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Ion mobility mass spectrometry of proteins in a modified commercial mass spectrometer

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Abstract

Ion mobility has emerged as an important technique for determining biopolymer conformations in solvent free environments. These experiments have been nearly exclusively performed on home built systems. In this paper we describe modifications to a commercial high performance mass spectrometer, the Waters UK "Ultima" Q-Tof, that allows high sensitivity measurement of peptide and protein cross sections. Arrival time distributions are obtained for a series of peptides (bradykinin, LHRH, substance P, bombesin) and proteins (bovine and equine cytochrome c, myoglobin, α-lactalbumin) with good agreement found with literature cross sections where available. In complex ATD's, mass spectra can be obtained for each feature confirming assignments. The increased sensitivity of the commercial instrument is retained along with the convenience of the data system, crucial features for analysis of protein misfolding systems.

Keywords: Ion mobility; Mass spectrometry; Peptide cross section; Protein structure; Protein folding

1. Introduction

The three dimensional conformation of a protein is one of its most important properties and plays a crucial role in determining its biological activity. The misfolding of proteins is thought to play an important role in the onset of a number of diseases and there is an urgent need to develop techniques that allow one to determine the conformations of proteins isolated from biological sources. Until relatively recently, most studies of the conformations of proteins have been carried out on crystals by means of X-ray methods [1] or in solution by means of nuclear magnetic resonance spectrometry [2,3]. Although studies in the condensed phase allow one to work with high molecular densities, the environments under which the proteins are studied are far removed from the biological conditions in which the proteins are normally found. Since the effects of differing environments on the conformation of individual proteins are largely unknown, attention has turned more recently to the study of protein conformation in the gas phase which allows the study of different, intrinsic conformations of a protein in the absence of solvent effects [4–6]. Once information on these has been obtained, it may be possible to study the changes in conformation that occur as the degree of solvation of the protein is increased, leading to an increased understanding of conformations in the normal biological environments of the protein.

The first investigations of protein conformation that made use of a mass spectrometer involved a study of the H/D exchange of exposed amide hydrogen atoms both in solution [7–9] and in the gas phase [10–12]. A somewhat more direct method is based on the determination of collisional cross sections of mass selected ions formed by electrospray ionisation. Ions are passed through a low pressure collision cell and detected by a second mass spectrometer [13–16]. An adaptation of this method, which gave promising results, involved the modification of a commercial mass spectrometer to study the conformations of a number of peptides [17]. A second method is based on ion mobility measure-

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ments in which the time taken to traverse a cell containing a collision gas can be related to the collision cross section of an ion [18–21]. These, in turn, can be related to the three-dimensional conformation of the ion by means of modelling studies [22,23]. This technique has been successfully applied to various types of clusters [24–27], polymers [28,29] and to the study of both small and larger biopolymers [30–34] but a drawback of the technique is that it has required the construction of a purpose-built mass spectrometer specifically designed for this type of work. This paper describes the modification of a commercial mass spectrometer and associated software in order to obtain data with improved sensitivity over typical home built instruments and with sufficient accuracy for structural characterization.

2. Instrumentation development and experimental details

The instrument chosen for modification to carry out ion mobility measurements was an API hybrid quadrupole orthogonal time-of-flight (Tof) mass spectrometer (Waters, UK) which is one to two orders of magnitude more sensitive than the "Quattro" triple quadrupole instrument previously used for collision cross section studies [17]. The use of a commercial instrument rather than a purpose built instrument for this work has a number of advantages:

(i) The sensitivity of the instrument is greater than that of purpose-built instruments described in the literature and allows work to be carried out at concentrations closer to those of biological interest.
(ii) The increased throughput of a commercial instrument increases the speed of analysis and facilitates the automation of the experiment.
(iii) The selectivity of the measurement can be increased by the addition of a mass measurement capability and, if required, by the addition of a conformational filter. This is particularly relevant for work in which a small fraction of abnormally folded protein is present in large excess of the normal protein.
(iv) The use of commercial data acquisition systems and software packages improves the analysis of information obtained from the experiment.

A schematic of the modified Waters UK "Ultima" Q-Tof instrument is shown in Fig. 1. The modifications are in the two transfer regions of the instrument between the source and the quadrupole mass filter. In the first of these, the usual RF-only guide was replaced by ion storage and ion mobility regions and in the second, the RF-only ion guide was modified to allow the generation of an axial voltage gradient. All the ion guides used in this experiment have a stacked ring-electrode geometry, as shown in Fig. 2, in which alternate electrodes have 180° different phases of RF voltage applied to them. The electrodes are 0.5 mm thick with a 5.0 mm diameter ion transmission aperture and are spaced 1.5 mm apart centre-to-centre. The RF-only ion storage region and the ion mobility region have lengths of 75 and 152 mm, respectively. The same RF voltage is applied to the two regions but in the ion mobility region, the field is segmented axially to facilitate the generation of an axial electric field. The electrodes in this region are grouped in sets of four to which is applied a constant dc voltage; the groups are interconnected by a resistor chain and the RF voltage is capacitatively coupled to each same-phase electrode. An axial field is produced by applying different voltages to each end of the resistor chain. The field generated is not axially uniform but has a "staircase" structure as illustrated in Fig. 3.

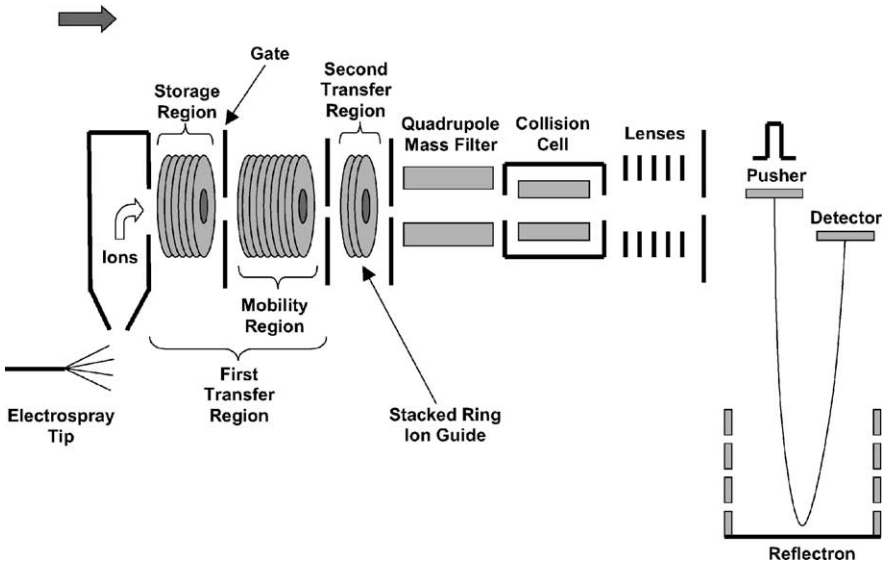

Fig. 1. A schematic of the Waters "Ultima" Q-TOF mass spectrometer modified for measurement of ion mobilities. See text for description of the new elements.

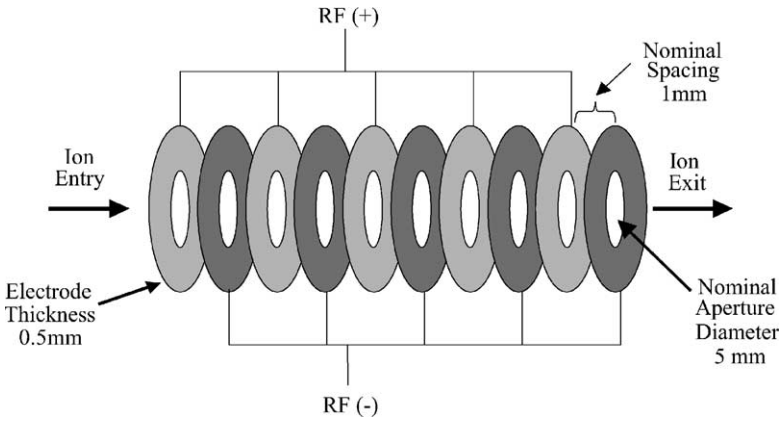

Fig. 2. A schematic of a stacked ring ion guide region of the instrument.

A gate between the storage and mobility sections allows the pulsed delivery of ions for mobility separation. The gate voltage is set at 10 V above that of the storage region to facilitate trapping of the ions but is dropped to the storage region voltage for a period of typically 200 μs to allow ions to enter the mobility region. The gate pulses are generated by means of a LeCroy LW120 Arbitrary Waveform Generator. The storage/mobility sections operate at a pressure of about 2.5 mbar. The frequency of the applied RF field is 0.8 MHz and the peak-to-peak voltages employed are dependent on the masses of the ions of interest. The mobility section operates with a potential difference of 200 V producing an average field of 13.2 V/cm.

The second stacked ring ion guide has a length of 30.5 mm and is also segmented axially to allow application of an axial field to reduce the transit time of the ion packets produced by mobility separation. Since the pressure in this region is approximately 10^{-3} mbar, the axial field is necessary to counter the effects of collisions between the ions and neutrals which would slow the ions, causing a reduction in separation and resolution. The collisions are sufficiently infrequent, however, for no further mobility separation to occur. This guide was operated with an RF field of 1.9 MHz and peak-to-peak voltages that depended on the mass range of interest. The potential difference across the device was 2 V giving rise to an average axial field of 0.66 V/cm.

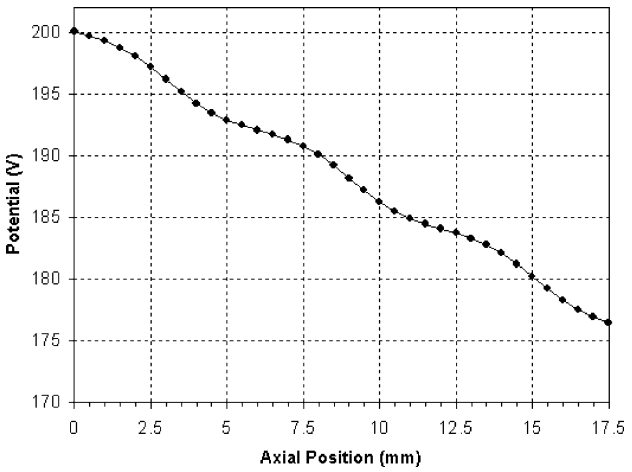

Fig. 3. A plot of a region of the axial potential in the ion mobility section vs. the positions of ring elements illustrating the slight non-uniformity in the gradient due to the grouping of rings into groups of four having the same dc potential.

Ions continually flow into the storage region from the source region and are prevented from exiting by the dc voltage applied to the gate. The gate voltage is pulsed to release ions into the mobility region where they separate according to their mobility and pass through the transfer lens and enter the ToF analyser for mass analysis. In this configuration the quadrapole and collision cell are set to pass ions of all masses.

Ion packets were separated by their relative mobilities and their arrival times at the ToF analyser were determined by use of the MassLynx control and data acquisition software after suitable modification. ToF data acquisition is initiated by the voltage pulse applied to the gate injecting ions into the mobility region. When the pulse of ions exiting the mobility region enters the ToF source it is subjected to two hundred orthogonal acceleration pulses. The acquisition process then awaits the next group of ions produced by a gate pulse prior to recording a further 200 spectra, which are stored together with the corresponding spectra from the first group of ions. This process is repeated for a time that depends on the mass range of interest to be acquired and consequently on the ToF pulse repeat time. Display of the total ion current recorded as a function of the pulse number gives an arrival time spectrum at the ToF mass analyser. For example, if a mass range of 1250 Da was required, this would correspond to a 50 μs pulse repeat time and the total mobility experiment would then be recorded over a 10 ms (200 × 50 μs) time period. The use of a constant 200 pulses per mobility spectrum was chosen in order to encompass all expected ion drift times in the mobility device. In these experiments, the mobility spectra were summed for five seconds then repeated for further intervals of five seconds until the acquisition was halted.

Samples were purchased from Sigma-Aldrich Company Limited (Poole, UK) and used without further purification. Ion mobility spectra of the following peptides were investigated: bombesin, luteinizing hormone-releasing hormone (LHRH), bradykinin and substance P, each at a concentration of 0.2 μM. Protein samples of bovine and equine cytochrome c, myoglobin, lysozyme and α-lactalbumin were investigated at a concentration of 1 μM.

3. Results and discussion

A number of proving experiments have been undertaken in order to determine the performance of the instrument under various conditions and to establish the reproducibility, sensitivity, speed, dynamic range and information content of each type of experiment.

3.1. Reproducibility of arrival time distributions

Fig. 4 shows the results of a typical ion mobility arrival time measurement in which the arrival time distribution of the +2 charged state of bombesin was determined. Each experiment consisted of 200 repeated scans, each of 75 μs duration, giving a total time for the experiment of 15 ms. Data were acquired for 5 s. The figure gives the results obtained for 20 such experiments. The figure indicates a signal occurs at the 45th pulse of each 200 pulse sequence, indicating good reproducibility. These experiments were conducted with a drift cell of length 150 mm, a bath gas of nitrogen at a pressure of ∼2.4 mbar and a voltage gradient of 200 V across the cell.

3.2. Calculation of cross sections from arrival time distributions

Fig. 5 shows the arrival time distribution for the +2 charge state of bradykinin (*m*/*z*, 531) and for this data, the arrival

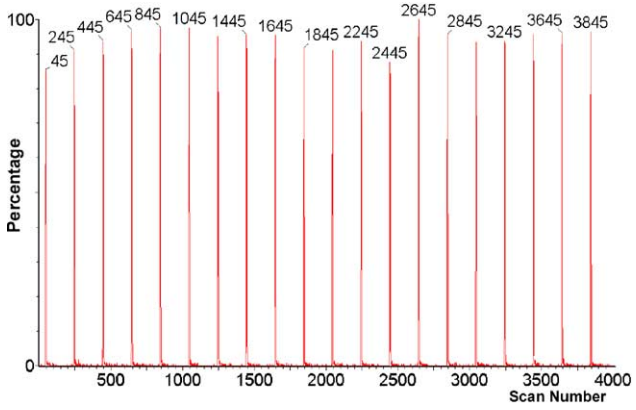

Fig. 4. Arrival time distributions for the +2 charge state of bombesin. For each group of ions exiting the mobility cell 200 time of flight spectra are taken at 75 μs intervals. In this example the ions arrive at the ToF source during the 45th spectra of the first 200 spectra. They continue to arrive on the 45th ToF spectra during repeated runs as well.

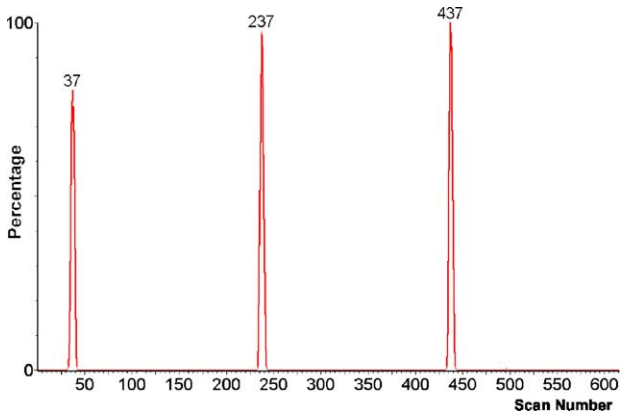

Fig. 5. Arrival time distributions for the +2 charge state of bradykinin (see caption for Fig. 4).

time is given by the expression

$$t_{AR} = \text{scan number} \times \text{scan time} \times \text{charge state}$$

which for the +2 state of bradykinin gives

$$t_{AR} = 37 \times 75 \times 2\,\mu s = 5.55\,ms$$

A correction must be applied to this arrival time to give the required time for passage through the drift cell, t_D, since after leaving the drift cell, the ions pass through the transfer optics, the quadrupole mass filter and the collision cell before reaching the Tof mass analyser. This value can be measured experimentally by varying the voltage drop across the drift cell but in these proving experiments an estimation, based on instrument geometry, has been employed. The additional flight time t_F is given by

$$t_F = K\left(\frac{m}{z}\right)^{1/2}\ \mu s$$

Here K is a constant and m/z the mass to charge ratio. K has been determined to have a value of 19.5 ± 2.5 for this particular instrument geometry [35]. This flight time needs to be subtracted from the measured arrival times in order to obtain the corrected drift times for passage through the drift cell. For Bradykinin (+2)

$$t_F = 19.5\sqrt{531} = 449\,\mu s$$

Hence for the +2 charge state of Bradykinin, $t_D = t_{AR} - t_F = 5.1$ ms.All cross sections in this work are calculated relative to that of the +2 charge state of bradykinin, which is assumed to be 241 Å^2 [36], and the drift time is related to the cross section by use of the equation [35]

$$\Omega_{AVG} = \frac{(18\pi)^{1/2}}{16}\left[\frac{1}{m} + \frac{1}{m_B}\right]^{1/2}\frac{Ze}{(k_B T)^{1/2}}\frac{t_D E}{L}\frac{1}{\rho}$$

where Ω_{AVG} is the average cross section of an ion of mass m (Da) and charge Ze, m_B is the mass of the bath gas of density ρ, E is the electric field strength, t_D the drift time (arrival time) in a cell of length L cm and k_B is the Boltzman constant.

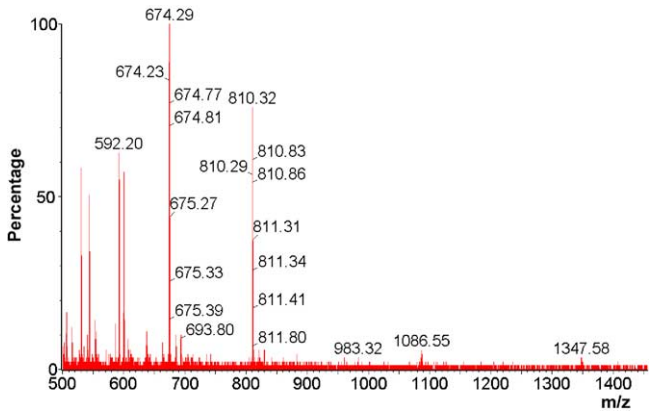

Fig. 6. The electrospray ionisation mass spectrum of a mixture of bombesin, bradykinin, LHRH and substance P.

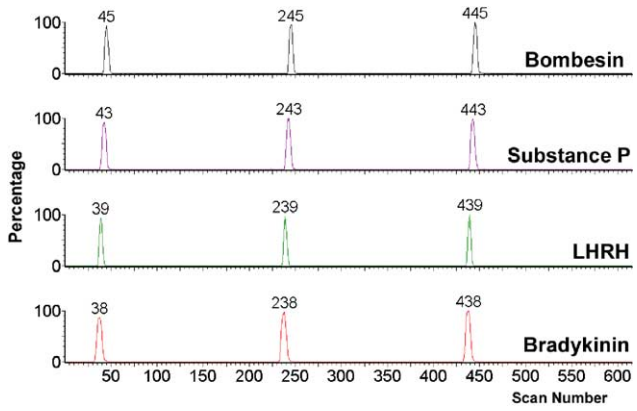

Fig. 7. Arrival time distributions for the four components in the peptide mixture.

3.3. Measurement of the cross sections of components in a peptide mixture

Fig. 6 shows an electrospray mass spectrum of a mixture of four peptides of similar mass-to-charge ratio. The arrival times for the peptides are collected as described above and the cross-scans of the +2 charge state ions are shown in Fig. 7. The corrected drift times and resulting cross sections are shown in Table 1 and clearly indicate that the experimental method allows one to distinguish between small peptides of similar cross section. The indicated values (based on a value of 241 Å^2 for bradykinin) are in good agreement with literature values [17].

Table 1
Cross sections of various peptides

Peptide	Mass to charge	Drift times (μs)	Cross section (Å^2)
Bombesin	810.5	6195	284
Substance P	674.5	5944	273
LHRH	591.5	5376	247
Bradykinin	531	5251	241

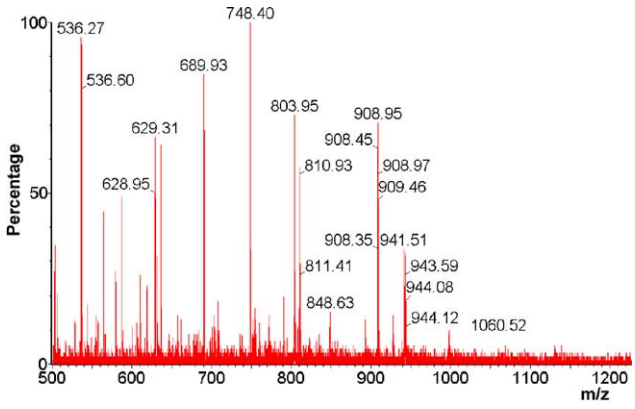

Fig. 8. The electrospray ionisation mass spectrum of a tryptic digest of myoglobin to which has been added a small quantity of bombesin.

3.4. Determination of the cross sections of peptides in complex digests

In order that ion mobility experiments can be used to study problems of biological significance, it is necessary to demonstrate that reliable measurements can be made on complex mixtures. This has often been accomplished by prior separation of the ions of the different components by passing them through a mass analyser but in these experiments no prior mass selection is used. There is therefore a need to establish that the presence of a range of different ions in the drift tube does not influence the data recorded. Fig. 8 shows an electrospray mass spectrum of a complex mixture formed by the tryptic digest of myoglobin to which has been added a small amount of the peptide bombesin. The peak at *m/z* 810.5, which corresponds to the +2 charge state of bombesin, is a minor component of the mixture. Fig. 9 shows the arrival time measurement for the Bombesin +2 ions which is excellent agreement with that measured for the pure component and shown in Fig. 7. A similar experiment was carried out in which a small amount of bradykinin was added to a tryptic digest of myoglobin and the arrival time distribution for the +2 charge state of bradykinin was

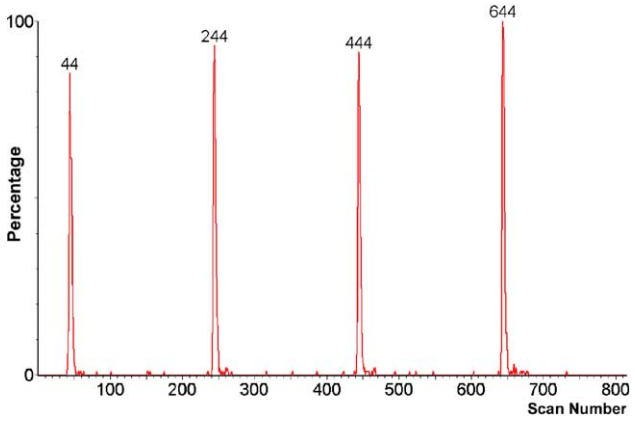

Fig. 9. Arrival time distributions for the +2 state of bombesin present in the tryptic digest mixture.

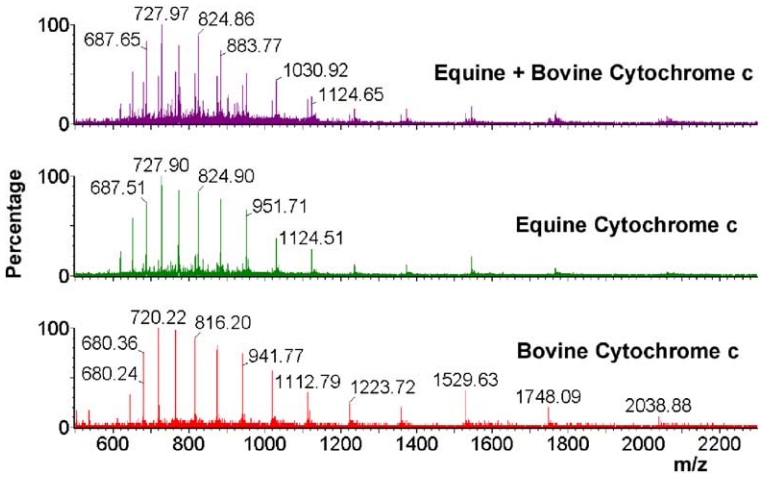

Fig. 10. The electrospray ionisation mass spectra of bovine cytochrome c, equine cytochrome c and an equimolar mixture of these.

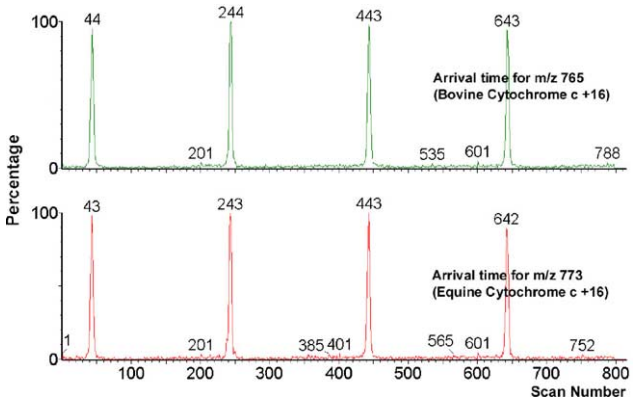

Fig. 11. Arrival time distributions for the +16 charge states of bovine and equine cytochrome c.

in excellent agreement with that shown in Fig. 7. This indicates that reliable data can be obtained without the need for separation of ions prior to their entering the drift cell.

3.5. Studies of bovine and equine cytochrome c

Although the experiments described above demonstrate that cross sections of simple peptides can be measured quite accurately, much of the interest in this type of measurement lies in determining the conformations of proteins. Studies have therefore been carried out on both bovine and equine cytochrome c, which have molecular masses of 12,230 and 12,360 Da respectively. The electrospray ionisation of proteins yields a range of multiple charge states resulting from different extents of protonation of the molecule. When the

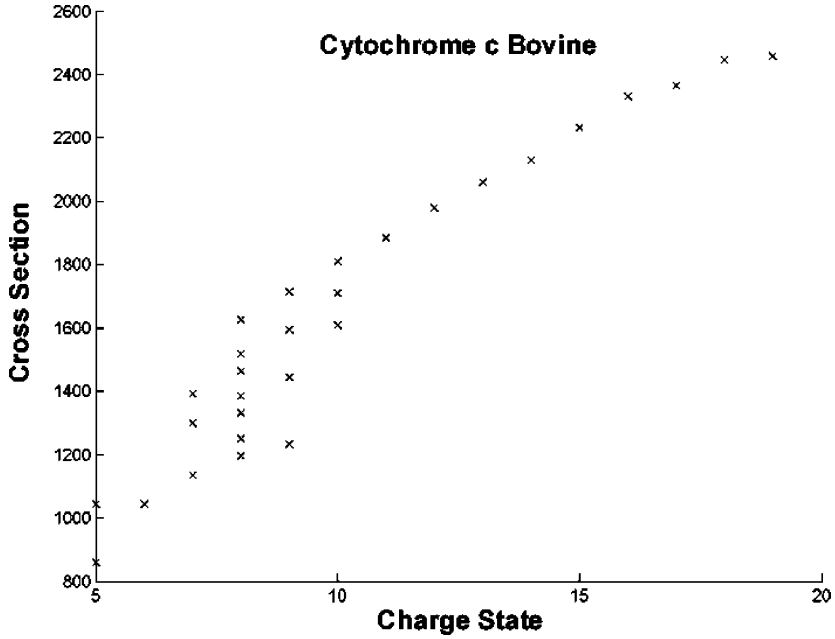

Fig. 12. A plot illustrating the variation of the cross section of bovine cytochrome c with its charge state.

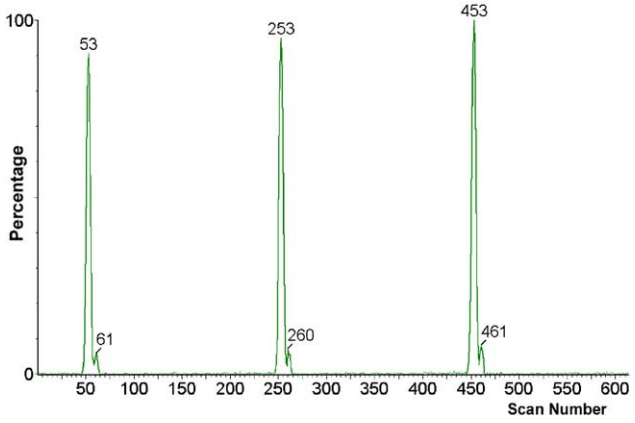

Fig. 13. Arrival time distributions for the +7 charge state of α-lactalbumin showing the presence of a small percentage of a conformer having a higher cross section than that of the dominant conform.

extent of protonation is small, it is assumed that the resulting ion has a conformation that approximates to the native conformation of the uncharged molecule. As the extent of protonation increases, producing more highly-charged ions, the configuration adopted becomes more open and a number of increasingly open conformations may be observed before the final configuration is attained.

Fig. 10 shows the ESI mass spectra of samples of bovine and equine cytochrome c and of an equimolar mixture. The spectrum of bovine cytochrome c shows peaks from *m*/*z* 2038.88 due to $[M + 6H]^{6+}$ to *m*/*z* 644.7 due to $[M + 20H]^{20+}$ ions and that of equine cytochrome c shows a similar series between *m*/*z* 2061 and *m*/*z* 619. In Fig. 11, arrival times measured for the +16 charge states for both species are shown; these are very similar as expected. The species can easily be distinguished, however, by means of their different mass to charge ratios. Data for all of the charge states for both species can be acquired in a single experiment lasting only 15 ms. and in Fig. 12 is shown the cross sections calculated from the experimental arrival times for the series of multiply-protonated bovine cytochrome c. Similar plots of data for multiply-protonated equine cytochrome c and myoglobin were obtained. In all cases, the cross sections agree well with literature values for these proteins [34,37].

A similar study was also carried out on the slightly larger proteins lysosyme c (14,313 Da) and α-lactalbumin (14,186 Da). As expected, the two proteins were found to have very similar cross sections that varied in a similar manner with the charge state but in the case of the +7 charge state of α-lactalbumin, the arrival time distribution indicated the presence of a small percentage of a conformer having a somewhat larger cross section than the main conformer as is seen in Fig. 13. It is interesting to note that the +11 charge state exhibits a single arrival time, indicating that it exists in a single conformation. The correlation of solution phase structures with those obtained following solvent evaporation is an area of intense interest at present. For very large systems, such as Gro EL [38], it is clear that solution structural integrity is retained in the gas phase while for very small systems, such as the peptides described earlier (Table 1) solution phase information is lost in the gas phase. In intermediate sizes, a case by case analysis is necessary.

3.6. Variation of the cross section of bradykinin with charge state: comparison with literature values

A detailed study [30] of the arrival times of various charge states of bradykinin in a purpose-built ion mobility instrument by Bowers et al. has shown that the +3 and +2 charge states each have a single conformation and show a single

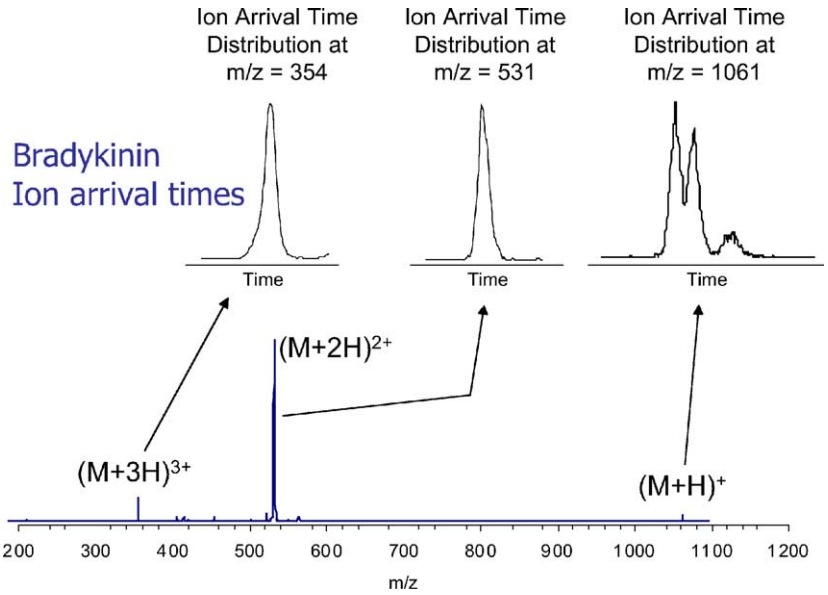

Fig. 14. Arrival times for the various charge states of bradykinin (from [30]).

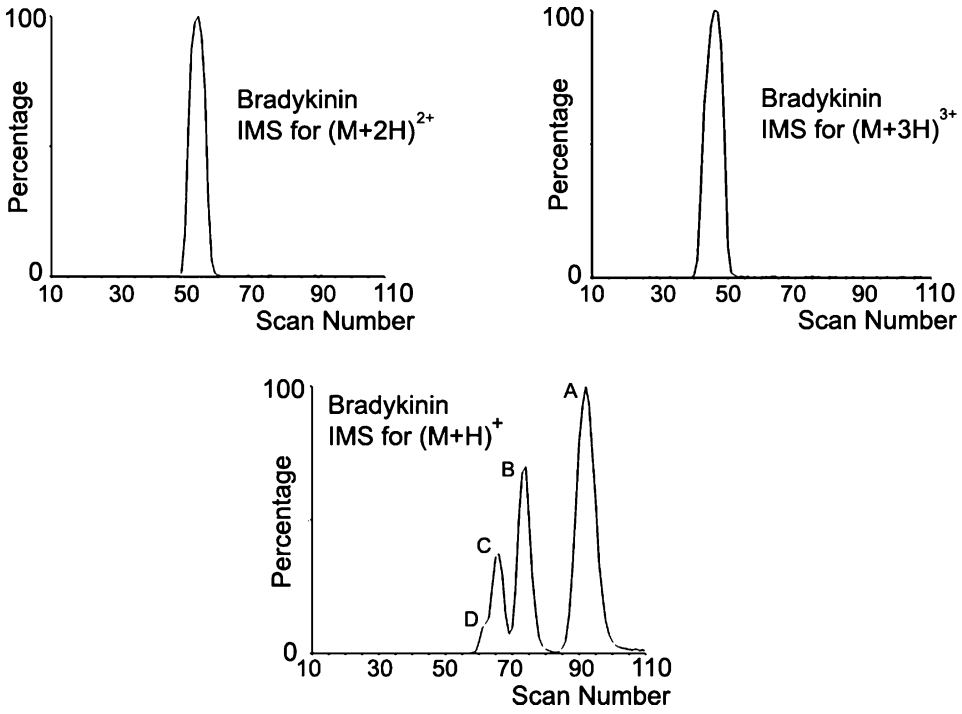

Fig. 15. Arrival times for the various charge states of bradykinin (present work).

peak in the arrival time distribution spectrum. The singly charged state, however, shows multiple peaks in its arrival time spectrum and the additional peaks have been assigned, on the basis of modelling studies, to oligomeric species. Their data for bradykinin is illustrated in Fig. 14 and are essentially identical to those obtained using the modified commercial instrument in the present work, shown in Fig. 15. An advantage of the present experiment, however, is that it is possible to obtain a reconstructed mass spectrum of ions that give rise to a specific peak in the arrival time spectrum. Fig. 16 shows the reconstructed mass spectra from the three main components of the +1 charge state arrival time distribution spectrum. These data confirm directly that the peaks in the $[M + H]^+$ ATD are due to the formation of multiply-charged oligomeric species as predicted theoretically [30].

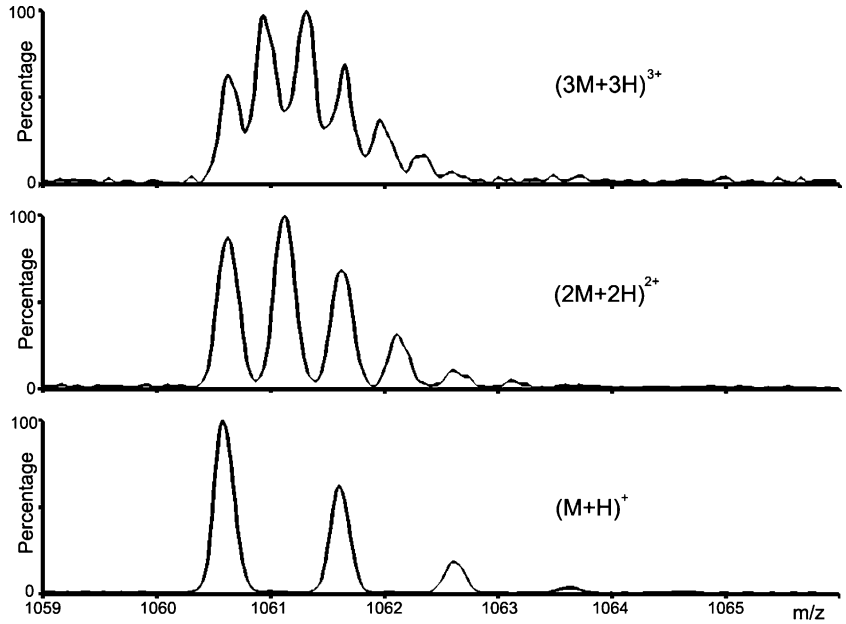

Fig. 16. Reconstructed mass spectra of species contributing to the arrival time distribution for the +1 charge state of bradykinin.

4. Conclusions

A commercial mass spectrometer has been successfully modified to produce a sensitive and selective instrument for the measurement of ion mobilities from which the cross sections of peptides and proteins may be determined and from which information on the conformations of these species in the gas phase may be obtained. The modifications to the instrument were accomplished without any loss of sensitivity so that work could be carried out on very small amounts of sample. The experiment is fast, allowing a high throughput, very small sample sizes, is reproducible and has a high information content. It is possible to work with complex mixtures and to obtain information on different components within a mixture. The ability to determine the reconstructed mass spectrum of species giving rise to a specific peak in the arrival time distribution spectrum provides valuable additional information. The results obtained agree well with those in the literature.

A particular advantage of the high sensitivity is the fact that it will provide a method of detecting relatively small quantities of a misfolded protein in the presence of an excess of normal protein. This is likely to be important in the early detection of the onset of a number of diseases and the ability to obtain the mass spectra of different conformers will assist in identifying any small changes in composition that occur as a result of the misfolding.

Acknowledgements

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References

[1] T.L. Blundell, L.N. Johnson, Protein Crystallography, Academic Press, New York, 1976.
[2] W. Braun, Quart. Rev. 19 (11987) 115.
[3] K. Wüthrich, Acc. Chem. Res. 22 (1989) 36.
[4] T. Wyttenbach, M.T. Bowers, Modern Mass Spectrom. Top. Curr. Chem. 225 (2003) 207.
[5] M.F. Jarrold, Ann. Rev. Phys. Chem. 51 (2000) 179.
[6] M.F. Jarrold, Acc. Chem. Res. 32 (1999) 360.
[7] V. Kattu, B.T. Chait, Rapid Commun. Mass Spectrom. 5 (1991) 2141. J. Am. Chem. Soc. 115 (1993) 6317.
[8] D.L. Smith, Y. Deng, Z. Zhang, J. Mass Spectrom. 32 (1997) 135.
[9] C. Woodward, J. Am. Soc. Mass Spectrom. 10 (1999) 627.
[10] B.E. Winger, K.J. Light-Wahl, A.L. Lockwood, R.D. Smith, J. Am. Chem. Soc. 114 (1992) 5897.
[11] X. Cheng, C. Fenselau, Int. J. Mass Spectom. Ion Processes 122 (1992) 109.
[12] T.D. Wood, R.A. Corush, F.M. Wampler III, D.P. Little, P.B. O'Connor, F.W. McLafferty, Proc. Natl. Acad. Sci. U.S.A. 92 (1995) 2451.
[13] T. Covey, D.J. Douglas, J. Am. Soc. Mass Spectrom. 4 (1993) 616.
[14] B.A. Collins, D.J. Douglas, J. Am. Chem. Soc. 118 (1996) 4488.
[15] Y.L. Chen, B.A. Collings, D.J. Douglas, J. Am. Soc. Mass Spectrom. 8 (1997) 681.
[16] K.A. Cox, R.K. Julian, R.G. Cooks, R.E. Kaiser, J. Am. Soc. Mass Spectrom. 5 (1994) 127.
[17] A.C. Gill, K.R. Jennings, T. Wyttenbach, M.T. Bowers, Int. J. Mass Spectrom. 195–196 (2000) 685.
[18] G. von Helden, M-T. Hsu, P.R. Kemper, M.T. Bowers, J. Chem. Phys. 95 (1991) 3835;
G. von Helden, T. Wyttenbach, M.T. Bowers, Science 267 (1995) 1483.
[19] T. Wyttenbach, P.R. Kemper, M.T. Bowers, Int. J. Mass Spectrom. 212 (2001) 13.
[20] J.L. Fye, M.F. Jarrold, Int. J. Mass Spectrom. 187 (1999) 507.
[21] S.J. Valentine, M. Kulchana, C.A.S. Barnes, D.E. Clemmer, Anal. Chem. 212 (2001) 97.
[22] J. Gidden, M.T. Bowers, J. Phys. Chem. B 107 (2003) 12829.
[23] M.D. Leavell, S.P. Gaucher, J.A. Leary, J.A. Taraszka, D.E. Clemmer, J. Am. Soc. Mass Spectrom. 13 (2002) 284.
[24] G. von Helden, M-T. Hsu, N. Gotts, M.T. Bowers, J. Phys. Chem. 97 (1993) 8182.
[25] J. Lerme, P. Dugourd, R.R. Hudgins, M.F. Jarrold, Chem. Phys. Lett. 304 (1999) 19.
[26] R.R. Hudgins, M. Imai, M.F. Jarrold, P. Dugourd, J. Chem. Phys. 111 (1999) 7865.
[27] A.A. Shvartsburg, R.R. Hudgins, P. Dugourd, M.F. Jarrold, Chem. Soc. Rev. 30 (2001) 26.
[28] T. Wyttenbach, G. von Helden, M.T. Bowers, Int. J. Mass Spectrom. Ion Proc. 165/166 (1997) 377;
J. Gidden, A.T. Jackson, J.H. Scrivens, M.T. Bowers, Int. J. Mass Spectrom. 188 (1999) 127.
[29] J. Gidden, M.T. Bowers, A.T. Jackson, J.H. Scrivens, J. Am. Soc. Mass Spectrom. 13 (2002) 499;
J. Gidden, T. Wyttenbach, M.T. Bowers, A.T. Jackson, J.H. Scrivens, J. Am. Chem. Soc. 122 (2000) 4692;
J. Gidden, T. Wyttenbach, J.J. Batka, P. Weis, A.T. Jackson, J.H. Scrivens, M.T. Bowers, J. Am. Soc. Mass Spectrom. 10 (1999) 883.
[30] T. Wyttenbach, G. von Helden, M.T. Bowers, J. Am Chem. Soc. 118 (1996) 8355.
[31] K.B. Shelimov, D.E. Clemmer, R.R. Hodgins, M.F. Jarrold, J. Am. Chem. Soc. 119 (1997) 2240.
[32] J. Gidden, M.T. Bowers, J. Am. Soc. Mass Spectrom. 14 (2003) 161.
[33] D.T. Kaleta, M.F. Jarrold, J. Phys. Chem. 107 (2003) 14529.
[34] E.R. Badman, C.S. Hoaglund-Hyzer, D.E. Clemmer, J. Am. Soc. Mass Spectrom. 13 (2002) 719.
[35] E.A. Mason, E.W. McDaniel, Transport Properties of Ions in Gases, Wiley, New York, 1988.
[36] T. Wyttenbach, J.E. Bushnell, M.T. Bowers, J. Am. Chem. Soc. 120 (1998) 5098.
[37] K.B. Shelimov, M.F. Jarrold, J. Am. Chem. Soc. 119 (1997) 2987.
[38] F. Sobott, C.V. Robinson, Int. J. Mass Spectrom., doi:10.1016/ j.ijms.2004.05.010.