

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
12 June 2008 (12.06.2008)

PCT

(10) International Publication Number
WO 2008/068515 A2

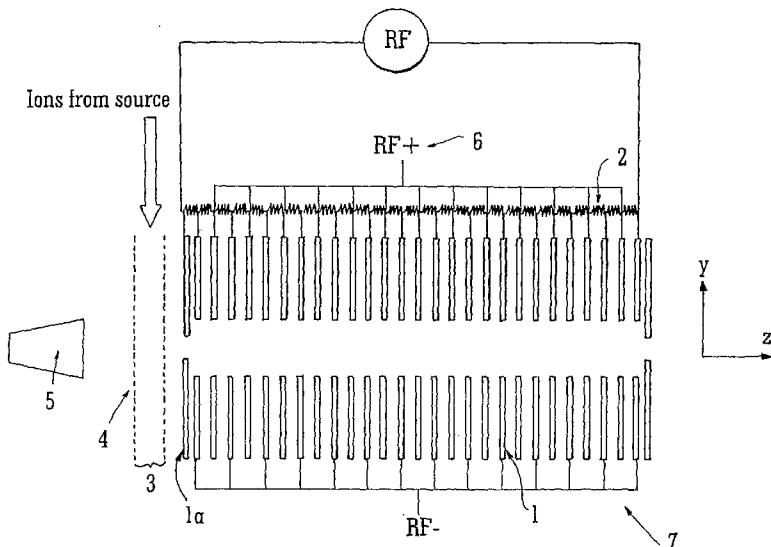
(51) International Patent Classification: Not classified (74) Agents: FRANK B. DEHN & CO. et al.; St Bride's House, 10 Salisbury Square, London EC4Y 8JD (GB).

(21) International Application Number: PCT/GB2007/004732 (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(22) International Filing Date: 10 December 2007 (10.12.2007) (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(25) Filing Language: English (72) Inventors; and (75) Inventors/Applicants (for US only): GREEN, Martin [GB/GB]; Grange Croft, Grange Road, Bowden, Altrincham, Cheshire WA14 3EE (GB). WILDGOOSE, Jason, Lee [GB/GB]; 110 Barcicroft Road, Heaton Mersey, Stockport SK4 3PJ (GB).

(54) Title: MASS SPECTROMETER



WO 2008/068515 A2

(57) Abstract: A mass spectrometer is disclosed comprising a time of flight mass analyser (7). The time of flight mass analyser (7) comprises an ion guide comprising a plurality of electrodes (1) which are interconnected by a series of resistors (2) forming a potential divider. Ions are confined radially within the ion guide by the application of a two-phase RF voltage to the electrodes (1). A single phase additional RF voltage is applied across the potential divider so that an inhomogeneous pseudo-potential force is maintained along the length of the ion guide.

1
MASS SPECTROMETER

5 The present invention relates to a mass spectrometer and a method of mass spectrometry.

A known mass spectrometer comprises an Electron Impact ("EI") ion source in combination with a reflectron Time of Flight mass analyser. The known reflectron Time of Flight mass analyser comprises a series of ring electrodes which are connected to a potential divider or resistor chain. A RF voltage and a static DC voltage are applied across the ends of the potential divider or resistor chain so that a static axial DC voltage gradient and an inhomogenous axial RF voltage are maintained along the length of the mass analyser. The mass spectrometer further comprises an electron multiplier ion detector which is arranged in line with the central axis of the mass analyser at the position of zero field. At a predetermined phase of the RF voltage applied to the ring electrodes, ions formed by the Electron Impact ion source are pulsed into the Time of Flight mass analyser by applying a voltage pulse to an acceleration grid which is arranged adjacent to an entrance aperture of the mass analyser. Ions which are accelerated into the Time of Flight mass analyser travel a proportion of the length of the mass analyser before being reflected back towards the entrance of the mass analyser. The ions then exit the mass analyser, pass through the acceleration grid and are subsequently detected by the ion detector. The time of flight of the ions from the time that the voltage pulse is applied to the acceleration grid to the subsequent detection of the ions by the ion detector is related to the mass to charge ratio of the ions and the field parameters within the Time of Flight mass analyser.

One problem with the known Time of Flight mass analyser is that ions are not effectively confined radially within the mass analyser. Therefore, the ion transmission efficiency is relatively low.

Another problem with the known Time of Flight mass analyser is that the ions entering the mass analyser have a relatively large spread of initial velocities and initial positions which results in the resolution of the known Time of Flight mass analyser being relatively poor.

5 A further problem with the known Time of Flight mass analyser is that the mass analyser is only arranged to operate with an Electron Impact ion source which operates at a low pressure and hence the mass analyser is not arranged to operate with an atmospheric pressure ionisation ion source.

It is therefore desired to provide an improved mass spectrometer and method of mass spectrometry.

According to an aspect of the present invention there is provided a time of flight mass analyser comprising:

10 an ion guide comprising a plurality of electrodes;

first means arranged and adapted and to confine ions radially within the ion guide; and

15 second means arranged and adapted to apply a time varying inhomogeneous axial electric field along at least a portion of the axial length of the ion guide.

The ion guide preferably comprises: (i) a multipole rod set or a segmented multipole rod set; (ii) an ion tunnel or ion funnel; or (iii) a stack or array of planar, plate or mesh electrodes.

20 According to an embodiment the multipole rod set preferably comprises a quadrupole rod set, a hexapole rod set, an octapole rod set or a rod set comprising more than eight rods.

According to an embodiment the ion tunnel or ion funnel preferably comprises a plurality of electrodes or at least 2, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 electrodes having apertures through which ions are transmitted in use, wherein at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the electrodes have apertures which are of substantially the same size or area or which have apertures which become progressively larger and/or smaller in size or in area. Preferably, at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the electrodes have internal diameters or dimensions selected from the group consisting of: (i) ≤ 1.0 mm; (ii) ≤ 2.0 mm; (iii) ≤ 3.0 mm; (iv) ≤ 4.0 mm; (v) ≤ 5.0 mm; (vi) ≤ 6.0 mm; (vii) ≤ 7.0 mm; (viii) ≤ 8.0 mm; (ix) ≤ 9.0 mm; (x) ≤ 10.0 mm; and (xi) > 10.0 mm.

The stack or array of planar, plate or mesh electrodes preferably comprises a plurality or at least 2, 3, 4, 5, 6, 7, 8,

9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 planar, plate or mesh electrodes wherein at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the planar, plate or mesh electrodes are arranged
5 generally in the plane in which ions travel in use. Preferably, at least some or at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the planar, plate or mesh electrodes are supplied with an AC or RF voltage and wherein adjacent planar, plate or mesh electrodes
10 are supplied with opposite phases of the AC or RF voltage.

The ion guide preferably comprises a plurality of axial segments or at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95 or 100 axial segments.

The centre to centre spacing between adjacent electrodes is
15 preferably selected from the group consisting of: (i) < 0.5 mm; (ii) 0.5-1.0 mm; (iii) 1.0-1.5 mm; (iv) 1.5-2.0 mm; (v) 2.0-2.5 mm; (vi) 2.5-3.0 mm; (vii) 3.0-3.5 mm; (viii) 3.5-4.0 mm; (ix) 4.0-4.5 mm; (x) 4.5-5.0 mm; (xi) 5.0-5.5 mm; (xii) 5.5-6.0 mm; (xiii) 6.0-6.5 mm; (xiv) 6.5-7.0 mm; (xv) 7.0-7.5 mm; (xvi) 7.5-
20 8.0 mm; (xvii) 8.0-8.5 mm; (xviii) 8.5-9.0 mm; (xix) 9.0-9.5 mm; (xx) 9.5-10.0 mm; and (xxi) > 10.0 mm.

The ion guide preferably has an axial length selected from the group consisting of: (i) < 20 mm; (ii) 20-40 mm; (iii) 40-60 mm; (iv) 60-80 mm; (v) 80-100 mm; (vi) 100-120 mm; (vii) 120-140 mm; (viii) 140-160 mm; (ix) 160-180 mm; (x) 180-200 mm; (xi) 200-
25 220 mm; (xii) 220-240 mm; (xiii) 240-260 mm; (xiv) 260-280 mm; (xv) 280-300 mm; and (xvi) > 300 mm.

The first means preferably comprises first AC or RF voltage means arranged and adapted to apply a first AC or RF voltage to at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the electrodes forming the ion guide in order to confine ions radially within the ion guide.

The first AC or RF voltage means is preferably arranged and adapted to supply a first AC or RF voltage to the electrodes of the ion guide having an amplitude selected from the group consisting of: (i) < 50 V peak to peak; (ii) 50-100 V peak to peak; (iii) 100-150 V peak to peak; (iv) 150-200 V peak to peak; (v) 200-250 V peak to peak; (vi) 250-300 V peak to peak; (vii)

300-350 V peak to peak; (viii) 350-400 V peak to peak; (ix) 400-450 V peak to peak; (x) 450-500 V peak to peak; and (xi) > 500 V peak to peak.

The first AC or RF voltage means is preferably arranged and adapted to supply a first AC or RF voltage to the electrodes of the ion guide having a frequency selected from the group consisting of: (i) < 100 kHz; (ii) 100-200 kHz; (iii) 200-300 kHz; (iv) 300-400 kHz; (v) 400-500 kHz; (vi) 0.5-1.0 MHz; (vii) 1.0-1.5 MHz; (viii) 1.5-2.0 MHz; (ix) 2.0-2.5 MHz; (x) 2.5-3.0 MHz; (xi) 3.0-3.5 MHz; (xii) 3.5-4.0 MHz; (xiii) 4.0-4.5 MHz; (xiv) 4.5-5.0 MHz; (xv) 5.0-5.5 MHz; (xvi) 5.5-6.0 MHz; (xvii) 6.0-6.5 MHz; (xviii) 6.5-7.0 MHz; (xix) 7.0-7.5 MHz; (xx) 7.5-8.0 MHz; (xxi) 8.0-8.5 MHz; (xxii) 8.5-9.0 MHz; (xxiii) 9.0-9.5 MHz; (xxiv) 9.5-10.0 MHz; and (xxv) > 10.0 MHz.

The phase difference of the first AC or RF voltage between adjacent electrodes or adjacent groups of electrodes is preferably selected from the group consisting of: (i) > 0°; (ii) 1-30°; (iii) 30-60°; (iv) 60-90°; (v) 90-120°; (vi) 120-150°; (vii) 150-180°; (viii) 180°; (ix) 180-210°; (x) 210-240°; (xi) 240-270°; (xii) 270-300°; (xiii) 300-330°; and (xiv) 330-360°.

The first AC or RF voltage applied, in use, to the electrodes preferably causes or generates a radial pseudo-potential well which acts to confine ions radially, in use, within the ion guide.

The first AC or RF voltage preferably comprises a two-phase or multi-phase AC or RF voltage.

According to an embodiment the second means is preferably arranged and adapted to apply a non-zero time varying inhomogeneous axial electric field along at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the axial length of the ion guide.

The second means preferably comprises means for applying a second AC or RF voltage to the electrodes. The second AC or RF voltage preferably comprises a single phase AC or RF voltage.

The phase difference of the second AC or RF voltage between adjacent electrodes or adjacent groups of electrodes is preferably substantially 0°.

According to the preferred embodiment the second AC or RF voltage is preferably applied across at least some of the

plurality of electrodes. The second AC or RF voltage is preferably applied to at least x electrodes, wherein x is selected from the group consisting of: (i) < 10; (ii) 10-20; (iii) 20-30; (iv) 30-40; (v) 40-50; (vi) 50-60; (vii) 60-70; (viii) 70-80; (ix) 80-90; (x) 90-100; (xi) 100-150; (xii) 150-200; and (xiii) > 200.

5 In a mode of operation the maximum amplitude of the second AC or RF voltage at one or more points along the axial length of the ion guide is preferably arranged to remain substantially constant with time. According to an alternative mode of 10 operation the maximum amplitude of the second AC or RF voltage at one or more points along the axial length of the ion guide may be arranged to vary, increase or decrease with time.

15 Preferably, at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the plurality of electrodes are connected at different points along a potential divider or resistor chain.

20 The second means is preferably arranged and adapted to apply a time varying axial electric field along at least a portion of the axial length of the ion guide. The axial electric field preferably increases or decreases along the length of the ion guide in a direction from an ion entrance region of the ion guide to an ion exit region of the ion guide. The axial electric field is preferably arranged to increase or decrease in a linear 25 or non-linear manner along the length of the ion guide in a direction from an ion entrance region of the ion guide to an ion exit region of the ion guide.

30 According to the preferred embodiment the second means is preferably arranged and adapted to accelerate or decelerate ions axially along at least a portion of the axial length of the ion guide.

35 According to a less preferred embodiment the second means may further comprise one or more auxiliary electrodes. The one or more auxiliary electrodes are preferably located external to the plurality of electrodes forming the ion guide.

The one or more auxiliary electrodes preferably have a cross-sectional area or shape which preferably varies, increases or decreases along the length of the ion guide in a direction

from an ion entrance region of the ion guide to an ion exit region of the ion guide.

The one or more auxiliary electrodes are preferably axially segmented.

5 According to an embodiment singly charged ions having a mass to charge ratio in the range of 1-100, 100-200, 200-300, 300-400, 400-500, 500-600, 600-700, 700-800, 800-900, 900-1000 or > 1000 have a drift or transit time through the ion guide in the range: (i) 0-50 μ s; (ii) 50-100 μ s; (iii) 100-150 μ s; (iv) 150-200 μ s; (v) 200-250 μ s; (vi) 250-300 μ s; (vii) 300-350 μ s; (viii) 350-400 μ s; (ix) 400-450 μ s; (x) 450-500 μ s; (xi) 500-550 μ s; (xii) 550-600 μ s; (xiii) 600-650 μ s; (xiv) 650-700 μ s; (xv) 700-750 μ s; (xvi) 750-800 μ s; (xvii) 800-850 μ s; (xviii) 850-900 μ s; (xix) 900-950 μ s; (xx) 950-1000 μ s; and (xxi) > 1000 μ s.

10 15. According to an embodiment singly charged ions having a mass to charge ratio in the range of 1-100, 100-200, 200-300, 300-400, 400-500, 500-600, 600-700, 700-800, 800-900, 900-1000 or > 1000 have a drift or transit time through the ion guide in the range: (i) 0-1 ms; (ii) 1-2 ms; (iii) 2-3 ms; (iv) 3-4 ms; (v) 4-5 ms; (vi) 5-6 ms; (vii) 6-7 ms; (viii) 7-8 ms; (ix) 8-9 ms; (x) 9-10 ms; (xi) 10-11 ms; (xii) 11-12 ms; (xiii) 12-13 ms; (xiv) 13-14 ms; (xv) 14-15 ms; (xvi) 15-16 ms; (xvii) 16-17 ms; (xviii) 17-18 ms; (xix) 18-19 ms; (xx) 19-20 ms; (xxi) 20-21 ms; (xxii) 21-22 ms; (xxiii) 22-23 ms; (xxiv) 23-24 ms; (xxv) 24-25 ms; 20 (xxvi) 25-26 ms; (xxvii) 26-27 ms; (xxviii) 27-28 ms; (xxix) 28-29 ms; (xxx) 29-30 ms; (xxxi) 30-35 ms; (xxxii) 35-40 ms; (xxxiii) 40-45 ms; (xxxiv) 45-50 ms; (xxxv) 50-55 ms; (xxxvi) 55-60 ms; (xxxvii) 60-65 ms; (xxxviii) 65-70 ms; (xxxix) 70-75 ms; (xl) 75-80 ms; (xli) 80-85 ms; (xlii) 85-90 ms; (xliii) 90-95 ms; 30 (xliv) 95-100 ms; and (xlv) > 100 ms.

35 According to an embodiment the time of flight mass analyser may further comprise DC voltage means for maintaining a substantially constant DC voltage gradient along at least a portion or at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the axial length of the ion guide in order to urge at least some ions along at least a portion or at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the axial length of the ion guide.

According to an embodiment the time of flight mass analyser may further comprise transient DC voltage means arranged and adapted to apply one or more transient DC voltages or potentials or one or more transient DC voltage or potential waveforms to at least some of the electrodes forming the ion guide in order to urge at least some ions along at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the axial length of the ion guide.

According to an embodiment the time of flight mass analyser may further comprise AC or RF voltage means arranged and adapted to apply two or more phase-shifted AC or RF voltages to electrodes forming the ion guide in order to urge at least some ions along at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the axial length of the ion guide.

The time of flight mass analyser preferably comprises a reflectron time of flight mass analyser wherein in a mode of operation ions travel in a first direction, are reflected within the ion guide and then travel in a second direction which is preferably substantially opposed to the first direction.

In a mode of operation ions preferably enter the ion guide via an entrance electrode, entrance region or entrance aperture and preferably traverse the length of the ion guide and preferably exit the ion guide via an exit electrode, exit region or exit aperture.

According to an embodiment ions are preferably not substantially reflected axially within the ion guide as they traverse from the entrance electrode, entrance region or entrance aperture to the exit electrode, exit region or exit aperture.

According to an embodiment at least a portion of the ion guide is arranged to be maintained at a pressure selected from the group consisting of: (i) > 0.001 mbar; (ii) > 0.01 mbar; (iii) > 0.1 mbar; (iv) > 1 mbar; (v) > 10 mbar; (vi) > 100 mbar; (vii) 0.001-100 mbar; (viii) 0.01-10 mbar; and (ix) 0.1-1 mbar.

According to an embodiment at least a portion of the ion guide is arranged to be maintained at a pressure selected from the group consisting of: (i) 0.001-0.005 mbar; (ii) 0.005-0.010 mbar; (iii) 0.01-0.05 mbar; (iv) 0.05-0.10 mbar; (v) 0.1-0.5

mbar; (vi) 0.5-1.0 mbar; (vii) 1-5 mbar; (viii) 5-10 mbar; (ix) 10-50 mbar; (x) 50-100 mbar; and (xi) > 100 mbar.

In a mode of operation ions are preferably substantially separated according to their mass to charge ratio without ions being substantially separated according to their ion mobility.

In a mode of operation ions are preferably substantially separated according to their mass to charge ratio and/or their ion mobility.

In a mode of operation the mass analyser is preferably arranged and adapted to operate as a collision, fragmentation or reaction device.

In a mode of operation the mass analyser is preferably arranged and adapted to collisionally cool or thermalise ions within the ion guide.

In a mode of operation the mass analyser is preferably arranged and adapted to operate as an ion mobility spectrometer or separator.

In a mode of operation ions are preferably arranged to pass through the ion guide in a first direction and a collision, background or other gas is arranged to flow through the ion guide in a second direction. The first direction may be substantially opposed to the second direction. Alternatively, the first direction may be substantially the same direction as the second direction.

According to another aspect of the present invention there is provided a mass spectrometer comprising a time of flight mass analyser as disclosed above.

The mass spectrometer preferably further comprises an acceleration electrode, pusher electrode, puller electrode or grid electrode wherein in a mode of operation ions are preferably accelerated into the ion guide by applying a voltage pulse to the acceleration electrode, pusher electrode, puller electrode or grid electrode. The acceleration electrode, pusher electrode, puller electrode or grid electrode is preferably arranged adjacent an entrance electrode, entrance region or entrance aperture of the ion guide.

The mass spectrometer preferably further comprises an ion detector arranged adjacent the entrance electrode, entrance region or entrance aperture of the ion guide. Alternatively, the

ion detector may be arranged adjacent an exit electrode, exit region or exit aperture of the ion guide, wherein the exit electrode, exit region or exit aperture is arranged at an opposite end of the ion guide to the entrance electrode, entrance region or entrance aperture.

5 The mass spectrometer preferably further comprises an further ion guide, ion trap or ion trapping region arranged upstream and/or downstream of the time of flight mass analyser. The further ion guide, ion trap or ion trapping region is 10 preferably arranged to trap, store or accumulate ions and then to periodically pulse ions into or towards the time of flight mass analyser.

In a mode of operation the maximum amplitude of the second 15 AC or RF voltage at one or more points along the axial length of the ion guide forming part of the time of flight mass analyser is preferably arranged to vary, increase or decrease with time in a synchronised manner with the release of ions from the further ion guide, ion trap or ion trapping region arranged upstream and/or downstream of the time of flight mass analyser.

20 The mass spectrometer may further comprise a second ion guide comprising a plurality of electrodes. The second ion guide is preferably arranged upstream and/or downstream of the time of flight mass analyser. The second ion guide preferably comprises: (i) a multipole rod set or a segmented multipole rod set; (ii) an 25 ion tunnel or ion funnel; or (iii) a stack or array of planar, plate or mesh electrodes.

According to an embodiment the multipole rod set comprises a quadrupole rod set, a hexapole rod set, an octapole rod set or a rod set comprising more than eight rods.

30 According to an embodiment the ion tunnel or ion funnel comprises a plurality of electrodes or at least 2, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 electrodes having apertures through which ions are transmitted in use, wherein at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 35% 85%, 90%, 95% or 100% of the electrodes have apertures which are of substantially the same size or area or which have apertures which become progressively larger and/or smaller in size or in area. Preferably, at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or

100% of the electrodes have internal diameters or dimensions selected from the group consisting of: (i) ≤ 1.0 mm; (ii) ≤ 2.0 mm; (iii) ≤ 3.0 mm; (iv) ≤ 4.0 mm; (v) ≤ 5.0 mm; (vi) ≤ 6.0 mm; (vii) ≤ 7.0 mm; (viii) ≤ 8.0 mm; (ix) ≤ 9.0 mm; (x) ≤ 10.0 mm; and (xi) > 10.0 mm.

According to an embodiment the stack or array of planar, plate or mesh electrodes comprises a plurality or at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 planar, plate or mesh electrodes wherein at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the planar, plate or mesh electrodes are arranged generally in the plane in which ions travel in use. Preferably, at least some or at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the planar, plate or mesh electrodes are supplied with an AC or RF voltage and wherein adjacent planar, plate or mesh electrodes are supplied with opposite phases of the AC or RF voltage.

The second ion guide preferably comprises a plurality of axial segments or at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95 or 100 axial segments.

The centre to centre spacing between adjacent electrodes of the second ion guide is preferably selected from the group consisting of: (i) < 0.5 mm; (ii) 0.5-1.0 mm; (iii) 1.0-1.5 mm; (iv) 1.5-2.0 mm; (v) 2.0-2.5 mm; (vi) 2.5-3.0 mm; (vii) 3.0-3.5 mm; (viii) 3.5-4.0 mm; (ix) 4.0-4.5 mm; (x) 4.5-5.0 mm; (xi) 5.0-5.5 mm; (xii) 5.5-6.0 mm; (xiii) 6.0-6.5 mm; (xiv) 6.5-7.0 mm; (xv) 7.0-7.5 mm; (xvi) 7.5-8.0 mm; (xvii) 8.0-8.5 mm; (xviii) 8.5-9.0 mm; (xix) 9.0-9.5 mm; (xx) 9.5-10.0 mm; and (xxi) > 10.0 mm.

The second ion guide preferably has an axial length selected from the group consisting of: (i) < 20 mm; (ii) 20-40 mm; (iii) 40-60 mm; (iv) 60-80 mm; (v) 80-100 mm; (vi) 100-120 mm; (vii) 120-140 mm; (viii) 140-160 mm; (ix) 160-180 mm; (x) 180-200 mm; (xi) 200-220 mm; (xii) 220-240 mm; (xiii) 240-260 mm; (xiv) 260-280 mm; (xv) 280-300 mm; and (xvi) > 300 mm.

According to an embodiment the mass spectrometer further comprises DC voltage means for maintaining a substantially constant DC voltage gradient along at least a portion or at least

5 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%,
70%, 75%, 80%, 85%, 90%, 95% or 100% of the axial length of the
second ion guide in order to urge at least some ions along at
least a portion or at least 5%, 10%, 15%, 20%, 25%, 30%, 35%,
40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or
100% of the axial length of the second ion guide.

10 According to an embodiment the mass spectrometer comprises
transient DC voltage means arranged and adapted to apply one or
more transient DC voltages or potentials or one or more transient
DC voltage or potential waveforms to at least some of the
electrodes forming the second ion guide in order to urge at least
some ions along at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%,
45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of
the axial length of the second ion guide.

15 According to an embodiment the mass spectrometer further
comprises AC or RF voltage means arranged and adapted to apply
two or more phase-shifted AC or RF voltages to electrodes forming
the second ion guide in order to urge at least some ions along at
least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%,
65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the axial length of
the second ion guide.

20 According to an embodiment the mass spectrometer further
comprises a second mass analyser arranged upstream and/or
downstream of the time of flight mass analyser. The second mass
analyser is preferably selected from the group consisting of: (i)
25 a quadrupole mass analyser; (ii) a 2D or linear quadrupole mass
analyser; (iii) a Paul or 3D quadrupole mass analyser; (iv) a
Penning trap mass analyser; (v) an ion trap mass analyser; (vi) a
magnetic sector mass analyser; (vii) Ion Cyclotron Resonance
("ICR") mass analyser; (viii) a Fourier Transform Ion Cyclotron
Resonance ("FTICR") mass analyser; (ix) an electrostatic or
30 orbitrap mass analyser; (x) a Fourier Transform electrostatic or
orbitrap mass analyser; (xi) a Fourier Transform mass analyser;
(xii) a Time of Flight mass analyser; (xiii) an orthogonal
35 acceleration Time of Flight mass analyser; (xiv) an axial
acceleration Time of Flight mass analyser; and (xv) a Wein
filter.

According to an embodiment the mass spectrometer further
comprises a collision, fragmentation or reaction device. The

collision, fragmentation or reaction device is preferably arranged and adapted to fragment ions by Collision Induced Dissociation ("CID"). According to an alternative embodiment the collision, fragmentation or reaction device is selected from the group consisting of: (i) a Surface Induced Dissociation ("SID") fragmentation device; (ii) an Electron Transfer Dissociation fragmentation device; (iii) an Electron Capture Dissociation fragmentation device; (iv) an Electron Collision or Impact Dissociation fragmentation device; (v) a Photo Induced Dissociation ("PID") fragmentation device; (vi) a Laser Induced Dissociation fragmentation device; (vii) an infrared radiation induced dissociation device; (viii) an ultraviolet radiation induced dissociation device; (ix) a nozzle-skimmer interface fragmentation device; (x) an in-source fragmentation device; (xi) an ion-source Collision Induced Dissociation fragmentation device; (xii) a thermal or temperature source fragmentation device; (xiii) an electric field induced fragmentation device; (xiv) a magnetic field induced fragmentation device; (xv) an enzyme digestion or enzyme degradation fragmentation device; (xvi) an ion-ion reaction fragmentation device; (xvii) an ion-molecule reaction fragmentation device; (xviii) an ion-atom reaction fragmentation device; (xix) an ion-metastable ion reaction fragmentation device; (xx) an ion-metastable molecule reaction fragmentation device; (xxi) an ion-metastable atom reaction fragmentation device; (xxii) an ion-ion reaction device for reacting ions to form adduct or product ions; (xxiii) an ion-molecule reaction device for reacting ions to form adduct or product ions; (xxiv) an ion-atom reaction device for reacting ions to form adduct or product ions; (xxv) an ion-metastable ion reaction device for reacting ions to form adduct or product ions; (xxvi) an ion-metastable molecule reaction device for reacting ions to form adduct or product ions; and (xxvii) an ion-metastable atom reaction device for reacting ions to form adduct or product ions.

According to an embodiment the mass spectrometer further comprises acceleration means arranged and adapted to accelerate ions into the collision, fragmentation or reaction device wherein in a mode of operation at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or

100% of the ions are caused to fragment or react upon entering the collision, fragmentation or reaction device.

According to an embodiment the mass spectrometer further comprises a control system arranged and adapted to switch or repeatedly switch the potential difference through which ions pass prior to entering the collision, fragmentation or reaction device between a relatively high fragmentation or reaction mode of operation wherein ions are substantially fragmented or reacted upon entering the collision, fragmentation or reaction device and a relatively low fragmentation or reaction mode of operation wherein substantially fewer ions are fragmented or reacted or wherein substantially no ions are fragmented or reacted upon entering the collision, fragmentation or reaction device. In the relatively high fragmentation or reaction mode of operation ions entering the collision, fragmentation or reaction device are preferably accelerated through a potential difference selected from the group consisting of: (i) ≥ 10 V; (ii) ≥ 20 V; (iii) ≥ 30 V; (iv) ≥ 40 V; (v) ≥ 50 V; (vi) ≥ 60 V; (vii) ≥ 70 V; (viii) ≥ 80 V; (ix) ≥ 90 V; (x) ≥ 100 V; (xi) ≥ 110 V; (xii) ≥ 120 V; (xiii) ≥ 130 V; (xiv) ≥ 140 V; (xv) ≥ 150 V; (xvi) ≥ 160 V; (xvii) ≥ 170 V; (xviii) ≥ 180 V; (xix) ≥ 190 V; and (xx) ≥ 200 V. In the relatively low fragmentation or reaction mode of operation ions entering the collision, fragmentation or reaction device are preferably accelerated through a potential difference selected from the group consisting of: (i) ≤ 20 V; (ii) ≤ 15 V; (iii) ≤ 10 V; (iv) ≤ 5 V; and (v) ≤ 1 V. The control system is preferably arranged and adapted to switch the collision, fragmentation or reaction device between the relatively high fragmentation or reaction mode of operation and the relatively low fragmentation or reaction mode of operation at least once every 1 ms, 5 ms, 10 ms, 15 ms, 20 ms, 25 ms, 30 ms, 35 ms, 40 ms, 45 ms, 50 ms, 55 ms, 60 ms, 65 ms, 70 ms, 75 ms, 80 ms, 85 ms, 90 ms, 95 ms, 100 ms, 200 ms, 300 ms, 400 ms, 500 ms, 600 ms, 700 ms, 800 ms, 900 ms, 1 s, 2 s, 3 s, 4 s, 5 s, 6 s, 7 s, 8 s, 9 s or 10 s.

The collision, fragmentation or reaction device is preferably arranged and adapted to receive a beam of ions and to convert or partition the beam of ions such that at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 separate groups or packets of ions are confined and/or isolated

in the collision, fragmentation or reaction device at any particular time, and wherein each group or packet of ions is separately confined and/or isolated in a separate axial potential well formed in the collision, fragmentation or reaction device.

5 According to an embodiment the mass spectrometer further comprises a further mass filter or mass analyser arranged upstream and/or downstream of the time of flight mass analyser. The further mass filter or mass analyser is preferably selected from the group consisting of: (i) a quadrupole rod set mass filter; (ii) a Time of Flight mass filter or mass analyser; (iii) a Wein filter; and (iv) a magnetic sector mass filter or mass analyser.

10 According to an embodiment the mass spectrometer further comprises an ion source. The ion source is preferably selected from the group consisting of: (i) an Electrospray ionisation ("ESI") ion source; (ii) an Atmospheric Pressure Photo Ionisation ("APPI") ion source; (iii) an Atmospheric Pressure Chemical Ionisation ("APCI") ion source; (iv) a Matrix Assisted Laser Desorption Ionisation ("MALDI") ion source; (v) a Laser Desorption Ionisation ("LDI") ion source; (vi) an Atmospheric Pressure Ionisation ("API") ion source; (vii) a Desorption Ionisation on Silicon ("DIOS") ion source; (viii) an Electron Impact ("EI") ion source; (ix) a Chemical Ionisation ("CI") ion source; (x) a Field Ionisation ("FI") ion source; (xi) a Field Desorption ("FD") ion source; (xii) an Inductively Coupled Plasma ("ICP") ion source; (xiii) a Fast Atom Bombardment ("FAB") ion source; (xiv) a Liquid Secondary Ion Mass Spectrometry ("LSIMS") ion source; (xv) a Desorption Electrospray Ionisation ("DESI") ion source; (xvi) a Nickel-63 radioactive ion source; (xvii) a Thermospray ion source; (xviii) a Particle Beam ("PB") ion source; and (xix) a Flow Fast Atom Bombardment ("Flow FAB") ion source.

15 The mass spectrometer preferably further comprises a continuous or pulsed ion source.

20 According to another aspect of the present invention there is provided a method of mass analysing ions according to their time of flight comprising:

25 providing an ion guide comprising a plurality of electrodes;

confining ions radially within the ion guide; and
5 applying a time varying inhomogeneous axial electric field
along at least a portion of the axial length of the ion guide.

According to another aspect of the present invention there
10 is provided a method of mass spectrometry comprising a method as
disclosed above.

According to another aspect of the present invention there
is provided a device for temporally separating ions according to
their mass to charge ratio and/or ion mobility, the device
15 comprising:

an ion guide comprising a plurality of electrodes;
first means arranged and adapted and to confine ions
radially within the ion guide; and
second means arranged and adapted to apply a time varying
15 inhomogeneous axial electric field along at least a portion of
the axial length of the ion guide.

According to another aspect of the present invention there
is provided a method of temporally separating ions according to
their mass to charge ratio and/or ion mobility, the device
20 comprising:

providing an ion guide comprising a plurality of
electrodes;
confining ions radially within the ion guide; and
25 applying a time varying inhomogeneous axial electric field
along at least a portion of the axial length of the ion guide.

The preferred embodiment relates to a mass spectrometer or
mass analyser comprising an RF ion guide. The RF ion guide
preferably comprises a ring stack ion guide wherein an AC or RF
voltage is applied to neighbouring ring electrodes. The AC or RF
30 voltage which is applied to the ring electrodes is preferably
such that the same amplitude AC or RF voltage is applied to
neighbouring electrodes but the phase of the AC or RF voltage is
preferably 180 degrees different between two neighbouring
electrodes. Therefore, according to the preferred embodiment
35 adjacent electrodes are preferably supplied with opposite phases
of the AC or RF voltage. The AC or RF voltage applied to the
electrodes preferably results in a radial pseudo-potential well
being formed or generated which preferably acts to contain or
confine ions radially within the ion guide.

A supplemental, secondary or additional AC, RF or time varying inhomogeneous electric field is preferably additionally applied or maintained along at least part of or substantially the whole length of the axial length of the ion guide. The resulting axial inhomogenous AC, RF or time varying electric field preferably acts to propel, force or urge ions in a particular direction along the length of the ion guide.

The supplemental, secondary or additional AC or RF or time varying voltage is preferably applied or maintained across the axial length of the ion guide such that preferably all the electrodes forming the ion guide experience the same phase of the supplemental, secondary or additional AC, RF or time varying voltage i.e. there is a zero phase difference between the electrodes. However, the amplitude of the supplemental, secondary or additional AC, RF or time varying voltage is preferably arranged to increase or decrease along the length of the ion guide. According to a preferred embodiment the amplitude varies in a nonlinear manner.

The axial pseudo-potential force preferably urges ions in a direction so that ions move towards a region of weakest axial pseudo-potential force. The axial pseudo-potential force experienced by an ion is preferably inversely proportional to the mass to charge ratio of the ion.

According to the preferred embodiment the ion guide comprises a plurality of ring electrodes. This embodiment is particularly advantageous since different AC or RF voltages can be applied to different axial segments. However, according to other less preferred embodiments the ion guide may comprise an elongated RF multipole rod set ion guide such as a quadrupole rod set ion guide, a hexapole rod set ion guide or an octopole rod set ion guide. No axial electric field is developed as a result of applying an AC or RF voltage to the rod electrodes in order to confine ions radially within the rod set ion guide.

According to another embodiment the multipole rod set ion guide may be axially segmented thereby enabling a supplemental, secondary or additional AC, RF or time varying voltage to be applied individually to the axial segments so that a non-zero axial inhomogenous pseudo-potential force is preferably generated along the length of the ion guide.

According to another embodiment, one or more auxiliary shaped electrodes may be used to create an axial pseudo-potential driving force. The one or more auxiliary electrodes may be located external to the multipole rod electrodes. The one or 5 more auxiliary electrodes may be supplied with a supplemental, secondary or additional AC, RF or time varying voltage which is preferably independent of the AC or RF voltage which is preferably applied to the multipole rod electrodes in order to confine ions radially within the ion guide. The one or more 10 auxiliary electrodes may be situated between the rod electrodes in regions of zero potential. The one or more auxiliary electrodes may be shaped to produce the required axial field. According to another embodiment the one or more auxiliary 15 electrodes may be segmented axially so that different amplitudes of the supplemental, secondary or additional AC or RF voltage may be applied to individual segments.

According to an embodiment a DC voltage may additionally be applied to the one or more auxiliary electrodes so that a smoothly varying potential or a travelling wave voltage or 20 potential may be created which preferably manipulates or urges ion populations within the ion guide and which preferably translates ions along the length of and through the ion guide.

According to another less preferred embodiment the RF ion 25 guide may comprise a segmented flat plate ion guide comprising a plurality of plate electrodes. The plate electrodes forming the ion guide may be arranged in a sandwich formation with the plane of the plates arranged parallel to the axis of the ion guide. An AC or RF voltage is preferably applied between neighbouring 30 plates in order to confine ions within the ion guide. The plates are preferably axially segmented such that different AC or RF voltages can be applied to different axial segments of the ion guide so that an axial non-zero AC or RF electric field may be maintained along the length of the ion guide.

An ion guide or mass analyser according to various 35 embodiments of the present invention is particularly advantageous since the AC or RF voltage or potential which is applied to the electrodes forming the ion guide in order to confine ions radially within the ion guide can be adjusted so that ions are confined radially within the ion guide in a substantially optimum

manner. The radial confinement of ions can be arranged and optimised in a manner which is essentially independent of applying or generating an axial pseudo-potential driving force along the length of the ion guide or mass analyser. An ion guide or mass analyser according to the preferred embodiment can therefore be optimised for a number of different applications.

Another advantage of the ion guide or mass analyser according to various embodiments of the present invention is that the preferred ion guide or mass analyser can be coupled to an atmospheric pressure ionisation source.

Various embodiments of the present invention together with an arrangement given for illustrative purposes only will now be described, by way of example only, and with reference to the accompanying drawings in which:

Fig. 1 shows a known reflectron Time of Flight mass analyser;

Fig. 2A shows a Time of Flight mass analyser according to an embodiment of the present invention wherein ions enter and exit the mass analyser via an entrance electrode and Fig. 2B shows how the axial pseudo-potential varies along the length of the mass analyser according to an embodiment;

Fig. 3A shows a Time of Flight mass analyser according to another embodiment of the present invention wherein ions enter the mass analyser via an entrance electrode and exit the mass analyser via an exit electrode arranged at the opposite end of the mass analyser and Fig. 3B shows how the axial pseudo-potential varies along the length of the mass analyser according to an embodiment;

Fig. 4 shows a mass spectrometer according to an embodiment of the present invention wherein a preferred Time of Flight mass analyser is coupled to an orthogonal acceleration Time of Flight mass analyser via an ion guide;

Fig. 5 shows the result of a SIMION (RTM) simulation of the trajectories of ten ions having mass to charge ratios of 500 which were modelled as entering a reflectron Time of Flight mass analyser wherein a supplemental, secondary or additional AC or RF potential was maintained along the length of the mass analyser but wherein ions were not confined radially within the mass analyser;

Fig. 6 shows the result of a SIMION (RTM) simulation of the trajectories of ten ions having mass to charge ratios of 500 which were modelled as entering a reflectron Time of Flight mass analyser wherein a supplemental, secondary or additional AC or RF potential was maintained along the length of the mass analyser and wherein ions were modelled as being confined radially within the mass analyser;

Fig. 7 shows a SIMION (RTM) simulation of the trajectories of five ions having mass to charge ratios of 500 which were modelled as being initially present within a Time of Flight mass analyser according to an embodiment of the present invention wherein ions were confined radially within the mass analyser and wherein a supplemental, secondary or additional AC or RF potential was modelled as being maintained along the length of the mass analyser and wherein the amplitude of the supplemental, secondary or additional AC or RF potential was modelled as increasing as a function of time; and

Fig. 8 shows a plot of the arrival time of ions as a function of mass to charge ratio for ions having different mass to charge ratios which were simulated as being initially present within a Time of Flight mass analyser as disclosed in relation to Fig. 7.

A known mass spectrometer comprising an Electron Impact ion source and a reflectron Time of Flight mass analyser will now be described, for illustrative purposes only, with reference to Fig. 1. The mass analyser comprises a series of ring electrodes 1 which are interconnected via a resistor chain 2 to both a RF power supply and a DC power supply. The resistor chain is arranged such that the potential applied to a given electrode is given by:

$$U_{z,x,y}(t) = \left(\frac{-1}{z_0^2 - \frac{r_0^2}{2}} \right) (V_{dc} + V_{ac} \cos(\Omega t)) \left(z^2 - \frac{(x^2 + y^2)}{2} \right) \quad (1)$$

wherein z_0 is the overall length of the ion guide or Time of Flight mass analyser, r_0 is the internal radius of each ring electrode, V_{dc} is the amplitude of the applied DC voltage, V_{ac} is

the amplitude of the applied AC voltage and Ω is the frequency of oscillation of the applied AC voltage.

The Electron Impact ("EI") ion source which generates ions is located in a low pressure region. Some of the ions which are generated by the ion source are present in a region 3 adjacent an entrance electrode 1a or entrance aperture of the Time of Flight mass analyser. Ions formed by the ion source are periodically accelerated into the Time of Flight mass analyser by applying a voltage pulse to an acceleration grid 4 which is arranged adjacent to the entrance electrode 1a or entrance aperture of the Time of Flight mass analyser. Ions are pulsed into the mass analyser and start to travel along the length of the mass analyser. As ions begin to approach the opposite end of the ion guide or Time of Flight mass analyser the ions are reflected back towards the entrance electrode 1a and the entrance aperture of the ion guide or mass analyser by the combination of an axial DC voltage gradient (which is maintained along the length of the ion guide or mass analyser) and a time averaged or pseudo-potential force which is also maintained along the length of the ion guide or mass analyser. The axial pseudo-potential force results from the application of an AC or RF voltage which is applied across the length of the ion guide or mass analyser. Ions exit the ion guide or mass analyser via the entrance electrode 1a and are then subsequently detected by an ion detector 5. The ion detector 5 is arranged co-axially with the central axis of the ion guide or mass analyser. The arrival time of ions at the ion detector 5 is related to the mass to charge ratio of the ions and the field parameters of the ion guide or mass analyser. Ions are not confined radially within the ion guide or mass analyser as they traverse the length of the ion guide or mass analyser which is maintained at a relatively low pressure.

Fig. 2A shows a reflectron Time of Flight ion guide or mass analyser 7 according to an embodiment of the present invention. The ion guide or mass analyser 7 preferably comprises a series or a plurality of ring electrodes 1 or electrodes having apertures through which ions are preferably transmitted in use. The electrodes 1 are preferably connected to a two-phase AC or RF voltage supply 6. Neighbouring electrodes 1 are preferably connected to opposite phases of the two-phase AC or RF voltage

supply 6. As a result, a radial pseudo-potential well is preferably produced or created within the ion guide or mass analyser 7 which preferably serves or acts to confine ions radially within the ion guide or mass analyser 7. This is in 5 contrast to the known Time of Flight mass analyser wherein ions are not confined radially within the known Time of Flight mass analyser. The application of the two-phase AC or RF voltage to the electrodes 1 forming the ion guide or mass analyser 7 preferably results in a series of axial pseudo-potential 10 corrugations being formed or created along the length of the ion guide or mass analyser 7. The axial pseudo-potential corrugations preferably have a relatively small amplitude and may have the effect of slowing down or substantially stopping the 15 onward passage of at least some ions through the ion guide or mass analyser 7 in the absence of any axial driving field or force. This effect may be particularly evident in the presence of a buffer gas.

According to the preferred embodiment of the present invention a supplemental, secondary or additional oscillating, AC 20 or RF voltage is preferably applied across the ion guide or mass analyser 7. The supplemental, secondary or additional oscillating, AC or RF voltage is preferably a single phase voltage. The maximum amplitude of the supplemental, secondary or additional oscillating, AC or RF voltage preferably varies along 25 the axial length of the ion guide or mass analyser 7. According to an embodiment the maximum amplitude of the supplemental, secondary or additional oscillating, AC or RF voltage may vary in a non-linear manner as shown in Fig. 2B along the axial length of the ion guide or mass analyser 7.

30 The general form of the supplemental, secondary or additional oscillating, AC or RF potential V_n applied to a particular electrode 1 or element of the ion guide or mass analyser 7 may be described by:

$$35 \quad V_n = f(n) \cos(\sigma t) \quad (2)$$

wherein n is the index number of the electrode, $f(n)$ is a function describing the amplitude of oscillation for the

particular electrode and σ is the frequency of modulation of the supplemental, secondary or additional oscillating, AC or RF potential.

If the maximum amplitude of the supplemental, secondary or additional oscillating, AC or RF potential described by $f(n)$ increases away from the entrance electrode 1a of the ion guide or mass analyser 7 in a non-linear manner as shown in Fig. 2B towards the opposite end of the ion guide or mass analyser 7, then a mass to charge ratio dependent pseudo-potential ramp will be formed, created or exist along the axial length of the ion guide or mass analyser 7. The pseudo-potential ramp will preferably be superimposed upon the relatively low amplitude regular pseudo-potential axial corrugations which preferably result from the application of the two-phase AC or RF voltage to the electrodes 1 in order to confine ions radially within the ion guide or mass analyser 7.

The axial pseudo-potential ramp preferably has the effect of propelling, directing or urging ions back along the length of the ion guide or mass analyser 7 towards a region of relatively weak axial pseudo-potential force i.e. back towards the entrance electrode 1a and the entrance aperture of the ion guide or mass analyser 7. The magnitude of the axial pseudo-potential ramp as experienced by an ion is preferably inversely proportional to the mass to charge ratio of the ion.

According to the preferred embodiment, the ion source which generates ions is not limited to an Electron Impact ion source and may comprise a pulsed ion source or a continuous ion source. According to an embodiment, ions from the ion source may be arranged to arrive at an orthogonal acceleration region 3 which is preferably located adjacent to an entrance electrode 1a and the entrance aperture of the ion guide or mass analyser 7. The ions which arrive at the orthogonal acceleration region 3 may comprise a continuous stream of ions or alternatively the ions may be grouped into a series of discrete packets of ions.

As ions arrive at the orthogonal acceleration region 3, ions are preferably periodically orthogonally accelerated into the ion guide or mass analyser 7 by applying a voltage pulse to an acceleration grid 4. The acceleration grid 4 is preferably arranged adjacent to the orthogonal acceleration region 3 and is

preferably also in close proximity to the entrance electrode 1a and the entrance aperture which leads into the ion guide or mass analyser 7. Ions which are injected into the ion guide or mass analyser 7 are preferably caused to traverse a proportion of the 5 length of the ion guide or mass analyser 7. The ions are then preferably reflected back towards the entrance electrode 1a and the entrance aperture by the axial pseudo-potential ramp. The ions then preferably exit the ion guide or mass analyser 7 via the entrance electrode 1a and the entrance aperture and 10 preferably pass through the acceleration grid 4. The ions are then preferably detected by an ion detector 5 which is preferably arranged co-axial with the central axis of the ion guide or mass analyser 7. The arrival time of ions at the ion detector 5 is 15 preferably recorded and the arrival time is preferably related in a substantially linear manner to the mass to charge ratio of the ions and the field parameters of the ion guide or mass analyser 7.

As ions traverse the ion guide or mass analyser 7 they are 20 preferably contained or confined radially within the ion guide or mass analyser 7 by a radial pseudo-potential well which preferably results from the application of the two-phase AC or RF voltage to the electrodes 1 of the ion guide or mass analyser 7.

The ion guide or mass analyser 7 according to the preferred 25 embodiment of the present invention may be used with or coupled to a variety of different ionisation sources including an Atmospheric Pressure Ionisation ion source. The ability of being able to couple an Atmospheric Pressure Ionisation ion source to the preferred ion guide or mass analyser 7 is particularly advantageous.

According to an embodiment the amplitude or strength of the 30 radial confining pseudo-potential may be adjusted substantially independently of the amplitude or strength of the axial pseudo-potential ramp. Accordingly, the ion guide or mass analyser 7 is preferably arranged so that ions are preferably radially confined 35 in an optimal manner and at the same time ions are preferably transported along and through the length of the ion guide or mass analyser 7 and separated according to their mass to charge ratio in an efficient and optimal manner.

An ion guide or Time of Flight mass analyser according to another embodiment of the present invention is shown in Fig. 3A. According to this embodiment, an ion guide or mass analyser 7 is provided wherein ions are not reflected within the ion guide or 5 mass analyser 7. Instead, ions preferably enter the ion guide or mass analyser 7 via an entrance electrode 1a and entrance aperture. The ions preferably traverse the length of the ion guide or mass analyser 7 and then preferably exit the ion guide or mass analyser 7 via an exit electrode 1b or exit aperture which is preferably located at the opposite end of the ion guide or mass analyser 7 to that of the entrance electrode 1a and the entrance aperture. An ion detector 5 is preferably arranged adjacent the exit electrode 1b or the exit aperture. The 10 orthogonal acceleration region 3 is therefore preferably arranged at an opposite end of the ion guide or mass analyser 7 to that of the ion detector 5.

A two-phase AC or RF voltage or potential is preferably applied to the electrodes 1 forming the ion guide or mass analyser 7 so that adjacent electrodes are preferably connected 20 to or maintained at opposite phases of the AC or RF voltage or potential. As a result, ions are preferably confined radially within the ion guide or mass analyser 7 by a radial pseudo-potential well. A supplemental, secondary or additional axial driving AC or RF potential is preferably applied or maintained 25 across the length of the ion guide or mass analyser 7. The axial driving AC or RF potential preferably acts to propel, direct or urge ions along the length of the ion guide or mass analyser 7 from the entrance region, entrance electrode 1a or entrance aperture of the ion guide or mass analyser 7 towards the exit region, exit electrode 1b or exit aperture of the ion guide or 30 mass analyser 7.

Ions present in the orthogonal acceleration region 3 are 35 preferably pulsed into the ion guide or mass analyser 7 at a time T_0 by the application of a voltage pulse to an acceleration electrode 4. The acceleration electrode 4 is preferably arranged close to and adjacent the entrance electrode 1a or entrance aperture of the ion guide or mass analyser 7. The supplemental, secondary or additional AC or RF potential which is preferably applied to the electrodes 1 may be arranged initially to have a

relatively low or zero amplitude. Once ions have entered the ion guide or mass analyser 7 at a subsequent time T1 (wherein T1>T0), the magnitude or amplitude of the supplemental, secondary or additional oscillating, AC or RF potential is preferably increased or switched from a relatively low or zero amplitude to a maximum value or amplitude.

According to an embodiment, the maximum amplitude of the supplemental, secondary or additional oscillating, AC or RF potential is preferably arranged to vary along the length of the ion guide or mass analyser 7 in a manner such that the maximum amplitude preferably decreases along the length of the ion guide or mass analyser 7 from the entrance region, entrance electrode 1a or entrance aperture of the ion guide or mass analyser 7 towards the exit region, exit electrode 1b or exit aperture of the ion guide or mass analyser 7. The axial pseudo-potential may decrease in a non-linear manner as shown, for example, in Fig.

3B. The axial pseudo-potential ramp is preferably mass to charge ratio dependent. The axial pseudo-potential ramp is preferably superimposed upon relatively low amplitude axial pseudo-potential corrugations which result from the application of the two-phase AC or RF voltage from the AC or RF voltage supply 6 to the electrodes 1 of the ion guide or mass analyser 7. The two-phase AC or RF voltage is preferably applied to the electrodes 1 in order to generate a radial pseudo-potential well which preferably acts to confine ions radially within the ion guide or mass analyser 7. The axial pseudo-potential ramp preferably acts to propel, direct or urge ions along the length of the ion guide or mass analyser 7 from the entrance region, entrance electrode 1a or entrance aperture of the ion guide or mass analyser 7 towards the exit region, exit electrode 1b or exit aperture of the ion guide or mass analyser 7.

The magnitude of the axial pseudo-potential ramp as experienced by an ion is preferably inversely proportional to the mass to charge ratio of the ion. The depth of the regular axial pseudo-potential corrugations resulting from applying the two-phase AC or RF voltage 6 to the electrodes 1 in order to confine ions radially within the ion guide or mass analyser 7 is also preferably inversely proportional to mass to charge ratio of the ions. According to an embodiment the axial electric field which

preferably propels, directs or urges ions along the length of the ion guide or mass analyser 7 may be matched to the depth of the axial pseudo-potential corrugations for all ions irrespective of their mass to charge ratio.

5 The arrival time of ions which emerge from the ion guide or mass analyser 7 via the exit electrode 1b or exit aperture and which then subsequently impinge upon the ion detector 5 are preferably recorded. The ion detector 5 is preferably arranged adjacent the exit electrode 1b of the ion guide or mass analyser 10 7. The arrival time of an ion at the ion detector 5 is preferably related to the mass to charge ratio of the ions and the field parameters of the ion guide or mass analyser 7.

15 As ions traverse the length of the ion guide or mass analyser 7 the ions are preferably contained radially within the ion guide or mass analyser 7 by a radial pseudo-potential well which is preferably formed or generated by the application of an AC or RF voltage to the electrodes 1 of the ion guide or mass analyser 7 so that adjacent electrodes are preferably maintained at opposite phases of the applied AC or RF voltage.

20 The time of flight of ions through the preferred ion guide or mass analyser 7 is preferably described by the following equation:

$$T \propto C \sqrt{\frac{m}{qV^*}} \quad (3)$$

25

wherein q is the electron charge, m is the mass of the ion, C is a constant related to the distance over which the ions travel and V^* is the time averaged axial potential difference or pseudo-potential difference.

30 The pseudo-potential may be described by:

$$V^* = \frac{qE(z)^2}{4m\sigma^2} \quad (4)$$

35 wherein $E(z)$ describes the electric field in the axial direction for the maxima of the applied oscillating voltage and σ is the frequency of modulation.

From Eqn. 4 it is apparent that the time of flight given in Eqn. 3 above may be re-written as:

$$T \propto C \sqrt{\frac{m^2}{q^2}} = C \cdot \frac{m}{q} \quad (5)$$

5

An expression for the mass resolution R^* of the mass analyser may be derived by differentiation of Eqn. 5:

$$R^* = \frac{m}{\partial m} = \frac{T}{\partial T} \quad (6)$$

10

It should be noted that the resolution of the preferred ion guide or mass analyser 7 as given in Eqn. 6 above is different to the relationship for ions accelerated in a DC potential which is given by Eqn. 7 below:

15

$$R = \frac{m}{\partial m} = \frac{T}{2\delta T} \quad (7)$$

It should also be noted that the pseudo-potential driving force according to the preferred embodiment acts equally upon 20 positive and negative ions and urges ions in the same direction irrespective of whether an ion is positively or negatively charged. This is in contrast to an arrangement wherein a static or DC potential is used to drive ions through an ion guide wherein the DC potential will accelerate positive ions in the 25 opposite direction to negative ions.

If a buffer gas is introduced into the preferred ion guide or mass analyser 7 then the time of flight of ions through the ion guide or mass analyser 7 may then become at least partially dependent upon the mobility of the ions. The mobility of an ion 30 is a function of the cross sectional area of the ion, the buffer gas number density, the charge of the ion, the mass of the ion, the mass of the gas molecules and the temperature.

The various parameters and relationships which govern the separation of ions having differing mass to charge ratios and 35 cross sections in an ion guide or mass analyser 7 according to

the preferred embodiment are more complicated than those which apply with a conventional ion mobility drift tube wherein a DC potential is employed to accelerate ions through a buffer gas. In the case of a known ion mobility drift tube wherein a linear DC electric field is maintained along the length of the drift tube, then the equation motion of an ion may be expressed as:

$$z'' + \frac{\lambda z'}{m} - \frac{E \cdot q}{m} = 0 \quad (8)$$

wherein E is a field constant and λ is a drag term related to the cross sectional area of the ion, the gas number density, the cross sectional area and the temperature.

Considering the case where ions undergo sufficient collisions within the drift tube such that they reach a terminal velocity u :

$$\frac{\lambda u}{m} = \frac{E \cdot q}{m} \quad (9)$$

For a given length of drift tube L , the drift time Dt of an ion having a charge q and a mobility λ will be given by:

$$Dt = \frac{L \cdot \lambda}{E \cdot q} \quad (10)$$

In the case where according to the preferred embodiment ions are subjected to an axial pseudo-potential driving force V^* (see Eqn. 4 above) then Eqn. 10 above is modified:

$$Dt^* = \frac{L \cdot \lambda \cdot m}{A \cdot q^2} \quad (11)$$

wherein A is the field constant of the axial pseudo-potential.

It is apparent that the drift time Dt^* is proportional both to the mobility λ of an ion and the mass m of an ion for ions having the same charge q .

Fig. 4 shows an embodiment of the present invention wherein a preferred ion guide or mass analyser 7 is arranged upstream of an orthogonal acceleration Time of Flight mass analyser or mass spectrometer 10. Ions from an ion source are preferably 5 accumulated in an ion trap or ion trapping region 8 which is preferably arranged upstream of the preferred ion guide or mass analyser 7. Ions are preferably pulsed out of the ion trap or ion trapping region 8 into the preferred ion guide or mass analyser 7 by altering the potential or voltage applied to a gate electrode 8a. The gate electrode 8a is preferably arranged 10 downstream of the ion trap or ion trapping region 8 and upstream of the preferred ion guide or mass analyser 7.

At a time T0 the magnitude of a supplemental, secondary or additional axial AC or RF voltage or potential which is 15 preferably applied to the electrodes of the preferred ion guide or mass analyser 7 is preferably relatively low or zero. Once ions have entered the preferred ion guide or mass analyser 7 at a subsequent time T1 (wherein $T1 > T0$), the magnitude or amplitude of the supplemental, secondary or additional AC or RF voltage or 20 potential is preferably increased to a maximum value.

According to an embodiment the maximum amplitude of the supplemental, secondary or additional AC or RF voltage or potential preferably decreases from the entrance region, entrance 25 electrode or entrance aperture of the preferred ion guide or mass analyser 7 towards the exit region, exit electrode or exit aperture of the preferred ion guide or mass analyser 7 in a non-linear manner. As discussed above, the transit time of ions through the preferred ion guide or mass analyser 7 is preferably related to the mass to charge ratio of the ions and the field 30 parameters of the ion guide or mass analyser 7.

According to an embodiment a travelling wave ion guide 9 or a second ion guide may be arranged downstream of the preferred ion guide or mass analyser 7. The travelling wave ion guide 9 or second ion guide is preferably arranged to sample the ions output 35 from or which emerge from the preferred ion guide or mass analyser 7. Ions having a restricted or a relatively narrow range of mass to charge ratios preferably emerge from the preferred ion guide or mass analyser 7 at any instance in time. The ions which emerge at any instance in time are then preferably

arranged to be received in one of a number of axial potential wells which are preferably created and then translated along the length of the travelling wave ion guide 9 or second ion guide. One or more transient DC voltages or potentials or one or more transient DC voltage or potential waveforms are preferably applied to the electrodes of the travelling wave ion guide 9 or second ion guide so that one or more axial potential wells are preferably continually transported or translated along the length of the travelling wave ion guide 9 or second ion guide. Ions are preferably released from an axial potential well which has been translated along the length of the travelling wave ion guide 9 or second ion guide as the axial potential well reaches the downstream end of the travelling wave ion guide 9 or second ion guide.

Ions which are released from the travelling wave ion guide 9 or second ion guide preferably pass or are onwardly transmitted to an orthogonal acceleration Time of Flight mass analyser 10 which is preferably arranged downstream of the travelling wave ion guide 9 or second ion guide. An orthogonal extraction pulse or voltage is preferably periodically applied to an extraction electrode or pusher and/or puller electrode 10a of the orthogonal acceleration Time of Flight mass analyser 10. The orthogonal extraction pulse or voltage is preferably applied in a substantially synchronised manner with the release of ions from the travelling wave ion guide 9 or second ion guide. According to this embodiment, ions released from an axial potential well of the travelling ion guide 9 or second ion guide are preferably transmitted to the orthogonal acceleration region of the Time of Flight mass analyser 10 and are then orthogonally accelerated into the drift region of the Time of Flight mass analyser 10 in a substantially optimal manner.

According to an embodiment a buffer gas may be introduced into the preferred ion guide or mass analyser 7. According to this embodiment the output of ions from the preferred ion guide or mass analyser 7 may be at least partially related to the mobility of the ions in the buffer gas (see Eqn. 11).

Fig. 5 shows the trajectories of ions in an ion guide or mass analyser 7 as modelled using SIMION (RTM) ion optics software. The ion guide or mass analyser 7 was modelled as

comprising 27 ring or annular electrodes 11 wherein the radius inscribed by the ring or annular electrodes 11 was set at 2.5 mm. The ring or annular electrodes 11 each had a thickness of 0.5 mm and were modelled as having 1 mm gaps between adjacent electrodes 11. At either end of the ion guide or mass analyser 7 an annular end plate electrode 12,13 was modelled as being provided. The annular end plate electrodes 12,13 were modelled as having an internal radius of 1 mm and were modelled as being set or maintained at ground potential.

A supplemental, secondary or additional AC or RF voltage or potential was modelled as being applied to the electrodes 11 so that neighbouring electrodes were maintained at the same phase of the AC or RF voltage. The amplitude of the supplemental, secondary or additional AC or RF voltage was modelled as varying along the length of the ion guide or mass analyser 7. The amplitude of the supplemental, secondary or additional AC or RF voltage or potential applied to each of the n ring electrodes $V_{ax}(n)$ was modelled as following the following general relationship:

$$V_{ax}(n) = \frac{V_0 n^{\frac{3}{2}}}{27^2} \cos(\sigma t) \quad (12)$$

wherein V_0 is the maximum peak amplitude of the supplemental, secondary or additional AC or RF voltage applied to electrode #27 and σ is the frequency of oscillation of the applied supplemental, secondary or additional AC or RF voltage or potential.

The relationship given in Eqn. 12 above was chosen such that the magnitude of the axial driving pseudo-potential was arranged to vary linearly along the length of the ion guide or mass analyser 7. However, according to other embodiments the axial pseudo-potential may be arranged to vary in another manner along the length of the ion guide or mass analyser 7.

The maximum amplitude V_0 as referred to in Eqn. 12 above was set at 800 V. The oscillating frequency σ of the supplemental, secondary or additional AC or RF voltage was set at 1 MHz.

The trajectories of ten ions each having a mass to charge ratio of 500 were simulated. Each ion was arranged to have an initial energy of 1 eV and the ions were arranged to have a spread of initial starting positions and trajectories. No gas 5 model was used in the simulation. In the case of the simulation, the results of which are shown in Fig. 5, the ions were not confined radially within the ion guide or mass analyser 7 (i.e. a two-phase AC or RF voltage was not modelled as being applied to the electrodes 11). The ions were simulated as entering the ion 10 guide or mass analyser 7 at an entry position 14. As the ions traverse the length of the ion guide or mass analyser 7 the ions move off or away from the central axis of the ion guide or mass analyser 7. Some of the ions come into close proximity with the electrodes 11. In the simulation shown in Fig. 5 only four of 15 the ten ions which were modelled as initially entering the ion guide or mass analyser subsequently emerge from the ion guide or mass analyser 7 via electrode 13. The other ions hit the electrodes 11 within the ion guide or mass analyser 7 and are lost to the system.

20 Fig. 6 shows the trajectories of ten ions which were modelled under similar conditions to those described above with reference to Fig. 5 but wherein the ions were modelled as being confined radially within the ion guide or mass analyser 7. In the simulation shown in Fig. 6, a two-phase AC or RF voltage 25 having a peak amplitude of 50V was modelled as being applied to the electrodes 11. The frequency of the two-phase AC or RF voltage was set at 1 MHz. No gas model was used in the simulation. It is apparent from Fig. 6 that the ions were confined radially within the ion guide or mass analyser 7. The 30 ions were confined to the central axis of the ion guide or mass analyser 7 more efficiently than in the case where no radially confining RF voltage was applied to the electrodes 11. In this example, all ten ions which initially entered the ion guide or mass analyser 7 at entry position 14 subsequently exit the ion 35 guide or mass analyser 7 and hence may be detected.

Fig. 7 shows the results of a simulation according to a different embodiment of the present invention wherein ions were modelled as being confined radially within the ion guide or mass analyser 7 and wherein a supplemental, secondary or additional AC

or RF voltage or potential was modelled as being applied to each of the ring electrodes 11. According to this embodiment the amplitude of the supplemental, secondary or additional AC or RF voltage or potential was modelled as increasing with time.

5 The peak amplitude of the two-phase AC or RF voltage which was applied to the electrodes 11 in order to confine ions radially was set at 200 V and had a frequency of 1 MHz. Neighbouring ring electrodes were maintained at opposite phases of the two-phase AC or RF voltage. The supplemental, secondary 10 or additional AC or RF potential was modelled such that adjacent electrodes 11 experienced the same phase of the supplemental, secondary or additional AC or RF potential. The amplitude of the supplemental, secondary or additional AC or RF potential was arranged to vary along the length of the ion guide or mass 15 analyser 7 both as a function of axial displacement and also of time. The amplitude of the supplemental, secondary or additional AC or RF voltage $V_{ax}(n)$ applied to each of the n electrodes was ramped from zero amplitude to a maximum amplitude over a period of time and was arranged to follow the following relationship:

20

$$V_{ax}(n) = \frac{V_0 \cdot n^{\frac{3}{2}}}{27^{\frac{3}{2}}} \cos(\sigma t) \cdot \frac{t}{10^{-3}} \quad (13)$$

wherein V_0 is the peak amplitude of the supplemental, secondary or additional AC or RF voltage applied to electrode #27 (see Fig. 25 7) and σ is the frequency of oscillation of the applied voltage.

In the simulation modelled in Fig. 7, the peak amplitude V_0 was set to 900 V and the oscillating frequency of the supplemental, secondary or additional AC or RF voltage σ was set to 0.5 MHz. The voltage applied to the exit lens or exit 30 electrode 1a was set to -2V.

Five ions having a mass to charge ratio of 500 were modelled as being initially present within the preferred ion guide or mass analyser 7 and located at a position 15. A hard sphere collision gas model was used to simulate a Helium buffer 35 gas which was modelled as being present at a pressure of 1×10^{-2} mbar within the preferred ion guide or mass analyser 7.

Ions cooled by the buffer gas were initially trapped within one of the axial pseudo-potential corrugations which result from the application of the two-phase AC or RF voltage or potential to the ring electrodes 11 in order to confine ions radially within the ion guide or mass analyser 7. As the amplitude of the axial driving RF potential was ramped or increased with time then ions were preferably driven through and along the preferred ion guide or mass analyser 7 towards the exit electrode 1a.

Fig. 8 shows a graph of the flight time of ions through a preferred ion guide or mass analyser 7 as modelled and described above in relation to Fig. 7. Fig. 8 shows the flight times of ions having mass to charge ratios of 350, 400, 450, 500, 550 and 600. Five ions were modelled at each mass to charge ratio. It can be seen from Fig. 8 that there is a linear relationship between the mass to charge ratio of the ions and the flight time. The linear relationship is in good agreement with the relationship described above by Eqns. 5 and 11.

Other embodiments are contemplated wherein the preferred ion guide or mass analyser 7 may be used with or coupled to other types of mass analysers. For example, the preferred ion guide or mass analyser 7 may be coupled to a scanning quadrupole rod set mass filter or mass analyser. According to this embodiment the duty cycle of the mass filter or mass analyser may advantageously be increased.

According to another embodiment the preferred ion guide or mass analyser 7 may be used in a mode of operation as a collision gas cell in a tandem mass spectrometer.

Other embodiments are also contemplated wherein a buffer gas may be arranged to flow through the preferred ion guide or mass analyser 7 in a direction which is preferably substantially opposite to the direction in which ions are preferably urged or propelled through the ion guide or mass analyser 7 by the pseudo-potential driving force.

Although the present invention has been described with reference to the 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.

9363303c12

Claims

5 1. A time of flight mass analyser comprising:
 an ion guide comprising a plurality of electrodes;
 first means arranged and adapted and to confine ions
 radially within said ion guide; and
 second means arranged and adapted to apply a time
10 varying inhomogeneous axial electric field along at least a
 portion of the axial length of said ion guide.

2. A time of flight mass analyser as claimed in claim 1,
wherein said ion guide comprises:
15 (i) a multipole rod set or a segmented multipole rod
set;
 (ii) an ion tunnel or ion funnel; or
 (iii) a stack or array of planar, plate or mesh
electrodes.

20 3. A time of flight mass analyser as claimed in claim 2,
wherein said multipole rod set comprises a quadrupole rod
set, a hexapole rod set, an octapole rod set or a rod set
comprising more than eight rods.

25 4. A time of flight mass analyser as claimed in claim 2,
wherein said ion tunnel or ion funnel comprises a plurality
of electrodes or at least 2, 5, 10, 20, 30, 40, 50, 60, 70,
80, 90 or 100 electrodes having apertures through which ions
30 are transmitted in use, wherein at least 5%, 10%, 15%, 20%,
25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%,
85%, 90%, 95% or 100% of said electrodes have apertures which
are of substantially the same size or area or which have
apertures which become progressively larger and/or smaller in
35 size or in area.

5. A time of flight mass analyser as claimed in claim 4, wherein at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of said electrodes have internal diameters or dimensions

5 selected from the group consisting of: (i) \leq 1.0 mm; (ii) \leq 2.0 mm; (iii) \leq 3.0 mm; (iv) \leq 4.0 mm; (v) \leq 5.0 mm; (vi) \leq 6.0 mm; (vii) \leq 7.0 mm; (viii) \leq 8.0 mm; (ix) \leq 9.0 mm; (x) \leq 10.0 mm; and (xi) $>$ 10.0 mm.

10 6. A time of flight mass analyser as claimed in claim 2, wherein said stack or array of planar, plate or mesh electrodes comprises a plurality or at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 planar, plate or mesh electrodes wherein at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of said planar, plate or mesh electrodes are arranged generally in the plane in which ions travel in use.

20 7. A time of flight mass analyser as claimed in claim 6, wherein at least some or at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of said planar, plate or mesh electrodes are supplied with an AC or RF voltage and wherein adjacent planar, plate or mesh electrodes are supplied with opposite phases of said AC or RF voltage.

30 8. A time of flight mass analyser as claimed in any preceding claim, wherein said ion guide comprises a plurality of axial segments or at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95 or 100 axial segments.

35 9. A time of flight mass analyser as claimed in any preceding claim, the centre to centre spacing between adjacent electrodes is selected from the group consisting of: (i) $<$ 0.5 mm; (ii) 0.5-1.0 mm; (iii) 1.0-1.5 mm; (iv) 1.5-2.0 mm; (v) 2.0-2.5 mm; (vi) 2.5-3.0 mm; (vii) 3.0-3.5 mm; (viii)

3.5-4.0 mm; (ix) 4.0-4.5 mm; (x) 4.5-5.0 mm; (xi) 5.0-5.5 mm; (xii) 5.5-6.0 mm; (xiii) 6.0-6.5 mm; (xiv) 6.5-7.0 mm; (xv) 7.0-7.5 mm; (xvi) 7.5-8.0 mm; (xvii) 8.0-8.5 mm; (xviii) 8.5-9.0 mm; (xix) 9.0-9.5 mm; (xx) 9.5-10.0 mm; and (xxi) > 10.0 mm.

5

10. A time of flight mass analyser as claimed in any preceding claim, wherein said ion guide has an axial length selected from the group consisting of: (i) < 20 mm; (ii) 20-40 mm; (iii) 40-60 mm; (iv) 60-80 mm; (v) 80-100 mm; (vi) 100-120 mm; (vii) 120-140 mm; (viii) 140-160 mm; (ix) 160-180 mm; (x) 180-200 mm; (xi) 200-220 mm; (xii) 220-240 mm; (xiii) 240-260 mm; (xiv) 260-280 mm; (xv) 280-300 mm; and (xvi) > 300 mm.

15

11. A time of flight mass analyser as claimed in any preceding claim, wherein said first means comprises first AC or RF voltage means arranged and adapted to apply a first AC or RF voltage to at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the electrodes forming said ion guide in order to confine ions radially within said ion guide.

25

12. A time of flight mass analyser as claimed in claim 11, wherein said first AC or RF voltage means is arranged and adapted to supply a first AC or RF voltage to the electrodes of said ion guide having an amplitude selected from the group consisting of: (i) < 50 V peak to peak; (ii) 50-100 V peak to peak; (iii) 100-150 V peak to peak; (iv) 150-200 V peak to peak; (v) 200-250 V peak to peak; (vi) 250-300 V peak to peak; (vii) 300-350 V peak to peak; (viii) 350-400 V peak to peak; (ix) 400-450 V peak to peak; (x) 450-500 V peak to peak; and (xi) > 500 V peak to peak.

30

35 13. A time of flight mass analyser as claimed in claim 11 or 12, wherein said first AC or RF voltage means is arranged and adapted to supply a first AC or RF voltage to the electrodes of said ion guide having a frequency selected from the group

consisting of: (i) < 100 kHz; (ii) 100-200 kHz; (iii) 200-300 kHz; (iv) 300-400 kHz; (v) 400-500 kHz; (vi) 0.5-1.0 MHz; (vii) 1.0-1.5 MHz; (viii) 1.5-2.0 MHz; (ix) 2.0-2.5 MHz; (x) 2.5-3.0 MHz; (xi) 3.0-3.5 MHz; (xii) 3.5-4.0 MHz; (xiii) 4.0-4.5 MHz; (xiv) 4.5-5.0 MHz; (xv) 5.0-5.5 MHz; (xvi) 5.5-6.0 MHz; (xvii) 6.0-6.5 MHz; (xviii) 6.5-7.0 MHz; (xix) 7.0-7.5 MHz; (xx) 7.5-8.0 MHz; (xxi) 8.0-8.5 MHz; (xxii) 8.5-9.0 MHz; (xxiii) 9.0-9.5 MHz; (xxiv) 9.5-10.0 MHz; and (xxv) > 10.0 MHz.

10

14. A time of flight mass analyser as claimed in claim 11, 12 or 13 wherein the phase difference of said first AC or RF voltage between adjacent electrodes or adjacent groups of electrodes is selected from the group consisting of: (i) > 0°; (ii) 1-30°; (iii) 30-60°; (iv) 60-90°; (v) 90-120°; (vi) 120-150°; (vii) 150-180°; (viii) 180°; (ix) 180-210°; (x) 210-240°; (xi) 240-270°; (xii) 270-300°; (xiii) 300-330°; and (xiv) 330-360°.

20

15. A time of flight mass analyser as claimed in any of claims 11-14, wherein said first AC or RF voltage applied, in use, to said electrodes causes or generates a radial pseudo-potential well which acts to confine ions radially, in use, within said ion guide.

25

16. A time of flight mass analyser as claimed in any of claims 11-15, wherein said first AC or RF voltage comprises a two-phase or multi-phase AC or RF voltage.

30

17. A time of flight mass analyser as claimed in any preceding claim, wherein said second means is arranged and adapted to apply a non-zero time varying inhomogeneous axial electric field along at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the axial length of said ion guide.

18. A time of flight mass analyser as claimed in any preceding claim, wherein said second means comprises means for applying a second AC or RF voltage to said electrodes.

5 19. A time of flight mass analyser as claimed in claim 18, wherein said second AC or RF voltage comprises a single phase AC or RF voltage.

10 20. A time of flight mass analyser as claimed in claim 18 or 19, wherein the phase difference of said second AC or RF voltage between adjacent electrodes or adjacent groups of electrodes is substantially 0°.

15 21. A time of flight mass analyser as claimed in claim 18, 19 or 20, wherein said second AC or RF voltage is applied across at least some of said plurality of electrodes.

20 22. A time of flight mass analyser as claimed in any of claims 18-21, wherein said second AC or RF voltage is applied to at least x electrodes, wherein x is selected from the group consisting of: (i) < 10; (ii) 10-20; (iii) 20-30; (iv) 30-40; (v) 40-50; (vi) 50-60; (vii) 60-70; (viii) 70-80; (ix) 80-90; (x) 90-100; (xi) 100-150; (xii) 150-200; and (xiii) > 200.

25

23. A time of flight mass analyser as claimed in any of claims 18-22, wherein in a mode of operation the maximum amplitude of said second AC or RF voltage at one or more points along the axial length of said ion guide is arranged to remain substantially constant with time.

30 35 24. A time of flight mass analyser as claimed in any of claims 18-22, wherein in a mode of operation the maximum amplitude of said second AC or RF voltage at one or more points along the axial length of said ion guide is arranged to vary, increase or decrease with time.

25. A time of flight mass analyser as claimed in any preceding claim, wherein at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 5 90%, 95% or 100% of said plurality of electrodes are connected at different points along a potential divider or resistor chain.

26. A time of flight mass analyser as claimed in any 10 preceding claim, wherein said second means is arranged and adapted to apply a time varying axial electric field along at least a portion of the axial length of said ion guide and wherein said axial electric field increases or decreases along the length of said ion guide in a direction from an ion 15 entrance region of said ion guide to an ion exit region of said ion guide.

27. A time of flight mass analyser as claimed in claim 26, wherein said axial electric field is arranged to increase or 20 decrease in a linear or non-linear manner along the length of said ion guide in a direction from an ion entrance region of said ion guide to an ion exit region of said ion guide.

28. A time of flight mass analyser as claimed in any 25 preceding claim, wherein said second means is arranged and adapted to accelerate or decelerate ions axially along at least a portion of the axial length of said ion guide.

29. A time of flight mass analyser as claimed in any 30 preceding claim, wherein said second means further comprises one or more auxiliary electrodes.

30. A time of flight mass analyser as claimed in claim 29, wherein said one or more auxiliary electrodes are located

external to said plurality of electrodes forming said ion guide.

31. A time of flight mass analyser as claimed in claim 29 or 5 30, wherein said one or more auxiliary electrodes have a cross-sectional area or shape which varies, increases or decreases along the length of said ion guide in a direction from an ion entrance region of said ion guide to an ion exit region of said ion guide.

10

32. A time of flight mass analyser as claimed in claim 29, 30 or 31, wherein said one or more auxiliary electrodes are axially segmented.

15

33. A time of flight mass analyser as claimed in any preceding claim, wherein singly charged ions having a mass to charge ratio in the range of 1-100, 100-200, 200-300, 300-400, 400-500, 500-600, 600-700, 700-800, 800-900, 900-1000 or > 1000 have a drift or transit time through said ion guide in 20 the range: (i) 0-50 μ s; (ii) 50-100 μ s; (iii) 100-150 μ s; (iv) 150-200 μ s; (v) 200-250 μ s; (vi) 250-300 μ s; (vii) 300-350 μ s; (viii) 350-400 μ s; (ix) 400-450 μ s; (x) 450-500 μ s; (xi) 500-550 μ s; (xii) 550-600 μ s; (xiii) 600-650 μ s; (xiv) 650-700 μ s; (xv) 700-750 μ s; (xvi) 750-800 μ s; (xvii) 800-850 25 μ s; (xviii) 850-900 μ s; (xix) 900-950 μ s; (xx) 950-1000 μ s; and (xxi) > 1000 μ s.

30

34. A time of flight mass analyser as claimed in any preceding claim, wherein singly charged ions having a mass to charge ratio in the range of 1-100, 100-200, 200-300, 300-400, 400-500, 500-600, 600-700, 700-800, 800-900, 900-1000 or > 1000 have a drift or transit time through said ion guide in the range: (i) 0-1 ms; (ii) 1-2 ms; (iii) 2-3 ms; (iv) 3-4 ms; (v) 4-5 ms; (vi) 5-6 ms; (vii) 6-7 ms; (viii) 7-8 ms; (ix) 8-9 ms; (x) 9-10 ms; (xi) 10-11 ms; (xii) 11-12 ms; (xiii) 12-13 ms; (xiv) 13-14 ms; (xv) 14-15 ms; (xvi) 15-16 ms; (xvii) 16-17 ms; (xviii) 17-18 ms; (xix) 18-19 ms; (xx)

19-20 ms; (xxi) 20-21 ms; (xxii) 21-22 ms; (xxiii) 22-23 ms;
(xxiv) 23-24 ms; (xxv) 24-25 ms; (xxvi) 25-26 ms; (xxvii) 26-
27 ms; (xxviii) 27-28 ms; (xxix) 28-29 ms; (xxx) 29-30 ms;
(xxxi) 30-35 ms; (xxxii) 35-40 ms; (xxxiii) 40-45 ms; (xxxiv)
5 45-50 ms; (xxxv) 50-55 ms; (xxxvi) 55-60 ms; (xxxvii) 60-65
ms; (xxxviii) 65-70 ms; (xxxix) 70-75 ms; (xl) 75-80 ms;
(xli) 80-85 ms; (xlii) 85-90 ms; (xliii) 90-95 ms; (xliv) 95-
100 ms; and (xlv) > 100 ms.

10 35. A time of flight mass analyser as claimed in any
preceding claim, further comprising DC voltage means for
maintaining a substantially constant DC voltage gradient
along at least a portion or at least 5%, 10%, 15%, 20%, 25%,
30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%,
15 90%, 95% or 100% of the axial length of said ion guide in
order to urge at least some ions along at least a portion or
at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%,
55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the
axial length of said ion guide.

20 36. A time of flight mass analyser as claimed in any
preceding claim, further comprising transient DC voltage
means arranged and adapted to apply one or more transient DC
voltages or potentials or one or more transient DC voltage or
25 potential waveforms to at least some of the electrodes
forming said ion guide in order to urge at least some ions
along at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%,
50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of
the axial length of said ion guide.

30 37. A time of flight mass analyser as claimed in any
preceding claim, further comprising AC or RF voltage means
arranged and adapted to apply two or more phase-shifted AC or
RF voltages to electrodes forming said ion guide in order to
35 urge at least some ions along at least 5%, 10%, 15%, 20%,
25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%,
85%, 90%, 95% or 100% of the axial length of said ion guide.

38. A time of flight mass analyser as claimed in any preceding claim, wherein said time of flight mass analyser comprises a reflectron time of flight mass analyser wherein in a mode of operation ions travel in a first direction, are 5 reflected within said ion guide and then travel in a second direction which is substantially opposed to said first direction.

39. A time of flight mass analyser as claimed in any of 10 claims 1-38, wherein in a mode of operation ions enter said ion guide via an entrance electrode, entrance region or entrance aperture and traverse the length of said ion guide and exit said ion guide via an exit electrode, exit region or exit aperture.

15

40. A time of flight mass analyser as claimed in claim 39, wherein ions are not substantially reflected axially within said ion guide as they traverse from said entrance electrode, entrance region or entrance aperture to said exit electrode, 20 exit region or exit aperture.

41. A time of flight mass analyser as claimed in any preceding claim, wherein at least a portion of said ion guide is arranged to be maintained at a pressure selected from the 25 group consisting of: (i) > 0.001 mbar; (ii) > 0.01 mbar; (iii) > 0.1 mbar; (iv) > 1 mbar; (v) > 10 mbar; (vi) > 100 mbar; (vii) 0.001-100 mbar; (viii) 0.01-10 mbar; and (ix) 0.1-1 mbar.

30 42. A time of flight mass analyser as claimed in any preceding claim, wherein at least a portion of said ion guide is arranged to be maintained at a pressure selected from the group consisting of: (i) 0.001-0.005 mbar; (ii) 0.005-0.010 mbar; (iii) 0.01-0.05 mbar; (iv) 0.05-0.10 mbar; (v) 0.1-0.5 35 mbar; (vi) 0.5-1.0 mbar; (vii) 1-5 mbar; (viii) 5-10 mbar; (ix) 10-50 mbar; (x) 50-100 mbar; and (xi) > 100 mbar.

43. A time of flight mass analyser as claimed in any preceding claims, wherein in a mode of operation ions are substantially separated according to their mass to charge ratio without ions being substantially separated according to their ion mobility.

44. A time of flight mass analyser as claimed in any of claims 1-42, wherein in a mode of operation ions are substantially separated according to their mass to charge ratio and/or their ion mobility.

45. A time of flight mass analyser as claimed in any preceding claim, wherein in a mode of operation said mass analyser is arranged and adapted to operate as a collision, fragmentation or reaction device.

46. A time of flight mass analyser as claimed in any preceding claim, wherein in a mode of operation said mass analyser is arranged and adapted to collisionally cool or thermalise ions within said ion guide.

47. A time of flight mass analyser as claimed in any preceding claim, wherein in a mode of operation said mass analyser is arranged and adapted to operate as an ion mobility spectrometer or separator.

48. A time of flight mass analyser as claimed in any preceding claim, wherein in a mode of operation ions are arranged to pass through said ion guide in a first direction and a collision, background or other gas is arranged to flow through said ion guide in a second direction.

49. A time of flight mass analyser as claimed in claim 48, wherein said first direction is substantially opposed to said second direction.

50. A time of flight mass analyser as claimed in claim 48, wherein said first direction is substantially the same direction as said second direction.

5

51. A mass spectrometer comprising a time of flight mass analyser as claimed in any preceding claim.

52. A mass spectrometer as claimed in claim 51, further comprising an acceleration electrode, pusher electrode, puller electrode or grid electrode wherein in a mode of operation ions are accelerated into said ion guide by applying a voltage pulse to said acceleration electrode, pusher electrode, puller electrode or grid electrode.

15

53. A mass spectrometer as claimed in claim 52, wherein said acceleration electrode, pusher electrode, puller electrode or grid electrode is arranged adjacent an entrance electrode, entrance region or entrance aperture of said ion guide.

20

54. A mass spectrometer as claimed in claim 51, 52 or 53, further comprising an ion detector arranged adjacent said entrance electrode, entrance region or entrance aperture of said ion guide.

25

55. A mass spectrometer as claimed in claim 51, 52 or 53, further comprising an ion detector arranged adjacent an exit electrode, exit region or exit aperture of said ion guide, wherein said exit electrode, exit region or exit aperture is arranged at an opposite end of said ion guide to said entrance electrode, entrance region or entrance aperture.

30

56. A mass spectrometer as claimed in any of claims 51-55, further comprising an further ion guide, ion trap or ion

trapping region arranged upstream and/or downstream of said time of flight mass analyser.

57. A mass spectrometer as claimed in claim 56, wherein said further ion guide, ion trap or ion trapping region is arranged to trap, store or accumulate ions and then to periodically pulse ions into or towards said time of flight mass analyser.

10 58. A mass spectrometer as claimed in claim 56 or 57, wherein in a mode of operation the maximum amplitude of said second AC or RF voltage at one or more points along the axial length of said ion guide forming part of said time of flight mass analyser is arranged to vary, increase or decrease with 15 time in a synchronised manner with the release of ions from said further ion guide, ion trap or ion trapping region arranged upstream and/or downstream of said time of flight mass analyser.

20 59. A mass spectrometer as claimed in any of claims 51-58, further comprising a second ion guide comprising a plurality of electrodes arranged upstream and/or downstream of said time of flight mass analyser.

25 60. A mass spectrometer as claimed in claim 59, wherein said second ion guide comprises:

- (i) a multipole rod set or a segmented multipole rod set;
- (ii) an ion tunnel or ion funnel; or
- 30 (iii) a stack or array of planar, plate or mesh electrodes.

61. A mass spectrometer as claimed in claim 60, wherein said multipole rod set comprises a quadrupole rod set, a hexapole 35 rod set, an octapole rod set or a rod set comprising more than eight rods.

62. A mass spectrometer as claimed in claim 60, wherein said ion tunnel or ion funnel comprises a plurality of electrodes or at least 2, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 electrodes having apertures through which ions are transmitted in use, wherein at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of said electrodes have apertures which are of substantially the same size or area or which have 5 apertures which become progressively larger and/or smaller in size or in area.

10

63. A mass spectrometer as claimed in claim 62, wherein at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 15 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of said electrodes have internal diameters or dimensions selected from the group consisting of: (i) \leq 1.0 mm; (ii) \leq 2.0 mm; (iii) \leq 3.0 mm; (iv) \leq 4.0 mm; (v) \leq 5.0 mm; (vi) \leq 6.0 mm; (vii) \leq 7.0 mm; (viii) \leq 8.0 mm; (ix) \leq 9.0 mm; (x) \leq 10.0 20 mm; and (xi) $>$ 10.0 mm.

64. A mass spectrometer as claimed in claim 60, wherein said stack or array of planar, plate or mesh electrodes comprises a plurality or at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 25 13, 14, 15, 16, 17, 18, 19 or 20 planar, plate or mesh electrodes wherein at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of said planar, plate or mesh electrodes are arranged generally in the plane in which ions travel in use.

30

65. A mass spectrometer as claimed in claim 64, wherein at least some or at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of said planar, plate or mesh electrodes are supplied with an 35 AC or RF voltage and wherein adjacent planar, plate or mesh electrodes are supplied with opposite phases of said AC or RF voltage.

66. A mass spectrometer as claimed in any of claims 59-65, wherein said second ion guide comprises a plurality of axial segments or at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95 or 100 axial segments.

5

67. A mass spectrometer as claimed in any of claims 59-66, wherein the centre to centre spacing between adjacent electrodes of said second ion guide is selected from the group consisting of: (i) < 0.5 mm; (ii) 0.5-1.0 mm; (iii) 1.0-1.5 mm; (iv) 1.5-2.0 mm; (v) 2.0-2.5 mm; (vi) 2.5-3.0 mm; (vii) 3.0-3.5 mm; (viii) 3.5-4.0 mm; (ix) 4.0-4.5 mm; (x) 4.5-5.0 mm; (xi) 5.0-5.5 mm; (xii) 5.5-6.0 mm; (xiii) 6.0-6.5 mm; (xiv) 6.5-7.0 mm; (xv) 7.0-7.5 mm; (xvi) 7.5-8.0 mm; (xvii) 8.0-8.5 mm; (xviii) 8.5-9.0 mm; (xix) 9.0-9.5 mm; (xx) 9.5-10.0 mm; and (xxi) > 10.0 mm.

10

68. A mass spectrometer as claimed in any of claims 59-67, wherein said second ion guide has an axial length selected from the group consisting of: (i) < 20 mm; (ii) 20-40 mm; (iii) 40-60 mm; (iv) 60-80 mm; (v) 80-100 mm; (vi) 100-120 mm; (vii) 120-140 mm; (viii) 140-160 mm; (ix) 160-180 mm; (x) 180-200 mm; (xi) 200-220 mm; (xii) 220-240 mm; (xiii) 240-260 mm; (xiv) 260-280 mm; (xv) 280-300 mm; and (xvi) > 300 mm.

15

69. A mass spectrometer as claimed in any of claims 59-68, further comprising DC voltage means for maintaining a substantially constant DC voltage gradient along at least a portion or at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the axial length of said second ion guide in order to urge at least some ions along at least a portion or at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the axial length of said second ion guide.

25

70. A mass spectrometer as claimed in any of claims 59-69, further comprising transient DC voltage means arranged and adapted to apply one or more transient DC voltages or

35

potentials or one or more transient DC voltage or potential waveforms to at least some of the electrodes forming said second ion guide in order to urge at least some ions along at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 5 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the axial length of said second ion guide.

71. A mass spectrometer as claimed in any of claims 59-70, further comprising AC or RF voltage means arranged and 10 adapted to apply two or more phase-shifted AC or RF voltages to electrodes forming said second ion guide in order to urge at least some ions along at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the axial length of said second ion 15 guide.

72. A mass spectrometer as claimed in any of claims 51-71, further comprising a second mass analyser arranged upstream and/or downstream of said time of flight mass analyser. 20

73. A mass spectrometer as claimed in claim 72, wherein said second mass analyser is selected from the group consisting of: (i) a quadrupole mass analyser; (ii) a 2D or linear quadrupole mass analyser; (iii) a Paul or 3D quadrupole mass 25 analyser; (iv) a Penning trap mass analyser; (v) an ion trap mass analyser; (vi) a magnetic sector mass analyser; (vii) Ion Cyclotron Resonance ("ICR") mass analyser; (viii) a Fourier Transform Ion Cyclotron Resonance ("FTICR") mass analyser; (ix) an electrostatic or orbitrap mass analyser; 30 (x) a Fourier Transform electrostatic or orbitrap mass analyser; (xi) a Fourier Transform mass analyser; (xii) a Time of Flight mass analyser; (xiii) an orthogonal acceleration Time of Flight mass analyser; (xiv) an axial acceleration Time of Flight mass analyser; and (xv) a Wein 35 filter.

74. A mass spectrometer as claimed in any of claims 51-73, further comprising a collision, fragmentation or reaction device.

5 75. A mass spectrometer as claimed in claim 74, wherein said collision, fragmentation or reaction device is arranged and adapted to fragment ions by Collision Induced Dissociation ("CID").

10 76. A mass spectrometer as claimed in claim 74, wherein said collision, fragmentation or reaction device is selected from the group consisting of: (i) a Surface Induced Dissociation ("SID") fragmentation device; (ii) an Electron Transfer Dissociation fragmentation device; (iii) an Electron Capture 15 Dissociation fragmentation device; (iv) an Electron Collision or Impact Dissociation fragmentation device; (v) a Photo Induced Dissociation ("PID") fragmentation device; (vi) a Laser Induced Dissociation fragmentation device; (vii) an infrared radiation induced dissociation device; (viii) an 20 ultraviolet radiation induced dissociation device; (ix) a nozzle-skimmer interface fragmentation device; (x) an in-source fragmentation device; (xi) an ion-source Collision Induced Dissociation fragmentation device; (xii) a thermal or temperature source fragmentation device; (xiii) an electric 25 field induced fragmentation device; (xiv) a magnetic field induced fragmentation device; (xv) an enzyme digestion or enzyme degradation fragmentation device; (xvi) an ion-ion reaction fragmentation device; (xvii) an ion-molecule reaction fragmentation device; (xviii) an ion-atom reaction 30 fragmentation device; (xix) an ion-metastable ion reaction fragmentation device; (xx) an ion-metastable molecule reaction fragmentation device; (xxi) an ion-metastable atom reaction fragmentation device; (xxii) an ion-ion reaction device for reacting ions to form adduct or product ions; 35 (xxiii) an ion-molecule reaction device for reacting ions to form adduct or product ions; (xxiv) an ion-atom reaction device for reacting ions to form adduct or product ions; (xxv) an ion-metastable ion reaction device for reacting ions

to form adduct or product ions; (xxvi) an ion-metastable molecule reaction device for reacting ions to form adduct or product ions; and (xxvii) an ion-metastable atom reaction device for reacting ions to form adduct or product ions.

5

77. A mass spectrometer as claimed in any of claims 74, 75 or 76, further comprising acceleration means arranged and adapted to accelerate ions into said collision, fragmentation or reaction device wherein in a mode of operation at least 10 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of said ions are caused to fragment or react upon entering said collision, fragmentation or reaction device.

15

78. A mass spectrometer as claimed in any of claims 74-77, further comprising a control system arranged and adapted to switch or repeatedly switch the potential difference through which ions pass prior to entering said collision, fragmentation or reaction device between a relatively high 20 fragmentation or reaction mode of operation wherein ions are substantially fragmented or reacted upon entering said collision, fragmentation or reaction device and a relatively low fragmentation or reaction mode of operation wherein substantially fewer ions are fragmented or reacted or wherein 25 substantially no ions are fragmented or reacted upon entering said collision, fragmentation or reaction device.

30

79. A mass spectrometer as claimed in claim 78, wherein in said relatively high fragmentation or reaction mode of operation ions entering said collision, fragmentation or reaction device are accelerated through a potential difference selected from the group consisting of: (i) ≥ 10 V; (ii) ≥ 20 V; (iii) ≥ 30 V; (iv) ≥ 40 V; (v) ≥ 50 V; (vi) ≥ 60 V; (vii) ≥ 70 V; (viii) ≥ 80 V; (ix) ≥ 90 V; (x) ≥ 100 V; 35 (xi) ≥ 110 V; (xii) ≥ 120 V; (xiii) ≥ 130 V; (xiv) ≥ 140 V; (xv) ≥ 150 V; (xvi) ≥ 160 V; (xvii) ≥ 170 V; (xviii) ≥ 180 V; (xix) ≥ 190 V; and (xx) ≥ 200 V.

80. A mass spectrometer as claimed in claim 78 or 79, wherein in said relatively low fragmentation or reaction mode of operation ions entering said collision, fragmentation or reaction device are accelerated through a potential difference selected from the group consisting of: (i) ≤ 20 V; (ii) ≤ 15 V; (iii) ≤ 10 V; (iv) ≤ 5 V; and (v) ≤ 1 V.

81. A mass spectrometer as claimed in any of claims 78, 79 or 80, wherein said control system is arranged and adapted to switch said collision, fragmentation or reaction device between said relatively high fragmentation or reaction mode of operation and said relatively low fragmentation or reaction mode of operation at least once every 1 ms, 5 ms, 10 ms, 15 ms, 20 ms, 25 ms, 30 ms, 35 ms, 40 ms, 45 ms, 50 ms, 55 ms, 60 ms, 65 ms, 70 ms, 75 ms, 80 ms, 85 ms, 90 ms, 95 ms, 100 ms, 200 ms, 300 ms, 400 ms, 500 ms, 600 ms, 700 ms, 800 ms, 900 ms, 1 s, 2 s, 3 s, 4 s, 5 s, 6 s, 7 s, 8 s, 9 s or 10 s.

82. A mass spectrometer as claimed in any of claims 74-81, wherein said collision, fragmentation or reaction device is arranged and adapted to receive a beam of ions and to convert or partition said beam of ions such that at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 separate groups or packets of ions are confined and/or isolated in said collision, fragmentation or reaction device at any particular time, and wherein each group or packet of ions is separately confined and/or isolated in a separate axial potential well formed in said collision, fragmentation or reaction device.

83. A mass spectrometer as claimed in any of claims 51-82, further comprising a further mass filter or mass analyser arranged upstream and/or downstream of said time of flight mass analyser.

84. A mass spectrometer as claimed in claim 83, wherein said further mass filter or mass analyser is selected from the

group consisting of: (i) a quadrupole rod set mass filter; (ii) a Time of Flight mass filter or mass analyser; (iii) a Wein filter; and (iv) a magnetic sector mass filter or mass analyser.

5

85. A mass spectrometer as claimed in any of claims 51-84, further comprising an ion source.

86. A mass spectrometer as claimed in claim 85, further comprising an ion source selected from the group consisting of: (i) an Electrospray ionisation ("ESI") ion source; (ii) an Atmospheric Pressure Photo Ionisation ("APPI") ion source; (iii) an Atmospheric Pressure Chemical Ionisation ("APCI") ion source; (iv) a Matrix Assisted Laser Desorption 10 Ionisation ("MALDI") ion source; (v) a Laser Desorption Ionisation ("LDI") ion source; (vi) an Atmospheric Pressure Ionisation ("API") ion source; (vii) a Desorption Ionisation on Silicon ("DIOS") ion source; (viii) an Electron Impact ("EI") ion source; (ix) a Chemical Ionisation ("CI") ion source; (x) a Field Ionisation ("FI") ion source; (xi) a Field Desorption ("FD") ion source; (xii) an Inductively Coupled Plasma ("ICP") ion source; (xiii) a Fast Atom Bombardment ("FAB") ion source; (xiv) a Liquid Secondary Ion 20 Mass Spectrometry ("LSIMS") ion source; (xv) a Desorption Electrospray Ionisation ("DESI") ion source; (xvi) a Nickel-63 radioactive ion source; (xvii) a Thermospray ion source; (xviii) a Particle Beam ("PB") ion source; and (xix) a Flow 25 Fast Atom Bombardment ("Flow FAB") ion source.

30

87. A mass spectrometer as claimed in claim 85 or 86, further comprising a continuous or pulsed ion source.

88. A method of mass analysing ions according to their time of flight comprising:

35

providing an ion guide comprising a plurality of electrodes;

confining ions radially within said ion guide; and

applying a time varying inhomogeneous axial electric field along at least a portion of the axial length of said ion guide.

5 89. A method of mass spectrometry comprising a method as claimed in claim 88.

90. A device for temporally separating ions according to their mass to charge ratio and/or ion mobility, said device
10 comprising:

an ion guide comprising a plurality of electrodes;
first means arranged and adapted and to confine ions radially within said ion guide; and
second means arranged and adapted to apply a time
15 varying inhomogeneous axial electric field along at least a portion of the axial length of said ion guide.

91. A method of temporally separating ions according to their mass to charge ratio and/or ion mobility, said device
20 comprising:

providing an ion guide comprising a plurality of electrodes;
confining ions radially within said ion guide; and
applying a time varying inhomogeneous axial electric
25 field along at least a portion of the axial length of said ion guide.

1/8

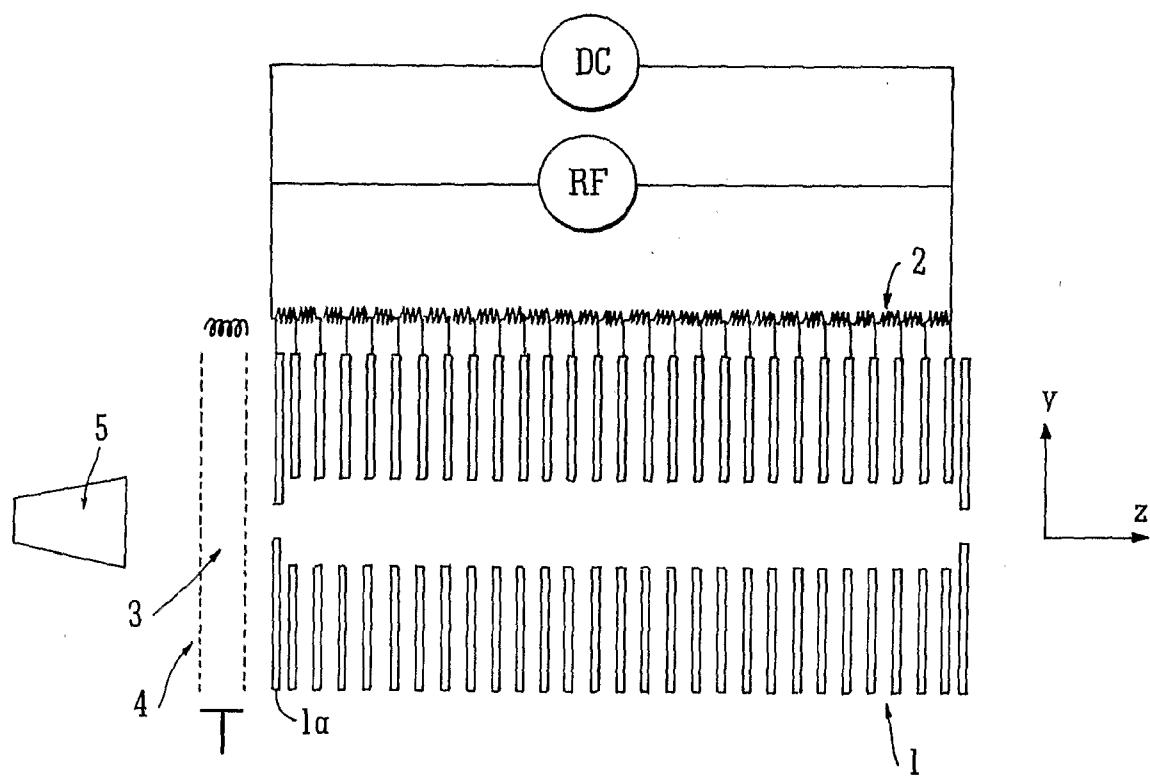


FIG. 1
PRIOR ART

2/8

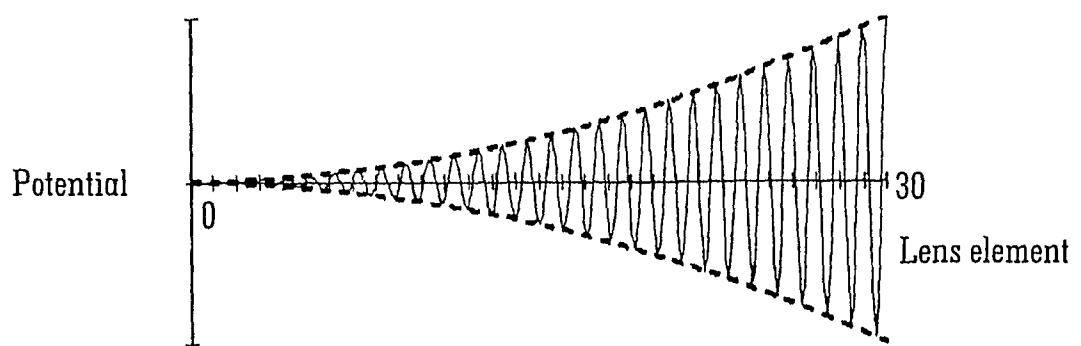
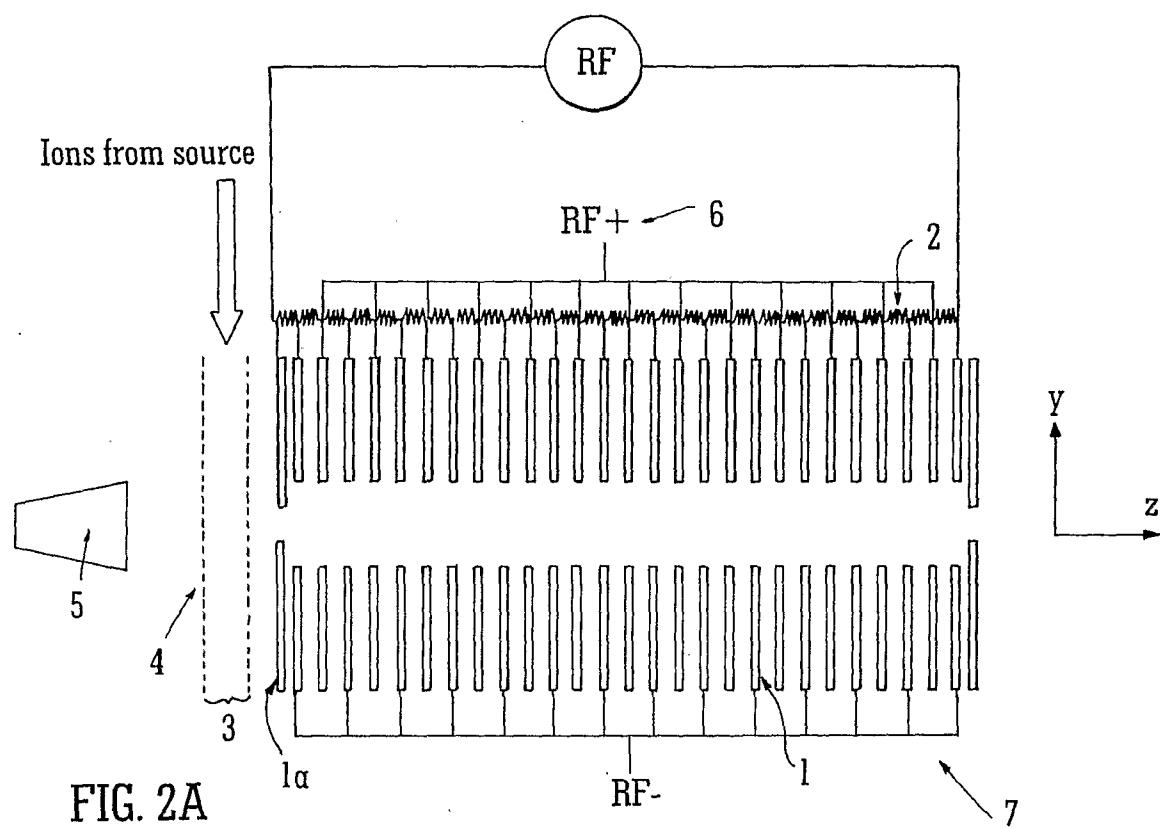


FIG. 2B

3/8

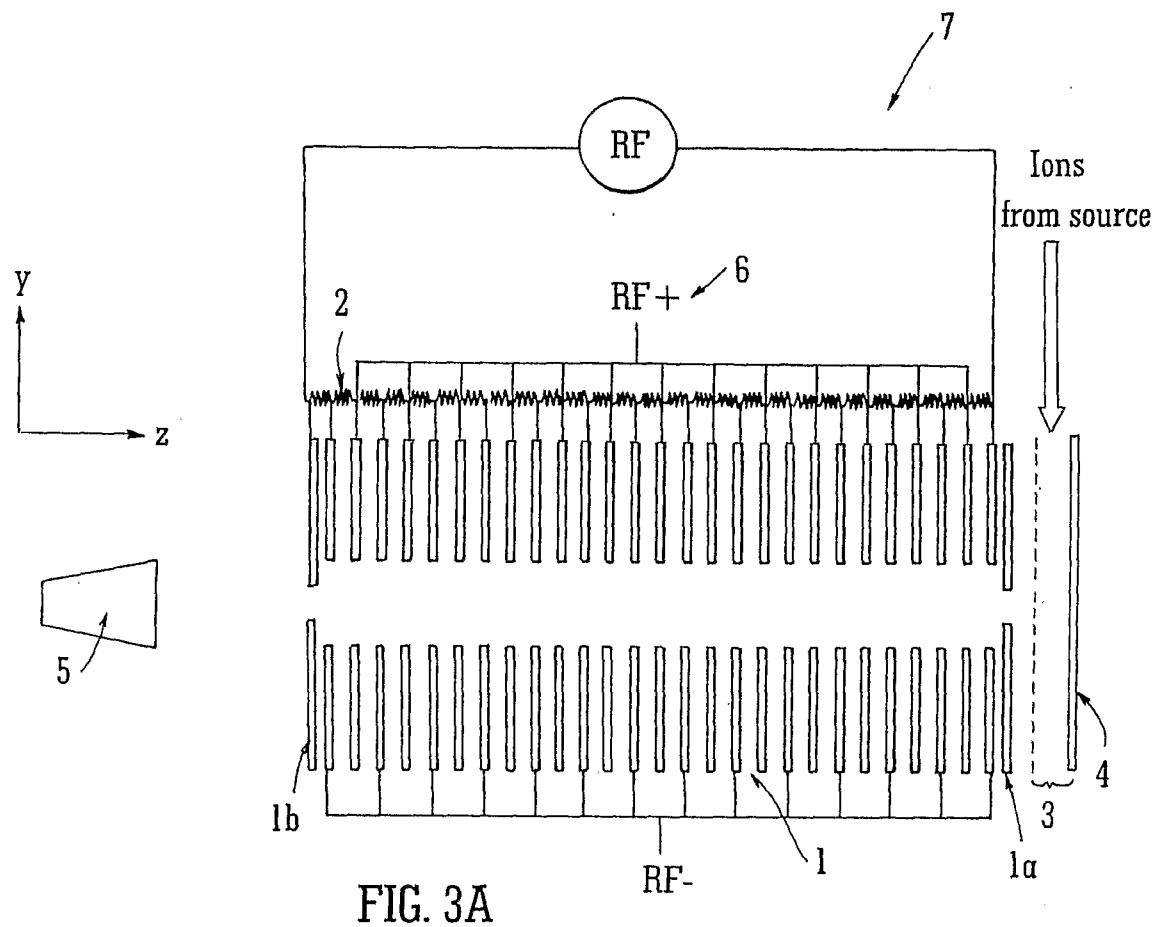


FIG. 3A

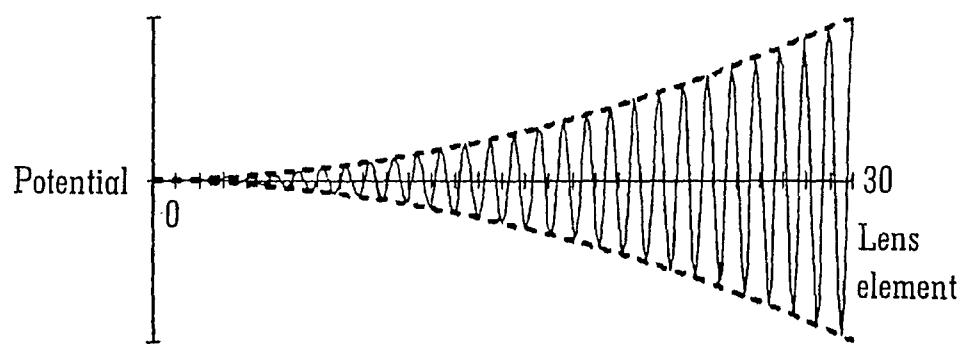


FIG. 3B

4/8

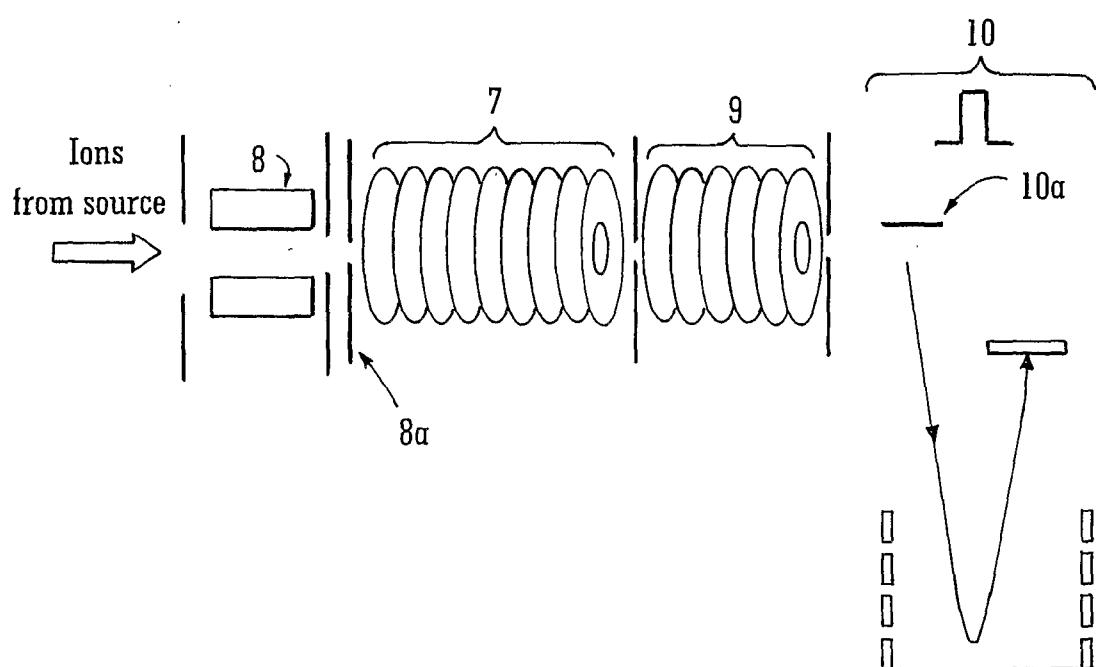


FIG. 4

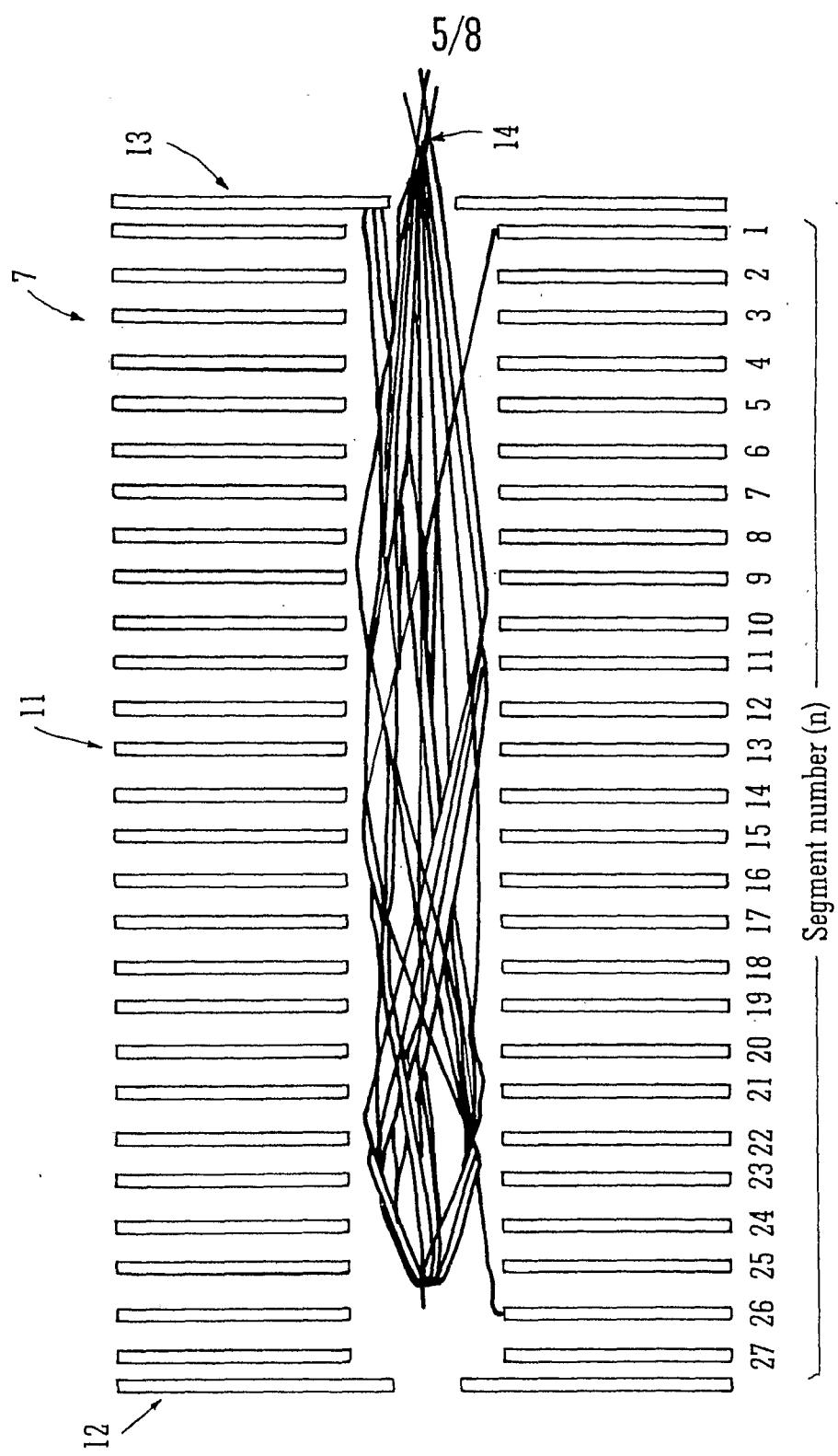


FIG. 5

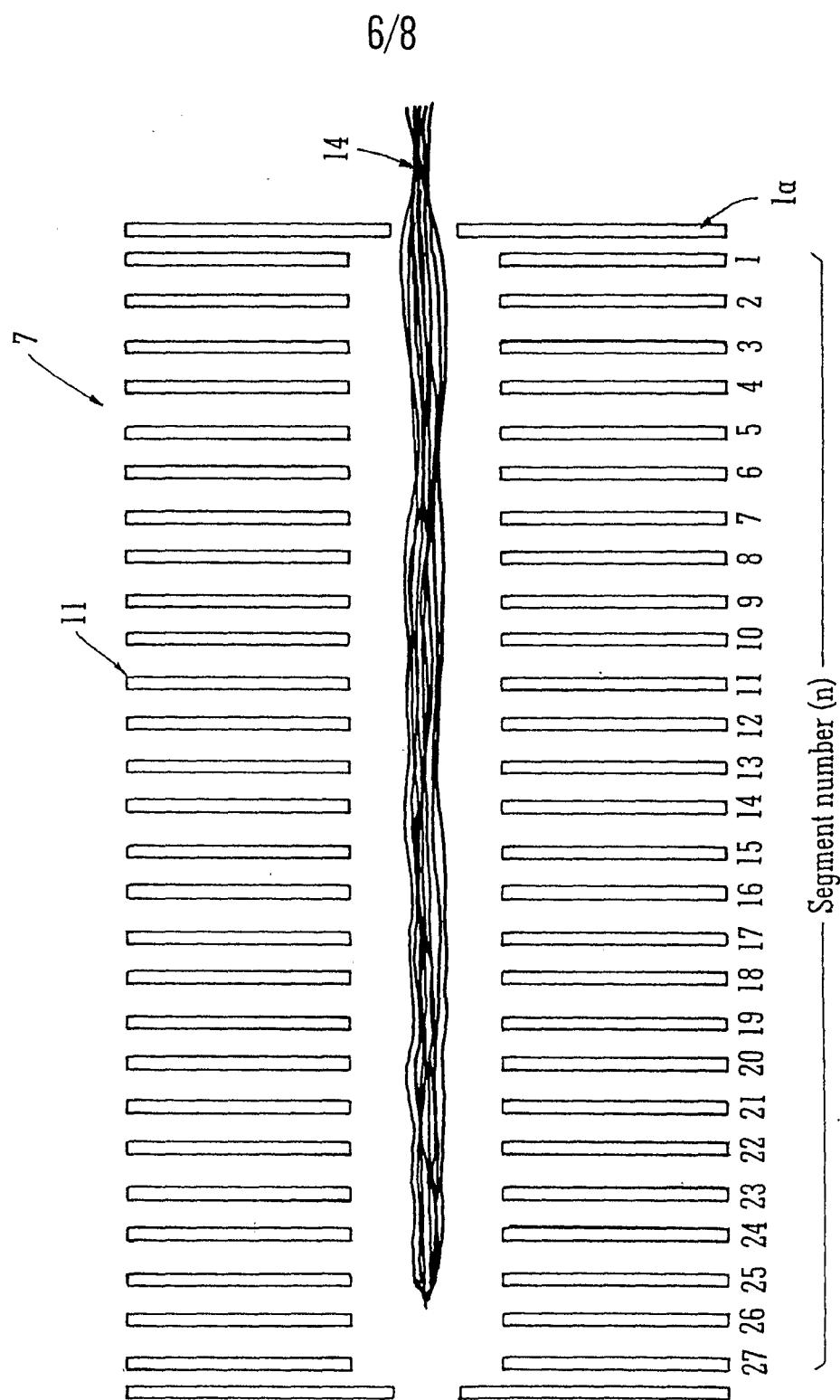


FIG. 6

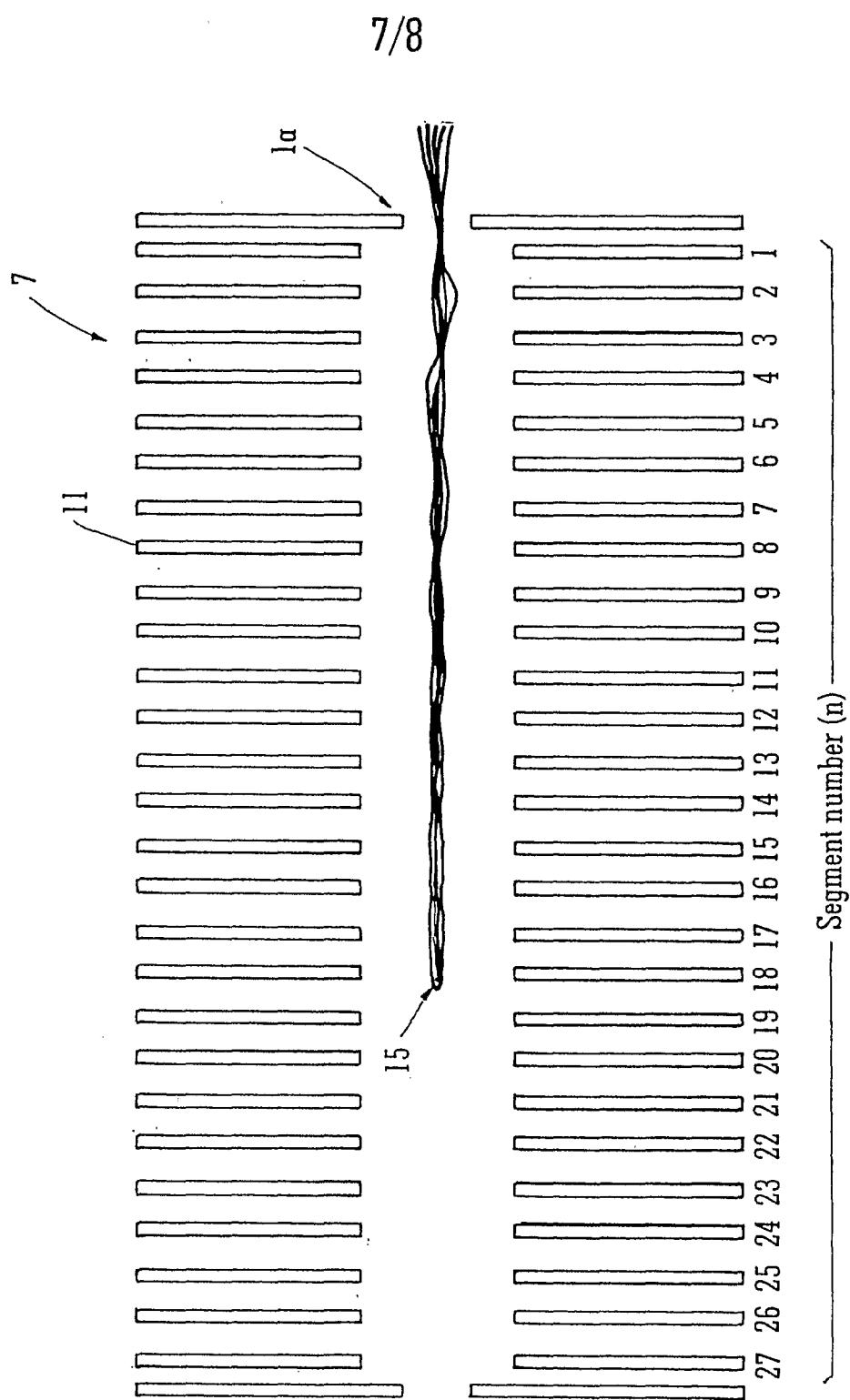


FIG. 7

8/8

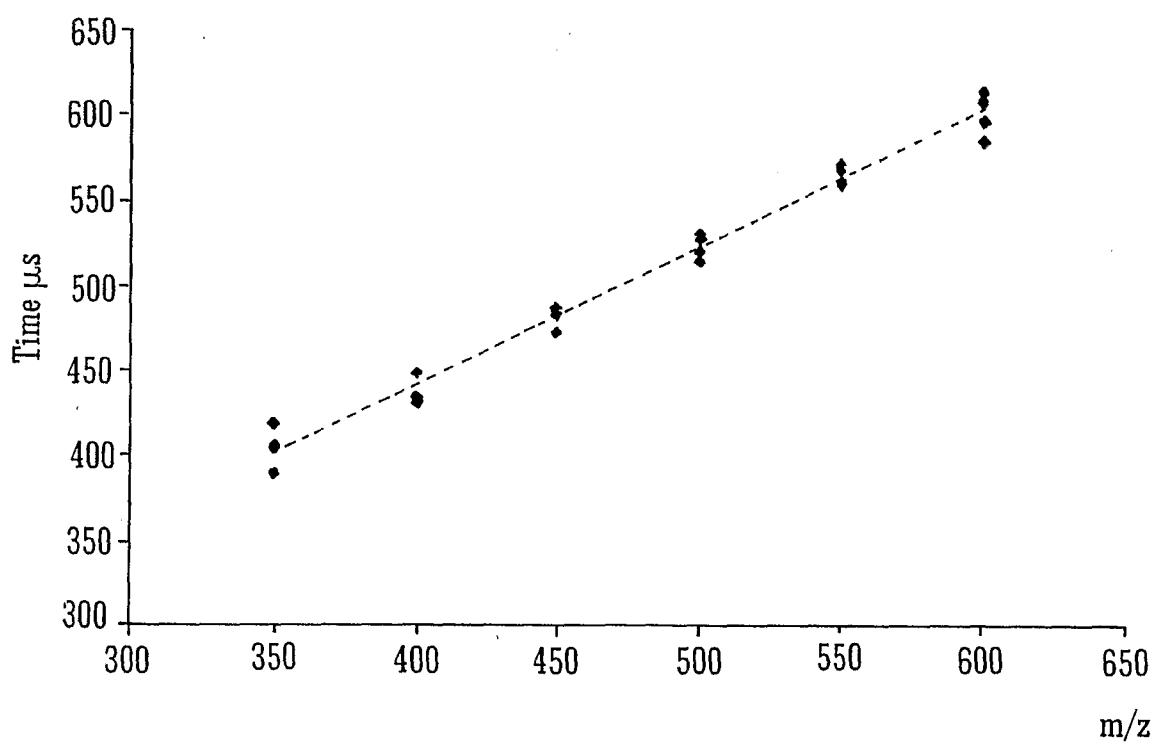


FIG. 8