Bio-Molecule Characterization Using a Novel Ion Mobility Orbitrap Mass Spectrometer

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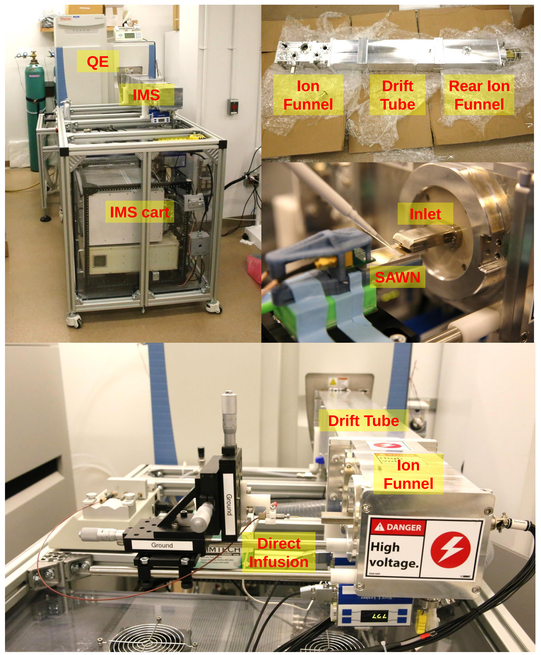
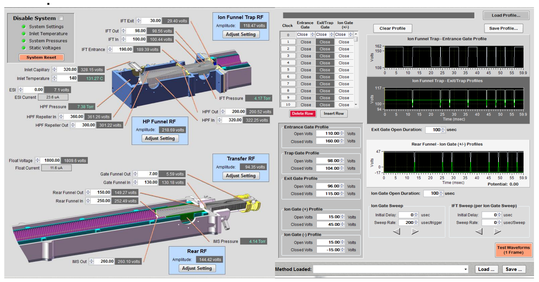
Introduction

Drift time - ion mobility spectrometry (DT-IMS) can offer improved resolving power compared to other classes of mobility separation systems. When coupled with mass spectrometry, IMS provides structural characterization with an added dimension of ion separation. Orbitrap mass spectrometers offer high mass resolution and accuracy that are widely used in biochemical studies. We have bridged the gap between DT-IMS (capable of operating >100Hz) and orbitrap (operating at around 1-10 Hz) capabilities and reported on a novel analytical system. We have expanded its applicability to intact proteins and a novel ionization method, surface acoustic wave nebulization (SAWN) been successfully coupled with IMS orbitrap.

All experiments were performed with a bespoke IMS instrument (Spectroglyph, Kennewick, WA) coupled to a QExactive orbitrap mass spectrometer (ThermoFisher, San Jose, CA) using nanoESI and/or surface acoustic wave nebulization (SAWN). The IMS incorporates an interface for orthogonal ion injection, followed by an ion funnel trap, a drift tube and an IMS Exit Gate. In each IMS experiment, 2^{N-1} ion packets are injected based on a pseudo-random sequence of N-bits. The same waveform is applied to the IMS Exit Gate but shifted sequentially in time. At each delay step, orbitrap mass spectra are acquired and the acquired multiplexed spectra are then inverse-transformed to reconstruct the original data vector.



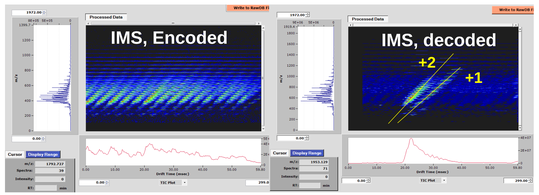
Instrument Layout & Control Software



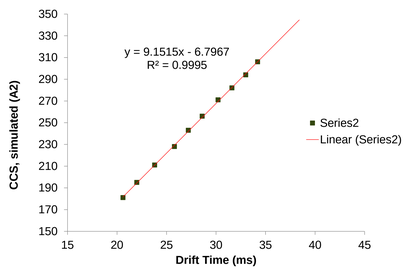
A) Ion Mobility Spectrometer (IMS) layout as shown in Graphical User Interface (GUI) of the instrument control software. B) Experimental sequences used for encoding raw data with Ion Mobility Spectrometer (IMS) coupled to Q Exactive mass spectrometer.

Results

Polyalanine IMS

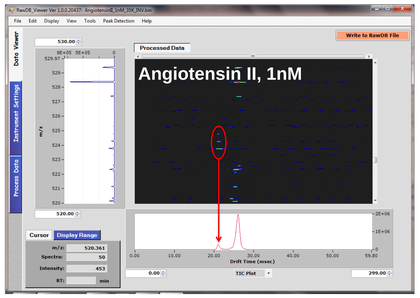


Polyalanine Drift Time vs. CCS Simulation

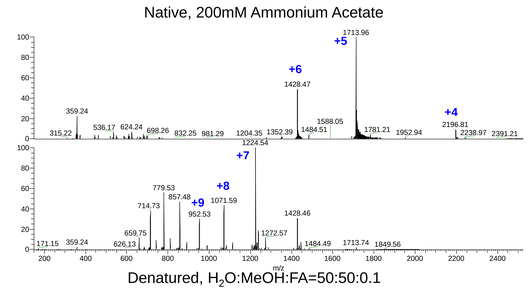


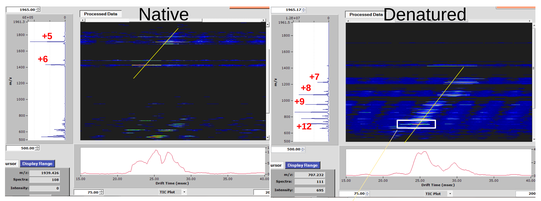
Simulated values are from Bush et al., Anal. Chem. 2012, *84*, 7124-7130.

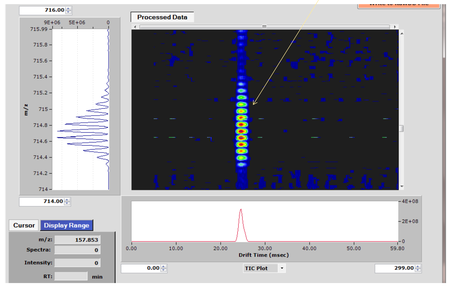
Limit of Detection



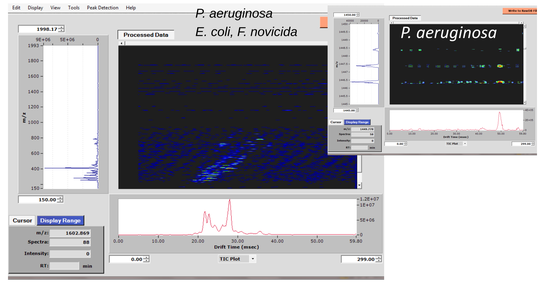
Ubiquitin IMS



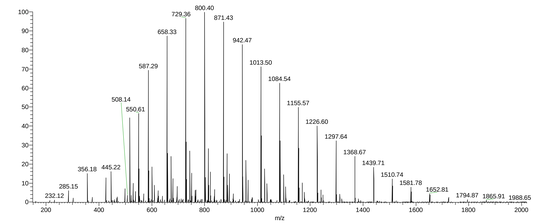


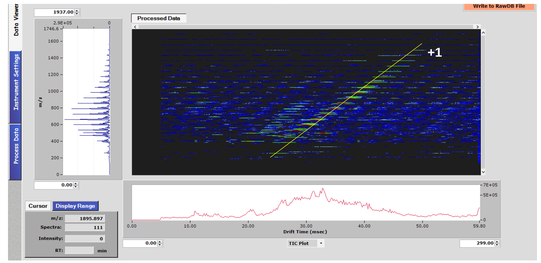


Lipid A Mixture



SAWN IMS - Polyalanine





Conclusions

- High performance Ion Mobility Spectrometer has been designed, integrated with a Q Exactive
- IMS-QE validated with a variety of biochemical samples
- IMS-HCD offered additional dimension
- SAWN could be coupled IMS-QE

Acknowledgments

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*DRG has a significant financial interest in Deurion.

Presentations from Goodlett and Ernst Laboratories

MP372 Bio-Molecule Characterization Using a Novel Ion Mobility Orbitrap Mass Spectrometer
MP440 Autopiquer – Introducing a New Approach to High Confidence Peak Detection, David Kilgour
MP712 Top-Down Mass Spectrometry Applications for Detection of N-Terminal Sequence Heterogeneity and PTMs for a Therapeutic Molecule

TOF pm 02:30 Absorption Mode Processing of MALDI-FT-ICR Imaging Data Improves Mapping of Gram-Negative Bacterial Virulence Factors on-Tissue

TP040 Phosphoproteomic Analysis of Differential Protein Expression in BRaf-Mutated Melanoma Cells with Acquired Resistance to BRaf, MEK1/2, or ERK1/2 Inhibitors
TP503 Structural Characterization of Membrane Glycolipids from Marine Sponge-associated Bacteria by Mass Spectrometry
TP506 Top-down Structural Elucidation of Gram-negative Bacterial Endotoxins by Tandem Mass Spectrometry
TP507 Structural Characterization of Lipid Biomarkers from Staphylococcus aureus following Microextraction for Mass Spectrometric Phenotyping

ThP025 Surface Acoustic Wave Nebulization Sample Introduction for Vacuum-Assisted Plasma Ionization
ThP026 Surface Acoustic Wave Nebulization – Mass Spectrometry: A Tool for Rapid Analysis of Food Products
ThP027 Performance Characterization of Surface Acoustic Wave Nebulization for Lipid A Mass Spectrometric Analysis
ThP028 Surface Acoustic Wave Nebulization – Mass Spectrometry on a TripleTOF Mass Spectrometer
ThP209 A Rapid, Cell Culture-Based Method for Biomarker Discovery and Drug Screening by MALDI-MSI