

**ASMS 2015**

**MP 132**

Analytical Implications for  
Conducting Precision Drift  
Tube Ion Mobility  
Measurements in Helium,  
Nitrogen, and Carbon  
Dioxide

Jody C. May,<sup>1</sup> Nichole M. Lareau,<sup>1</sup>  
James N. Dodds,<sup>1</sup> Ruwan T.  
Kurulugama,<sup>2</sup> Alex Mordehai,<sup>2</sup>  
George C. Stafford,<sup>2</sup> John C.  
Fjeldsted,<sup>2</sup> and John A. McLean<sup>1</sup>

## Introduction and Scope of Work

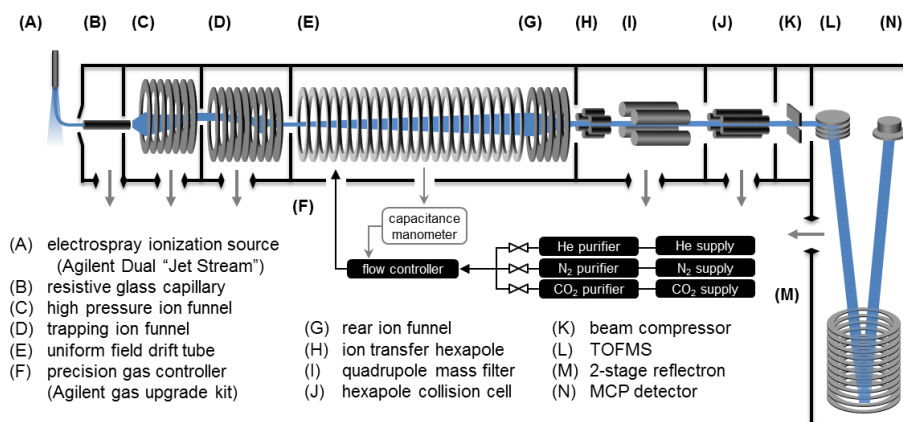
- This report describes recent improvements in the gas delivery and monitoring system of a commercial drift tube ion mobility-mass spectrometer (Ion Mobility Q-TOF 6560A, Agilent Technologies).
- With this instrument (shown below), the measured ion transport data (reduced mobilities and collision cross sections, CCS) exhibit a precision of better than 1% RSD, with most measurements better than 0.5% RSD [1].
- The instrument supports a variety of drift gases at ca. 4 Torr, to facilitate direct comparison of empirical result.
- This work presents results for helium, nitrogen, and carbon dioxide drift gases. Gas-specific dependencies on the ion mobility resolving power and other practical considerations for conducting ion mobility experiments in alternative drift gases are discussed.

**At Right** – Table summarizing the properties of the three gases investigated in this study.

	He	N <sub>2</sub>	CO <sub>2</sub>
Gas Mass (Da):	4.00	28.01	44.01
Gas Polarizability (Å <sup>3</sup> ):	0.21	1.74	2.91

## Instrumentation and Methods

### Ion Mobility Q-TOF MS Instrument (Agilent 6560)

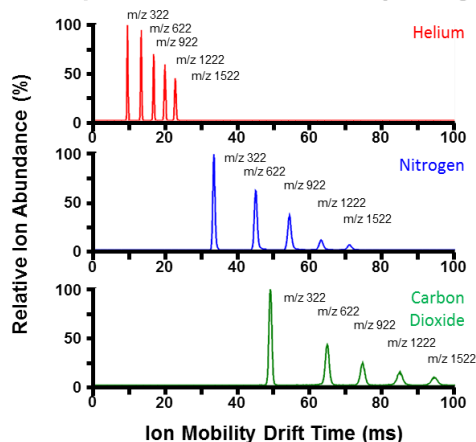


**Above Schematic** – Conceptual schematic of the Agilent 6560 IM-MS Instrument.

**Below Spectra** – Ion mobility spectra of an MS calibration mixture (Agilent ESI tuning mix) in the three drift gases obtained under the same drift field and gas pressure conditions (9.6 V/cm, 4,000 Torr, and ca. 303 K).

**Below Table** – Measured reduced mobility values demonstrate the wide range of mobilities surveyed.

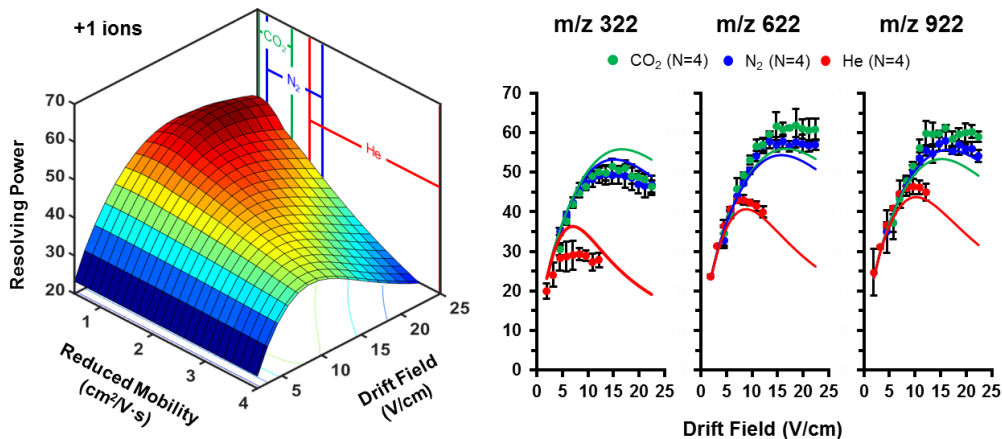
### Gas-Specific Reduced Mobility Ranges



	Empirically Determined Reduced Mobility Value (cm <sup>2</sup> /V·s)		
	Helium	Nitrogen	Carbon Dioxide
m/z 118	--	1.83±0.05 (60)	1.08±0.01 (111)
m/z 322	5.44±0.12 (88)	1.37±0.01 (68)	0.88±0.01 (113)
m/z 622	3.99±0.09 (112)	1.01±0.01 (94)	0.67±0.01 (113)
m/z 922	3.17±0.07 (112)	0.84±0.01 (58)	0.58±0.01 (112)
m/z 1222	2.62±0.06 (98)	0.73±0.01 (58)	0.51±0.01 (112)
m/z 1522	2.29±0.06 (98)	0.65±0.01 (59)	0.46±0.01 (111)
m/z 1822	2.05±0.05 (49)	0.58±0.00 (27)	--
m/z 2122	1.86±0.05 (49)	0.53±0.00 (27)	--
m/z 2422	1.73±0.08 (44)	0.49±0.00 (27)	--
m/z 2722	1.60±0.08 (44)	0.46±0.00 (27)	--
Min:	1.60 cm <sup>2</sup> /V·s	0.46 cm <sup>2</sup> /V·s	ca. 0.3 cm <sup>2</sup> /V·s
Max:	5.44 cm <sup>2</sup> /V·s	1.83 cm <sup>2</sup> /V·s	1.08 cm <sup>2</sup> /V·s

**Above** – Significantly disparate ranges of gas-phase mobilities are observed in the different drift gases.

## Resolving Power Surface Plot



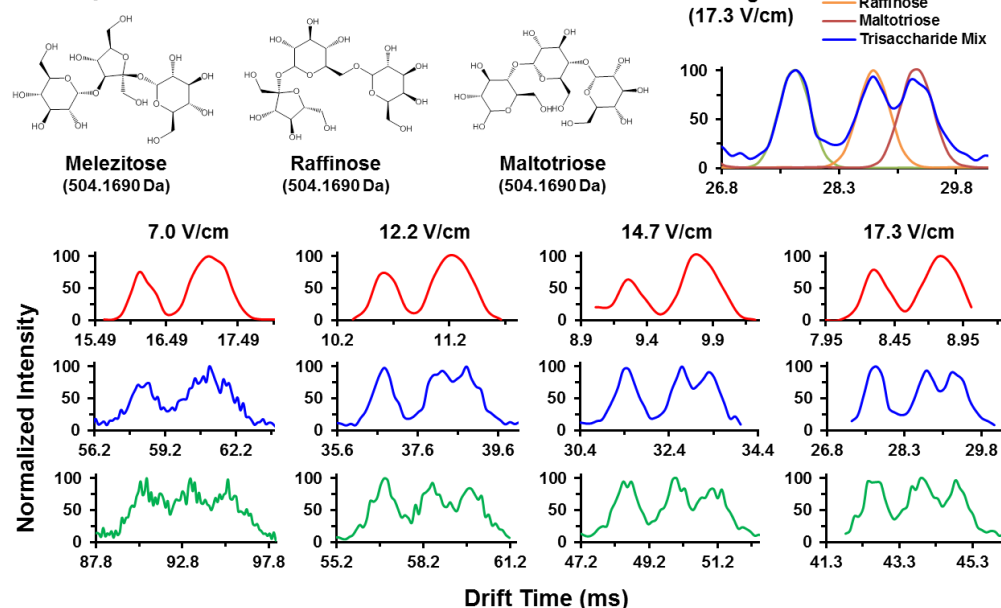
**Above Left** – 3D surface plot of the instrument resolving power mapped for +1 ions. Plot was generated using a theoretical resolving power equation developed by Siems *et al.* (at **right**) [2] and trained against empirical measurements. This model utilizes three semi-empirical terms ( $\alpha$ ,  $\beta$ , and  $\gamma$ ) to fit empirical data and theoretical results can be used to infer separation performance across a range of experimental conditions.

$$R_{SE} = \frac{t_{drift}}{\left( \alpha \cdot \frac{T \cdot t_{drift}^2}{V \cdot z} + \beta \cdot t_{gate}^2 + \gamma \right)^{0.5}}$$

**Above Right** – Extracted resolving power curves representing m/z 322, 622, and 922 ions in three different drift gases. The different drift gases enable different reduced mobility ranges to be accessed by the instrument. In this case, nitrogen and carbon dioxide represent lower mobilities, which access higher resolving powers.

## Resolution of Isomers for Alternative Drift Gases

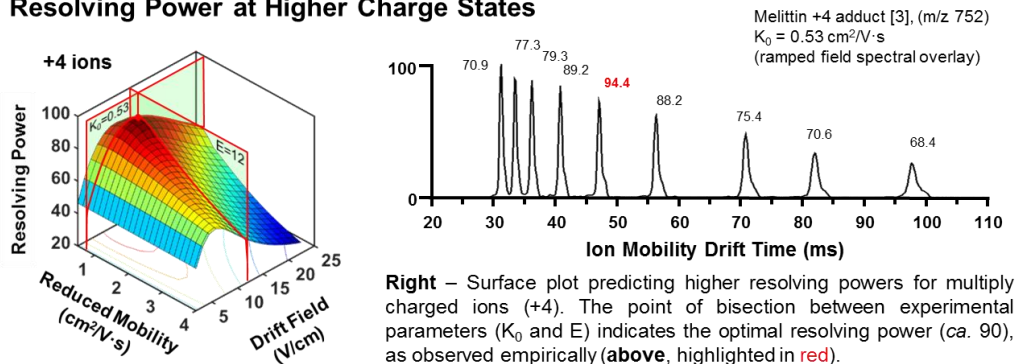
### 3-Component Trisaccharide Mixture



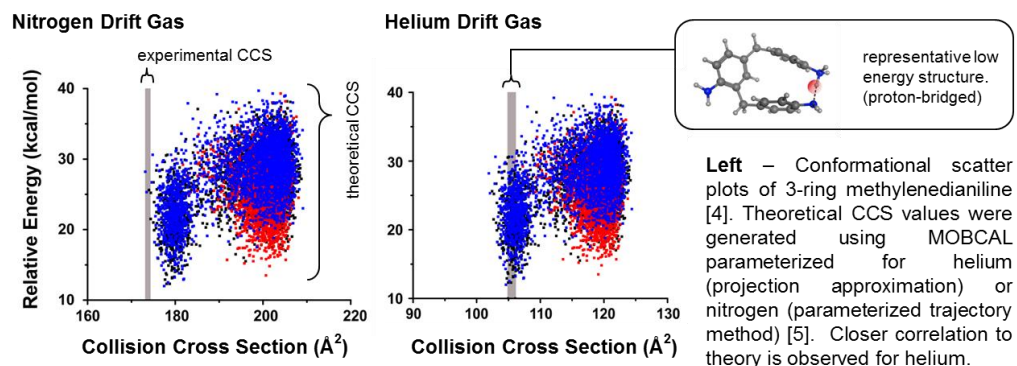
**Above** – Ion mobility spectra of a three component mixture of isomeric carbohydrates (Melezitose, Raffinose, and Maltotriose) obtained in helium (red trace), nitrogen (blue trace), and carbon dioxide (green trace) at four different drift fields. All spectra are unsmoothed, which results in “jagged” traces for the broader peaks due to increased sampling across the trace (more bins). Higher resolution is observed for nitrogen and carbon dioxide.

## Additional Considerations

### Resolving Power at Higher Charge States



### Correlation of Collision Cross Section Measurements to Theory



## Conclusions and Future Directions

- This work demonstrates the capabilities of the instrument towards supporting studies using various drift gases.
- The instrument is capable of operating at the same pressure, temperature, and similar fields for all three drift gases investigated (He,  $\text{N}_2$ ,  $\text{CO}_2$ ), which facilitates direct comparisons between experimental results.
- Carbon dioxide and nitrogen access the highest resolving powers. Resolving power was found to depend on the ion's reduced mobility, which enabled theoretical mapping of the instrument resolving power.
- Higher resolving power does correlate to better separations as observed from measurements obtained on a mixture of three isomeric carbohydrates, but the differences in resolution are subtle.
- Helium based CCS measurements are found to correlate better to current theoretical methods.

## References & Acknowledgements

- [1] J.C. May, C.R. Goodwin, N.M. Lareau, K.L. Leaptrot, C.B. Morris, R.T. Kurulugama, A. Mordehai, C. Klein, W. Barry, E. Darland, G. Overney, K. Imatani, G.C. Stafford, J.C. Fjeldsted, J.A. McLean, "Conformational Ordering of Biomolecules in the Gas-Phase: Nitrogen Collision Cross Sections Measured on a Prototype High Resolution Drift Tube Ion Mobility-Mass Spectrometer", *Analytical Chemistry* 86(4), 2107-2116 (2014).
- [2] W.F. Siems, C. Wu, E.E. Tarver, H.H. Hill, Jr., P.R. Larsen and D.G. McMin "Measuring the Resolving Power of Ion Mobility Spectrometers", *Analytical Chemistry* 66, 4195-4201 (1994).
- [3] J.C. May and J.A. McLean, "A Uniform Field Ion Mobility Study of Melittin and Implications of Low-Field Mobility for Resolving Fine Cross-Sectional Detail in Peptide and Protein Experiments", *Proteomics*, DOI: 10.1002/pmic.201400551 (2015).
- [4] S.M. Stow, T.M. Onifer, J.G. Forsythe, H. Nefzger, N.W. Kwiecien, J.C. May, J.A. McLean and D.H. Hercules, "Structural Characterization of Methylenedianiline Regioisomers by Ion Mobility-Mass Spectrometry, Tandem Mass Spectrometry, and Computational Strategies: II. Electrospray Spectra of 3-Ring and 4-Ring Isomers", *Analytical Chemistry*, DOI: 10.1021/acs.analchem.5b01084 (2015).
- [5] (a) I.D.G. Campuzano, M.F. Bush, C.V. Robinson, C. Beaumont, K. Richardson, H. Kim, H.I. Kim, "Structural Characterization of Drug-Like Compounds by Ion Mobility-Mass Spectrometry", *Analytical Chemistry* 84(2), 1026-1033 (2012). (b) H. Kim, H.I. Kim, P.V. Johnson, L.W. Beegle, J.L. Beauchamp, W.A. Goddard, I. Kanik, "Experimental and Theoretical Investigation into the Correlation Between Mass and Ion Mobility for Choline and other Ammonium Cations in  $\text{N}_2$ ", *Analytical Chemistry* 80(6), 1928-1936 (2008).

The authors gratefully acknowledge Sarah Stow for providing the theoretical CCS results. Financial support for Vanderbilt authors was provided by the National Science Foundation (NSF MRI CHE-1229341); and the National Institutes of Health National Center for Advancing Translational Sciences (NIH NCATS UH2TR000491).