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EDITORIAL

Travelling wave ion mobility

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The first commercial availability of travelling wave ion mobility (TWIM) was in 2006 with the launch of the SYNAPT High Definition Mass Spectrometry (HDMS) system at the 54th American Society for Mass Spectrometry (ASMS) meeting in Seattle, USA. However, development of this technology began several years before the instrument became available.

The use of ion mobility coupled with mass spectrometry for the analysis of biological samples started to take hold in the 1990's through the pioneering work of several groups including Prof. Mike Bowers (University of California Santa Barbara, USA), Prof. Herb Hill (Washington State University, USA), Prof. Martin Jarrold (Indiana University, USA) and Prof. David Clemmer (Indiana University, USA). However, the early work on ion mobility separation at Waters was particularly prompted by some excellent data shown by Prof. Clemmer and co-workers in the late 90's early 00's on the mobility separation of complex mixtures of peptides, illustrating the potential benefit of increased analytical peak capacity offered by the inclusion of ion mobility. (e.g. Valentine SJ, Kulchania M, Srebalus Barnes CA, Clemmer DE (2001) Multidimensional separations of complex peptide mixtures: a combined high-performance liquid chromatography/ion mobility/time-of-flight mass spectrometry approach. Int. J. Mass Spectrom. 212: 97).

The first system design at Waters in 2001 utilised stacked ring ion guides (SRIG) with axial electric fields to produce the mobility separation in the millibar pressure source region of a quadrupole time-of-flight mass spectrometer. Beyond the separative capability, two key performance features were considered essential for the commercial viability of this new design: firstly that operation with ion mobility did not compromise sensitivity of the instrument, and secondly that, if not required, the ion mobility functionality could be disabled and would appear essentially transparent to the ion beam. To achieve this, ion guides with radio frequency (RF) confining voltages were used to both accumulate ions whilst the previous mobility separation occurred (adapted from Prof. Clemmer's work) and to radially confine ions as the mobility separation took place. A fuller description of this apparatus can be found in: Thalassinos K, Slade SE, Jennings KR, Scrivens JH, Giles K, Wildgoose J, Hoyes J, Bateman RH, Bowers MT (2004) Ion mobility mass spectrometry of proteins in a modified commercial mass spectrometer. Int. J. Mass Spectrom. 236: 55.

In 2002 work was being undertaken on the first designs of travelling wave (T-Wave) ion guide (TWIG), primarily for propelling ions through the collision cells of the tandem quadrupole instruments, facilitating fast scanning/switching experiments. The TWIG is an adaptation of the SRIG where direct current (DC) voltage pulses are superimposed on the confining RF and propagate through the device as waves. It was considered that, under the right conditions, it might be possible to use T-Waves for mobility separation, with the benefits over axial fields of flexibility of ion control through adjustment of the T-wave parameters, and removal of the need for large voltages to generate the fields, thus reducing the problem of electrical discharge. In 2003, the first mobility separation was performed using T-Waves with the TWIG in place of the standard collision

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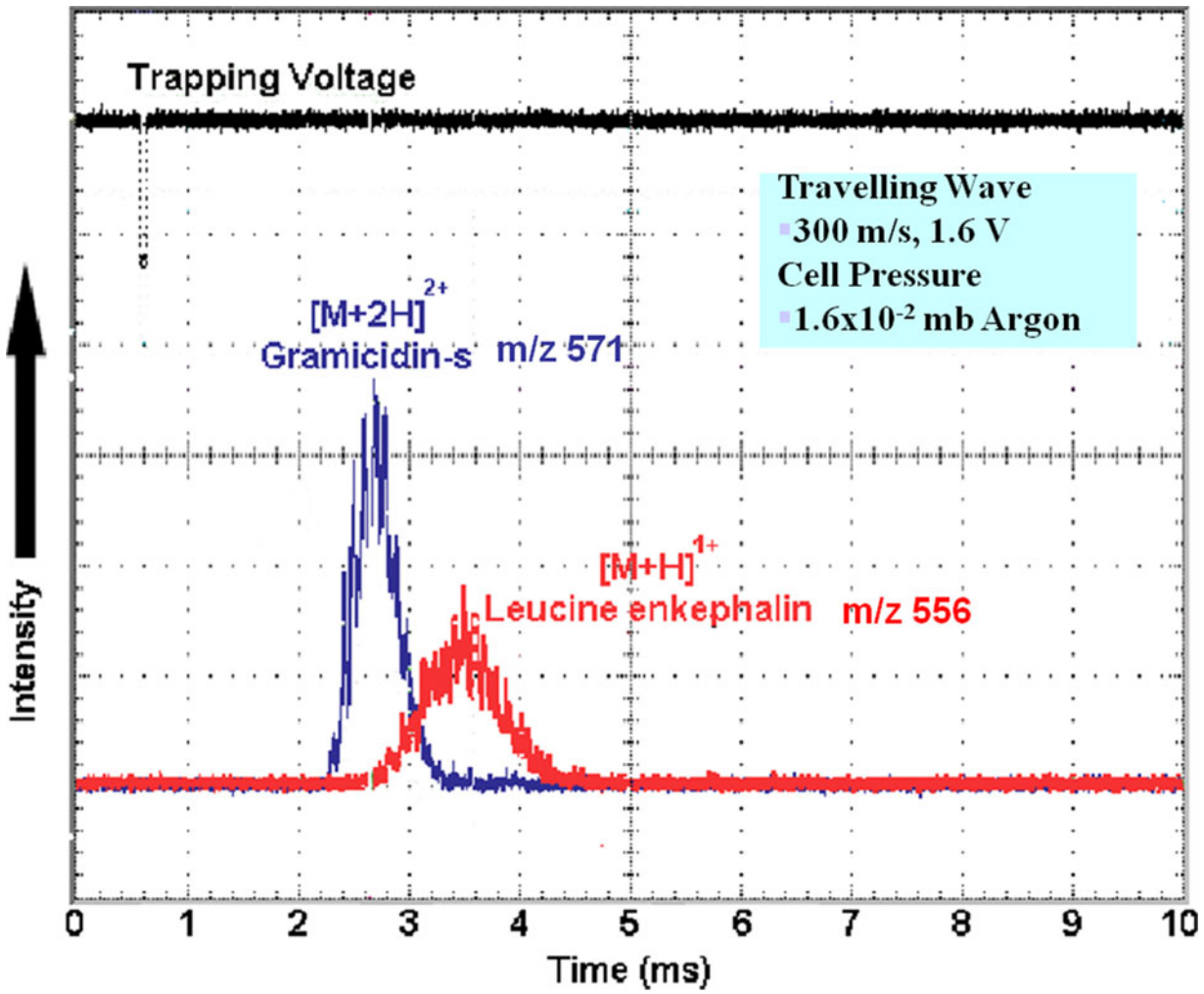
cell on a tandem quadrupole instrument. The figure shows the result obtained for two peptide species:



Following the success of this investigation, the first TWIM system was built with the mobility cell in place of the standard collision cell on a Q-ToF instrument. The TWIM cell was located in its own differentially pumped chamber to allow use of higher pressures than had been readily attainable on the preliminary instrument, providing higher mobility resolution. This system is described more fully in: Giles K, Pringle SD, Worthington KR, Little D, Wildgoose JL, Bateman RH (2004) Applications of a travelling wave-based radio-frequency only stacked ring ion guide. Rapid Commun. Mass Spectrom. 18: 2401. The first major application paper from the TWIM system was produced through a collaboration with Prof. Carol Robinson, Dr Brandon Ruotolo and co-workers at Cambridge University, UK where investigations were conducted into the gas-phase conformations of large protein complexes: Ruotolo BT, Giles K, Campuzano I, Sandercock AM, Bateman RH, Robinson CV (2005) Evidence for Macromolecular Protein Rings in the Absence of Bulk Water. Science 310: 1658.

With the mobility device located after the quadrupole in this instrument, unlike most research instrument geometries, more system flexibility could be realised through the capability to m/z select ion species prior to mobility separation. Also, with the design incorporating short ion guides pre- and post-mobility to reduce gas streaming from the TWIM cell into adjacent chambers, ion fragmentation could be undertaken in these regions. The concept of pre- and post-mobility fragmentation was developed further in the next generation of TWIM instruments, resulting in the 'Triwave' region found in the Synapt HDMS instrument launched in 2006, described more fully in: Pringle SD, Giles K, Wildgoose JL, Williams JP, Slade SE, Thalassinos K, Bateman RH, Bowers MT, Scrivens JH (2007) An investigation of the mobility separation of some peptide and

protein ions using a new hybrid quadrupole/travelling wave IMS/oa-ToF instrument. Int. J. of Mass Spectrom. 261: 1. The TWIM device in this system operated at around 0.5–1.0 mbar of nitrogen and gave a mobility resolution of around 10 ($\Omega/\Delta\Omega$) (where Ω is the collision cross-section). Much of the work performed on these instruments has been in the areas of protein, protein complex and peptide analysis.

The subsequent generation of TWIM instrument, the Synapt G2 HDMS, was launched at the 57th ASMS meeting, Philadelphia, USA in 2009. The TWIM focus on this instrument was towards increased mobility resolution. For this, the Triwave region was modified to allow use of higher TWIM pressure and, consequently, higher T-Wave amplitudes, which resulted in approximately a four-fold increase in the mobility resolution to around 40 ($\Omega/\Delta\Omega$). One of the key features of the new TWIM cell was implementation of a short helium-filled cell at the entrance of the nitrogen-filled mobility separation region facilitating efficient transport of ions from the lower pressure pre-mobility region into the 2.5–3.0 mbar mobility cell. More detail on the mobility performance of the latest TWIM design can be found in: Giles K, Williams JP and Campuzano I (2011) Enhancements in travelling wave ion mobility resolution. Rapid Commun. Mass Spectrom. 25: 1559. Another significant development on this instrument was the implementation of an analogue-to-digital conversion detection system capable of ion mobility acquisitions. This provided an order of magnitude increase in spectral dynamic range, which was critical to expanding the TWIM capability where the ion concentration effects of mobility separation are particularly challenging.

For completeness, I mention that the latest version of the TWIM instrument, the Synapt G2-S, was launched in 2011 at the 59th ASMS meeting in Denver, USA. In this product, the new ‘StepWave’ source ion optics were implemented, providing around 25-fold increase in ion current, however, the TWIM region of this instrument remained unchanged from that of the Synapt G2.

The application areas of the Synapt instruments has been continually growing as more researchers look to harness the combined power of ion mobility with mass spectrometry both for the improved selectivity in complex mixtures and for more fundamental investigations into ion structure. In the two volumes of this special issue, a snapshot of the wide array of studies being undertaken using the TWIM capability of the Synapt instrument is presented. I’m certain this collection of papers will be of interest to a broad range of scientists whether working in research or routine analysis.

Finally, I am deeply grateful to each of the authors for their contribution and support in producing this special issue on travelling wave ion mobility.

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