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ENHANCEMENT OF PRECURSOR ION SCANNING ON A Q-TOF INSTRUMENT USING A TRAVELLING WAVE ION MOBILITY SEPARATOR

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OVERVIEW

AIM

- To enhance precursor ion sensitivity on a Q-ToF instrument

METHOD

- T-Wave ion mobility separator used to replace scanning quadrupole
- ToF duty cycle increase using synchronization with T-Wave ion guide

RESULTS

- TOF duty cycle enhancement up to x10
- Combination with ion mobility separation of precursors provides up to x100 increase in response over precursor ion scanning on a tandem quadrupole

INTRODUCTION

Precursor ion experiments on scanning tandem MS instruments are of relatively low efficiency due to the requirement to scan the first mass analyser over a selected mass range. With tandem quadrupole instruments, the second quadrupole operates at the fixed m/z of the product ion and so transmission efficiency is high, however, with Q-ToF type instruments MS2 is the ToF analyser which introduces further losses in ion transmission, in part due to low duty cycle, especially at low m/z. The resulting duty cycle can be typically less than 0.1%.
The oa-TOF duty cycle may be significantly increased by transporting ions to the orthogonal acceleration region using a travelling wave (T-Wave) ion guide[1]. The T-Wave ion guide converts the continuous ion beam into discrete packets and by subsequent synchronization of the arrival of ions of a specific m/z value from each packet with the ToF acceleration step, signal enhancement occurs over a m/z window centred on the ion of interest. Here we report a method of further improving the duty cycle on a Q-ToF instrument by replacing the scanning quadrupole with a T-Wave ion mobility separator[1].

EXPERIMENTAL

T-Wave Ion Mobility Separator

The T-Wave ion guide is a stacked ring electrode device with opposite phases of RF applied to adjacent electrodes to provide radial ion confinement. A DC voltage pulse pattern is applied to the ring electrodes so as to provide travelling voltage pulses which propel ions through the gas-filled device. Through appropriate choice of the wave parameters mobility separation can be achieved as less mobile ions roll over the 'wave' more often than the high mobility ions[1]. Experiments were performed on a modified Q-Tof Premier instrument, shown in Figure 1. Modifications include a separately pumped chamber which houses the T-Wave IMS cell, followed by a further pumped chamber containing a hexapole ion guide and a T-Wave collision cell. To perform mobility-based separations, ions are stored in the source T-Wave ion guide and gated out for 100 µs every 15 ms. The ion packet then enters the T-Wave IMS cell where mobility separation occurs and the ions then pass to the T-Wave collision cell through which they are transported to the ToF analyser. The temporal arrival of the mobility separated ions at the ToF is recorded by synchronisation of the orthogonal acceleration pushes (mass spectra) with the ion gate such that 200 mass spectra are recorded per mobility spectrum (total time per mobility spectrum = 200 x pusher period). The combination of ion accumulation during mobility separation and the high TOF repetition rate compared to mobility seaparation time scales significantly enhances duty cycle over that of a scanning quadrupole.

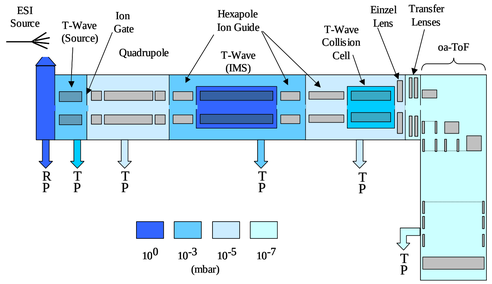

Figure 1 Schematic diagram of the modified Q-ToF Premier instrument

The mobility separated ions can be injected into the T-Wave collision cell with low energy to allow recording of the precursor ions, or with high energy to record fragment ions. The continually running T-Wave in the cell maintains the mobility profile in both low and high energy cases and thus enables correlation of fragment ions with associated precursors.

Enhancement of the ToF duty cycle (EDC) for a product ion is achieved by synchronising the ToF pusher with the ion packet release from the cell T-Wave and introducing a fixed delay to account for the time of flight of the ion of interest from the cell to the pusher region.

Experimental Parameters

Nano ESI interface - samples infused at 400 nL/min

	Quattro Premier	**Modified Q-ToF Premier**	
		T-Wave	
	Collision Cell	*IMS Cell*	*Collision Cell*
Pressure	4.0×10^{-3} mbar Ar	1.0 mbar N_2	2.0×10^{-2} mbar N_2
Pulse Height	5 V	21 V	3.5 V
Pulse Velocity	300 m/s	600 m/s	300 m/s
Acquisition Time	Precursor ion scan 50-1100 Da in 1s 30 s	IMS ToF MS 0-1950 Da 30 s	

RESULTS

Figure 2 shows the mass spectra obtained by conventional tandem quadrupole precursor ion scanning for decreasing concentrations of verapamil in 70/30 acetonitrile/water (0.1% formic acid). From a comparison of rows 2 and 3 of Figure 2, it is reasonable to assume that the limit of detection (LOD) for this technique, defined by a continuous peak half-width, is approximately 1-2pg/µL.

The ion mobility spectra and associated mass spectra of Figure 3 illustrate the technique of enhanced precursor ion scanning on a modified Q-ToF Premier MS. Row 1 shows the low collision energy ion mobility separation and the summed mass spectrum for 500fg/µL of verapamil.

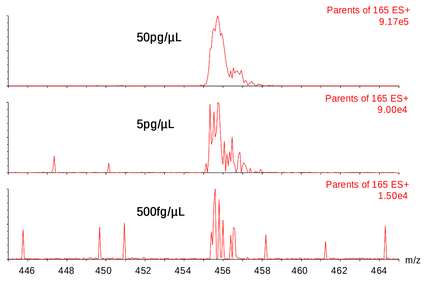

Figure 2 Conventional tandem quadrupole precursor ion scans for decreasing amounts of verapamil

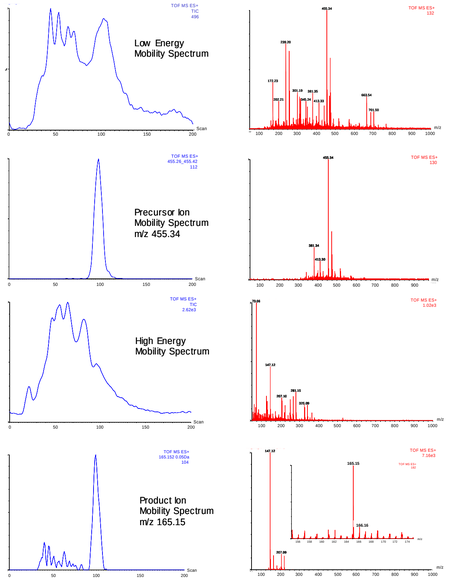

Figure 3 Ion mobility separations and their associated mass spectra obtained under low and high energy conditions for 500fg/µL verapamil

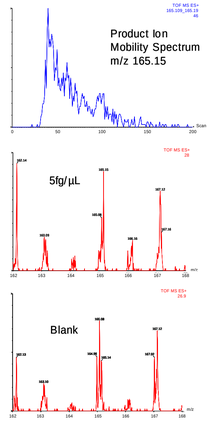

Figure 4 LOD for precursor ion scanning of 5fg/µL verapamil with the modified Q-Tof Premier

Row 2 of Figure 3 shows the selected ion mobility spectrum for the precursor ion of verapamil at m/z 455.34. By repeating this experiment at a high collision energy, we obtain the corresponding selected ion mobility spectrum for the product ion at m/z 165.15 and the associated mass spectrum obtained by selectively summing over the time-separated product ion mobility peak. The retention time and peak shape correlation between the two selected ion mobility spectra provides a high degree of precursor ion confirmation. Furthermore, high sensitivity is demonstrated in the EDC product ion mass spectrum shown in row 4 (≈10x signal enhancement over the non-EDC acquisition mode). The LOD of verapamil at approximately 5fg/µL (Figure 4), represents an improvement factor of at least x200 when compared to the tandem quadrupole data.

Figure 5 shows the mass spectra obtained by conventional tandem quadrupole precursor ion scanning for decreasing concentrations of a beta casein digest in 25/75 acetonitrile/water (0.1% formic acid).

At a total digest concentration of 100fmol/µL (row 3), we can estimate that the doubly charged precursor ion (FQBEEQQQTEDELQDK) contains around 10 ions! In contrast, the 100fmol/µL data for the modified Q-ToF Premier, shown in Figure 6, demonstrates a high degree of precursor ion confirmation (rows 2 and 4). Furthermore, the first two isotopes for the dephosphorylated product ion spectrum (Figure 6, row 4) contain approximately 1000 ion counts (EDC factor ≈4x). These data reinforce the assertion that the modified Q-ToF premier precursor ion scanning technique can show x100 improvements in sensitivity when compared to a tandem quadrupole instrument.

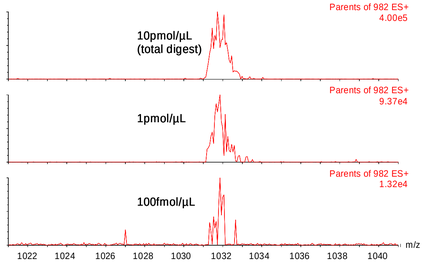

Figure 5 Conventional tandem quadrupole precursor ion scans for decreasing amounts of beta casein digest

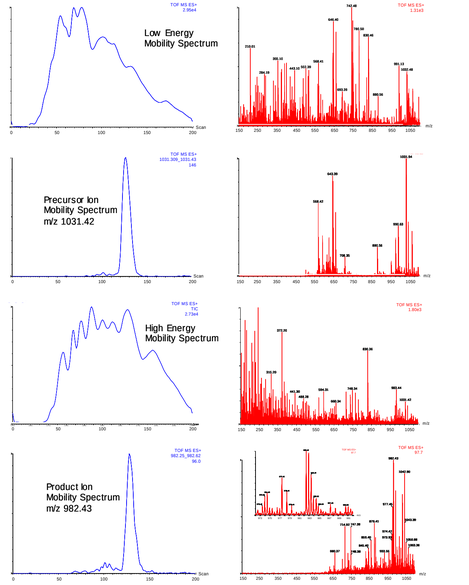

Figure 6 Ion mobility separations and their associated mass spectra obtained under low and high energy conditions for 100fmol/µL beta casein digest

CONCLUSIONS

- This study has demonstrated the feasibility of using a mobility-based separation of precursor ions to enhance duty cycle when compared with a scanning quadrupole.
- Further increases in performance have been demonstrated by using EDC acquisition on the oa-TOF analyser.
- This technique has been shown to enhance the sensitivity of precursor ion detection by at least a factor of 100 when compared with a scanning tandem quadrupole.

REFERENCES

1 'Applications of a Travelling Wave-Based Radio-Frequency-Only Stacked Ring Ion Guide', Giles K, Pringle SD, Worthington KR, Little D, Wildgoose JL and Bateman RH, *Rapid Commun. Mass Spectrom.*, **14** (2004) 2401

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