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A COMPARISON OF METHODS OF IMPROVING THE DUTY CYCLE ON ORTHOGONAL TOF MASS ANALYSERS

Jason Wildgoose; Steven Pringle; Kevin Giles; Robert Bateman; Steve Bajic
Waters MS Technology Center, Floats Road, Wythenshawe, Manchester, UK

OVERVIEW

Aim

- To compare methods of increasing the duty cycle of oa-ToF.

Results

- The observed duty cycle has been significantly increased over the whole of the mass range by utilising Ion Mobility Separation in conjunction with a T-Wave device synchronised with the application of the oa extraction field.

INTRODUCTION

When a continuous ion source is coupled to an oa-ToF mass analyser the duty cycle, or sampling efficiency, is typically about 25% for the highest m/z ions. The duty cycle decreases for ions of lower m/z in proportion to the square root of their m/z values. An established method of increasing the duty cycle involves accumulating ions from a continuous ion source and then extracting them in a pulse. This can increase the duty cycle over a restricted mass range, but for ions outside that range the duty cycle will be reduced.

It has been shown previously that the movement of ions can be precisely controlled in a collision cell utilising a combination of a stacked ring rf ion guide and programmable travelling wave. A photograph of the device is shown in figure 1.

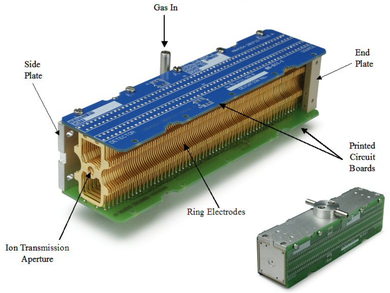


Figure 1: T-Wave collision cell

The application of a pulse to several ring electrodes distributed evenly along the length of the ion guide effectively divides ions axially into small packets.

PREVIOUS RESULTS

Previously[1] we reported a method that increases the duty cycle across a restricted m/z range. A travelling wave ion guide samples the continuous ion beam and converts it into a series of packets which are periodically released into the oa-TOF extraction region.

The oa-TOF push is synchronised with the arrival of the ions of interest from each packet, thereby increasing the duty cycle. Figure 2 shows the duty cycle enhancement obtained when the oa-TOF push delay is optimised for m/z 658 compared with the duty cycle achieved with asynchronous pushes.

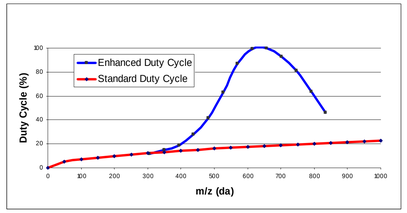


Figure 2: Single delay duty cycle window

The duty cycle improvement is evident over a significant m/z range, approximately 300 Da for a duty cycle of greater than 50% in the example illustrated. In general the m/z range for which the duty cycle is greater than 50% is around 45% of the center m/z.

To extend the duty cycle window over a wider m/z range, an additional stage of separation is required prior to the T-Wave ion guide. This extra stage of separation would act to restrict the m/z range in each packet of ions. As each packet is released, the oa-TOF extraction pulse would be synchronised with the m/z range within each packet.

Previously[1] we reported using an axial TOF as a means of achieving this extra stage of separation. This method involves accumulating ions from a continuous ion beam and ejecting them as a pulse into a flight tube. On exit from the flight tube, the ions are sample by the T-Wave ion guide. As the flight time is proportional to the square root of the m/z value, the first ions to exit the flight tube are of low m/z so only low m/z ions are present in the first packets released into the oa-TOF. The delay from packet release to oa-TOF push is incremented so that it is optimised for the particular m/z range being released from the cell at any given time. The results from this method may be seen in figure 3. The duty cycle is better than in the standard mode but is non-uniform across the m/z range

A second approach presented here is to use an Ion Mobility Separator (IMS) as the extra stage of separation in place of the axial TOF.

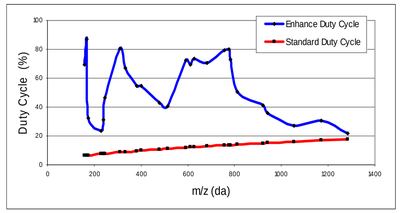


Figure 3: Wide m/z range duty cycle enhancement

EXPERIMENTAL

The test platform was modified by replacing the first T-Wave collision cell with a T-Wave IMS with a short hexapole before and after its entrance and exit lens plates. This system has been described in detail elsewhere[2]. A schematic diagram of the system is shown in figure 4.

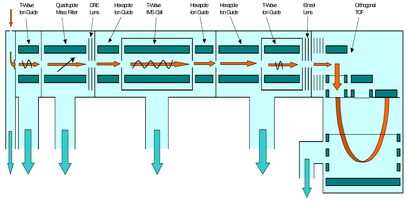


Figure 4: Schematic diagram of the modified test platform

Ion mobility spectra are obtained by periodically accumulating and releasing ions from the source T-Wave ion guide. The ions then enter the T-Wave IMS cell where they separate according to their mobility. On exit of the IMS the separation is maintained through two hexapole ion guides and a T-Wave ion guide before entering the oa-ToF. The oa-ToF push number is recorded with push 1 being the first push after the ions are released from the source T-Wave. After 200 pushes have been recorded the process is repeated until the acquisition is complete. Each block of 200 pushes is summed with all the push 1's added together, all the push 2's added together etc. Each push number now corresponds to a particular drift time where the drift time is equal to the push number multiplied by the pusher period. Mass chromatograms can then be produced showing the drift time profiles for each ion.

The temporal separation characteristic of a typical ion mobility separator is shown in figure 5 where ions from a peptide mixture are distributed in two distinct bands. For a given m/z value, multiply charged ions tend to traverse the IMS in a shorter time

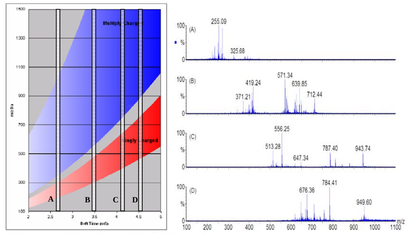


Figure 5: Ion Mobility Separation

than singly charged ions or alternatively for a given drift time the lower m/z ions tend to be singly charged and the higher m/z ions tend to be multiply charged. More importantly, when considering any particular charge state, the lower m/z ions tend to traverse the IMS in a shorter time than the higher m/z ions. It is this relationship between drift time and m/z for a particular charge state that can be exploited to enhance the oa-ToF duty cycle.

RESULTS

Figure 6 shows the ion mobility spectrum obtained for the fragment ions of Glu-fibrino Peptide (GFP). The doubly charged GFP parent at m/z 785.8 was isolated with the quadrupole and accelerated into the first hexapole ion guide operating at a pressure of around 5e-3 mbar allowing the parent ion to undergo collision induced dissociation. The fragment ions then undergo ion mobility separation and mass chromatograms of the major fragment ions are shown in figure 6. The drift time to m/z correlation previously described is clear from figure 6.

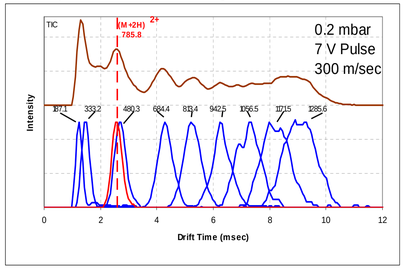
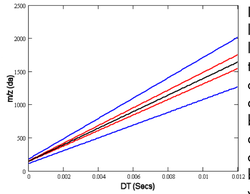


Figure 6: GFP fragment ions drift time data

Figure 7 shows a plot of the drift time versus m/z value for the ions in figure 6 (black line). The two red lines correspond to the half height drift time values for a particular ion versus the m/z value.



If the collision cell release to oa-ToF pulse delay is set so that at a particular drift time the duty cycle transmission window is centred on the black line then we can derive the two 50% duty cycle lines shown in blue ion versus the m/z value.

Figure 7: Drift time V's m/z

For a particular ion we can now plot the drift time profile and the duty cycle profile as shown in figure 8.

In figure 8 the true drift time profile of the 813 fragment ion from GFP is shown in red . The efficiency with which m/z 813 is pushed into the oa-ToF versus drift time is shown in blue. The product of these two plots is shown in black. The integral of the this product divided by the integral of the true drift time profile leads to the overall duty cycle for the GFP fragment at m/z 813. In this case the two plots are almost the same so the overall duty

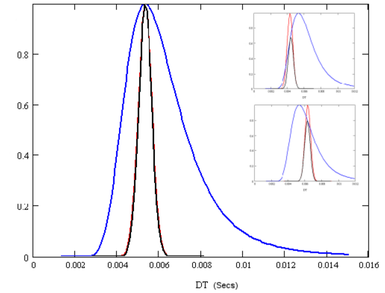


Figure 8: Duty cycle window

cycle is high at over 97%. However as this technique is based on ion mobility, it is possible for ions of the same charge state and the same nominal m/z value to have differing drift times.

Figure 8 (inset) shows the anticipated effect of these drift time variations. The two inset plots show the duty cycle for ions of m/z 813 but with drift times that vary by +/- 1msec. The resultant duty cycle for these ions is 78% and 66% respectively.

A comparison of high duty cycle mode compared with standard duty cycle mode for GFP fragment ions (sample consumption 100 fmols) is shown in figure 9.

It is clear that this method improves the duty cycle across the entire m/z range, a duty cycle of over 90% for m/z 480 and above was achieved. At m/z 333 a duty cycle of approximately 60% was achieved. The results shown so far are for singly charged product ions, however the principle can be readily applied to multiply charged precursor ion spectra also.

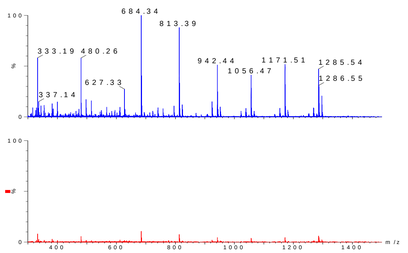


Figure 9: GFP sensitivity gain

In figure 10 the synchronisation has been optimised for the doubly charged band of ions, however there is also a comparable

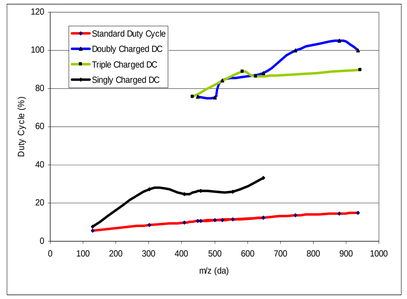


Figure 10: Multiply charged duty cycle enhancement

enhancement of triple charged ions. Additionally there is an enhancement in the singly charged ions but to a lesser degree. This discrimination effect could further improve detection limits for multiply charged precursor ions when background signal is dominated by singly charged ions.

CONCLUSIONS

- The duty cycle may be increased over a limited m/z range by using a T-Wave device synchronised with the oa-TOF pusher
- Additional separation prior to the T-Wave device extends the m/z range over which the duty cycle is enhanced.
- Both time of flight and ion mobility can be used as the extra stage of separation.

REFERENCES

1 Investigation into improving the Duty Cycle on oa-TOF mass analysers. S.Pringle, J.Wildgoose, K.Giles, K.Worthington, R.Bateman. Poster Presentation ASMS 2004

2 Applications of a travelling wave-based radio frequency only stacked ring ion guide. K.Giles, S.Pringle, K.Worthington, D.Little, J.Wildgoose, R.Bateman. *Rapid Commun. Mass Spectrom.* 2004; 18: 2401-2414 ***The travelling wave device described here is similar to that described by Kirchner in US Patent 5,206,506 (1993).***

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