Erin S. Baker, Xueyun Zheng, Noor A. Aly, Kristin E. Burnum-Johnson, Matthew E. Monroe, and Richard D. Smith
Biological Sciences Division, Pacific Northwest National Laboratory, Richland, WA,

INSERT DEPARTMENT / COLLEGE LOGO

Overview

- Rapid and highly sensitive small molecule measurements are not possible to date for untargeted studies
- Measurements using ion mobility spectrometry combined with mass spectrometry (IMS-MS) are both rapid (<1 s) and highly sensitive
- To date, small molecule information for IMS-MS is sparse
- An IMS-MS small molecule database was created using >500 small molecule standards enabling rapid screening of biological and environmental samples

Introduction

- The confident identification of metabolites and xenobiotics in biological and environmental studies is an analytical challenge due to their immense dynamic range, vast chemical space and structural diversity.
- IMS is widely used for small molecule analyses since it can separate isomeric species and be easily coupled with front end separations and mass spectrometry for multidimensional characterizations. However, to date IMS metabolomic and exposomic studies have been limited by an inadequate number of accurate collision cross section (CCS) values for small molecules, causing features to be detected, but not confidently identified.
- In this work, we utilized drift tube IMS (DTIMS) to directly measure CCS values for >500 small molecules including primary metabolites, secondary metabolites and xenobiotics. This CCS database and structural information are freely available for download at http://panomics.pnnl.gov/metabolites/ with new molecules being added monthly [1].

Methods

The standards were characterized with an Agilent 6560 IMS-QTOF MS platform (Figure 1). All measurements were performed in triplicate in both positive and negative polarities with nitrogen gas and seven different electric fields, allowing the assessment of structural differences and relative standard deviations for each molecule [2].

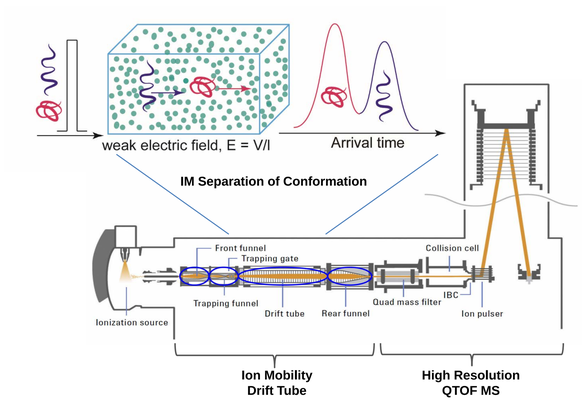
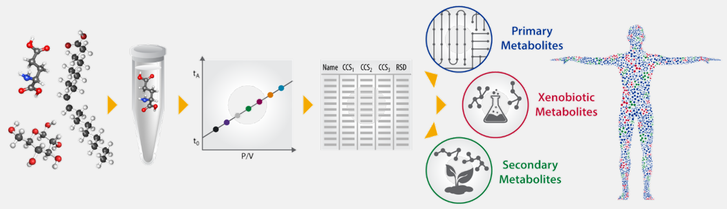


Figure 1. Schematic of an IMS separation and the Agilent 6560 IMS-QTOF MS platform

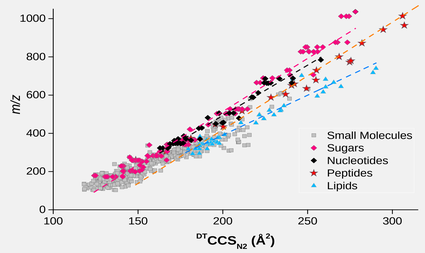
Results

1. Development of a large scale DTIMS CCS database for metabolites and xenobiotics

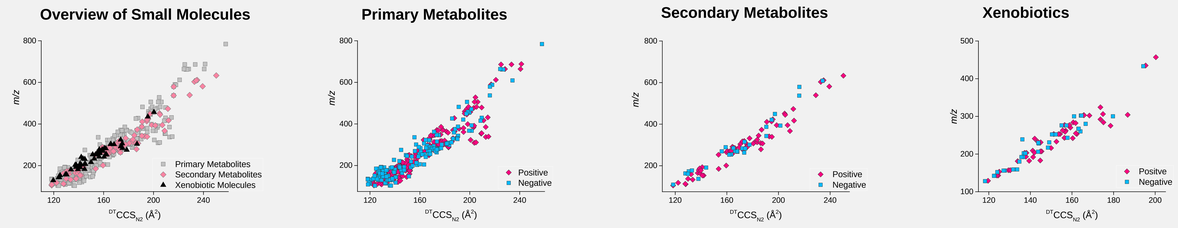
Workflow for developing a DTIMS CCS database



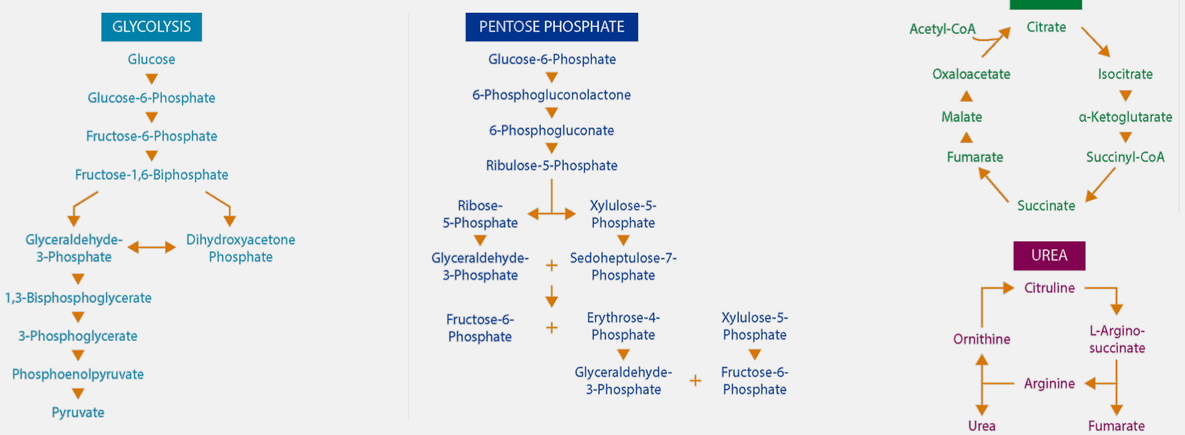
Resulting DTIMS CCS database



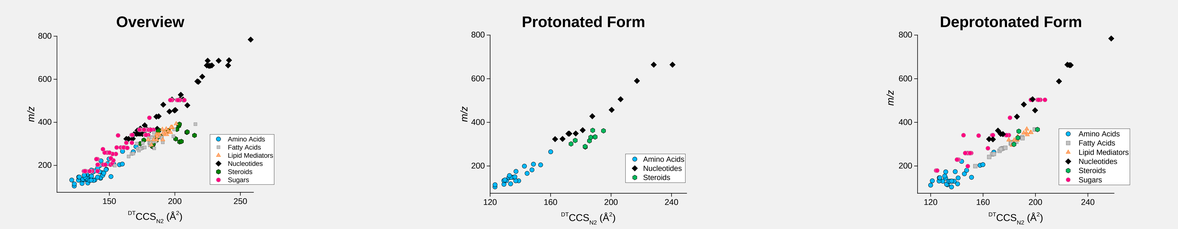
DTIMS CCS of metabolites and xenobiotics



Mapping CCS values for molecules from metabolic pathways

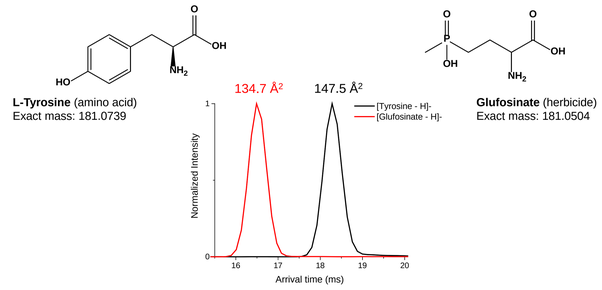


CCS trend lines for different classes of primary metabolites

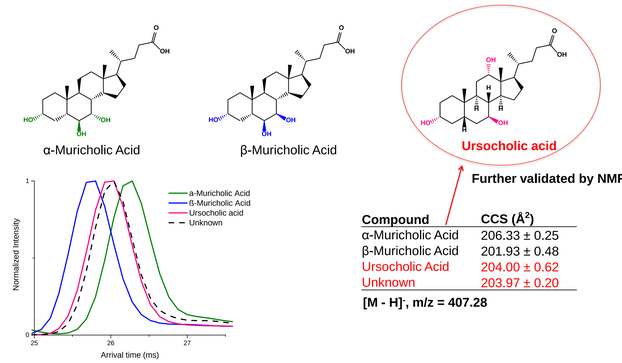


2. Application of the CCS database to small molecule studies

Increasing identification confidence using CCS information



Isomer separation and Identification of unknown bile acid



Compound	CCS (Å^2)
α-Muricholic Acid	206.33 ± 0.25
β-Muricholic Acid	201.93 ± 0.48
Ursocholic Acid	204.00 ± 0.62
Unknown	203.97 ± 0.20

[M - H]$^-$, m/z = 407.28

Conclusions

- A large-scale IMS-MS database for metabolites and xenobiotics was developed
- Adding IMS structural information to MS measurements increased the confidence of small molecule identifications
- This database enables the rapid screening of environmental and biological samples

Acknowledgements

This research were supported by grants from the National Institute of Environmental Health Sciences of the NIH (R01ES022190), National Institute of General Medical Sciences (P41 GM103493), NIH (P42 ES027704), and the Laboratory Directed Research and Development Program at PNNL. The work was performed in the W. R. Wiley Environmental Molecular Sciences Laboratory (EMSL), a DOE national scientific user facility at PNNL operated by Battelle under contract DE-AC05-76RL01830.

References

1. X. Zheng et al. *Chemical Science*, **2017**, DOI: 10.1039/c7sc03464d
2. S. M. Stow, *Analytical Chemistry* **2017**, 89, 9048-9055

CONTACT: Erin Baker, Ph.D.
Biological Sciences Division
Pacific Northwest National Laboratory
E-mail: erin.baker@pnnl.gov

www.omics.pnl.gov