

MULTI-REFLECTING TOF MASS SPECTROMETRY

5 CROSS-REFERENCE TO RELATED APPLICATION

This application claims priority from and the benefit of United Kingdom patent application No. 2301462.4 filed on 1 February 2023. The entire contents of this application are incorporated herein by reference..

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FIELD OF THE INVENTION

The present invention relates generally to mass spectrometers and in particular to time of flight mass spectrometers, such as Multi-Reflecting Time-of-Flight (MRTOF) mass spectrometers, and methods of their use.

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BACKGROUND

Time of Flight (TOF) mass analysers are well known devices that use an ion accelerator to pulse a packet of ions into a field-free region towards an ion detector. The pulsed ions separate according to their mass to charge ratios as they travel towards the detector, such that ions having different mass to charge ratios arrive at, and are detected by, the detector at different times. The mass analyser is then able to determine the mass to charge ratios of the detected ions based on the duration of time between the ions being pulsed and the respective times at which they are detected.

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It is known to be advantageous in TOF mass analysers to provide a relatively long ion flight path from the ion accelerator to the detector, because this enables ions having different mass to charge ratios to separate to a relatively high degree and hence the mass analyser is able to have a relatively high mass resolution and mass measurement accuracy. Alternatively, providing such a relatively long ion flight path enables a target mass resolution or mass measurement accuracy to be achieved whilst being relatively less stringent parameters with other parameters relating to the mass analyser, such as detector peak width and mechanical tolerances.

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Multi-Reflecting Time of Flight (MRTOF) mass analysers are known that provide the above-described relatively long ion flight path length by repeatedly reflecting the ions between two ion mirrors as the ions drift in a drift dimension from the ion accelerator to the ion detector. Such arrangements enable a relatively long ion flight path in an instrument having a relatively small volume. It is also known to reflect the ions in the drift dimension so as to cause them to make multiple passes along the mass analyser in the drift dimension, the ions being reflected back and forth between the mirrors during each pass. This increases the number of mirror reflections that the ions perform, and hence increase the ion flight path length, without increasing the size of the mass analyser. This mode of operation is referred to in the art as a “zoom” mode or a “multi-pass” mode.

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However, it can be difficult to operate a mass analyser in the above-described mode without ions undergoing different ion flight path lengths to the detector, since lower mass to charge ratios travel faster in the drift dimension than higher mass to charge ratios and so may have undergone more passes along the mass analyser, and hence more mirror reflections, than the ions of higher mass to charge ratio. Such modes can also limit the mass analyser to having a relatively low sensitivity, as the relatively long ion flight times limit the duty cycle of the instrument.

SUMMARY

From a first aspect the present invention provides a mass spectrometer comprising: an ion accumulation device for accumulating and pulsing out ions and a time of flight mass analyser. The mass analyser comprises: a plurality of ion mirrors for reflecting ions; an ion accelerator arranged and configured to receive ions from the ion accumulation device and pulse them into one of the ion mirrors such that ions are reflected back and forth between the mirrors in a first dimension as the ions drift in a drift dimension; reflectors for reflecting the ions in the drift dimension; an ion detector for detecting ions; and control circuitry configured to activate the reflectors so as to cause the ions to make multiple passes along the drift dimension and then deactivate one of the reflectors so as to allow ions to pass to the ion detector and be detected, wherein the timings at which the reflectors are activated and deactivated is such that only ions within a first range of mass to charge ratios are capable of having undergone the same number of passes in the drift dimension at the time that they are detected by the ion detector. The mass spectrometer has control circuitry that synchronises the time that ions are pulsed out of the ion accumulation device with the time that ions are pulsed by the ion accelerator such that only ions having mass to charge ratios within said first range are pulsed by the ion accelerator into said one of the ion mirrors.

The spectrometer is configured such that the ion accumulation device pulses ions having a certain range of mass to charge ratios to the ion accelerator, where said first range is smaller than and within said certain range. In other words, the control circuitry synchronises the time that ions are pulsed out of the ion accumulation device with the time that ions are pulsed by the ion accelerator such that ions having mass to charge ratios within said first range are pulsed by the ion accelerator, and ions having mass to charge ratios outside said first range are transmitted from the ion accumulation device to the ion accelerator but are not pulsed by the ion accelerator.

It has been realised that synchronising the ion accumulation device with the ion accelerator is a particularly convenient technique for restricting the range of mass to charge ratios that are mass analysed so that only ions that have made the same number of passes along the mass analyser reach the detector, whilst also providing the mass analyser with a relatively high sampling duty cycle and sensitivity.

The mass analyser may be configured to determine the mass to charge ratios of the detected ions based on the durations of time between the ions being pulsed by the ion accelerator and the respective times at which they are detected.

The mass spectrometer may be configured such that the ions that are pulsed out of the ion accumulation device separate according to mass to charge ratio as they travel to the ion accelerator, and so that ions of different mass to charge ratio enter the ion accelerator at different times.

5 For example, the region between the exit of the ion accumulation device and the ion accelerator may be substantially free of electric fields (in the average direction of travel of the ions). This region may also have a length and be at a pressure such that there are relatively few, or substantially no, collisions between the ions and background gas molecules.

10 The time at which ions are pulsed out of the ion accumulation device and the time at which ions are pulsed out of the ion accelerator are synchronised such that only ions having the first range of mass to charge ratio (or a narrower range that is within the first range) is within the ion accelerator at the time that ions are pulsed out of it. Ions having mass to charge ratios outside this first range will have already passed through the ion
15 accelerator or will not have entered it yet at the time that the ions are pulsed out of the ion accelerator.

The ion accumulation device may comprise an ion guide having a trapping electrode at its downstream exit.

20 The ion guide may be an RF ion guide, i.e. in which RF voltages are applied to electrodes of the ion guide so as to confine ions therein.

The ion accumulation device may be configured to accumulate ions and periodically pulse a packet of ions towards the MRTOF mass analyser. The ion accelerator may be synchronised with the ion accumulation device in the manner described herein for each pulse from the ion accumulation device. The ion accelerator may be configured to
25 repeatedly pulse packets of ions towards the ion accelerator during a single experimental run, and the ion accelerator may be synchronised with the ion accumulation device for each pulse from the ion accumulation device.

The mass spectrometer may be configured to pulse ions into the MRTOF mass analyser such that ions in different ion packets are detected at the detector during separate
30 non-overlapping time periods. In other words, no ions that are injected into the MRTOF in one ion packet are detected at the detector before all of the ions in the preceding ion packet have been detected at the detector, i.e. the MRTOF mass analyser may not be operated in an encoded frequent pulsing mode.

Ion optics may be arranged between the ion accumulation device and the ion
35 accelerator for transferring ions from the ion accumulation device to the ion accelerator. The ion optics may comprise, for example, at least one of an ion lens, one or more ion beam collimator plates, or an ion guide.

The ion accelerator may be configured to pulse ions in a substantially orthogonal direction to the drift dimension, e.g. the first dimension is orthogonal to the drift dimension.

40 The ion accelerator may receive ions as they are traveling in a first direction and pulse them such that they are accelerated in a substantially orthogonal direction into one of

the ion mirrors. The ions received at the ion accelerator from the ion accumulation device may be travelling substantially in the drift dimension.

Alternatively, the ions received at the ion accelerator may be travelling in a dimension that is substantially orthogonal to the drift dimension. In these embodiments, 5 the ion accelerator may be configured such that when it pulses the ions, the ions are urged in the drift dimension as well as in the first dimension into the ion mirror.

The plurality of ion mirrors may comprise two mirrors that are spaced apart in the first dimension. It is contemplated that more than two ion mirrors may be provided.

The mass spectrometer may be configured to allow a user to select what the first 10 range of mass to charge ratios is; and the control circuitry may be configured to control the timings at which the reflectors are activated and deactivated, and the time that ions are pulsed out of the ion accumulation device relative to the time that ions are pulsed by the ion accelerator, in response to the selection by the user.

The mass spectrometer may be configured to allow a user to select the number of 15 passes that the ions should perform prior to detection; and the control circuitry may be configured to control the timings at which the reflectors are activated and deactivated, and the time that ions are pulsed out of the ion accumulation device relative to the time that ions are pulsed by the ion accelerator, in response to the selection by the user so that ions having the first range of mass to charge ratios undergo the selected number of passes 20 prior to detection.

Accordingly, the mass spectrometer has a use interface for selecting the first range of mass to charge ratios and/or for selecting the number of passes that the ions should perform prior to detection.

The mass spectrometer may comprise a mass filter upstream of the ion 25 accumulation device for mass filtering ions passing to the ion accumulation device.

The mass spectrometer may comprise control circuitry configured to control the mass filter so that the mass filter only transmits ions having mass to charge ratios within a second range into the ion accumulation device, wherein said first range is narrower than and within the second range.

30 The provision of such a mass filter reduces the ion current entering the ion accumulation device and consequently the amount of charge per push of the ion accelerator (for a given accumulation time), thereby reducing space-charge effects in the ion accumulation device and/or mass analyser and improving dynamic range. This may improve the mass accuracy and mass resolution of the instrument. The provision of the 35 mass filter also enables a greater proportion of the ions that enter the ion accumulation device to have mass to charge ratios corresponding to those that will be pulsed by the ion accelerator. This is particularly beneficial in an MRTOF mass analyser, which conventionally have had a relatively low sensitivity.

40 It is contemplated that a device other than a mass filter may be used to selectively transmit ions having mass to charge ratios in said second range to said ion accumulation device. For example, a mass selective ion trap may be provided upstream of the ion accumulation device and the mass selective ion trap may be controlled so as to only

transmit ions having mass to charge ratios in the said second range to the ion accumulation device.

5 A first of the reflectors may be arranged at a first end, in the drift dimension, of the mass analyser; the ion accelerator and ion detector may be arranged at a second opposite end, in the drift dimension, of the mass analyser; and a second of the reflectors may be arranged between, in the drift dimension, the first reflector and the ion detector; wherein the timings at which the reflectors are activated and deactivated is such that ions within the first range of mass to charge ratios undergo an even number of passes in the drift dimension at the time that they are detected by the ion detector.

10 Ions passing through the mass analyser will have different speeds in the drift dimension depending on their mass to charge ratios, i.e. ions having a lower mass to charge ratio will have a higher speed in the drift dimension than ions having a higher mass to charge ratio.

15 The control circuitry may be configured to maintain the first reflector activated so as to be capable of reflecting ions for a duration starting when ions having the lowest mass to charge ratio in said first range would reach the first reflector for the first time, wherein the duration lasts at least until ions having the highest mass to charge ratio in said first range would be reflected by the first reflector so as to make their final pass in the drift dimension.

20 The control circuitry may be configured to activate the second reflector starting when ions having the highest mass to charge ratio in said first range would have passed the second reflector for the first time after having been injected into the mirrors by the ion accelerator.

25 The control circuitry may be configured to: (i) maintain the second reflector activated until ions having the highest mass to charge ratio in said first range would have been reflected by the second reflector so as to start their penultimate pass in the drift dimension; and (ii) deactivate the second reflector before ions having the lowest mass to charge ratio in said first range would have reached the second reflector during their final pass in the drift dimension, so as to allow ions to reach the ion detector.

30 Ions may be caused to undergo, for example, 4, 6, 8, 10 or 12 (or any even number that is greater than 12) passes along the drift dimension prior to the ions being detected at the ion detector.

35 Alternatively, the ion detector may be arranged at a first end, in the drift dimension, of the mass analyser; the ion accelerator may be arranged at a second opposite end, in the drift dimension, of the mass analyser; a first and a second of the reflectors may be arranged between, in the drift dimension, the ion accelerator and the ion detector such that the first reflector is closer to the ion detector than the second reflector; and the timings at which the reflectors are activated and deactivated is such that ions within the first range of mass to charge ratios undergo an odd number of passes in the drift dimension at the time that they are detected by the ion detector.

40 Ions having a lower mass to charge ratio will have a higher speed in the drift dimension than ions having a higher mass to charge ratio.

The control circuitry may be configured to: (i) activate the first reflector so as to reflect ions at a time prior to the time that ions having the lowest mass to charge ratio in said first range would reach the first reflector for the first time; (ii) maintain the first reflector activated until ions having the highest mass to charge ratios in the first range would have been reflected by the first reflector so as to make their penultimate pass in the drift dimension; and (iii) deactivate the first reflector before ions having the lowest mass to charge ratio in said first range would have reached the first reflector during their final pass in the drift dimension, so as to allow ions to reach the ion detector.

The control circuitry may be configured to: (i) activate the second reflector starting when ions having the highest mass to charge ratio in said first range would have passed the second reflector for the first time after having been injected into the mirrors by the ion accelerator; and (ii) maintain the second reflector activated until ions having the highest mass to charge ratio in said first range would have been reflected by the second reflector so as to make their final pass in the drift dimension.

It will be appreciated that the mass spectrometer may control the timings at which the first reflector is activated and deactivated so as to cause ions to have undergone any odd number of passes along the drift dimension at the point that the ions are detected. For example, ions may be caused to undergo 3, 5, 7, 9 or 11 (or any odd number that is greater than 11) passes along the drift dimension prior to the ions being detected at the ion detector.

The mass spectrometer disclosed herein may comprise a plurality of electrodes arranged between the ion mirrors and spaced apart in the drift dimension such that the ions pass between adjacent ones of the electrodes as the ions travel between the mirrors. A first of said electrodes may be the first reflector, and the mass spectrometer may be configured to apply a first voltage to the first electrode when the first reflector is activated for reflecting ions in the drift dimension, and to apply a different voltage to the first electrode when the first reflector is deactivated so that the first electrode and an adjacent one of the electrodes focus ions passing therebetween in the drift dimension. Alternatively, or additionally, a second of said electrodes may be the second reflector, and the mass spectrometer may be configured to apply a second voltage to the second electrode when the second reflector is activated for reflecting ions in the drift dimension, and to apply another voltage to the second electrode when the second reflector is deactivated so that the second electrode and an adjacent one of the electrodes focus ions passing therebetween in the drift dimension.

Less preferred embodiments are also contemplated that do not synchronise the time that ions are pulsed from an ion accumulation device with the time that the ion accelerator pulses ions, in order to select the range of mass to charge ratios that are mass analysed.

Accordingly, from a second aspect the present invention provides a mass spectrometer comprising: a first device for transmitting ions; and a time of flight mass analyser. The mass analyser comprises: a plurality of ion mirrors for reflecting ions; an ion accelerator arranged and configured to receive ions from the first device and pulse them

into one of the ion mirrors such that ions are reflected back and forth between the mirrors in a first dimension as the ions drift in a drift dimension; reflectors for reflecting the ions in the drift dimension; an ion detector for detecting ions; and control circuitry configured to activate the reflectors so as to cause the ions to make multiple passes along the drift dimension and then deactivate one of the reflectors so as to allow ions to pass to the ion detector and be detected, wherein the timings at which the reflectors are activated and deactivated is such that only ions within a first range of mass to charge ratios are capable of having undergone the same number of passes in the drift dimension at the time that they are detected by the ion detector. The first device is configured to supply ions to the ion accelerator such that only ions having mass to charge ratios within said first range are present in the ion accelerator when it pulses ions into said one of the ion mirrors.

The mass spectrometer according to the second aspect of the invention may have any of the features described in relation to the first aspect of the invention, except that the ion accelerator that is synchronised with the ion accumulation device is not provided, but said first device is provided instead for supplying ions to the ion accelerator.

For example, the spectrometer is configured such that the first device supplies ions having a certain range of mass to charge ratios to the ion accelerator, where said first range is smaller than and within said certain range.

The first device may be a mass selective ion trap and the mass spectrometer is configured to eject ions from the mass selective ion trap to the ion accelerator.

The operation of the mass selective ion trap may be synchronised with the time that ions are pulsed out of the ion accumulation device such that only ion having mass to charge ratios within said first range are pulsed by the ion accelerator into said one of the ion mirrors.

Alternatively, the first device may be a mass filter configured to only transmit ions having mass to charge ratios within a certain range and to filter out other ions, wherein said first range is smaller than and within said first range.

The present invention provides a multi-reflecting time of flight mass spectrometer configured to cause ions to be reflected multiple times between ion mirrors in a first dimension whilst the ions are also reflected back and forth in a drift dimension by reflectors; wherein the spectrometer is configured to activate and deactivate the reflectors at times such that ions having mass to charge ratios within a first range have undergone the same number of reflections in the drift dimension at the time that they are detected; and wherein the mass spectrometer is configured so as to only admit ions having mass to charge ratios within the first range into the ion mirrors.

This mass spectrometer may have any of the features described herein.

The present invention provides a method of mass spectrometry that uses the mass spectrometer described herein.

Accordingly, the present invention provides a method of mass spectrometry comprising: providing a mass spectrometer as described herein; supplying ions from the ion accumulation device or first device to the ion accelerator; applying a voltage pulse to an electrode of the ion accelerator so as to pulse ions into one of the ion mirrors such that ions

are reflected back and forth between the mirrors in a first dimension as the ions drift in a drift dimension; activating the reflectors so as to cause the ions to make multiple passes along the drift dimension and then deactivating one of the reflectors so as to allow ions to pass to the ion detector and be detected, wherein the timings at which the reflectors are
5 activated and deactivated is such that only ions within a first range of mass to charge ratios are capable of having undergone the same number of passes in the drift dimension at the time that they are detected by the ion detector; wherein the ion accumulation device or first device supplies ions to the ion accelerator such that only ions having mass to charge ratios within said first range are present in the ion accelerator when it pulses ions into said one of
10 the ion mirrors.

BRIEF DESCRIPTION OF THE DRAWINGS

Various embodiments of the present invention will now be described, by way of
15 example only, and with reference to the accompanying drawings in which:

Fig. 1 is a schematic illustration of an MRTOF mass analyser operating in a known mode of operation;

Fig. 2 shows an MRTOF mass analyser configured to operate in a multi-pass or zoom mode of operation;

20 Fig. 3 shows a schematic of a portion of a mass spectrometer according to an embodiment of the present invention in which the ions undergo an even number of passes in the drift dimension before being detected;

Fig. 4 shows a schematic of a portion of a mass spectrometer according to an embodiment of the present invention in which the ions undergo an odd number of passes
25 in the drift dimension before being detected;

Fig. 5 shows a timing diagram illustrating an example of how components of the spectrometer may be operated relative to each other in the embodiment shown in Fig. 3;

Figs. 6A-6B shows mass spectra obtained for the third isotope of Leucine Enkephalin when using an embodiment of the present invention and when using a
30 conventional approach, and Fig. 6C shows a computer simulation of mass spectral data for the third isotope of Leucine Enkephalin; and

Fig. 7 shows an embodiment that is substantially the same as that of Fig. 4, except that the drift-dimension reflectors are in different positions.

35 DETAILED DESCRIPTION

Fig. 1 is a schematic illustration of an MRTOF mass analyser operating in a known mode of operation. The instrument comprises two ion mirrors 2 that are elongated in a drift dimension (i.e. the z-dimension) for reflecting ions, an ion accelerator 4 for pulsing ions into
40 one of the mirrors, and a detector 6 for detecting the ions at the end of their flight path through the mass analyser.

In use, a beam of ions 8 enters the mass analyser travelling along the drift dimension and passes into the ion accelerator 4. Voltages are applied to electrodes of the ion accelerator so as to orthogonally accelerate a packet of the ions in the x-dimension towards one of the ion mirrors 2. The ions therefore have a velocity component in the x-dimension and also retain a velocity component in the drift dimension. As such, the ions are injected towards a first of the ion mirrors at an angle to the x-dimension. The ions pass into the first ion mirror and are reflected back towards a second of the ion mirrors. The ions then enter the second ion mirror and are reflected back to the first ion mirror. The first ion mirror then reflects the ions back to the second ion mirror. This continues and the ions are continually reflected between the two ion mirrors as they drift along the device in the drift dimension until the ions impact upon the ion detector 6. The ions therefore follow a substantially sinusoidal mean trajectory within the x-z plane.

A series of ion lenses 10 is provided between the ion mirrors 2. The ions pass through these lenses as they travel between the ion mirrors and the lenses are configured to provide electric fields that prevent the ion packet from expanding in the drift dimension to an extent that the ion packet has a larger width in the drift dimension than the detecting area of the ion detector.

The mass analyser determines the mass to charge ratios of the ions based on the duration between the time that they were pulsed by the ion accelerator and their respective times of detection at the ion detector.

It will be appreciated that because the ions are reflected back and forth between the ion mirrors, this provides a relatively long ion flight path between the ion accelerator and the detector, whilst enabling the instrument to have a relatively small volume.

It is known to increase the ion flight path length within the mass analyser still further by reflecting the ions in the drift dimension such that the ions make multiple passes along the mass analyser in the drift dimension, whilst being reflected between the ion mirrors multiple times during each pass in the drift dimension. This mode is known in the art as a "multi-pass" or "zoom" mode of operation.

Fig. 2 shows an MRTOF mass analyser configured to operate in a multi-pass or zoom mode of operation. The mass analyser has the same configuration as described in relation to Fig. 1, except that the ion detector 6 is arranged at the same end of the mass analyser (in the drift dimension) as the ion accelerator 4, and a drift-dimension reflector 12 is arranged at the other end of the mass analyser. In use, the ion accelerator 4 pulses ions into one of the mirrors 2 and the ions are reflected back and forth between the mirrors in the same way as described in relation to Fig. 1, until the ions reach the drift-dimension reflector 12. The ions are then reflected in the drift dimension by the reflector 12 such that they travel back towards the detector 6, being reflected back and forth between the mirrors 2 as they do so. The ions may then strike the ion detector 6. It will be appreciated that the use of the drift-dimension reflector 12 doubles the flight path length of the ions.

Fig. 3 shows a schematic of a portion of a mass spectrometer according to an embodiment of the present invention. The spectrometer comprises an MRTOF mass analyser and an ion accumulation device 14 that is configured to accumulate ions and then

periodically pulse a packet of ions 8 towards the MRTOF mass analyser. Ion optics 16 may be arranged between the ion accumulation device 14 and an ion accelerator 4 of the MRTOF mass analyser for transferring ions from the ion accumulation device to the MRTOF mass analyser. The ion optics 16 may comprise, for example, at least one of an
5 ion lens, one or more ion beam collimator plates, or an ion guide.

The MRTOF mass analyser comprises two ion mirrors 2a,2b that are extended along a drift dimension (z-dimension) for reflecting ions, an ion accelerator 4 arranged to receive ions from the accumulation device 14 and pulse them into one of the ion mirrors 2a, a first drift-dimension reflector 12a at a first end of the mass analyser for reflecting ions
10 in the drift dimension, a second drift-dimension reflector 12b at a second opposite end of the mass analyser for reflecting ions in the drift dimension, and an ion detector 6 for detecting the ions.

In use, ions are accumulated in the ion accumulation device 14 and are periodically pulsed out of the ion accumulation device in the drift dimension towards the MRTOF mass
15 analyser. These ions are received in the ion accelerator 4 of the MRTOF mass analyser. As the ions are passing through the ion accelerator, a voltage pulse is applied to one or more electrodes of the ion accelerator so as to orthogonally accelerate a packet of the ions in the x-dimension towards one of the ion mirrors 2a. As the ions entered the mass analyser in the drift dimension they retain a velocity component in this direction and so
20 leave the ion accelerator with a mean ion trajectory that is inclined relative to the x-dimension. The ions therefore have a main velocity component in the x-dimension and also a velocity component in the drift dimension. The ions enter into a first of the ion mirrors 2a and are reflected back towards a second of the ion mirrors 2b. The ions then enter the second mirror 2b and are reflected back to the first ion mirror 2a. The first ion
25 mirror then reflects the ions back to the second ion mirror. This continues and the ions are continually reflected between the two ion mirrors as they drift along the mass analyser in the z-dimension until the ions reach the first drift-dimension reflector 12a located at the first end of the mass analyser. At this point the ions have undergone a first pass along the mass analyser in the drift dimension. A static DC voltage may be applied to the reflector
30 12a so as to reflect the ions in the drift dimension back towards the ion accelerator 4. The ions continue to be reflected between the two ion mirrors 2a,2b as they drift back along the mass analyser in the drift dimension until they hit the ion detector 6 at the second end of the mass analyser. At this point the ions have undergone two passes along the mass analyser in the drift dimension. As is conventional in a TOF mass analyser, the mass
35 analyser determines the mass to charge ratios of the ions based on the duration between the time that they were pulsed by the ion accelerator 4 and their respective times of detection at the ion detector 6.

It is contemplated that the ions may be caused to perform more than two passes along the mass analyser in the drift dimension prior to being detected. Accordingly, instead
40 of the ions being allowed to strike the detector 6 at the time that they complete two passes along the mass analyser, the ions may be reflected again in the drift dimension by the second drift-dimension reflector 12b so that the ions perform one or more additional passes

along the mass analyser in the drift dimension prior to striking the detector 6, where the ions are continually reflected between the two ion mirrors 2a,2b as they perform each pass.

In such embodiments, the ions may be caused to have undergone an even number of passes at the time that they are detected. In such embodiments, the second drift dimension reflector 12b may be activated after the ions have passed the second drift-dimension reflector 12b for the first time, i.e. the first time after having been injected into the mirrors by the ion accelerator 4. The first drift-dimension reflector 12a remains active at least until all of the ions to be detected have been reflected by it so as to make their final pass in the drift dimension along the mass analyser. After having been activated, the second drift-dimension reflector 12b must remain activated until all of the ions to be detected have been reflected by it so as to make their penultimate pass along the mass analyser. The second reflector 12b must subsequently be deactivated before any ions to be detected have reached the second reflector during their final pass along the mass analyser. This is necessary so as to allow the ions to reach the ion detector 6.

It will be appreciated that the mass spectrometer may control the timings at which the second reflector 12b is activated and deactivated so as to cause ions to have undergone any even number of passes along the drift dimension at the point that the ions are detected. For example, ions may be caused to undergo 4, 6, 8, 10 or 12 (or any even number that is greater than 12) passes along the drift dimension prior to the ions being detected at the ion detector.

Alternatively, the ions may be caused to have undergone an odd number of passes in the drift dimension at the time that they are detected. Fig. 4 shows an example of such an embodiment. In these embodiments, an ion detector 6 is arranged at the first end of the mass analyser, further from the ion accelerator 4 than the first drift-dimension reflector 12a. In these embodiments, the second drift dimension reflector 12b may be activated after the ions have passed the second drift-dimension reflector for the first time, i.e. the first time after having been injected into the mirror 2a by the ion accelerator 4. The second drift-dimension reflector 12b then remains activated at least until all of the ions to be detected have been reflected by it so as to make their final pass along the mass analyser. The first drift-dimension reflector 12a must be activated before any ions to be detected reach it for the first time. The first reflector 12a must then remain active until all of the ions to be detected have been reflected by it so as to make their penultimate pass along the mass analyser in the drift dimension. The first reflector 12a must subsequently be deactivated before any ions to be detected have reached it during their final pass along the mass analyser.

It will be appreciated that the mass spectrometer may control the timings at which the first reflector 12a is activated and deactivated so as to cause ions to have undergone any odd number of passes along the drift dimension at the point that the ions are detected. For example, ions may be caused to undergo 3, 5, 7, 9 or 11 (or any odd number that is greater than 11) passes along the drift dimension prior to the ions being detected at the ion detector 6.

It is contemplated that ion detectors may be arranged at both the first and second ends of the mass analyser such that the mass analyser is capable of being operated in a first mode in which ions have undergone an even number of passes at their time of detection, and such that the mass analyser is also capable of being operated in a second mode (at a different time to the first mode) so as to cause ions to have undergone an odd number (greater than 1) of passes at the time of their detection.

It is also contemplated that in another mode the mass spectrometer may control the mass analyser so as to cause ions to have undergone only a single pass along the mass analyser before being detected. In order to perform such a mode an ion detector is arranged at the first end of the mass analyser and the first and second deflectors are not activated.

One or more ion lenses may be arranged between the ion mirrors such that the ions pass through the one or more lenses as they travel between the mirrors. The one or more lenses may be arranged such that the ions pass through them during each pass in the drift dimension, i.e. when travelling from the first end to the second end of the mass analyser and also when travelling from the second end to the first end of the mass analyser. One or more voltages may be applied to one or more electrodes of the ion lenses so as to focus ions passing therethrough in the drift dimension in order to prevent each ion packet pulsed into the mass analyser from diverging too much in the drift dimension by the time that its ions are detected. For example, the one or more lenses may be configured to focus the ions such that the width of the ion packet is smaller than the width of the detecting area of the detector, in the drift dimension, at the time that the ions strike the detector. Additionally, or alternatively, the one or more lenses may focus the ions in the drift dimension so as to ensure that substantially all of the ions have undergone the same total number of mirror reflections during each pass along the drift dimension.

In embodiments that include the one or more ion lenses, an electrode of an ion lens may be controlled so as to perform the function of the first and/or second drift-dimension reflector. For example, referring to Figs. 3 and 4, each ion lens may comprise two adjacent electrodes that are spaced apart in the drift dimension so that ions pass between the two electrodes as they are reflected from one mirror to another. The two electrodes may be maintained at substantially the same electric potential so as to focus the ions in the drift dimension. However, when it is desired to reflect ions in the drift dimension the two electrodes may be maintained at different electric potentials so as to cause the reflection of ions in the drift dimension.

However, it is also contemplated that the mass analyser need not comprise one or more ion lens between the mirrors.

Causing the ions to undergo multiple passes along the drift dimension prior to their detection significantly increases the ion flight path length, and hence enables the mass resolution and mass accuracy to be increased. This can be seen in the example depicted in Fig. 3. For example, if the ions only undergo only a single pass in the drift dimension prior to detection then the ions undergo 14 mirror reflections prior to being detected. If the ions undergo only two passes in the drift dimension prior to detection then the ions undergo

28 mirror reflections prior to being detected. If the ions undergo N passes in the drift dimension prior to detection, where N is ≥ 3 , then the ions undergo $[(N \times 13) + 14]$ reflections. The ion flight path is primarily made up of the distance that the ions travel when passing between the ion mirrors, as this distance is much larger than the total distance that the ions travel in the drift dimension. As such, in the illustrated example, the ion flight path is increased by a factor of approximately 1.9 when the ions undergo two passes prior to detection, as compared to a single pass (i.e. 27 reflections divided by 14 reflections). Similarly, when N passes are performed, the ion flight path is increased by a factor of approximately $[13(N-13)+14]/14$, as compared to a single pass.

Although causing the ions to perform multiple passes along the drift dimension prior to detection is beneficial for increasing the flight path length, it has been recognised that unless certain precautions are undertaken this technique can result in different ions from the same ion packet reaching the detector after having undergone flight paths of different lengths. This is problematic as the mass analyser is configured to determine the mass to charge ratios of the ions based on the duration between the time that the ions are pulsed by the ion accelerator and their respective times of detection at the ion detector, assuming that the ions all travel the same flight path length. In other words, the mass analyser determines the mass to charge ratios of the ions detected on the assumption that the ions arrive at the detector in order of mass to charge ratio and having arrival times at the detector that are related to their mass to charge ratios. However, if ions having relatively high mass to charge ratios travel a shorter flight path to the detector than lower mass to charge ratio ions, then these higher mass to charge ratio ions may be detected before the lower mass to charge ratios and so may be assigned mass to charge ratios that are too low.

It can be difficult to control the timings that the drift-dimension reflectors should be activated and deactivated in order to cause all of the ions in an ion packet to have undergone the same number of passes (i.e. same flight path length) at the time of detection. For example, it is necessary to deactivate a drift dimension reflector to allow ions to reach the detector at a time just before they have completed the desired number of passes. However, ions having higher mass to charge ratios travel slower in the drift dimension than ions having lower mass to charge ratios. As such, at the point in time just before relatively low mass to charge ratio ions have undergone the desired number of passes and the reflector needs to be deactivated, some higher mass to charge ratio ions may still need to be reflected by that reflector in order to ensure that they perform the same desired number of passes as the relatively low mass to charge ratio ions. Accordingly, if the drift dimension reflector is deactivated in this situation in order to allow the lower mass to charge ratio ions to be detected, then some ions of higher mass to charge ratio will reach the detector having undergone fewer passes than the relatively low mass to charge ratios. On the other hand, if the deactivation of the reflector is delayed so that the higher mass to charge ratio ions perform the desired number of passes, then the drift dimension reflector may reflect the lower mass to charge ratio ions such that they perform more than the desired number of passes.

By way of example, and with reference to Fig. 3, it may be desired for all of the ions to undergone four passes in the drift dimension at the time that they are detected. In other words, it may be desired for the ions to pass from the ion accelerator 4 to the first drift-dimension reflector 12a, be reflected back to the second drift-dimension reflector 12b, be reflected back to the first drift-dimension reflector 12a and then be reflected back to the detector 6. In this example, the first drift-dimension reflector 12a may remain active the whole time that the ions are in the mass analyser, but the second drift-dimension reflector 12b must be activated and deactivated as the ions pass through the mass analyser. The second drift-dimension reflector 12b may be deactivated at the time that the ions are pulsed into the first mirror 2a by the ion accelerator 4. The second drift-dimension reflector 12b may remain deactivated until the point at which all of the ions have passed the second drift-dimension reflector 12b for the first time (after having been pulsed into the mirror by the ion accelerator). The second drift-dimension reflector 12b is then activated at time T_{on} and may remain activated until it is deactivated at time T_{off} so as to allow ions to pass to the detector 6.

In this example, time T_{off} is selected to be the time at which ions having a mass to charge ratio M_{Low} have performed four passes in the drift dimension and are just arriving again at the second drift-dimension reflector 12b. As such, ions having a mass to charge ratio M_{Low} will pass to the detector and be detected, as will ions having higher mass to charge ratios since they will arrive at the second drift-dimension reflector after time T_{off} . In contrast, ions having a mass to charge ratio lower than M_{Low} will have a higher speed in the drift dimension than the ions of mass to charge ratio M_{Low} and will therefore reach the second drift-dimension reflector 12b before time T_{off} and whilst it is still activated. These lower mass to charge ratio ions will therefore be reflected by the second drift-dimension reflector 12b so as to be caused to perform more than four passes in the drift dimension before being detected. This is undesirable since these ions will have travelled a greater flight path by the time that they are detected than ions having a mass to charge ratio M_{Low} .

Ions having a mass to charge ratio higher than M_{Low} will have a lower speed in the drift dimension than the ions of mass to charge ratio M_{Low} . Ions having mass to charge ratios that are substantially higher than M_{Low} will not have completed two passes in the drift dimension until after time T_{off} at which the second drift-dimension reflector 12b is deactivated. These higher mass to charge ratio ions will therefore pass to the detector after having undergone only two passes in the drift dimension. This is undesirable since these ions will have travelled a shorter flight path length at the time they are detected than the ions having a mass to charge ratio M_{Low} .

It will therefore be appreciated that at time T_{off} when the second drift-dimension reflector 12b is deactivated, ions having a mass to charge ratio M_{High} will have only just performed two passes in the drift dimension and will have just been reflected in the drift dimension by the second drift-dimension reflector. Accordingly, only ions having mass to charge ratios between M_{Low} and M_{High} will have undergone the same number of passes in the drift dimension, and hence travelled the same flight path length, at the time they are detected by detector 6. It is therefore desirable to restrict the range of mass to charge

ratios that is pulsed into the mass analyser by the ion accelerator 4 so as to avoid the above described problems.

The present invention restricts the range of mass to charge ratios in the ion packet that is pulsed into the mass analyser by the ion accelerator 4 so that the ions being mass
5 analysed have undergone the same number of passes in the drift dimension at the time that they are detected.

Embodiments on the present invention perform this in the following manner. Ions are accumulated in the ion accumulation device 14 and are then pulsed out of this device towards and the ion accelerator 4. The ions are transmitted from the ion accumulation
10 device to the ion accelerator, optionally via ion optics 16, in a manner such that the ions separate according to their mass to charge ratios as they pass towards the ion accelerator 4. For example, the region between the exit of the ion accumulation device 14 and the ion accelerator 4 may be substantially free of electric fields (in the average direction of travel of the ions). This region may also have a length and be at a pressure such that there are
15 relatively few, or substantially no, collisions between the ions and background gas molecules. Ions of different mass to charge ratio enter the ion accelerator at different times. As such, the time at which the ion accelerator pulses ions into the first mirror will determine the range of mass to charge ratios that are mass analysed.

Embodiments of the present invention synchronise the time at which the ion
20 accelerator 4 pulses ions into the first mirror 2a with the time at which the ions are pulsed out of the ion accumulation device 14 so that only ions having mass to charge ratios within a preselected range will be pulsed into the first ion mirror 2a. This preselected range may be the same range of mass to charge ratios as the range of mass to charge ratios that the mass analyser is configured to cause to perform the same number of passes in the drift
25 dimension during mass analysis, i.e. a range from M_{Low} and M_{High} in the above example. Alternatively, the preselected range may be a range that is narrower and within the range of mass to charge ratios that the mass analyser is configured to cause to perform the same number of passes in the drift dimension during mass analysis.

The ion accumulation device 14 is therefore controlled in a manner that helps select
30 and restrict the range of mass to charge ratios that are mass analysed. Additionally, the use of the ion accumulator to accumulate and then pulse ions to the mass analyser provides the mass analyser with a relatively high orthogonal sampling duty cycle.

The ion accumulation device 14 may comprise an ion guide, such as an RF ion guide, having a trapping electrode 18 at its downstream exit. The mass spectrometer may
35 control the ion accumulation device 14 so as to operate in an ion accumulation mode, during which a voltage is applied to the trapping electrode 18 so as to prevent ions leaving through the exit. Ions may however pass into an upstream entrance of the ion guide during this mode. Subsequently, when it is desired to mass analyse the ions, the mass spectrometer may control the ion accumulation device so as to operate in an ion ejection
40 mode, during which the voltage applied to the trapping electrode 18 is altered so as to allow ions to leave through the exit and pass to the ion accelerator. In this mode the voltage applied to the trapping electrode may attract ions out of the ion guide, i.e. the

trapping electrode may operate as an extraction electrode. Additionally, or alternatively, one or more electrodes of the ion guide may be maintained at a voltage so as to eject ions through the exit. Ions may or may not be prevented from entering the ion accumulation device during the ejection mode.

5 The ion guide of the ion accumulation device 14 may be a linear ion guide having an elongated ion confinement volume. Alternatively, the ion accumulation device may have another ion confinement structure.

 The ion accumulation device 14 may accumulate ions in a region having a pressure in the range of 10^{-4} mbar to 5×10^{-2} mbar. This may be useful in collisionally cooling the
10 ions prior to pulsing the ions to the mass analyser. Additionally, or alternatively, it is contemplated that the ion accumulation device may be or form part of an ion fragmentation cell. For example, the ion accumulation device may be or form part of a collision induced dissociation (CID) device, an ion-ion reaction cell, or an electron triggered dissociation device.

15 Fig. 5 shows a timing diagram illustrating an example of how the ion accumulation device 14, ion accelerator 4 and second drift-dimension reflector 12b may be operated relative to each other in the embodiment shown in Fig. 3. The top plot in Fig. 5 shows an example of how the electric potential applied to the trapping electrode 18 of the ion accumulation device 14 may be varied with time. It can be seen that the potential is
20 generally maintained high so as to trap ions in the ion accumulation device, but that it is dropped for a short period so as to release ions to the ion accelerator 4.

 The middle plot in Fig. 5 shows an example of how the electric potential applied to an electrode of the ion accelerator 4 may be varied with time. The potential is generally low so as not to pulse ions into the ion mirrors 2. However, at a time T_{pulse} after the
25 potential applied to the trapping electrode 18 of the ion accumulation device 14 has been reduced so as to release ions, the potential applied to the electrode of the ion accelerator 4 is increased for a short duration so as to pulse ions into the ion mirrors 2. As described above, the duration T_{pulse} is selected so that only ions having a certain range of mass to charge ratios are pulsed into the ion mirrors 2. The time it takes for an ion to travel from
30 the exit of the ion accumulation device 14 to the ion accelerator 4 may be proportional to the square root of the mass to charge ratio of that ion. Although the exact value for this time will be dependent on the geometry of the ion accumulation device, ion optics, and ion accelerator, the value envisaged for an ion having a mass to charge ratio of 1000 would be in the range of 5-500 μs .

35 The bottom plot in Fig. 5 shows how the electric potential applied to the second drift-dimension reflector 12b may be varied with time in the embodiments illustrated by Fig. 3, i.e. where an even number of passes have been performed at the time of detection. The potential applied to the second drift-dimension reflector 12b is initially low, so that ions that are pulsed into the mirrors 2 by the ion accelerator are able to pass the deflector 12b and
40 travel to the first end of the mass analyser. After a duration T_{on} from the start of the ion accelerator pulse, the potential applied to the second drift-dimension reflector 12b is increased so that it is capable of reflecting ions passing from the first end to the second

end of the mass analyser. The time T_{on} is selected to be great enough that ions having the highest mass to charge ratio that are to be detected have had time to travel from the ion accelerator 4 passed the second reflector 12b before the reflector 12b is activated. The time that ions take to travel this distance may be proportional to the square root of their mass to charge ratio and therefore T_{on} may also be proportional to the square root of the maximum mass to charge ratio that is to be detected.

The duration T_{on} is also selected to be short enough so that the deflector 12b is activated by the time that ions having the lowest mass to charge ratio have passed back to the second drift-dimension reflector 12b for the first time, having been reflected in the drift dimension by the first drift-dimension reflector 12a at the first end of the mass analyser. Although the exact value for the duration T_{on} will be dependent on the geometry of the ion accumulation device, ion optics, and ion accelerator, the value envisaged for an ion having a mass to charge ratio of 1000 would be in the range of 100-4000 μs (e.g. 750 μs).

After a duration T_{off} from the start of the ion accelerator pulse, the potential applied to the second drift-dimension reflector 12b is decreased so that the second reflector 12b is deactivated and ions are able to pass to the detector 6. The time T_{off} may be selected to be the time just before ions having the lowest mass to charge ratio arrive back at the second drift-dimension reflector 12b after having just completed the desired number of passes in the drift dimension. Although the exact value for this time will be dependent on the geometry of the ion accumulation device, ion optics, and ion accelerator, the value envisaged for an ion having a mass to charge ratio of 1000 would be in the range of 100 – 5000 μs .

As described above in relation to Fig. 4, embodiments are contemplated in which an ion detector 6 is arranged at the first end of the mass analyser and the ions have undergone an odd number of passes in the drift dimension when they are detected. Such embodiments are operated in a corresponding manner to those described above, except that the second drift-dimension reflector 12b may remain activated after T_{on} and need not be deactivated since ions do not pass to a detector 6 at the second end of the mass analyser. Rather, the ions pass to a detector at a first end of the mass analyser and so the first drift-dimension reflector 12a must be deactivated at a certain time. More specifically, the first drift-dimension reflector 12a must be activated before ions having the lowest mass to charge ratio to be detected arrive at the first drift-dimension reflector 12a, and must be deactivated just before those ions arrive back at the first drift-dimension reflector 12a after having just completed the desired number of passes in the drift dimension. However, the first drift-dimension reflector 12a is not deactivated until the highest mass to charge ratio ions to be detected have been reflected by the first drift-dimension reflector to perform their penultimate pass in the drift dimension.

Each of Figs. 6A-6B shows mass spectra obtained for the third isotope of Leucine Enkephalin ($C_{28}H_{38}N_5O_7$) when using an embodiment of the type described above and also when using a conventional approach. Fig. 6A shows the absolute intensity of the ion signal as a function of mass to charge ratio. It can be seen that the mass spectral data obtained according to an embodiment of the present invention is significantly more intense

than the mass spectral data 22 obtained according to the conventional technique. The higher sensitivity of the embodiment of the present invention is enabled by accumulating ions in the ion accumulation device.

Fig. 6B shows the same mass spectral data as shown in Fig. 6A, except that the intensities have been normalised. It can be seen by comparing the mass spectral data 20 and 22 that the embodiment of the present invention provides mass spectral data of a higher mass resolution than the conventional technique, e.g. so as to allow determination of fine isotopic structures.

Fig. 6C shows a computer simulation of mass spectral data for the third isotope of Leucine Enkephalin ($C_{26}H_{38}N_5O_7$) at a high resolution of 300,000 FWHM. This data was generated using at envipat.eawag.ch. It can be seen by comparing Fig. 6A or 6B with Fig. 6C that the mass spectral data obtained according to the embodiment of the present invention has a good agreement with the simulated high resolution mass spectral data of Fig. 6C.

Although the present invention has been described with reference to preferred embodiments, it will be understood by those skilled in the art that various changes in form and detail may be made without departing from the scope of the invention as set forth in the accompanying claims.

For example, although embodiments have been described in which the ions are caused to have undergone a certain number of mirror reflections and passes in the drift dimension by the time they have been detected, it will be appreciated that a different number of mirror reflections and/or passes may be performed.

Additionally, or alternatively, the position within the mass analyser of the first and/or second drift-dimension reflector may be different to those shown and described above. For example, Fig. 7 shows an embodiment that is substantially the same as that of Fig. 4, except that the first and second drift-dimension reflectors 12a, 12b are further from the detector 6 and ion accelerator 4, respectively.

Embodiments are contemplated in which a mass filter is provided upstream of the ion accumulation device 14 so as to mass filter the ions passing into the accumulation device 14. The mass filter may be operated so as to only transmit ions having mass to charge ratios within a certain range into the ion accumulation device 14. As described above, the mass analyser of the embodiments may be configured such that only ions within a first range of mass to charge ratios have undergone the same number of passes in the drift dimension at the time that they are detected by the detector 6. As also described above, the synchronisation between the pulsing of ions out of the ion accumulation device 14 and the pulsing of ions into the mirrors 2 using the ion accelerator 4 may be selected so that only ions having mass to charge ratios within the first range are capable of being pulsed into the ion mirrors 2. The provision of a mass filter upstream of the ion accumulation device 14 reduces the ion current entering the ion accumulation device 14 and the amount of charge per push of the ion accelerator 4 (for a given accumulation time), thereby reducing space-charge effects in the ion accumulation device and/or mass analyser and improving dynamic range. This may improve the mass accuracy and mass

resolution of the instrument. The provision of the mass filter also enables a greater proportion of the ions that enter the ion accumulation device to have mass to charge ratios corresponding to those that will be pulsed by the ion accelerator.

5 The mass filter may be a quadrupole mass filter, although other types of mass filter may be used instead.

Claims

- 5 1. A mass spectrometer comprising:
 an ion accumulation device for accumulating and pulsing out ions;
 a time of flight mass analyser comprising:
 a plurality of ion mirrors for reflecting ions;
 an ion accelerator arranged and configured to receive ions from the ion
10 accumulation device and pulse them into one of the ion mirrors such that ions are reflected
 back and forth between the mirrors in a first dimension as the ions drift in a drift dimension;
 reflectors for reflecting the ions in the drift dimension;
 an ion detector for detecting ions; and
 control circuitry configured to activate the reflectors so as to cause the ions
15 to make multiple passes along the drift dimension and then deactivate one of the reflectors
 so as to allow ions to pass to the ion detector and be detected, wherein the timings at
 which the reflectors are activated and deactivated is such that only ions within a first range
 of mass to charge ratios are capable of having undergone the same number of passes in
 the drift dimension at the time that they are detected by the ion detector;
20 wherein control circuitry of the mass spectrometer synchronises the time that ions
 are pulsed out of the ion accumulation device with the time that ions are pulsed by the ion
 accelerator such that only ions having mass to charge ratios within said first range are
 pulsed by the ion accelerator into said one of the ion mirrors.
- 25 2. The mass spectrometer of claim 1, wherein the mass spectrometer is configured
 such that the ions that are pulsed out of the ion accumulation device separate according to
 mass to charge ratio as they travel to the ion accelerator, and so that ions of different mass
 to charge ratio enter the ion accelerator at different times.
- 30 3. The mass spectrometer of claim 1 or 2, wherein the ion accumulation device
 comprises an ion guide having a trapping electrode at its downstream exit.
4. The mass spectrometer of any preceding claim, wherein the mass spectrometer is
 configured to allow a user to select what the first range of mass to charge ratios is; and
35 wherein the control circuitry is configured to control the timings at which the reflectors are
 activated and deactivated, and the time that ions are pulsed out of the ion accumulation
 device relative to the time that ions are pulsed by the ion accelerator, in response to the
 selection by the user.
- 40 5. The mass spectrometer of any preceding claim, wherein the mass spectrometer is
 configured to allow a user to select the number of passes that the ions should perform prior
 to detection; and wherein the control circuitry is configured to control the timings at which

the reflectors are activated and deactivated, and the time that ions are pulsed out of the ion accumulation device relative to the time that ions are pulsed by the ion accelerator, in response to the selection by the user so that ions having the first range of mass to charge ratios undergo the selected number of passes prior to detection.

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6. The mass spectrometer of any preceding claim, comprising a mass filter upstream of the ion accumulation device for mass filtering ions passing to the ion accumulation device.

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7. The mass spectrometer of claim 6, comprising control circuitry configured to control the mass filter so that the mass filter only transmits ions having mass to charge ratios within a second range into the ion accumulation device, wherein said first range is narrower than and within the second range.

15

8. The mass spectrometer of any preceding claim, wherein a first of the reflectors is arranged at a first end, in the drift dimension, of the mass analyser; wherein the ion accelerator and ion detector are arranged at a second opposite end, in the drift dimension, of the mass analyser; and wherein a second of the reflectors is arranged between, in the drift dimension, the first reflector and the ion detector; and wherein the timings at which the reflectors are activated and deactivated is such that ions within the first range of mass to charge ratios undergo an even number of passes in the drift dimension at the time that they are detected by the ion detector.

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9. The mass spectrometer of claim 8, wherein the control circuitry is configured to maintain the first reflector activated so as to be capable of reflecting ions for a duration starting when ions having the lowest mass to charge ratio in said first range would reach the first reflector for the first time, wherein the duration lasts at least until ions having the highest mass to charge ratio in said first range would be reflected by the first reflector so as to make their final pass in the drift dimension.

30

10. The mass spectrometer of claim 8 or 9, wherein the control circuitry is configured to activate the second reflector starting when ions having the highest mass to charge ratio in said first range would have passed the second reflector for the first time after having been injected into the mirrors by the ion accelerator.

35

11. The mass spectrometer of claim 8, 9 or 10, wherein the control circuitry is configured to:

(i) maintain the second reflector activated until ions having the highest mass to charge ratio in said first range would have been reflected by the second reflector so as to start their penultimate pass in the drift dimension; and

40

(ii) deactivate the second reflector before ions having the lowest mass to charge ratio in said first range would have reached the second reflector during their final pass in the drift dimension, so as to allow ions to reach the ion detector.

- 5 12. The mass spectrometer of any one of claims 1-7, wherein the ion detector is arranged at a first end, in the drift dimension, of the mass analyser; wherein the ion accelerator is arranged at a second opposite end, in the drift dimension, of the mass analyser; wherein a first and a second of the reflectors are arranged between, in the drift dimension, the ion accelerator and the ion detector such that the first reflector is closer to
- 10 the ion detector than the second reflector; and wherein the timings at which the reflectors are activated and deactivated is such that ions within the first range of mass to charge ratios undergo an odd number of passes in the drift dimension at the time that they are detected by the ion detector.
- 15 13. The mass spectrometer of claim 12, wherein the control circuitry is configured to:
- (i) activate the first reflector so as to reflect ions at a time prior to the time that ions having the lowest mass to charge ratio in said first range would reach the first reflector for the first time;
- (ii) maintain the first reflector activated until ions having the highest mass to charge
- 20 ratios in the first range would have been reflected by the first reflector so as to make their penultimate pass in the drift dimension; and
- (iii) deactivate the first reflector before ions having the lowest mass to charge ratio in said first range would have reached the first reflector during their final pass in the drift dimension, so as to allow ions to reach the ion detector.
- 25 14. The mass spectrometer of claim 12 or 13, wherein the control circuitry is configured to:
- (i) activate the second reflector starting when ions having the highest mass to charge ratio in said first range would have passed the second reflector for the first time
- 30 after having been injected into the mirrors by the ion accelerator; and
- (ii) maintain the second reflector activated until ions having the highest mass to charge ratio in said first range would have been reflected by the second reflector so as to make their final pass in the drift dimension.
- 35 15. The mass spectrometer of any preceding claim, comprising a plurality of electrodes arranged between the ion mirrors and spaced apart in the drift dimension such that the ions pass between adjacent ones of the electrodes as the ions travel between the mirrors;
- (i) wherein a first of said electrodes is the first reflector, and the mass spectrometer is configured to apply a first voltage to the first electrode when the first reflector is activated
- 40 for reflecting ions in the drift dimension, and to apply a different voltage to the first electrode when the first reflector is deactivated so that the first electrode and an adjacent one of the electrodes focus ions passing therebetween in the drift dimension; and/or

(ii) wherein a second of said electrodes is the second reflector, and the mass spectrometer is configured to apply a second voltage to the second electrode when the second reflector is activated for reflecting ions in the drift dimension, and to apply another voltage to the second electrode when the second reflector is deactivated so that the second electrode and an adjacent one of the electrodes focus ions passing therebetween in the drift dimension.

16. A mass spectrometer comprising:
a first device for transmitting ions;
10 a time of flight mass analyser comprising:
a plurality of ion mirrors for reflecting ions;
an ion accelerator arranged and configured to receive ions from the first device and pulse them into one of the ion mirrors such that ions are reflected back and forth between the mirrors in a first dimension as the ions drift in a drift dimension;
15 reflectors for reflecting the ions in the drift dimension;
an ion detector for detecting ions; and
control circuitry configured to activate the reflectors so as to cause the ions to make multiple passes along the drift dimension and then deactivate one of the reflectors so as to allow ions to pass to the ion detector and be detected, wherein the timings at
20 which the reflectors are activated and deactivated is such that only ions within a first range of mass to charge ratios are capable of having undergone the same number of passes in the drift dimension at the time that they are detected by the ion detector;
wherein the first device is configured to supply ions to the ion accelerator such that only ions having mass to charge ratios within said first range are present in the ion
25 accelerator when it pulses ions into said one of the ion mirrors.

17. The mass spectrometer of claim 16, wherein the first device is a mass selective ion trap and the mass spectrometer is configured to eject ions from the mass selective ion trap to the ion accelerator.

18. The mass spectrometer of claim 16, wherein the first device is a mass filter configured to only transmit ions having mass to charge ratios within a certain range and to filter out other ions, wherein said first range is smaller than and within said first range.

19. A multi-reflecting time of flight mass spectrometer configured to cause ions to be reflected multiple times between ion mirrors in a first dimension whilst the ions are also reflected back and forth in a drift dimension by reflectors;
wherein the spectrometer is configured to activate and deactivate the reflectors at times such that ions having mass to charge ratios within a first range have undergone the
40 same number of reflections in the drift dimension at the time that they are detected; and
wherein the mass spectrometer is configured so as to only admit ions having mass to charge ratios within the first range into the ion mirrors.

20. A method of mass spectrometry comprising:
- providing a mass spectrometer as claimed in any one of claims 1-18;
- supplying ions from the ion accumulation device or first device to the ion
- 5 accelerator;
- applying a voltage pulse to an electrode of the ion accelerator so as to pulse ions into one of the ion mirrors such that ions are reflected back and forth between the mirrors in a first dimension as the ions drift in a drift dimension;
- activating the reflectors so as to cause the ions to make multiple passes along the
- 10 drift dimension and then deactivating one of the reflectors so as to allow ions to pass to the ion detector and be detected, wherein the timings at which the reflectors are activated and deactivated is such that only ions within a first range of mass to charge ratios are capable of having undergone the same number of passes in the drift dimension at the time that they are detected by the ion detector;
- 15 wherein the ion accumulation device or first device supplies ions to the ion accelerator such that only ions having mass to charge ratios within said first range are present in the ion accelerator when it pulses ions into said one of the ion mirrors.