ASMS 2006

A COMPARISON OF TRAVELLING WAVE AND DRIFT TUBE ION MOBILITY SEPARATIONS

Jason Wildgoose[1]; Kevin Giles[1]; Steven Pringle[1]; Stormy Koeniger[2]; Stephen Valentine[3]; Robert Bateman[1]; David Clemmer[2]
[1]Waters MS Technology Center, Manchester, UK [2]Indiana University, Bloomington, IN [3]Predictive Physiology and Medicine, Bloomington, IN

OVERVIEW

Aim

- To compare travelling wave and DC drift tube ion mobility separations with a view towards calibrating the travelling wave device.

Results

- The general trends in ion mobility separation of the travelling wave device are the same as the standard dc-only drift tube.
- A fundamental difference between the two separation techniques is that the dc-only ion mobility system provides a continuous mobility separation where an ions transit time through the device is proportional to the inverse of its mobility. However, in the travelling wave device ions above a certain mobility are carried through the device on a single wave with no separation, for ions with a mobility below this value the transit time through the device increases asymptotically away from this limit.

INTRODUCTION

Currently one of the major attractions of ion mobility spectrometry in the researchers laboratory is that the interaction cross-section between an ion and neutral gas can be determined, providing structural information of the ion for comparison with, or validation of, calculated values. This approach is possible since the factors affecting the mobility of an ion drifting through a gas under the influence of a weak electric field are well understood. A new approach to mobility separation has been developed where a travelling voltage wave (TW) is used to propel ions through a background gas. Whilst this device was primarily developed as a high transmission orthogonal separation technique, its possible use for measuring ion-neutral interaction cross-sections requires investigating.

EXPERIMENTAL

The travelling wave ion mobility separator (TWIMS) is incorporated in a Waters Synapt HDMS system. This system takes the form of a quadrupole/TWIMS/oa-Tof [1] a schematic of which is shown in figure 1.

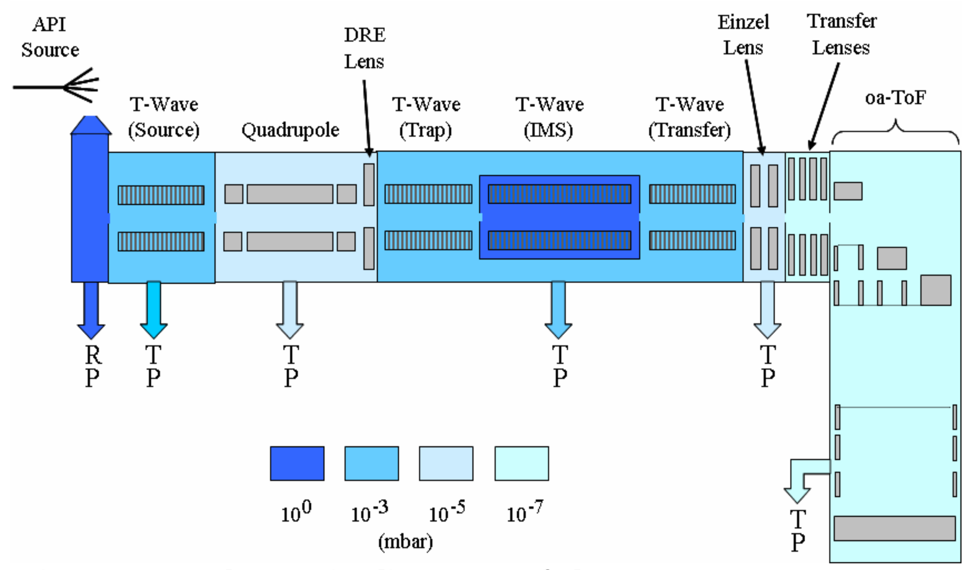

Figure 1: Schematic diagram of the Synapt HDMS system

The TWIMS device is based on a gas-filled stacked ring ion guide (figure 2) which has alternate phases of rf voltage applied to adjacent ring electrodes, providing radial confinement. Packets of ions are propelled through the device by repeating patterns of dc voltages (waves) applied sequentially to the ring electrodes. Ion mobility spectra are obtained by periodically accumulating and releasing ions from the Trap T-Wave ion guide. The ions then enter the TWIMS cell where they separate according to their mobility, those of lower mobility being 'overtaken' by the DC pulses more often than those of a higher mobility. On exit of the IMS the separation is maintained through a Transfer 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 Trap 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.

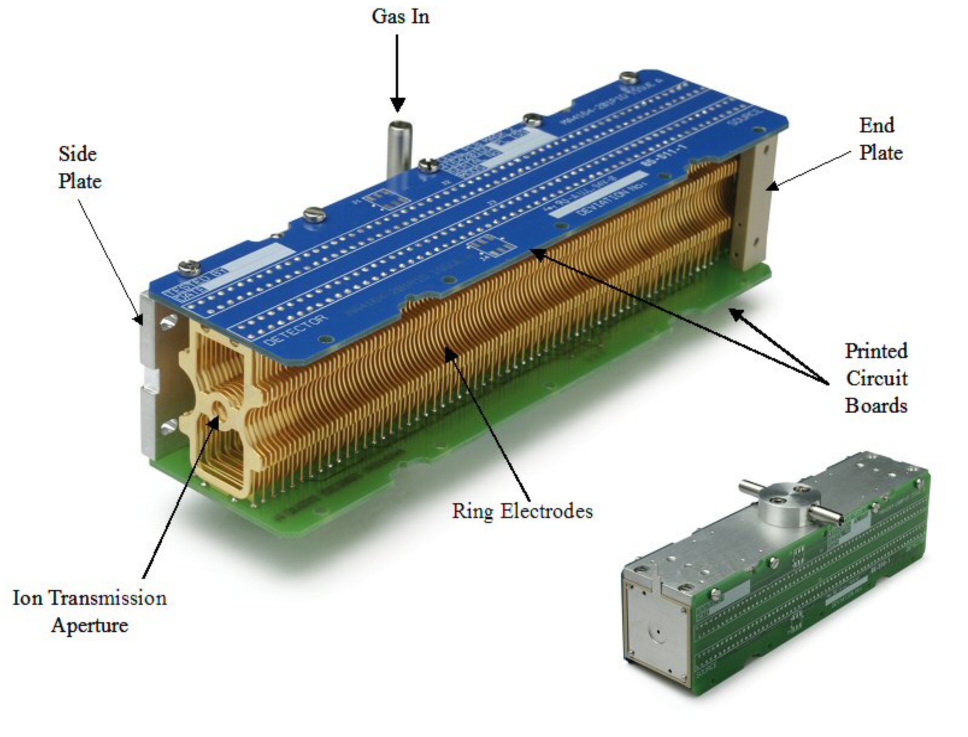

Figure 2: T-Wave collision cell

Digests of the proteins horse myoglobin, horse cytochrome C, horse albumin and bovine apotransferrin at a concentration of 1pmol/µl (50:50 ACN/H_2O, 0.1% formic acid) were infused separately at 5µl/min. The TWIMS was operated at an indicated pressure of 0.4 torr N_2 and a traveling wave pulse height of 10 Volts and velocity of 600 m/s. Relative transit times of various electrosprayed ions were then compared with results obtained from a dc-only drift tube described in reference [2].

RESULTS

Figure 3 shows a typical TWIMS data set for a digest of horse albumin. The left hand trace corresponds to the total ion current recorded over a 200 push experiment whilst right hand traces correspond to the reconstructed mass chromatograms for three doubly charged species at m/z 468.2, 575.3 and 734.4 Th respectively. For this experiment the pusher period was set to 100 µS resulting in an ion mobility experimental time of 20 mS. The three displayed species have drift times of approximately 2.7, 3.2 and 4.2 mS respectively. The resolution of the device is approximately 5 although this could be pushed closer to 10 if the experiment required.

Figure 4(a) shows the m/z versus drift time plot for a mixture of peptides obtained from the tryptic digests of horse myoglobin, horse cytochrome c, horse albumin and bovine apotransferrin when separated using a drift tube [2].

Figure 4 (b) shows the m/z versus drift time plot for the same mixture of peptides when separated using the TWIMS device.

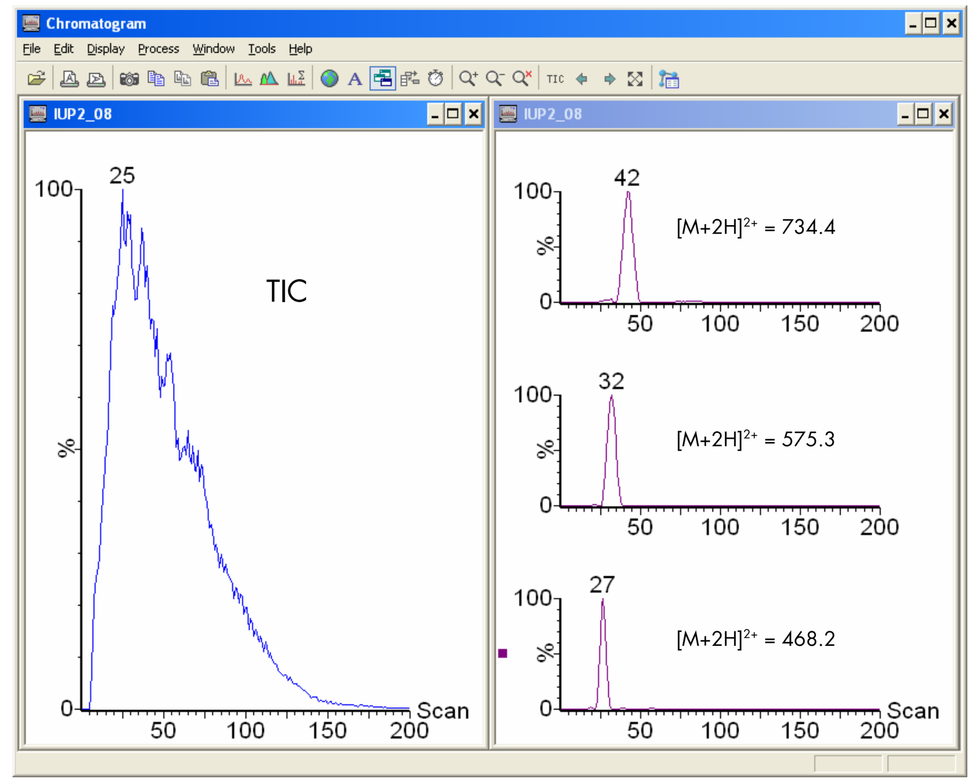

Figure 3: TWIMS of 1pmol/µL Horse Albumin digest

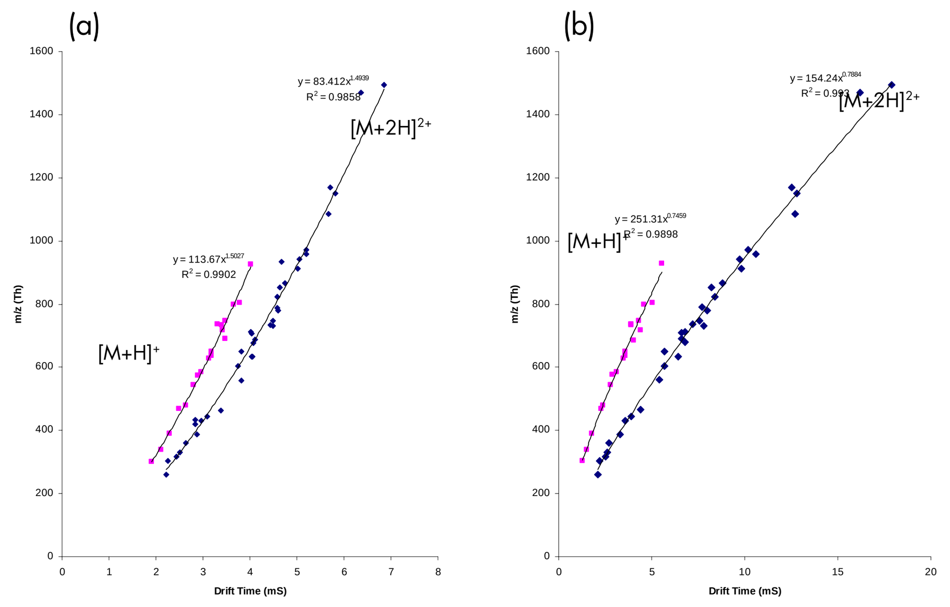

Figure 4: Comparison of m/z / drift time plots for a drift tube IMS and the TWIMS

These plots indicate that two of the general trends observed within a typical drift tube IMS data set are also observed within the TWIMS data set, these are.

- For a given m/z value, ions of a higher charge state tend to have shorter drift times.
- For a given charge state ions of lower m/z tend to have shorter drift times.

However, differences can be seen in the relationship between m/z and drift time for both data sets. To illustrate this a best fit curve of the form y=Ax^N was applied to both data sets. For the drift tube data (figure 4(a)) the values of N were 1.4939 and 1.5027 for the singly and doubly charged ion trend lines respectively. A value of N =1.5 would be expected for ions that are approximately spherical where the cross sectional area is proportional to Mass$^{2/3}$.

The same form of curve fitted to the TWIMS data set yields values for N of 0.7884 and 0.7459 for the singly and doubly charged ions respectively implying that the drift time through the TWIMS device is not inversely proportional to ion mobility as is the case with the drift tube. The relationship between ion mobility and drift time in the TWIMS device was investigated further using the singly charged data set from figure 4.

Figure 5 shows the singly charged ion drift time through the TWIMS device versus ion mobility where the mobility was calculated using published[2] cross-sectional areas and the pressure/gas within the TWIMS device. For comparison, the drift time versus ion mobility for an ideal DC drift tube is also plotted.

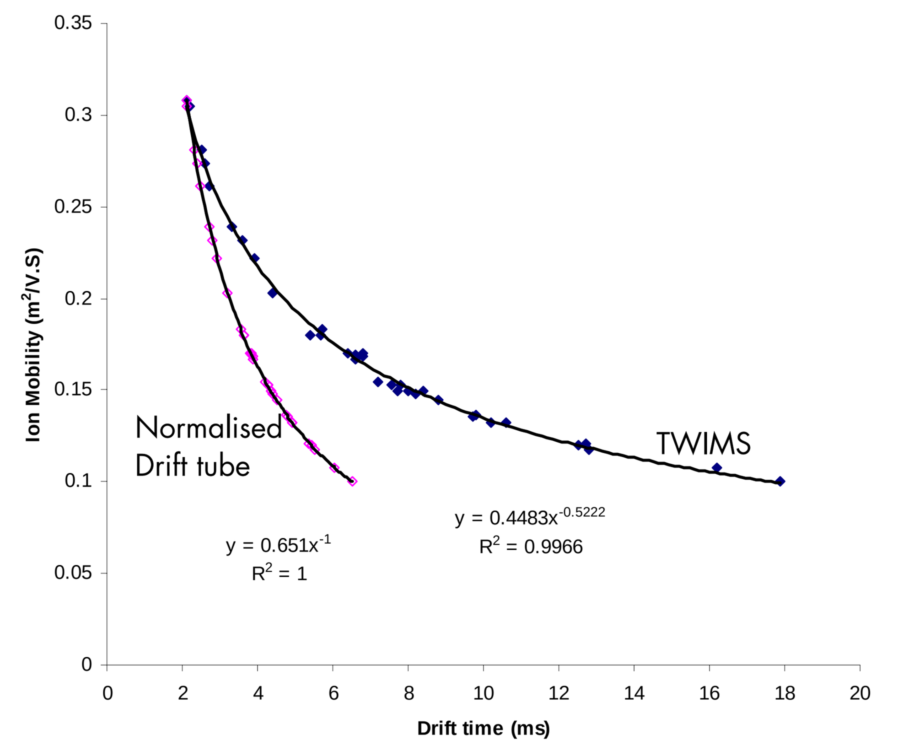

Figure 5: TWIMS drift time vs mobility plot

A curve of the form y=Ax^N was fitted to the data in figure 5. N for the TWIMS data was –0.5222 compared with N = -1 for the ideal drift tube. The fit to the TWIMS data is reasonably good with an R^2 value greater than 0.995. The value N = -0.5222 indicates that there may be close to an inverse square relationship between TWIMS drift time and ion mobility, however this would need to be confirmed by operating the TWIMS device over a wide range of pulse heights, pulse velocities and pressures.

When calculating the collision cross-sections from the measured drift times in a DC drift tube[2], equation 1 below is typically used.

$$\Omega = \frac{(18\pi)^{1/2}}{16}\frac{ze}{(k_bT)^{1/2}}\left[\frac{1}{m_I}+\frac{1}{m_N}\right]^{1/2} \times \frac{760}{P}\frac{T}{273.2}\frac{1}{N}\frac{t_D E_D}{L}$$

Equation 1

Where t_D, E_D, L, P and T correspond to the average drift time, electric field strength, the drift tube length, buffer gas pressure (in torr) and the temperature respectively. The other terms ze, N, k_b, m_I and m_B are the charge of the ion, the neutral number density, Boltzmann's constant, mass of the ion and mass of the neutral gas respectively. This equation is derived from the inverse relationship between drift time and ion mobility for drift tube ion mobility separators.

When calculating collision cross sections for the TWIMS device, equation 1 is generalised into equation 2.

$$\Omega = \frac{(18\pi)^{1/2}}{16}\frac{ze}{(k_bT)^{1/2}}\left[\frac{1}{m_I}+\frac{1}{m_N}\right]^{1/2} \times \frac{760}{P}\frac{T}{273.2}\frac{1}{N}At_D^B$$

Equation 2

Equation 2 transforms to equation 1 when we set A=E_D/L and B=1. The TWIMS data from figure 5 give A=1/0.4483 and B=0.5222. To test this equation a tryptic digest of horse albumin was infused and separated with the TWIMS device. A drift time versus ion mobility plot of the data is shown in figure 6. The curve fit yields values for A and B of 2.2227 and 0.524 respectively.

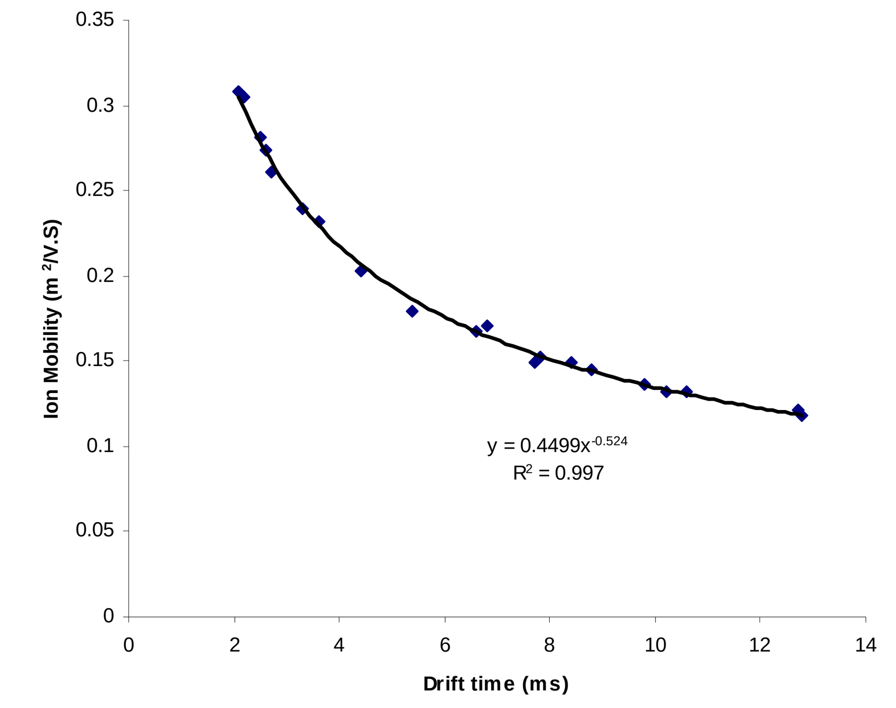

Figure 6: Horse albumin drift time versus mobility plot

Separate digests of horse myoglobin, horse cytochrome c and bovine apotransferrin were infused and the collision cross sections were calculated using equation 2 with values of 2.227 and 0.524 for A and B respectively. These cross sections were then compared with those in the published literature[2]. The results are shown in Table 1.

Protein	Cross Section [2]	Cross Section (TWIMS)	Delta Cross Section (%)
Horse Myoglobin	202.99	198.58	-2.22
Horse Myoglobin	172.29	170.96	-0.78
Horse Myoglobin	182.54	184.76	1.2
Horse Myoglobin	227.91	226.21	-0.75
Horse Cytochrome C	169.34	171.32	1.15
Horse Cytochrome C	181.96	182.01	0.03
Horse Cytochrome C	183.75	187.85	2.18
Horse Cytochrome C	207.13	204.47	-1.3
Horse Cytochrome C	257.73	258.12	0.15
Horse Cytochrome C	309.03	311.43	0.77
Horse Cytochrome C	286.74	295.58	2.99
Bovine Apotransferrin	139.78	140.59	0.58
Bovine Apotransferrin	200.45	193.51	-3.58
Bovine Apotransferrin	209.3	207.08	-1.07

Table 1

The delta cross section (%) column from table 12 has a mean of –0.05% and a standard deviation of 1.74%, the total spread being 6.57%.

Although equation 2 leads to a reasonably accurate determination of collision cross sections, the reason why B is the value it is (0.5222) needs further investigation. One approach to this would be to derive an expression describing an ions motion within the TWIMS device.

This was attempted by modelling the travelling wave as a simple sinusoid with the instantaneous velocity of an ion being the product of the ion mobility and the local field. This simplification allows an analytical expression to be derived for a given ion's velocity within the TWIMS. This velocity expression can then be integrated to give an equation describing the distanced travelled by an ion in each wave increment (equation 3).

$$\int_{t_n}^{t_{n+1}} \partial t = \int_{x_n}^{x_{n+1}} \frac{\partial x}{K.V.D.Cos(D.x)}$$

Equation 3

Where t_{n+1} - t_n is one travelling wave increment time step, K is the ion mobility, V is a constant related to the travelling wave pulse height and D is a constant related to the travelling wave repeat length. x_{n+1} - x_n is the distance an ion moves in one travelling wave increment.

This equation forms the basis of an iterative model that predicts the drift time through the TWIMS device for an ion of a given mobility. The model was applied to the ions from figure 5, the modelled drift time versus measured drift time plot can be seen in figure 7. The error bars correspond to the TWIMS vacuum gauge accuracy and the effect this error would have on the modelled drift time.

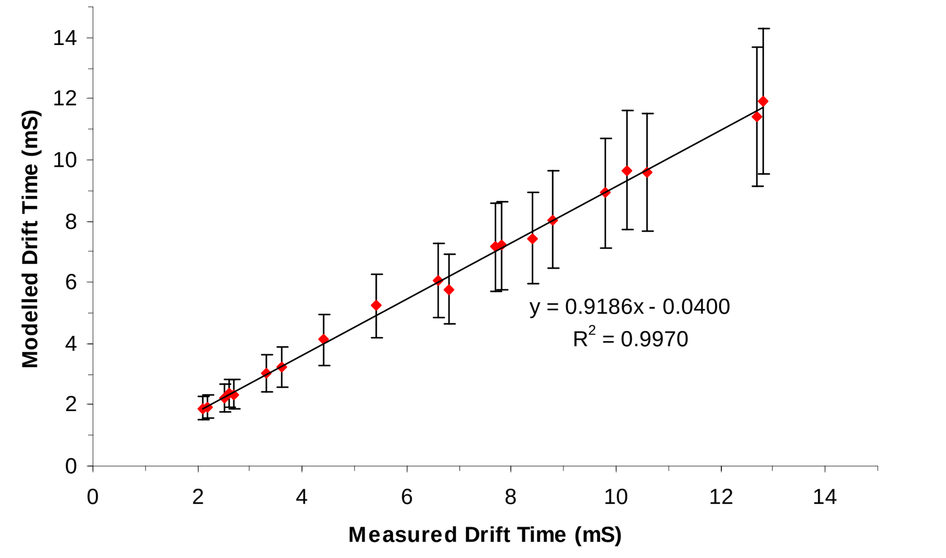

Figure 7: Model versus measured TWIMS drift time

CONCLUSIONS

- TWIMS displays the same general trends of charge separation and mass correlation seen in drift tube IMS.
- A generalisation of the collision cross section versus drift time equation allows for an accurate calibration of the TWIMS device resulting in calculated collision cross sections within +/- 3.5% (2SD).
- The coefficients in the generalised equation needs further investigation both in terms of reproducibility over a range of TWIMS conditions and in terms of origin.
- A simple periodic voltage waveform together with a drag model for ion motion gives a reasonable prediction of drift time through the TWIMS device.

REFERENCES

1 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).*

2 A Database of 660 Peptide Ion Cross Sections : Use of Intrinsi Size Parameters for Bona Fide Predictions of Cross Sections. Stephen Valentine, Anne Counterman, David Clemmer. *J Am Soc Mass Spectrom 1999, 10, 1188-1211.*

720001745EN