

# Trapped Ion Mobility Spectrometry: past, present and future trends

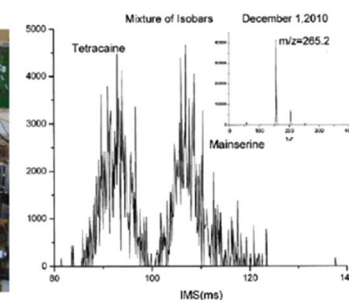
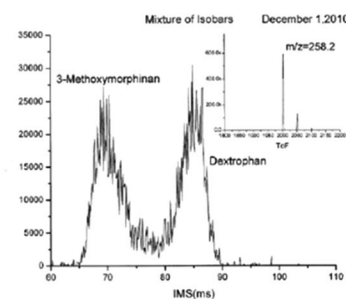
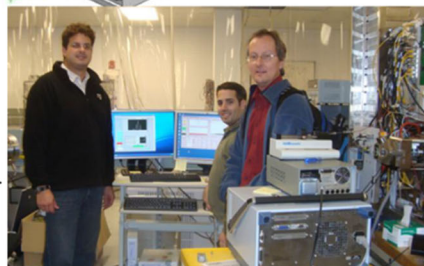
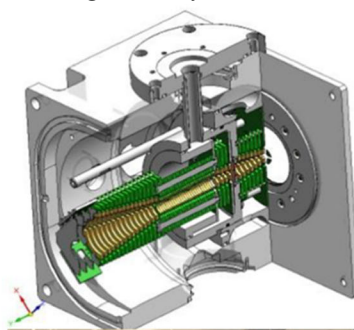
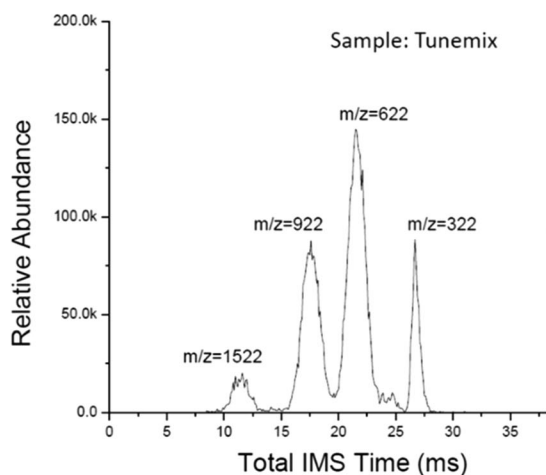
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Five years after the first publication on Trapped Ion Mobility Spectrometry entitled “Gas-phase separation using a trapped ion mobility spectrometer” on this journal [4], we celebrate the recent developments on TIMS technology with this special issue. This issue features an example of the high mobility resolving

power of TIMS (up to 400); TIMS potential for the analysis of high molecular weight biomolecules and biomolecular complexes; the use of nonlinear scan functions for targeted high resolution TIMS; and gated TIMS coupled to ultrahigh resolution FT-ICR MS analyzers.

## First TIMS spectrum



First TIMS spectrum (left) of TuningMix sample obtained in a prototype TIMS analyzer coupled to a Bruker micro q-TOF (center top) and first isobaric separation (right) of 3-methoxymorphinan and dextrophan ( $m/z$  258.2) and tetracaine

and mainserine ( $m/z$  265.2). In the picture, from left to right, Dr. Francisco Fernandez-Lima, Dr. Desmond A. Kaplan and Dr. Melvin A. Park

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Many major breakthroughs in IMS have occurred over the last decades. The large number of flavors (e.g., DT-IMS, PF-IMS, DIMS/FAIMS, TWIMS, and TIMS) and operating condition (low pressure to atmospheric) has allowed the IMS community to solve problems in a broad range of fields (e.g., biomedical, forensic, environmental, out-of-space, and basic science). Initially, IMS-MS developments were mainly restricted to research groups that focused on the development of IMS instrumentation and potential applications. With the recent increase of commercially available IMS-MS variants, there will be an exponential growth in number of IMS-MS users and it will soon become a required analysis for most MS service laboratories. In particular, the first Bruker Daltonics Inc. TIMS-MS commercial instrument was launched on the summer of 2016 at the ASMS conference.

Since the introduction of TIMS-MS in 2011 [4, 5], my group at Florida International University [1–3, 6, 8, 11, 14–17] and others [7, 9, 10, 12, 13, 18], [19, 20] has shown the potential of TIMS-MS for fast, gas-phase separation and for molecular structural elucidation. Different from other IMS variants, TIMS enables the interrogation and manipulation of mobility separated ion populations in the gas-phase, with high resolving power in millisecond-second time-scales, and with the possibility to measure CCS using first principles that can be further utilized for structural assignments. Briefly, the concept behind TIMS is the use of an electric field to hold ions stationary against a moving gas, so that the drift force is compensated by the electric field and ion packages are separated based on their respective ion mobilities. This concept follows the idea of a parallel flow ion mobility analyzer [21], with the main difference that ions are also confined radially using a quadrupolar field to guarantee higher ion transmission and sensitivity. The separation in a TIMS device can be described in the center of mass frame using the same principles as in a conventional IMS drift tube.

A brief biographical sketch and overall research interest is provided below for the main authors and groups that contributed to this issue on the development of TIMS in its fifth anniversary.



Mark Ridgeway is a scientist in the research Innovation and intellectual property group at Bruker Daltonics Inc. He earned

B.Sc. (2005) in Chemistry at Erskine College, Due West, South Carolina, and a Ph.D. (2010) in Analytical Chemistry at the University of North Carolina at Chapel Hill working in Prof. Gary Glish's group. He was hired by Bruker Daltonics, Inc. in 2010 where he is focused on mass spectrometry and ion mobility instrument research and development.



Dr. Melvin Park is Director of Research at Bruker Daltonics, Inc.. He received bachelor's degrees in Chemistry and Physics from NC State University in 1986 and a Ph.D. in Chemistry from Texas A&M in 1991 under the guidance of Prof. Emile A. Schweikert. He performed postdoctoral studies at the Naval Research Laboratories in 1994 with Dr. John Callahan. Over the past two decades he has produced more than 60 issued patents and 40 reviewed journal articles on various areas of mass spectrometry including ion sources and optics, and various methods of ion manipulation, mass analysis, and detection. More recently, he and his group have been active in the area of ion mobility spectrometry combined with mass spectrometry – pioneering the technique now known as trapped ion mobility spectrometry.



Dr. Francisco Fernandez-Lima is an Assistant Professor (2012-present) in the Department of Chemistry and Biochemistry at Florida International University. He received a BS (2001) and MS (2003) in Nuclear Physics at the Institute of Nuclear Sciences and Technology (Havana, Cuba) and a

PhD (2006) in Applied Physics at PUC-Rio (Brazil) under the guidance of Dr. Enio F. da Silveira. He performed post-doctoral studies (2007–2010) at Texas A&M University under the supervision of Dr. David H. Russell and Dr. Emile A. Schweikert. He is the recipient of a K99 (2010–2012) and R00 (2012–2016) Pathway to Independence Award by the National Institute of Health.

## References

- Benigni P, Fernandez-Lima F (2016) Oversampling selective accumulation trapped ion mobility spectrometry coupled to FT-ICR MS: fundamentals and applications. *Anal Chem* 88:7404–7412. doi:10.1021/acs.analchem.6b01946
- Benigni P, Thompson CJ, Ridgeway ME, Park MA, Fernandez-Lima F (2015) Targeted high-resolution ion mobility separation coupled to ultrahigh-resolution mass spectrometry of endocrine disruptors in complex mixtures. *Anal Chem* 87:4321–4325. doi:10.1021/ac504866v
- Castellanos A, Benigni P, Hernandez DR, DeBord JD, Ridgeway ME, Park MA, Fernandez-Lima FA (2014) Fast screening of polycyclic aromatic hydrocarbons using trapped ion mobility spectrometry – mass spectrometry. *Anal Meth* 6:9328–9332
- Fernandez-Lima F, Kaplan D, Suetering J, Park M (2011a) Gas-phase separation using a trapped ion mobility spectrometer. *Int J Ion Mobility Spectrom* 14:93–98. doi:10.1007/s12127-011-0067-8
- Fernandez-Lima FA, Kaplan DA, Park MA (2011b) Note: Integration of trapped ion mobility spectrometry with mass spectrometry. *Rev Sci Instr* 82:126106
- Hernandez DR, DeBord JD, Ridgeway ME, Kaplan DA, Park MA, Fernandez-Lima FA (2014) Ion dynamics in a trapped ion mobility spectrometer. *Analyst* 139:1913–1921. doi:10.1039/C3AN02174B
- Liu FC, Kirk SR, Bleiholder C (2016) On the structural denaturation of biological analytes in trapped ion mobility spectrometry–mass spectrometry. *Analyst* 141:3722–3730
- McKenzie A, DeBord JD, Ridgeway ME, Park MA, Eiceman GA, Fernandez-Lima F (2015) Lifetimes and Stabilities of familiar explosives molecular adduct complexes during ion mobility measurements. *Analyst* 140:5692–5699. doi:10.1039/c5an00527b
- Meier F, Beck S, Grassl N, Lubeck M, Park MA, Raether O, Mann M (2015) Parallel accumulation–serial fragmentation (PASEF): multiplying sequencing speed and sensitivity by synchronized scans in a trapped ion mobility device. *J Proteome Res* 14:5378–5387. doi:10.1021/acs.jproteome.5b00932
- Michelmann K, Silveira JA, Ridgeway ME, Park MA (2015) Fundamentals of trapped ion mobility spectrometry. *J Am Soc Mass Spectrom* 26:14–24. doi:10.1007/s13361-014-0999-4
- Molano-Arevalo JC, Hernandez DR, Gonzalez WG, Miksovska J, Ridgeway ME, Park MA, Fernandez-Lima F (2014) Flavin adenine dinucleotide structural motifs: from solution to gas-phase. *Anal Chem* 86:10223–10230
- Pu Y, Ridgeway ME, Glaskin RS, Park MA, Costello CE, Lin C (2016) Separation and identification of isomeric Glycans by selected accumulation-trapped ion mobility spectrometry-electron activated dissociation tandem mass spectrometry. *Anal Chem* 88:3440–3443. doi:10.1021/acs.analchem.6b00041
- Ridgeway ME, Silveira JA, Meier JE, Park MA (2015) Microheterogeneity within conformational states of ubiquitin revealed by high resolution trapped ion mobility spectrometry. *Analyst* 140:6964–6972. doi:10.1039/C5AN00841G
- Schenk ER, Almeida R, Miksovska J, Ridgeway ME, Park MA, Fernandez-Lima F (2015a) Kinetic intermediates of Holo- and Apo-myoglobin studied using HDX-TIMS-MS and molecular dynamic simulations. *J Am Soc Mass Spectrom* 26:555–563. doi:10.1007/s13361-014-1067-9
- Schenk ER, Mendez V, Landrum JT, Ridgeway ME, Park MA, Fernandez-Lima F (2014a) Direct observation of differences of carotenoid polyene chain cis/trans isomers resulting from structural topology. *Anal Chem* 86:2019–2024. doi:10.1021/ac403153m
- Schenk ER, Nau F, Fernandez-Lima F (2015b) Theoretical predictor for candidate structure assignment from IMS data of biomolecule-related conformational space. *Int J Ion Mobility Spectrom* 18:23–29. doi:10.1007/s12127-015-0165-0
- Schenk ER, Ridgeway ME, Park MA, Leng F, Fernandez-Lima F (2014b) Isomerization kinetics of AT hook Decapeptide solution structures. *Anal Chem* 86:1210–1214. doi:10.1021/ac403386q
- Silveira JA, Michelmann K, Ridgeway ME, Park MA (2016a) Fundamentals of Trapped Ion Mobility Spectrometry Part II: Fluid Dynamics. *J Am Soc Mass Spectrom* 27:585–595. doi:10.1007/s13361-015-1310-z
- Silveira JA, Ridgeway ME, Laukien FH, Mann M, Park MA (2016b) Parallel accumulation for 100 % duty cycle trapped ion mobility-mass spectrometry. *Int J Mass Spectrom*. doi:10.1016/j.ijms.2016.03.004
- Silveira JA, Ridgeway ME, Park MA (2014) High resolution trapped ion mobility Spectrometry of peptides. *Anal Chem* 86:5624–5627. doi:10.1021/ac501261h
- Zeleny J (1898) On the ratio of velocities of the two ions produced in gases by Röntgen radiation, and on some related phenomena. *Philos Mag* 46:120–154