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Clemmer et al.

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(54) **ION MOBILITY SPECTROMETER INSTRUMENT AND METHOD OF OPERATION**

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(22) Filed: **Nov. 22, 2010**

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Related U.S. Application Data

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(60) Provisional application No. 61/021,785, filed on Jan. 17, 2008.

(51) **Int. Cl.**
H01J 49/42 (2006.01)

(52) **U.S. Cl.**

USPC **250/281**; 250/282; 250/288

(58) **Field of Classification Search**

USPC 250/281
See application file for complete search history.

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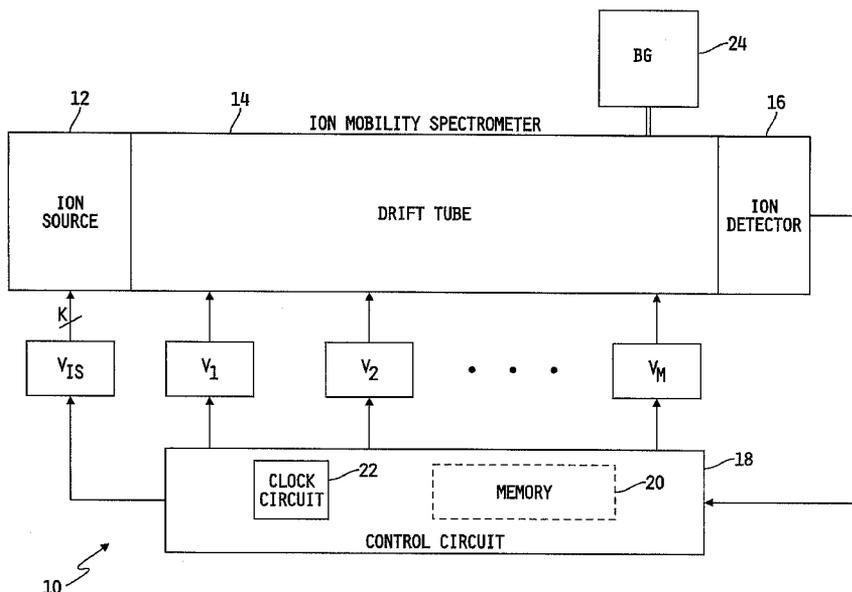
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(57) **ABSTRACT**

An ion mobility spectrometer instrument has a drift tube that is partitioned into a plurality of cascaded drift tube segments. A number of electric field activation sources may each be coupled to one or more of the plurality of drift tube segments. A control circuit is configured to control operation of the number of electric field activation sources in a manner that sequentially applies electric fields to the drift tube segments to allow only ions having a predefined ion mobility or range of ion mobilities to travel through the drift tube. The drift tube segments may define a linear drift tube or a closed drift tube with a continuous ion travel path. Techniques are disclosed for operating the ion mobility spectrometer to produce highly resolved ion mobility spectra.

16 Claims, 24 Drawing Sheets



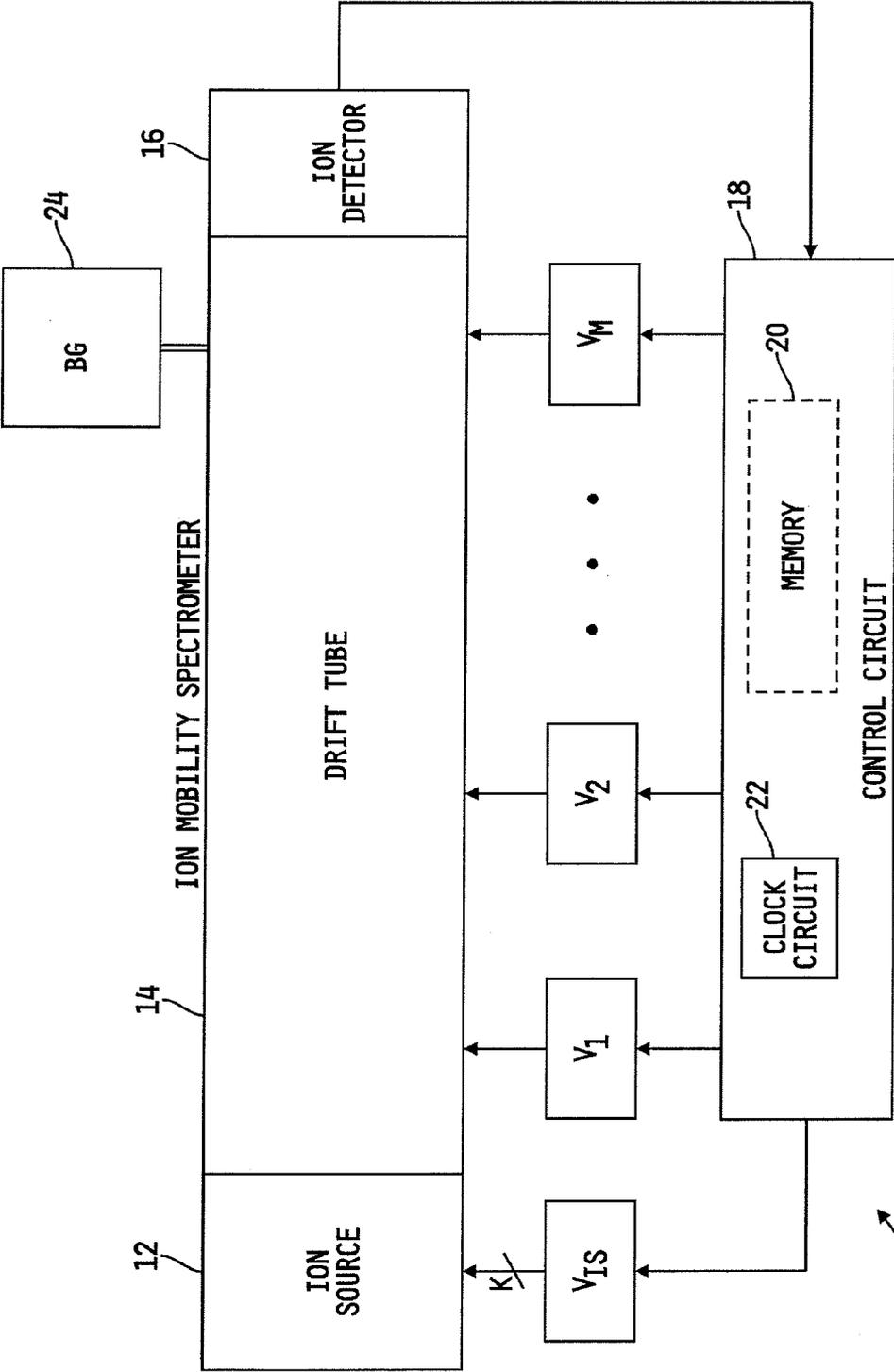


FIG. 1

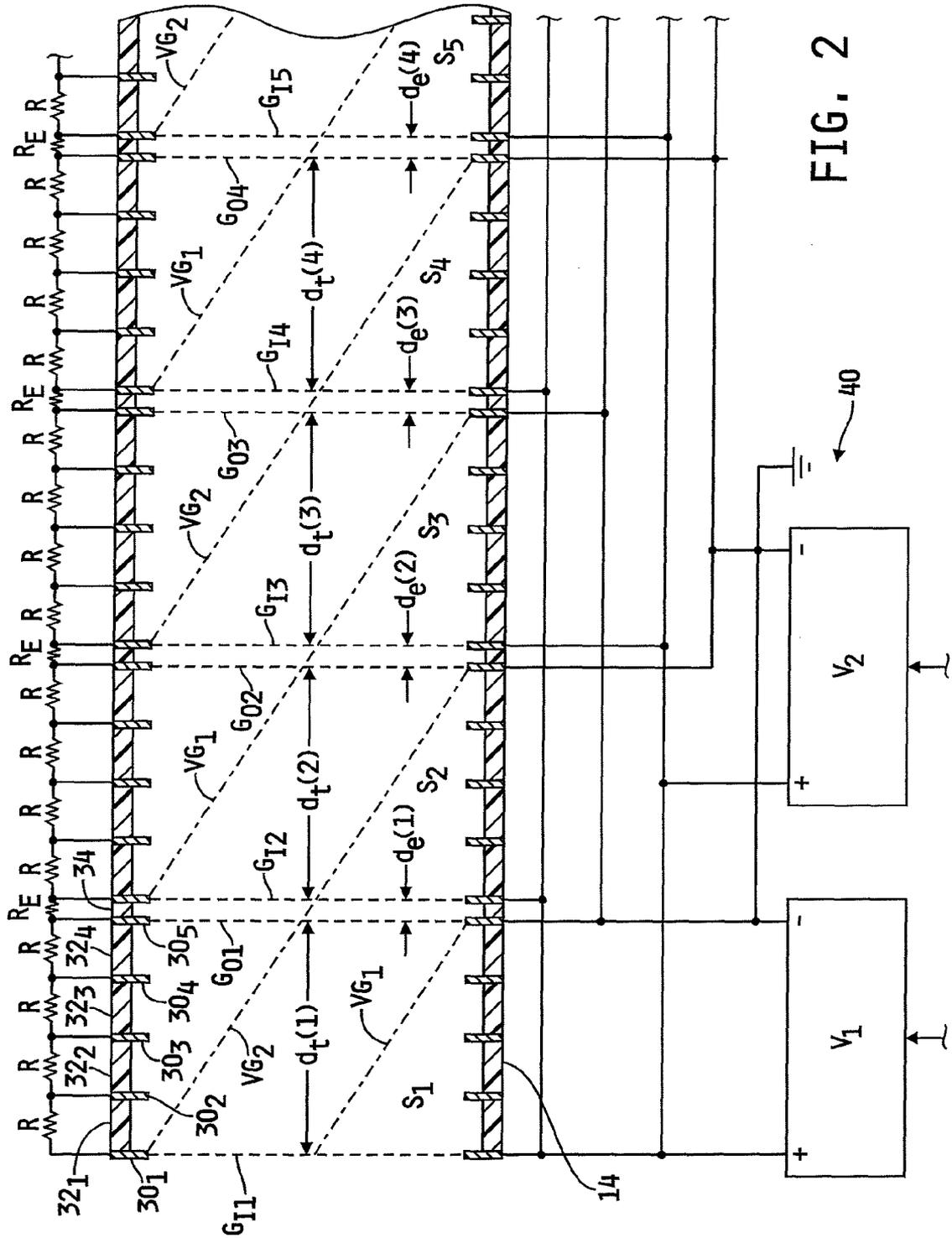


FIG. 2

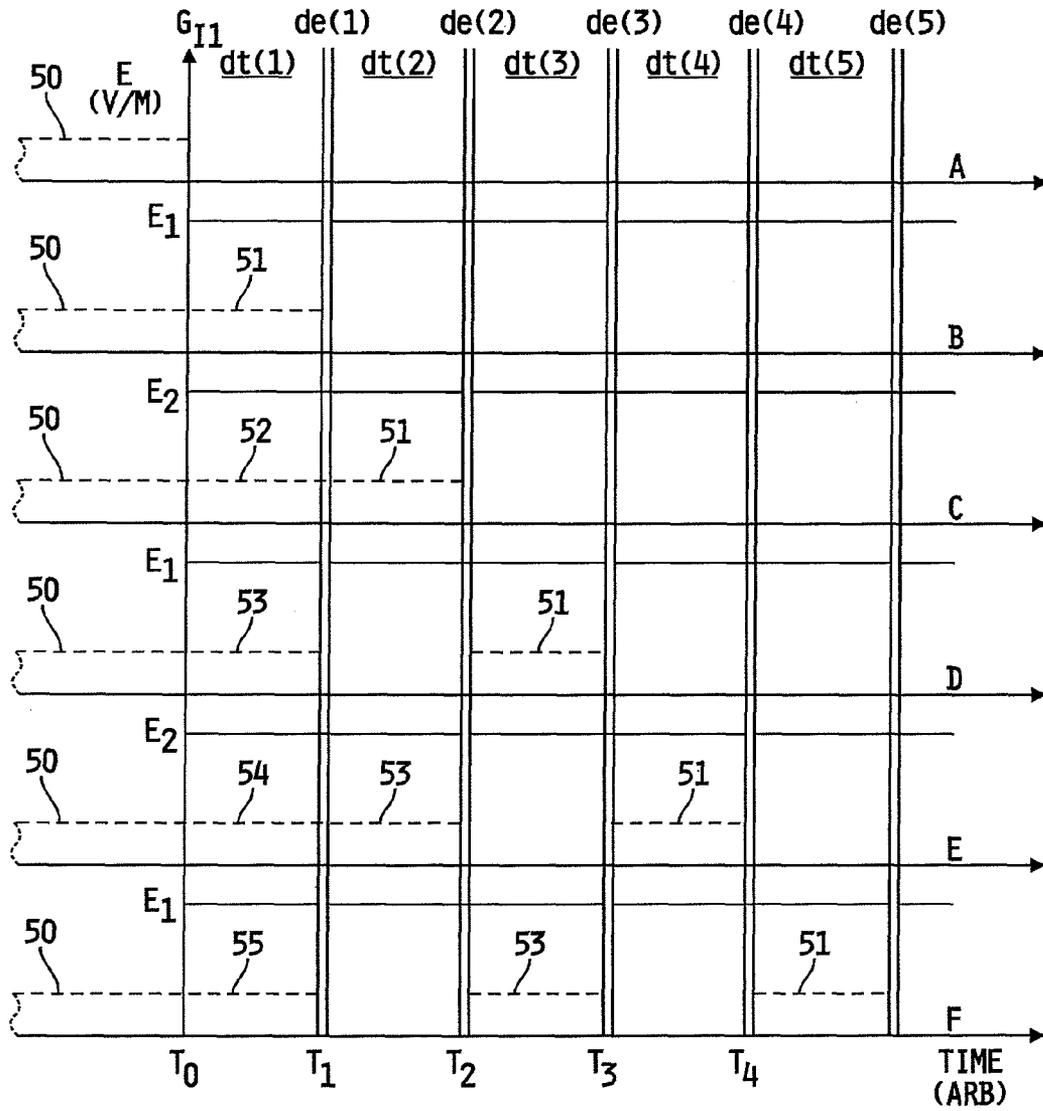
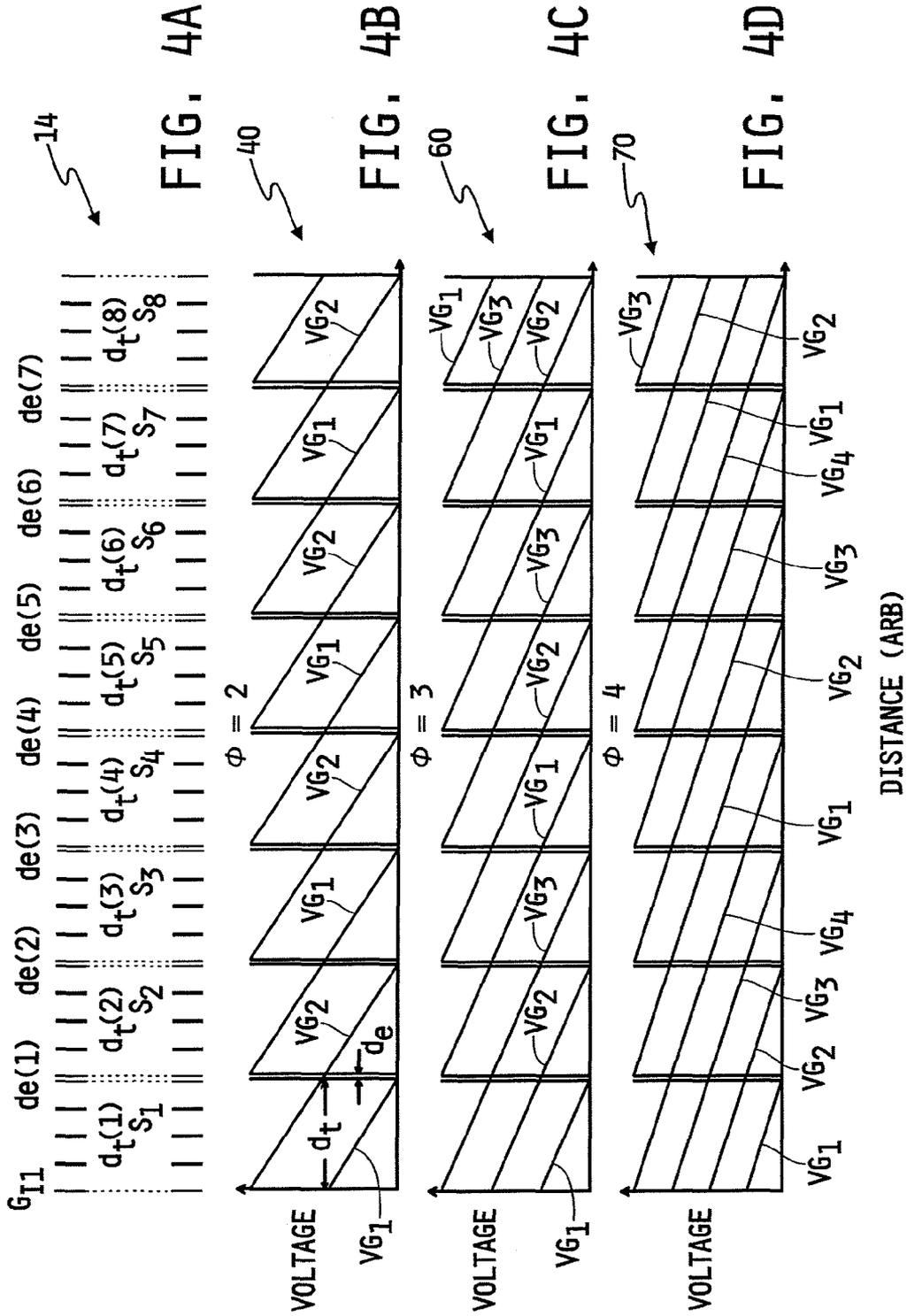


FIG. 3



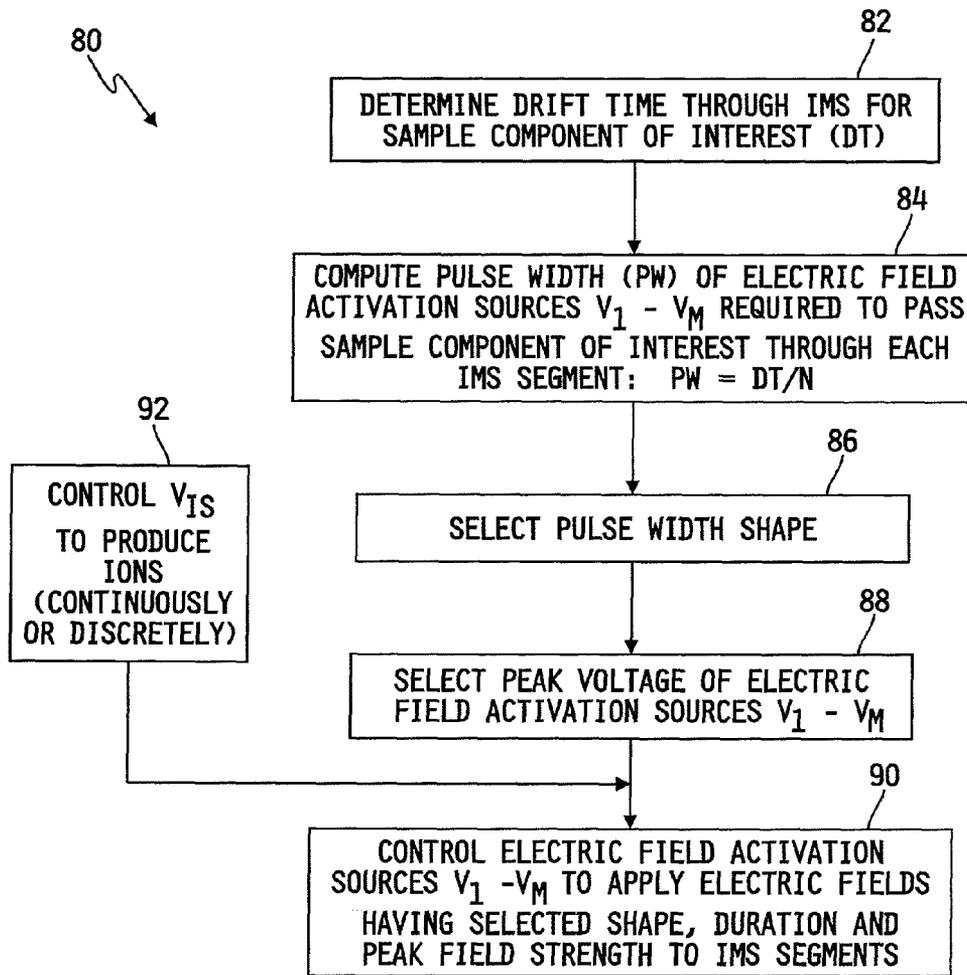


FIG. 5

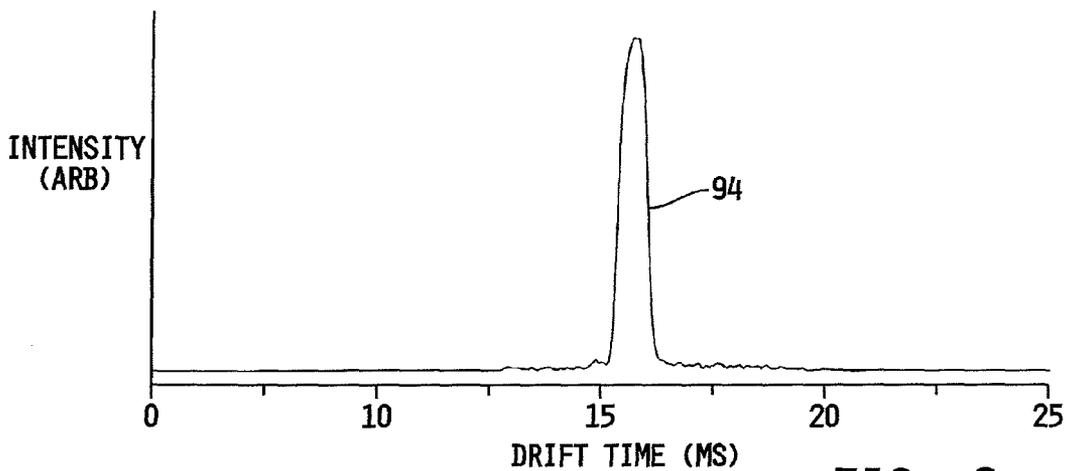


FIG. 6

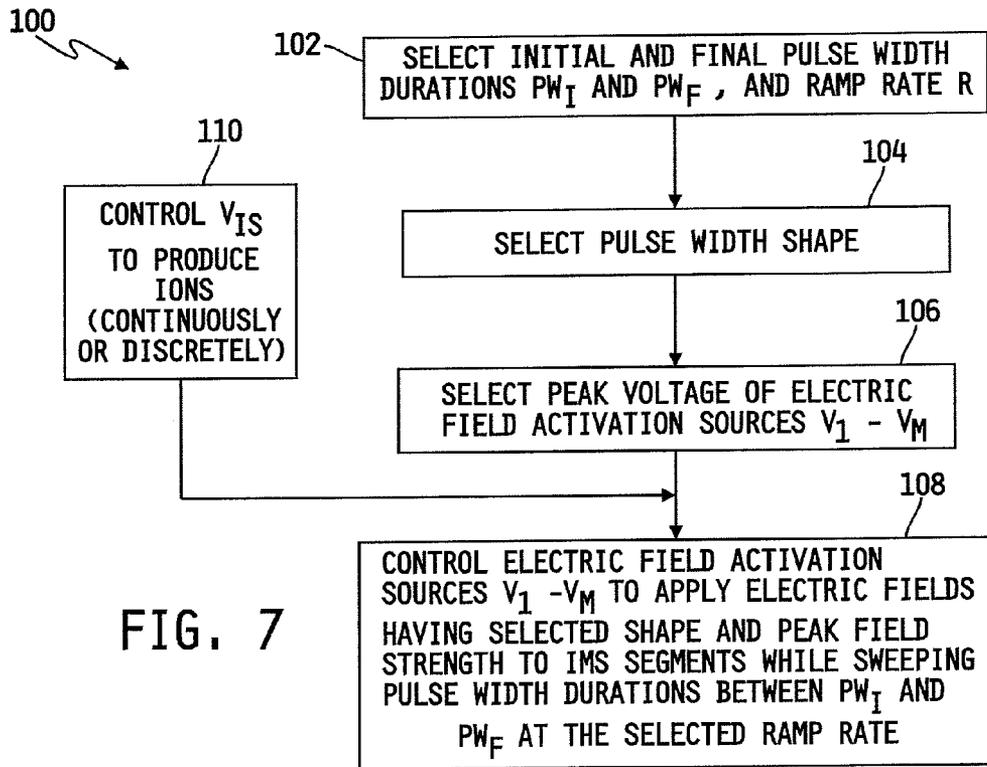


FIG. 7

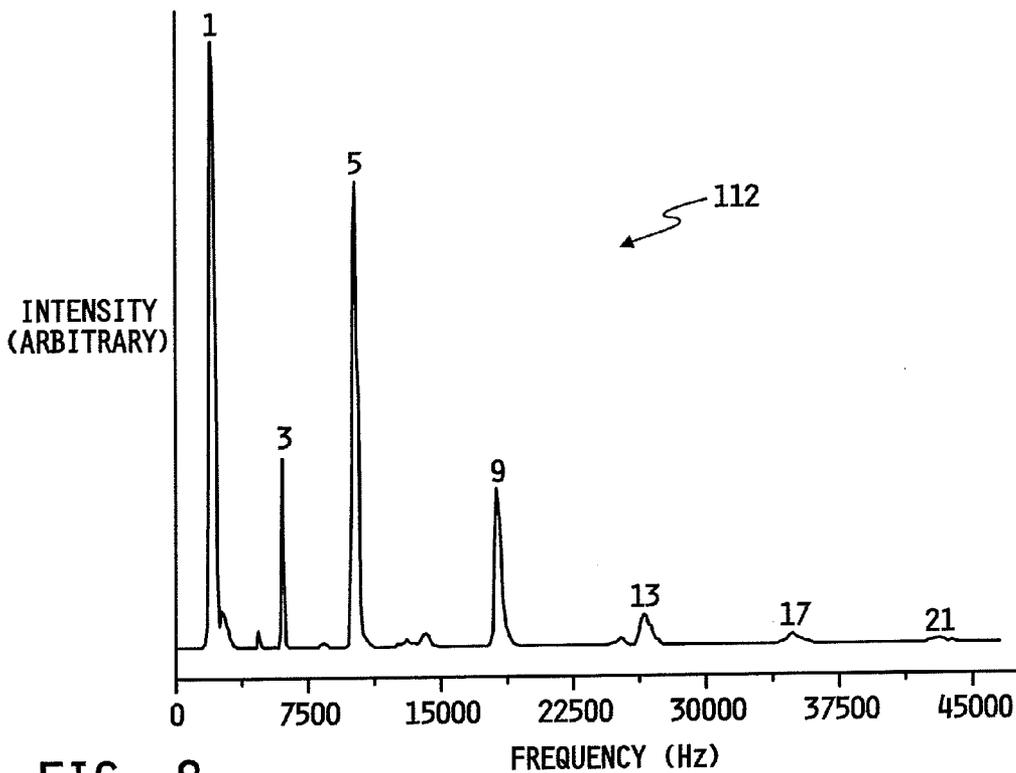


FIG. 8

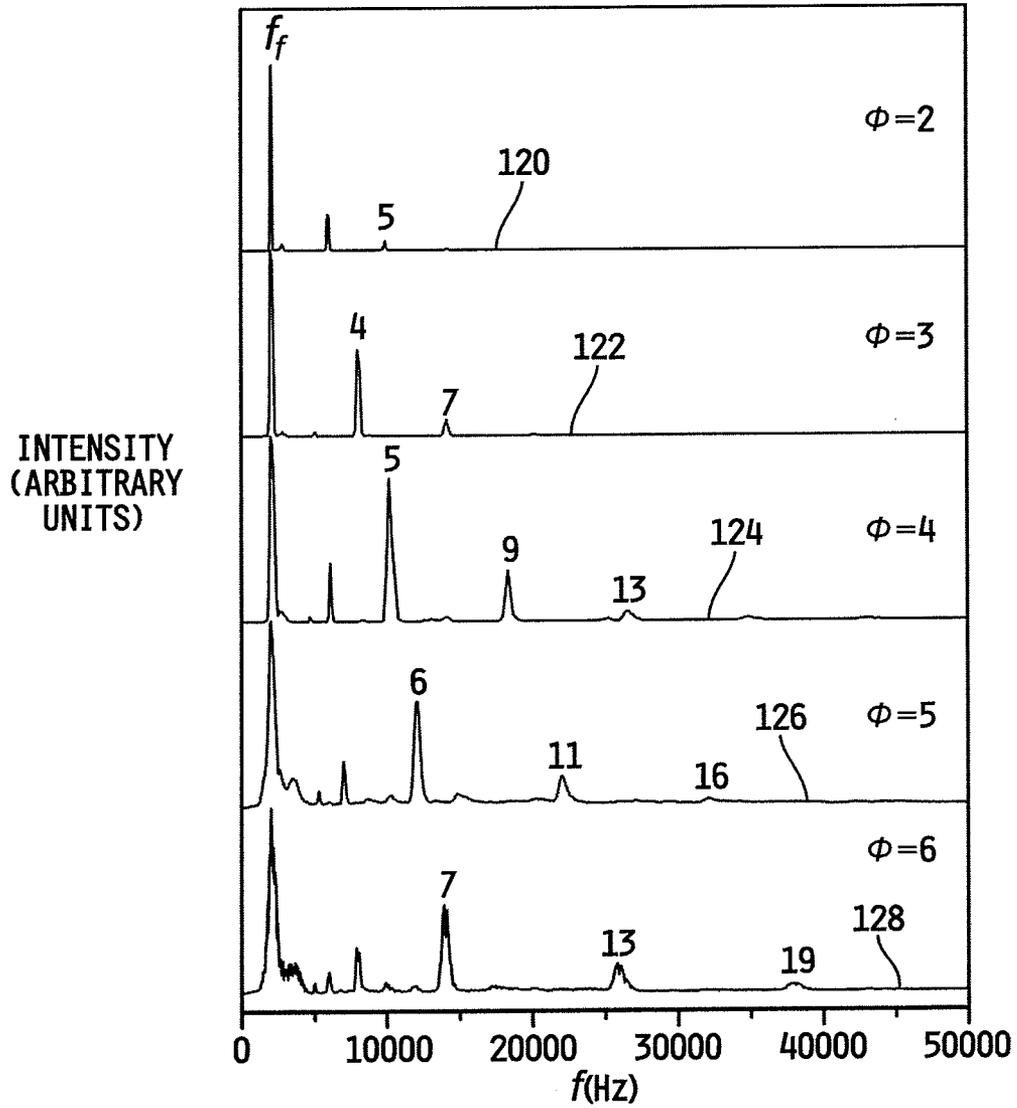


FIG. 9

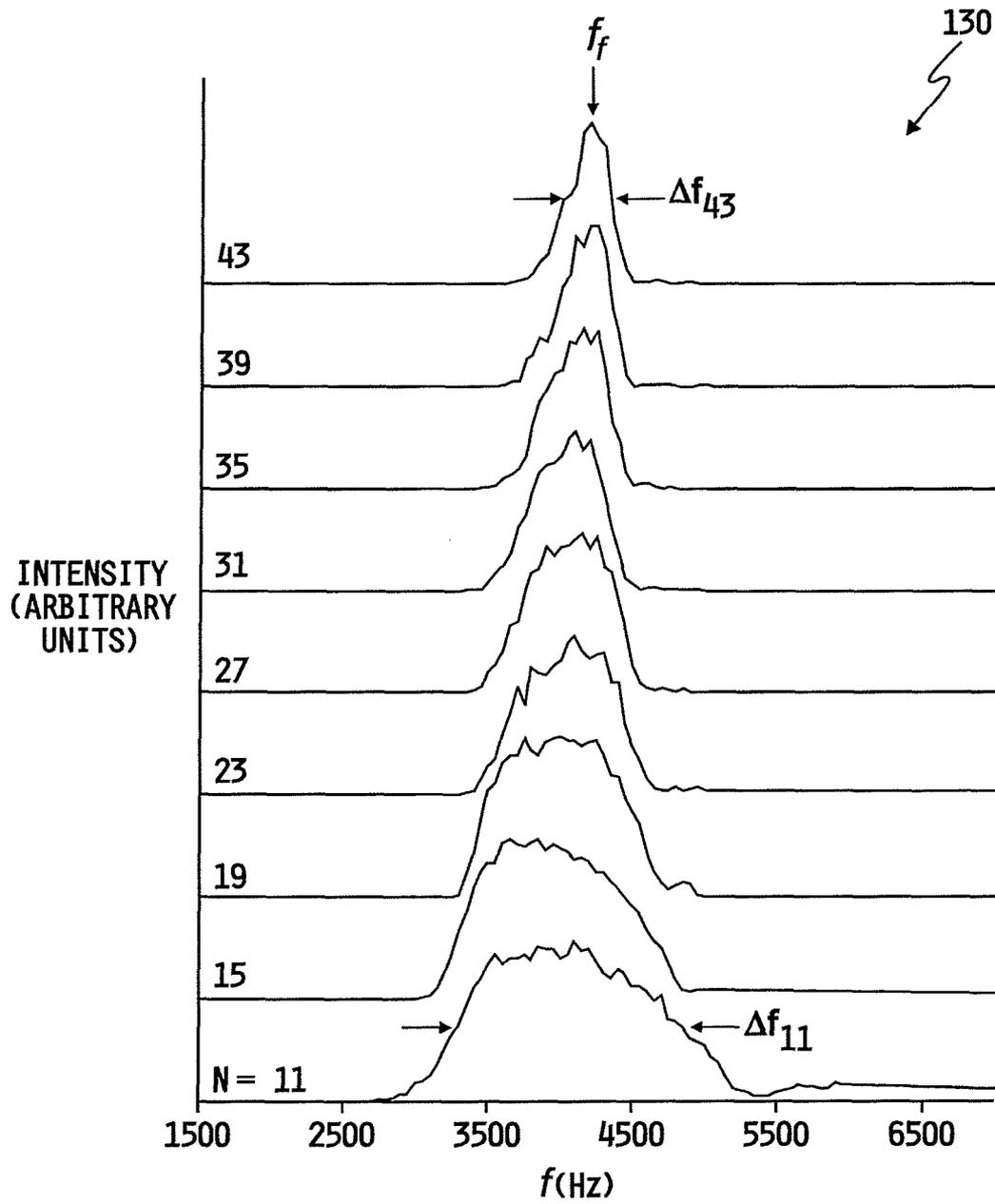


FIG. 10

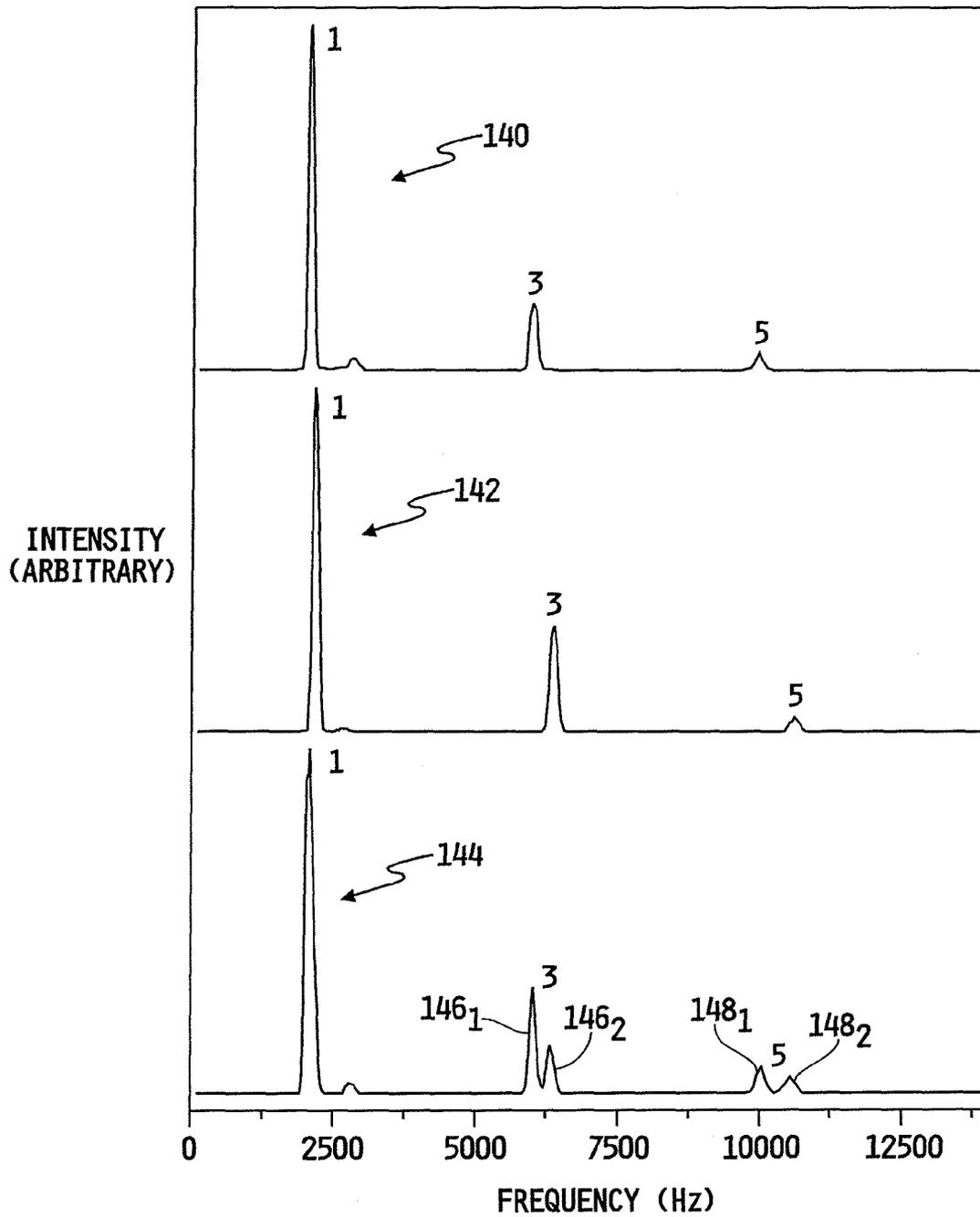
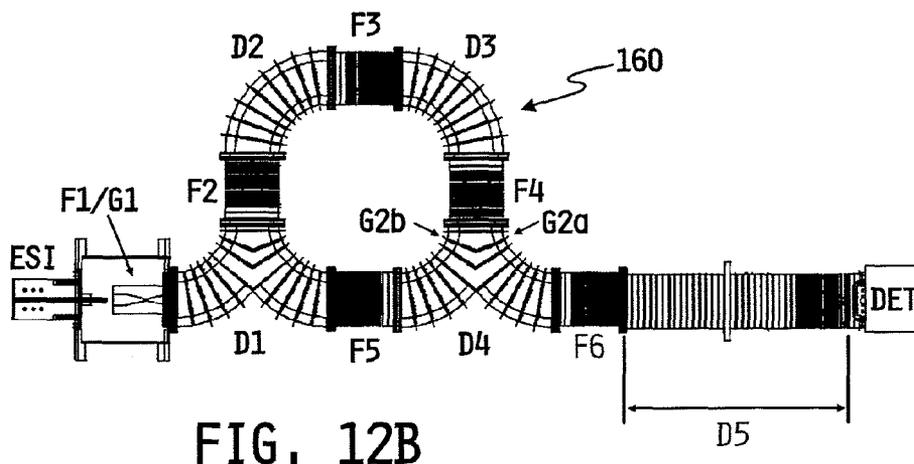
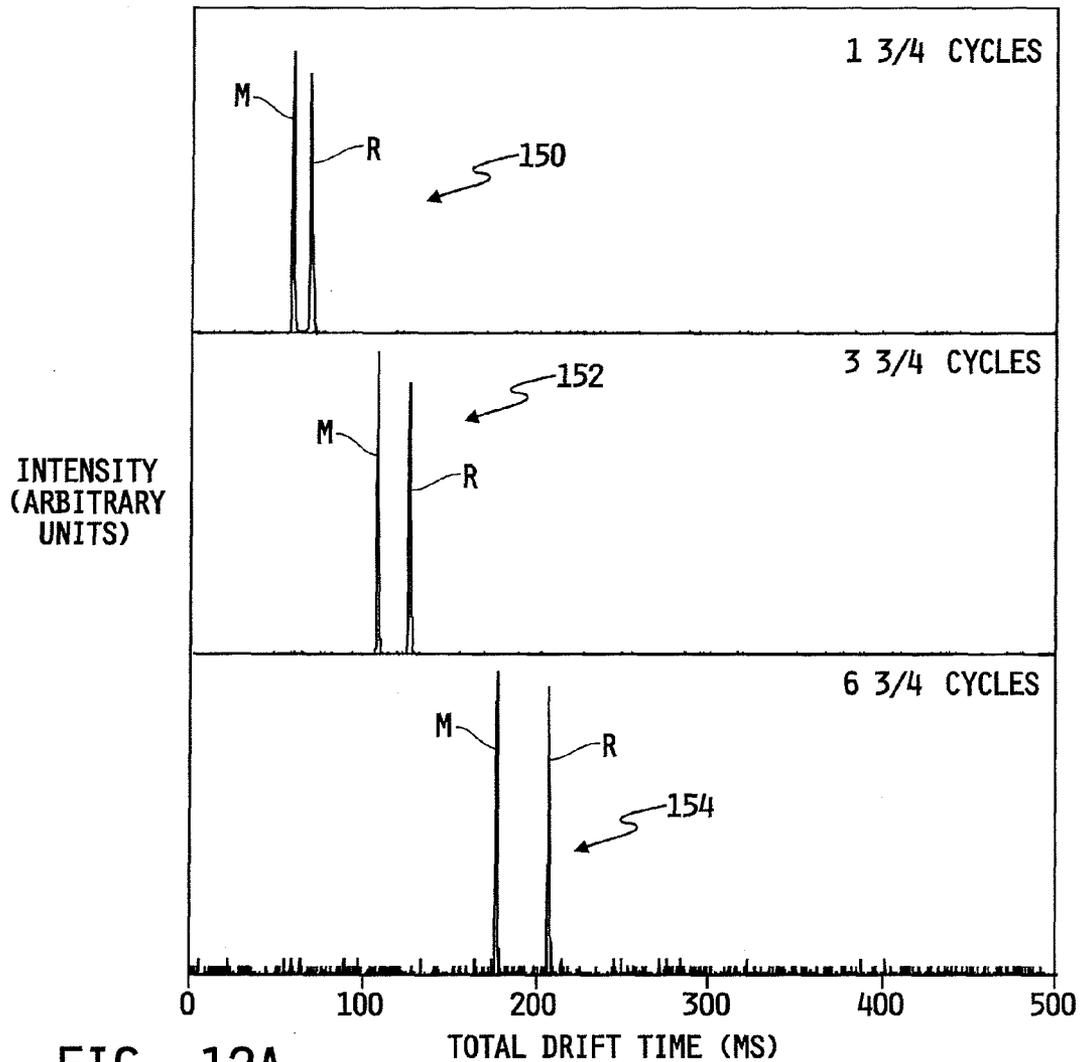


FIG. 11



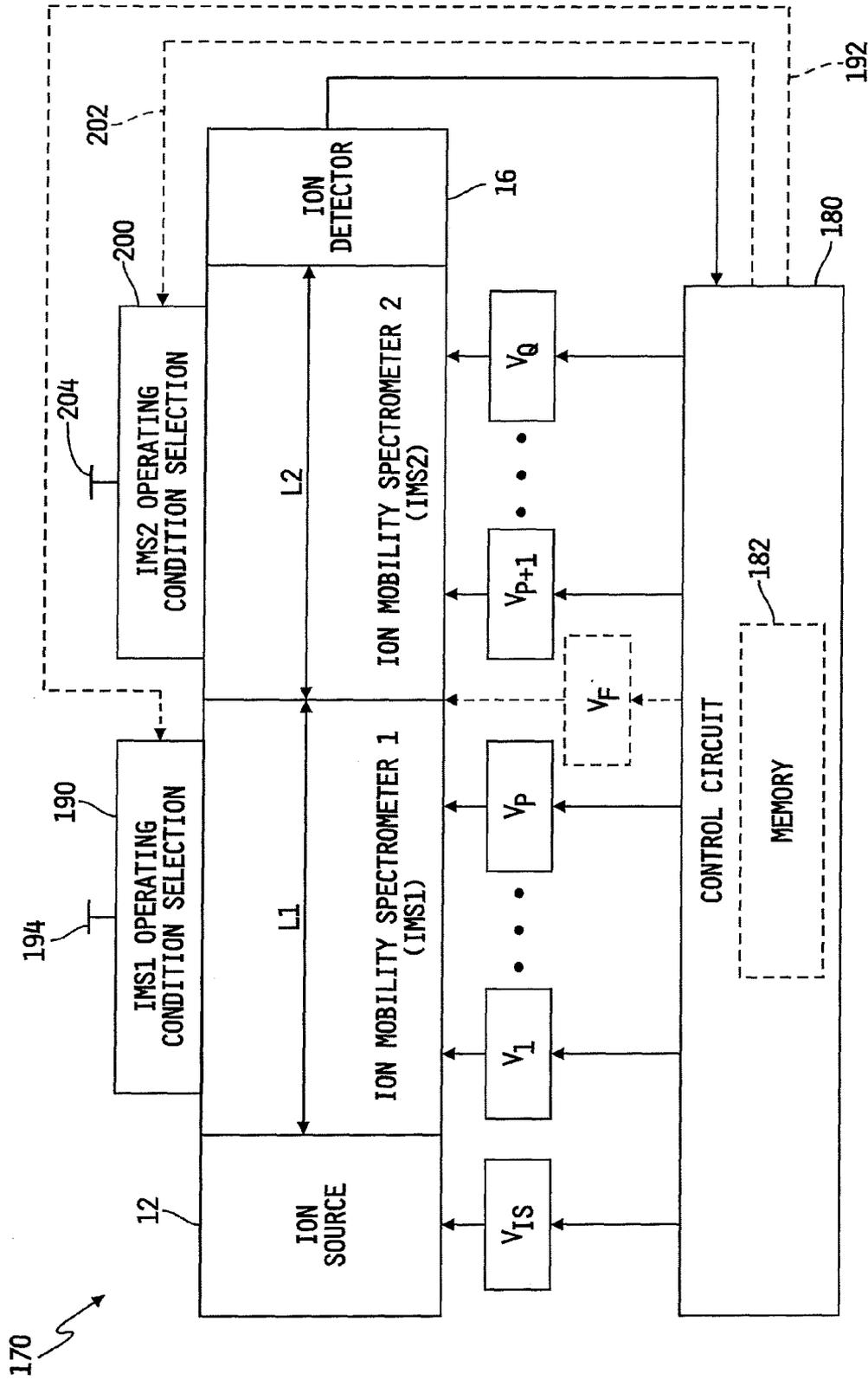


FIG. 13

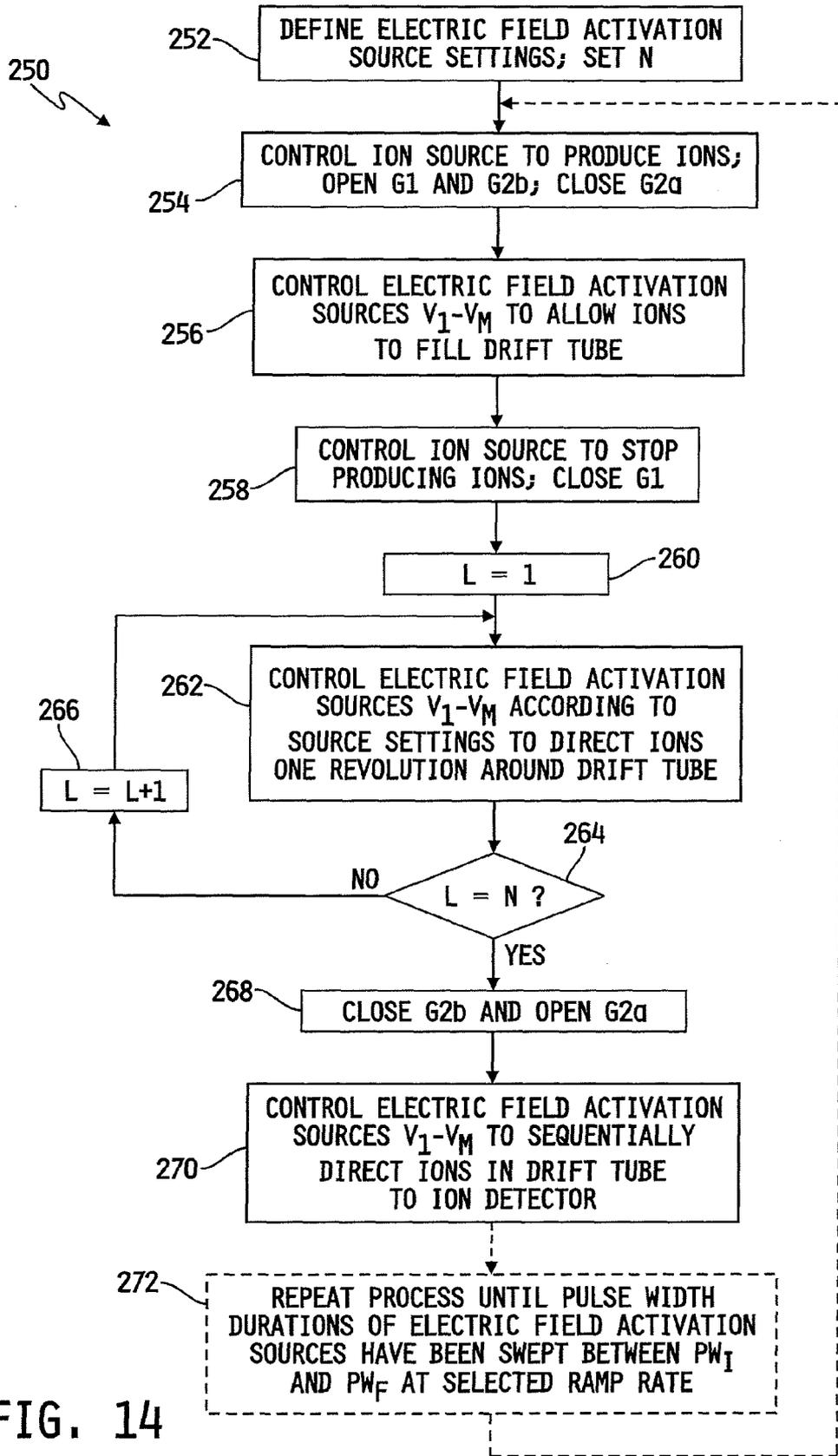


FIG. 14

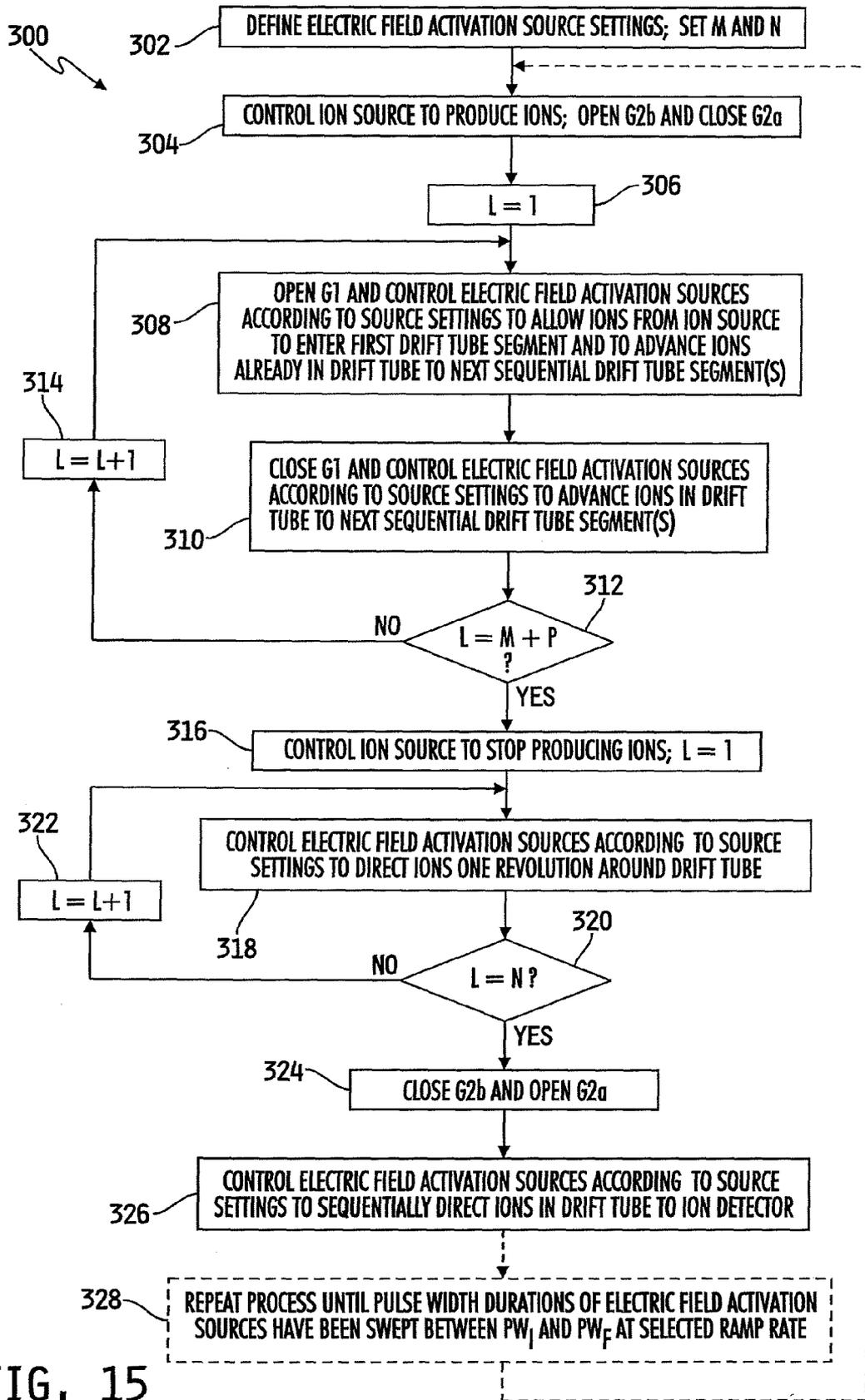
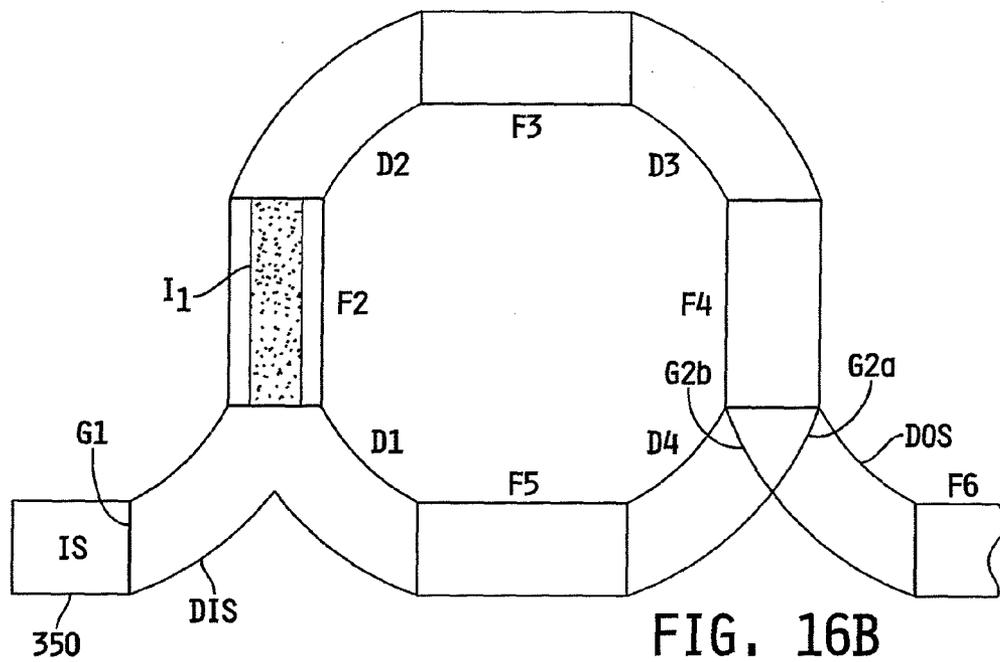
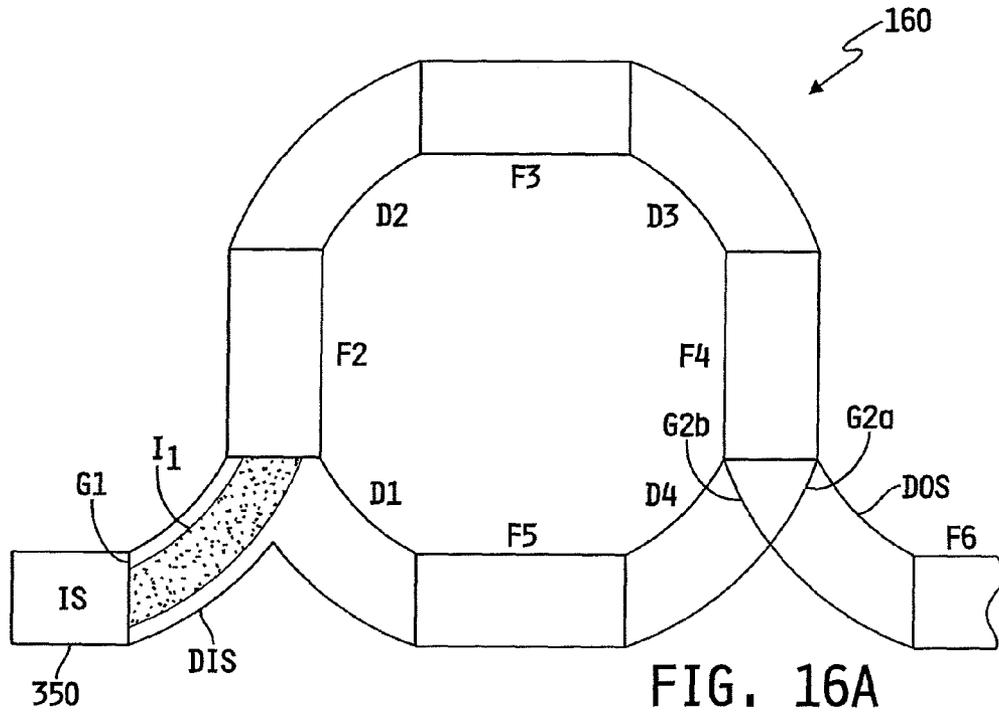
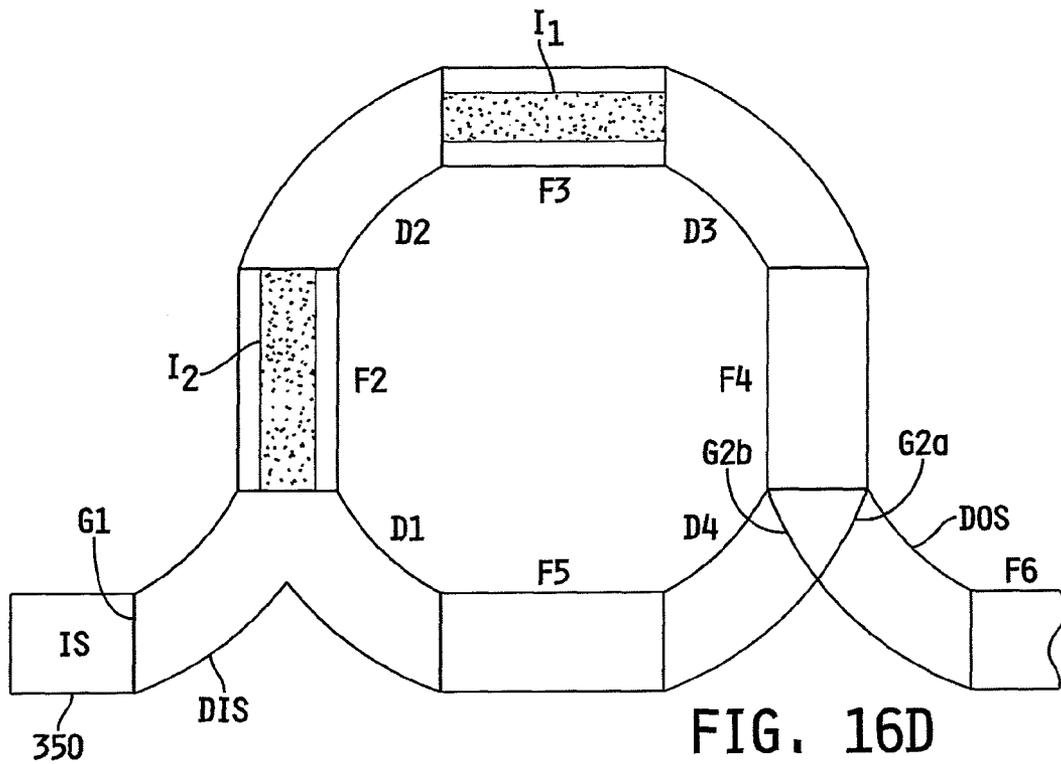
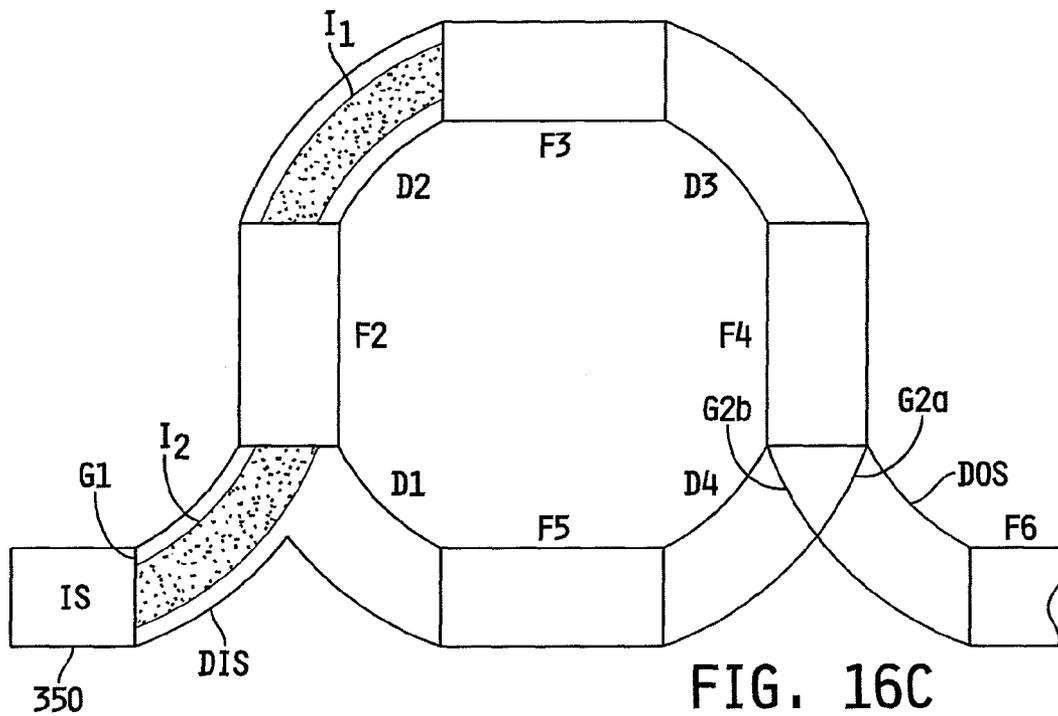
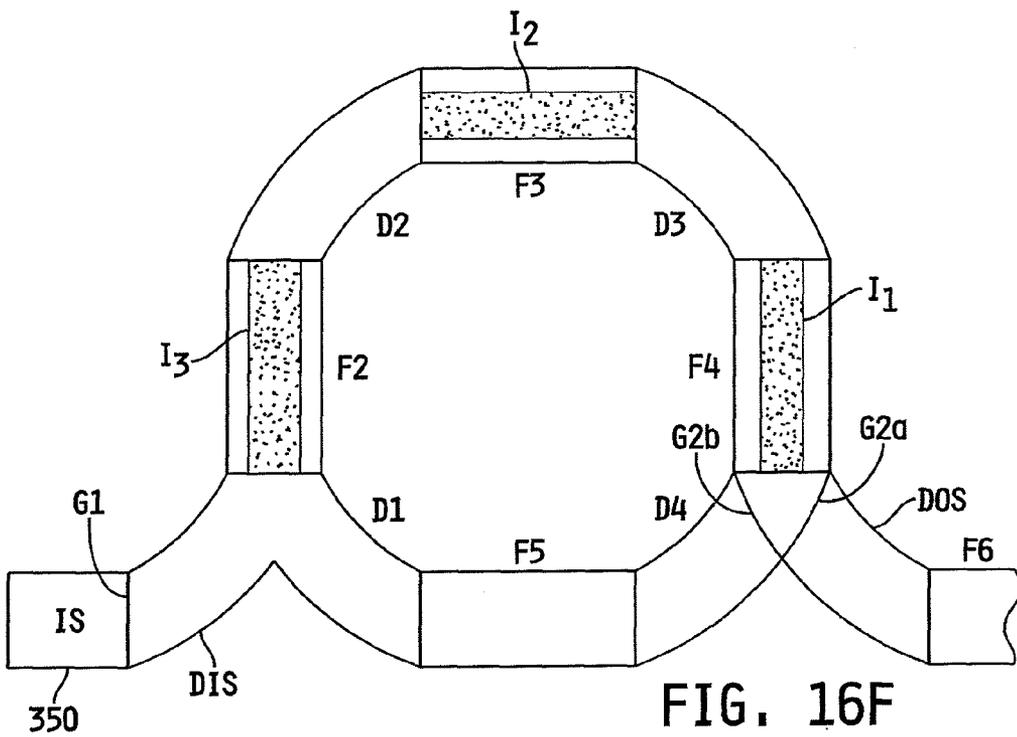
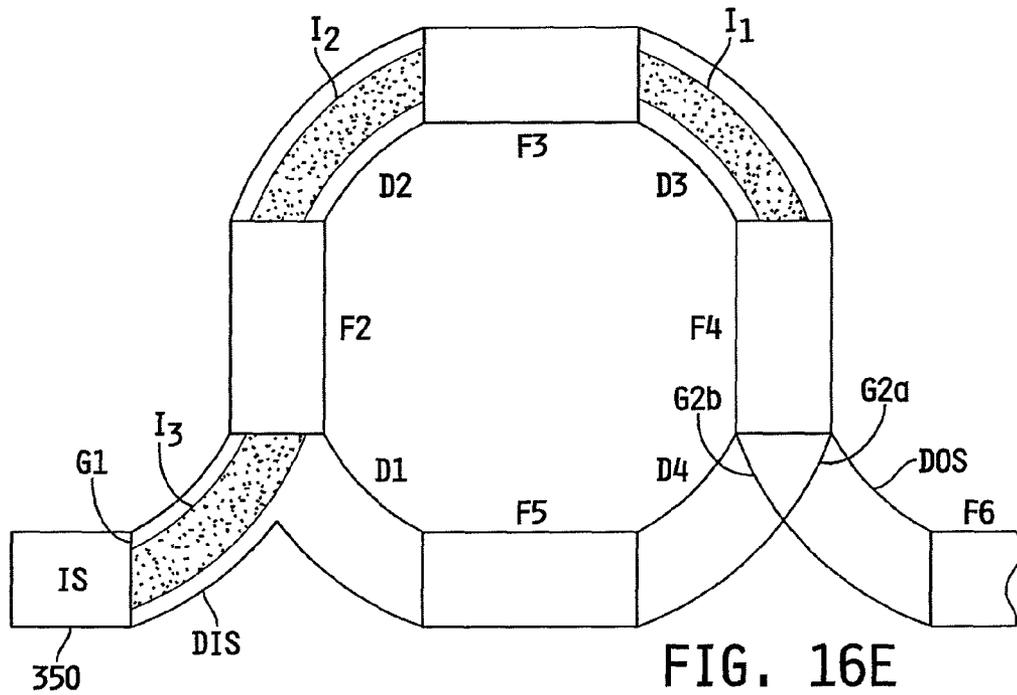
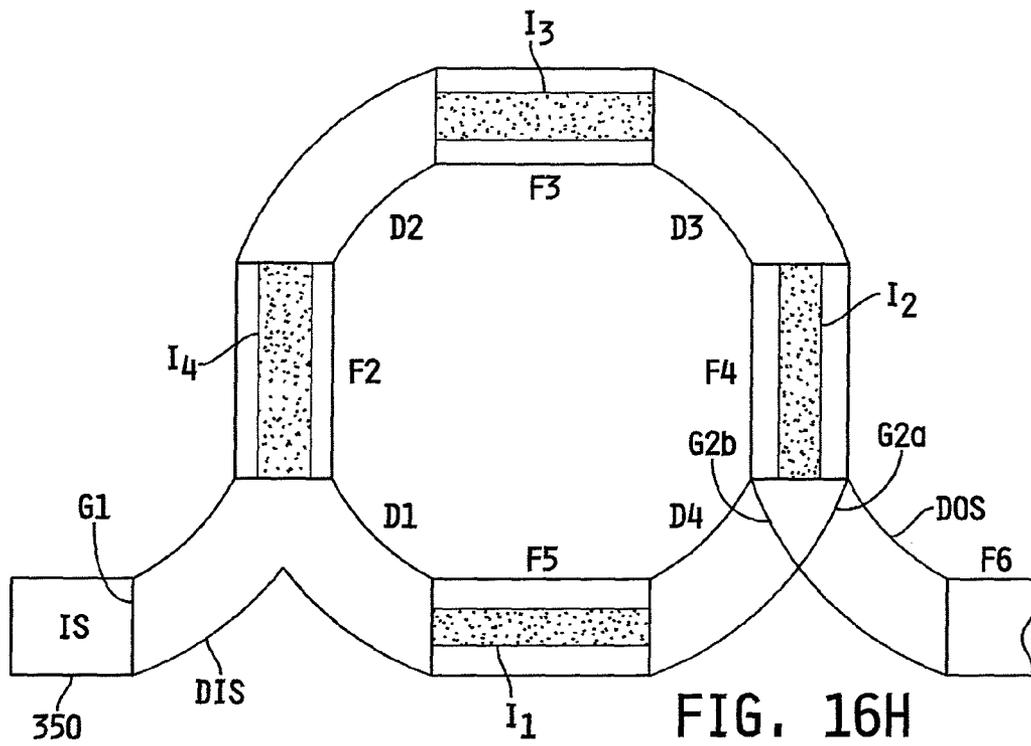
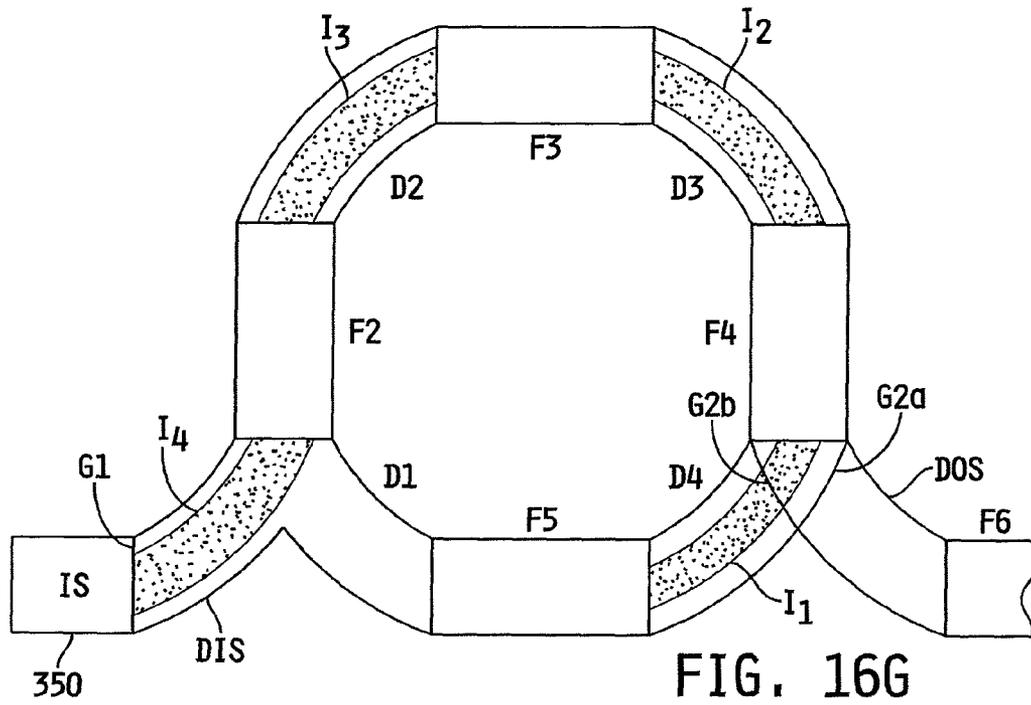


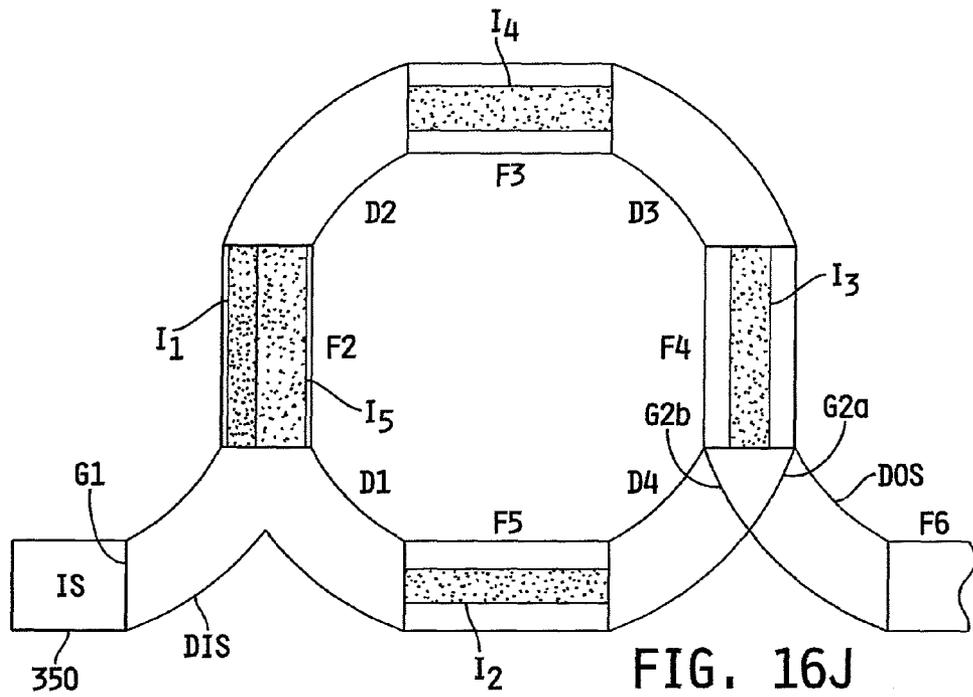
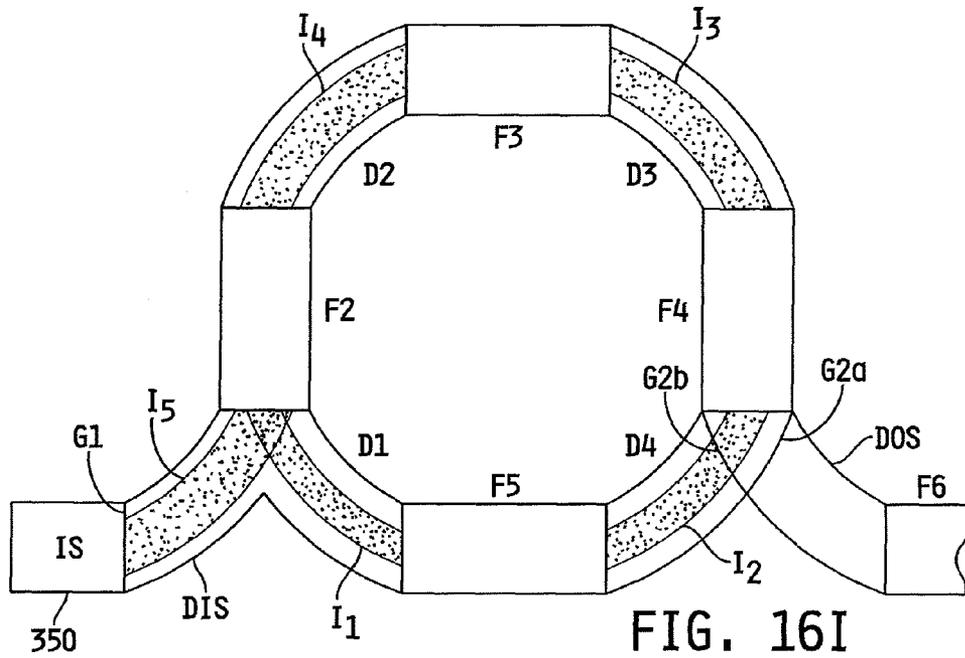
FIG. 15

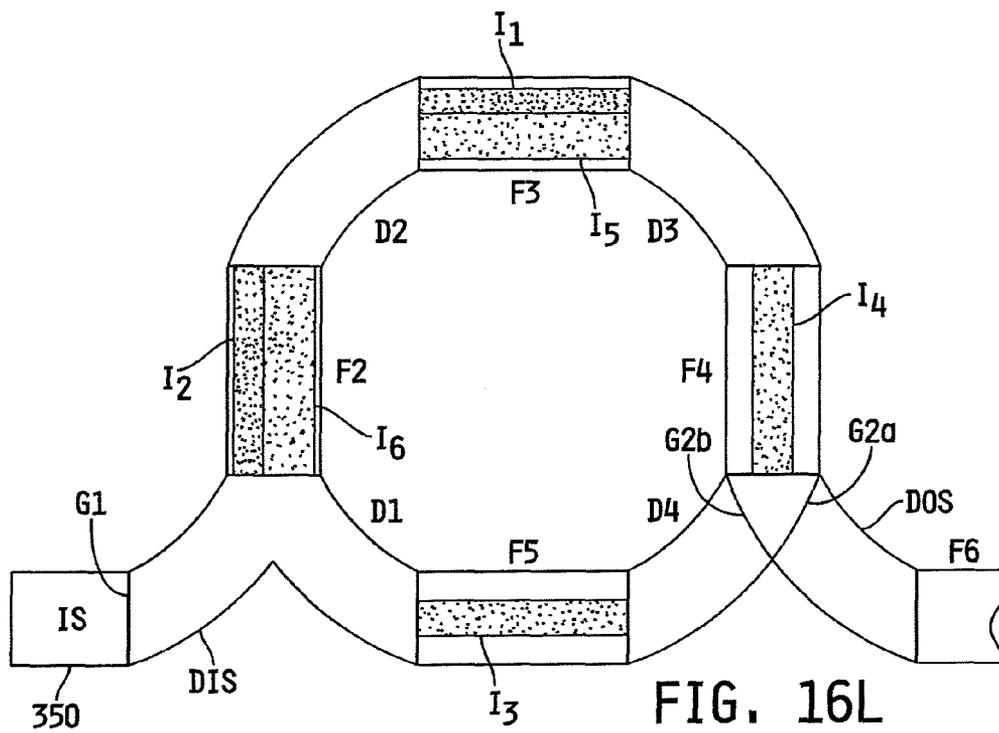
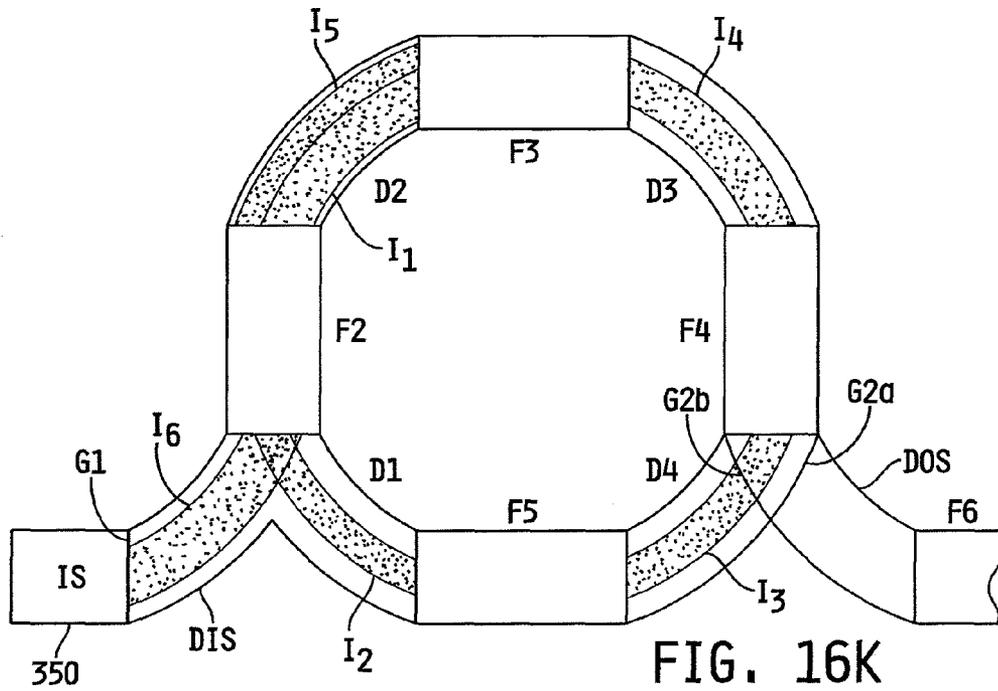












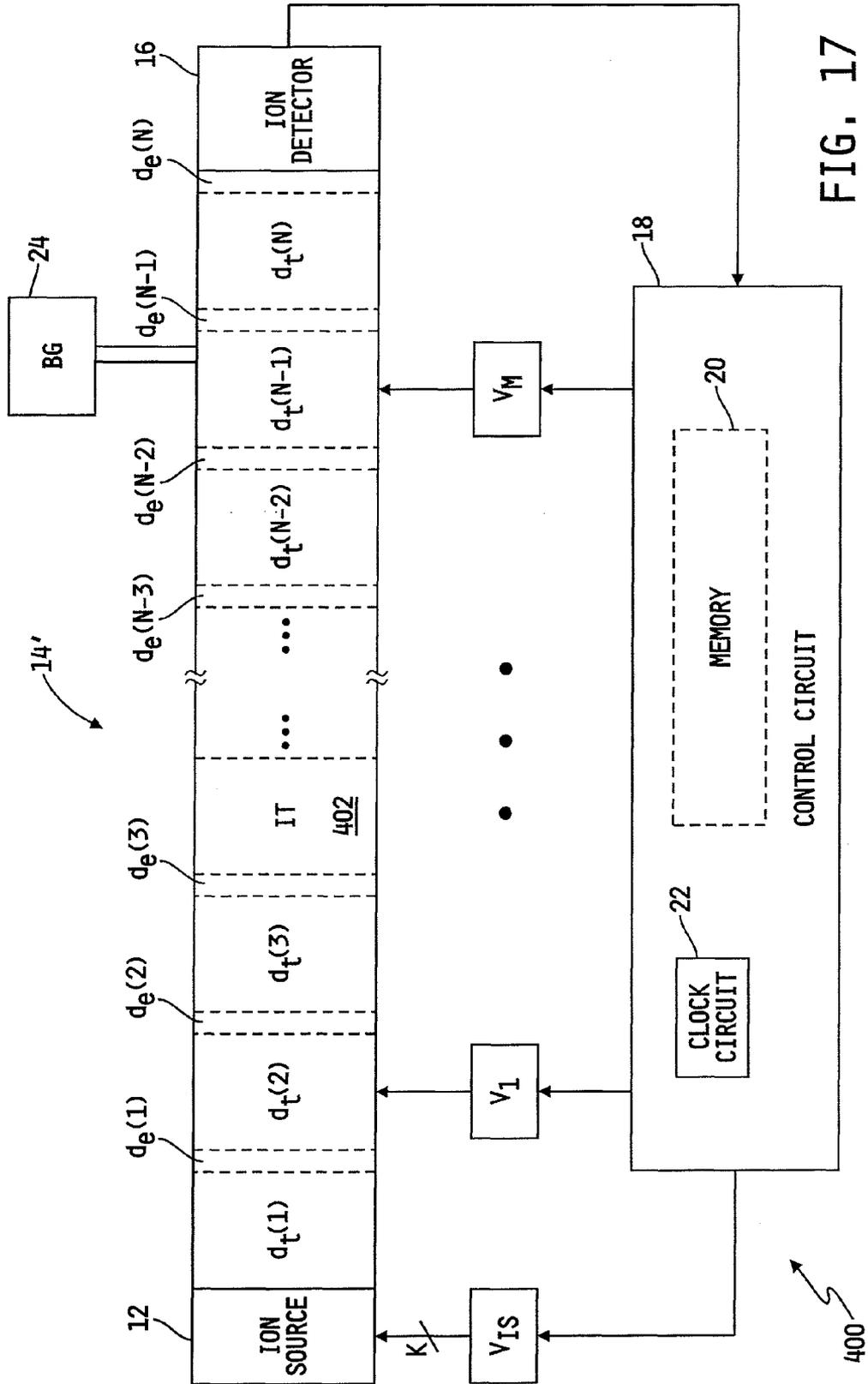


FIG. 17

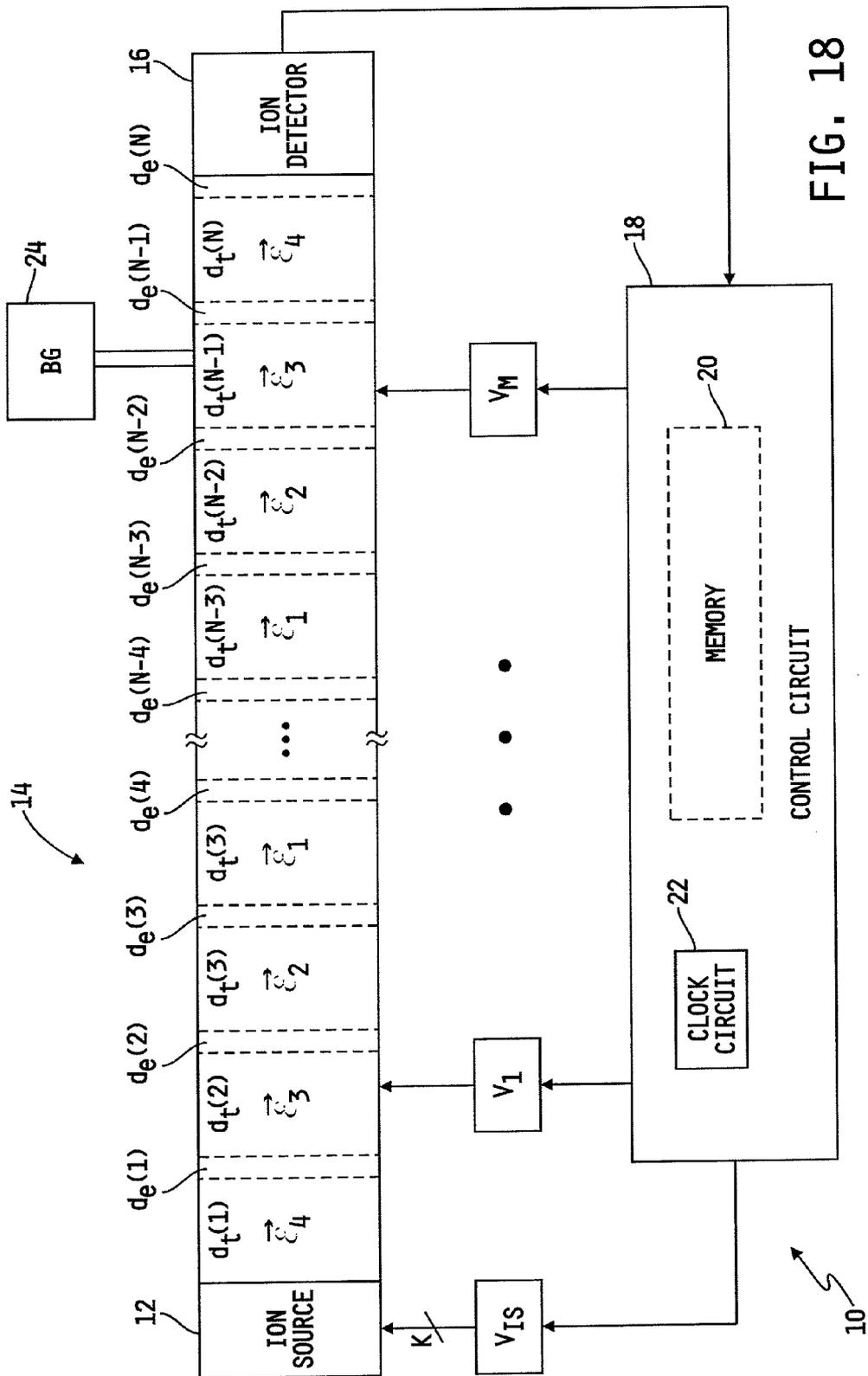


FIG. 18

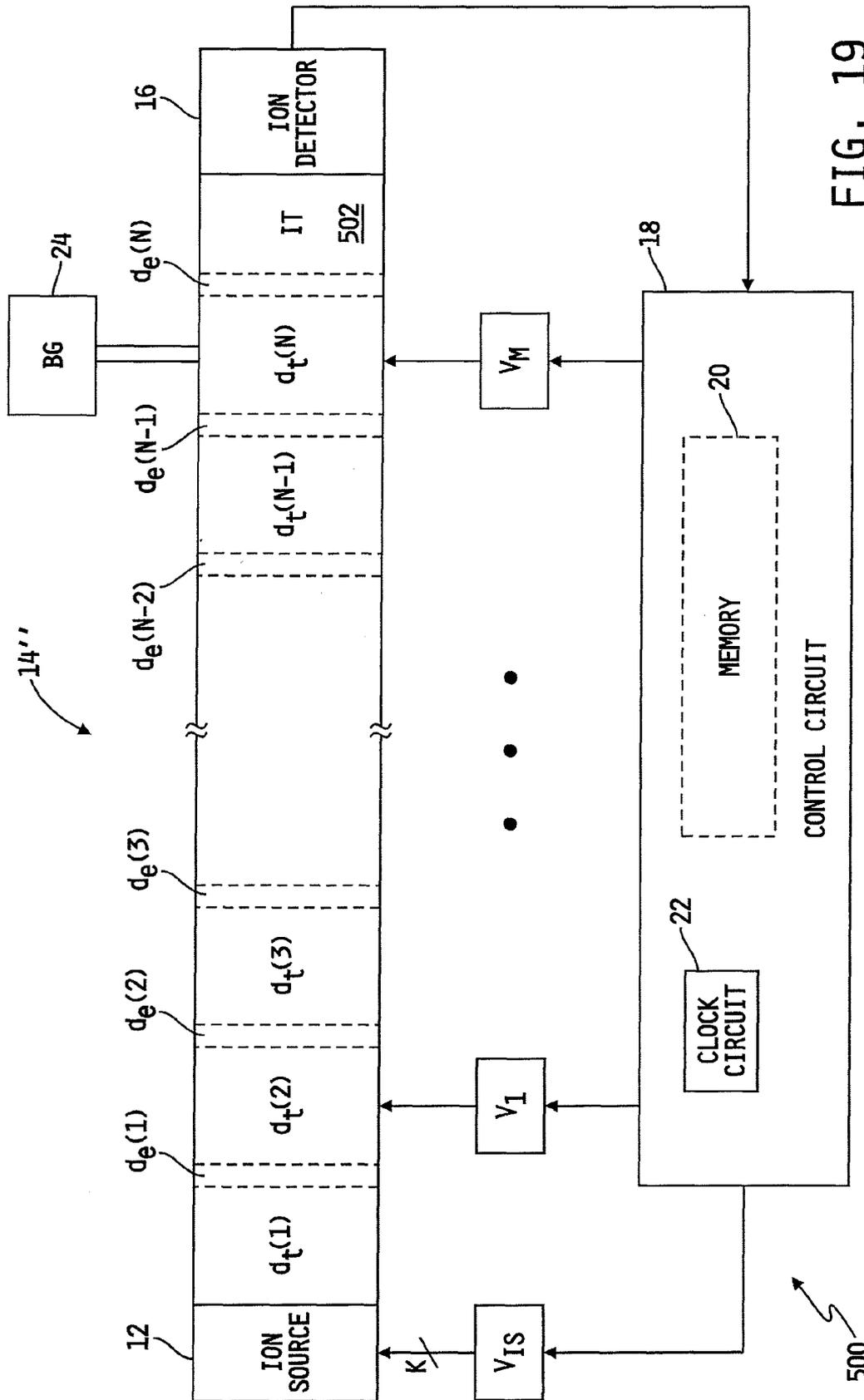


FIG. 19

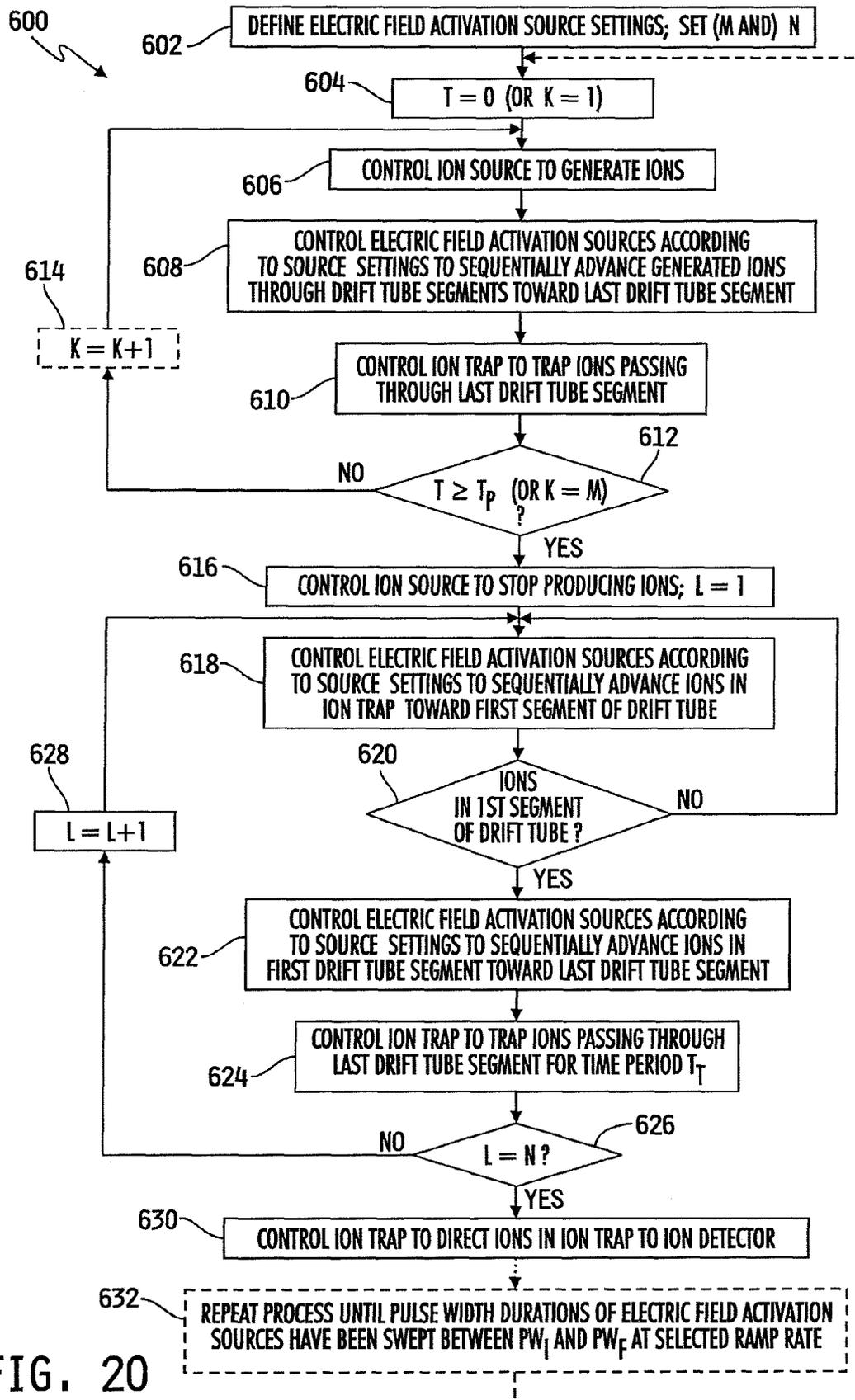


FIG. 20

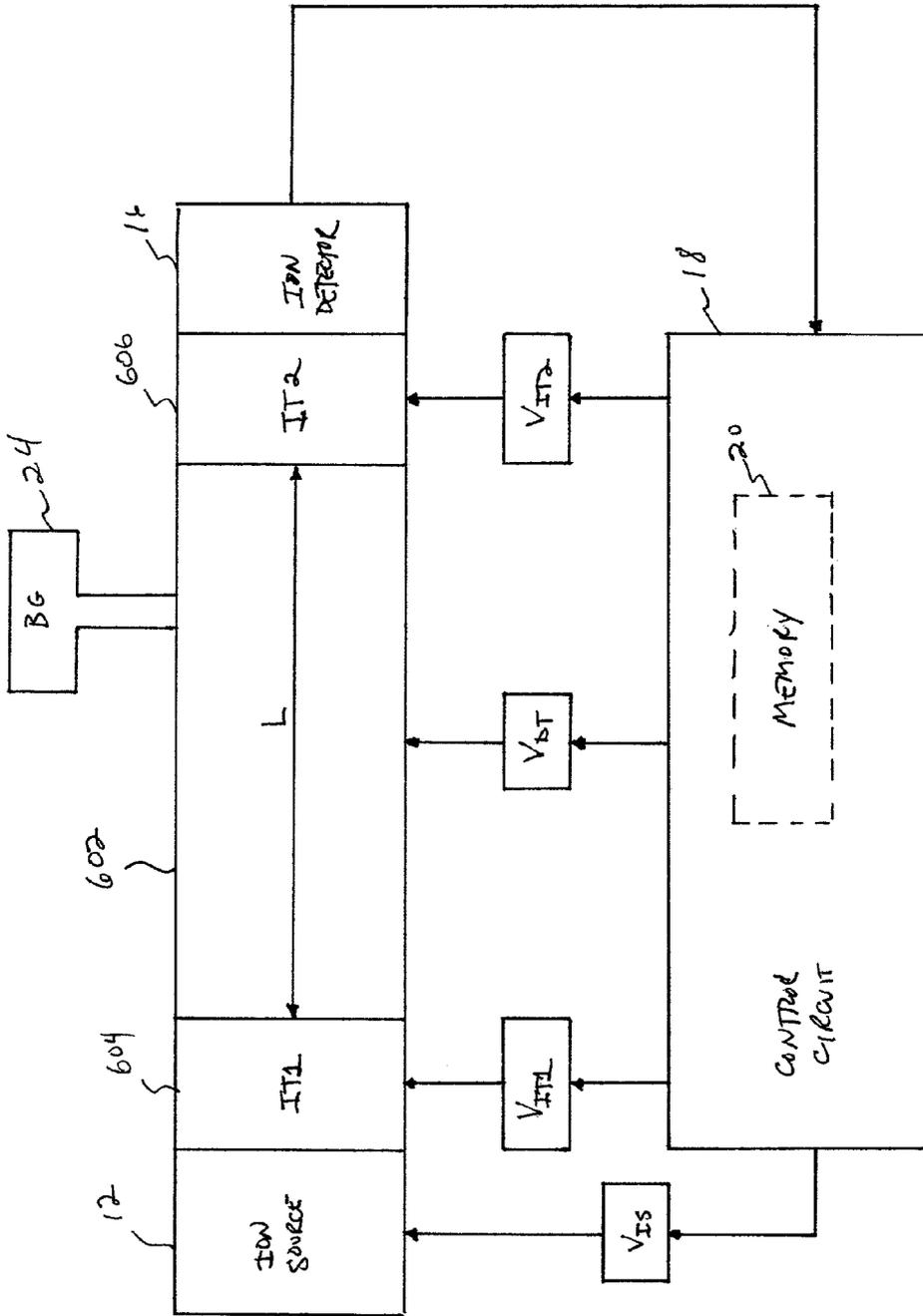


FIG. 21

600

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ION MOBILITY SPECTROMETER INSTRUMENT AND METHOD OF OPERATION

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a continuation-in-part of U.S. patent application Ser. No. 12/357,198, filed Jan. 21, 2009, which claims the benefit of, and priority to, U.S. Provisional Patent Application Ser. No. 61/021,785, the disclosures of which are incorporated herein by reference.

GOVERNMENT RIGHTS

This invention was made with government support under AG024547 and RR018942 awarded by the National Institutes of Health. The U.S. government has certain rights in the invention.

FIELD OF THE INVENTION

The present invention relates generally to ion separation instruments, and more specifically to instruments that operate to separate ions in time as a function of ion mobility.

BACKGROUND

Ion mobility spectrometers are analytical instruments that are used to separate ions in time as a function of ion mobility. It is desirable to be able to control electric fields applied to such instruments in order to investigate properties of charged particles.

SUMMARY

The present invention may comprise one or more of the features recited in the attached claims, and/or one or more of the following features and combinations thereof. An ion mobility spectrometer instrument may comprise a drift tube partitioned into a plurality of cascaded drift tube segments, each defining an ion inlet at one end and an ion outlet at an opposite end, with an ion elimination region defined between the ion outlet and an ion inlet of each adjacent drift tube segment. The ion elimination region of a last one of the drift tube segments may be coupled to the ion inlet of a first one of the drift tube segments such that the drift tube defines therein a closed and continuous ion travel path. An ion entrance drift tube segment may have an ion inlet coupled to an ion source and an ion outlet coupled to one of the plurality of cascaded drift tube segments, and an ion exit drift tube segment may have an ion inlet coupled to the one or another one of the plurality of drift tube segments, and an ion outlet. An ion gate arrangement may be responsive to a first set of one or more ion gate signals to direct ions moving through the drift tube through the one or another one of the plurality of cascaded drift tube segments while blocking the ions from entering the ion exit drift tube segment, and to a second set of one or more ion gate signals to direct the ions moving through the drift tube into the ion exit drift tube segment while blocking the ions from moving through the one or another one of the plurality of cascaded drift tube segments. A number, M, of electric field activation sources may each be operatively connected to one or more of the plurality of drift tube segments such that, when activated, each establishes a repulsive electric field in at least one of the first M ion elimination regions and in every following Mth ion elimination region, and estab-

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lishes an electric drift field in all remaining ion elimination regions and in all of the plurality of cascaded drift tube segments. A control circuit may include a memory having instructions stored therein that are executable by the control circuit to produce the first set of one or more ion gate signals and sequentially activate each of the number, M, of electric field activation sources for a time duration while deactivating the remaining number, M, of electric field activation sources to thereby cause only ions supplied by the ion source that have a predefined ion mobility or range of ion mobilities defined by the time duration to travel through the drift tube, and after the ions have traveled around the drift tube a selected number of times to produce the second set of one or more ion gate signals to draw ions moving through the drift tube out of the drift tube and into the ion exit drift tube segment.

The ion mobility spectrometer may further comprise an ion detector configured to detect ions exiting the ion exit drift tube segment and produce corresponding ion detection signals. The instructions stored in the memory may further include instructions executable by the control circuit to process the ion detection signals to determine ion mobility spectral information therefrom.

The ion gate arrangement may comprise a first ion gate positioned in the one or another one of the plurality of cascaded drift tube segments, and a second ion gate positioned in or at the ion inlet of the ion exit drift tube segment. The first set of one or more ion gate signals may comprise a first ion gate signal to which the first ion gate is responsive to allow ions to pass therethrough and a second ion gate signal to which the second ion gate is responsive to block ions from passing therethrough, and the second set of one or more ion gate signals may comprise a third ion gate signal to which the first ion gate is responsive to block ions from passing therethrough and a fourth ion gate signal to which the second ion gate is responsive to allow ions to pass therethrough.

The ion mobility spectrometer may further comprise a voltage supply operatively connected to the ion source and to the control circuit. The instructions stored in the memory may further include instructions executable by the control circuit to control the voltage source to thereby selectively cause the ion source to produce ions and to selectively supply produced ions to the ion entrance drift tube segment.

The instructions stored in the memory may further include instructions executable by the control circuit to produce the first set of one or more ion gate signals, to control the ion source to produce ions and control the number, M, of electric field activation sources in a manner that allows ions produced by the ion source to enter and fill each of the plurality of drift tube segments, to then control the ion source to stop producing ions and sequentially activate each of the number, M, of electric field activation sources for the time duration while deactivating the remaining number, M, of electric field activation sources to thereby cause only ions within the drift tube that have the predefined ion mobility or range of ion mobilities defined by the time duration to travel through the drift tube, and after the ions have traveled around the drift tube a selected number of times to produce the second set of one or more ion gate signals and control the number, M, of electric field activation sources to draw ions moving through the drift tube out of the drift tube and into the ion exit drift tube segment. The instructions stored in the memory may further include instructions executable by the control circuit to control the number, M, of electric field activation sources in the manner that allows ions produced by the ion source to enter and fill each of the plurality of drift tube segments by controlling the number, M, of electric field activation sources to

pass all ions generated by the ion source from each of the plurality of drift tube segments to the next adjacent drift tube segment.

The predefined ion mobility or range of ion mobilities may be resonant with a fundamental frequency defined by the time duration, and the instructions stored in the memory may further include instructions executable by the control circuit to control the number, M, of electric field activation sources to sweep the time duration between first and second predefined time durations to thereby cause ions within the drift tube that have at least one of ion mobilities defined by overtone frequencies of the time duration and ion mobilities resonant with fundamental frequencies of discrete time durations between the first and second time durations to travel through the drift tube.

The ion mobility spectrometer may further comprise a voltage supply operatively connected to the ion source and to the control circuit. The instructions stored in the memory may further include instructions executable by the control circuit to control the ion source to produce ions by controlling the voltage source to cause the ion source to produce ions and to supply the produced ions to the ion entrance drift tube segment, and to control the ion source to stop producing ions by controlling the voltage source to cause the ion source to stop producing ions.

The ion outlet of the ion entrance drift tube segment may be coupled to a first one of the plurality of drift tube segments. The instructions stored in the memory may further include instructions executable by the control circuit to produce the first set of the one or more gate signals, and to then control the ion source and the number, M, of electric field activation sources to alternately (a) supply ions to the first one of the plurality of cascaded drift tube segments via the ion entrance drift tube segment while also advancing ions in even-numbered ones of the plurality of drift tube segments to next adjacent odd-numbered ones of the plurality of drift tube segments and blocking advancement of ions in odd-numbered ones of the plurality of drift tube segments to next adjacent even-numbered ones of the plurality of drift tube segments, and (b) stop the supply of ions to the first one of the plurality of cascaded drift tube segments via the ion entrance drift tube segment while also advancing ions in odd-numbered ones of the plurality of drift tube segments to next adjacent even-numbered ones of the plurality of drift tube segments and blocking advancement of ions in even-numbered ones of the plurality of drift tube segments to next adjacent odd-numbered ones of the plurality of drift tube segments, a first number of times to thereby sequentially add ions selectively produced by the ion source to every other one of the plurality of drift tube segments. The instructions stored in the memory may further include instructions that are executable by the control circuit to, after ions selectively produced by the ion source have been added to every other one of the plurality of drift tube segments the first number of times, control the ion source to stop producing ions and sequentially activate each of the number, M, of electric field activation sources for the time duration while deactivating the remaining number, M, of electric field activation sources to thereby cause only ions within the drift tube that have the predefined ion mobility or range of ion mobilities defined by the time duration to travel through the drift tube, and after the ions have traveled around the drift tube a second number of times to produce the second set of the one or more ion gate signals to draw ions moving through the drift tube out of the drift tube and into the ion exit drift tube segment. The ion mobility spectrometer may further comprise a voltage supply operatively connected to the ion source and to the control

circuit. The instructions stored in the memory may further include instructions executable by the control circuit to control the ion source to produce ions by controlling the voltage source to cause the ion source to produce ions and to supply the produced ions to the ion entrance drift tube segment, and to control the ion source to stop producing ions by controlling the voltage source to cause the ion source to stop producing ions.

An ion mobility spectrometer instrument may comprise a linear drift tube partitioned into a plurality of cascaded drift tube segments, each defining an ion inlet at one end and an ion outlet at an opposite end, with an ion elimination region defined between the ion outlet and an ion inlet of each adjacent drift tube segment. An ion source coupled to the ion inlet of a first one of the plurality of cascaded drift tube segments.

A number, M, of electric field activation sources may each be operatively connected to one or more of the plurality of drift tube segments such that, when activated, each establishes a repulsive electric field in at least one of the first M ion elimination regions and in every following Mth ion elimination region, and also establishes an electric drift field in all remaining ion elimination regions and in all of the plurality of cascaded drift tube segments. A control circuit may include a memory having instructions stored therein that are executable by the control circuit to sequentially activate each of the number, M, of electric field activation sources for a time duration while deactivating the remaining number, M, of electric field activation sources to thereby cause only ions supplied by the ion source that have a predefined ion mobility or range of ion mobilities defined by the time duration to travel through the drift tube from the first drift tube segment to a last one of the plurality of drift tube segments, and to then, for a first predefined number of times, sequentially activating each of the number, M, of electric field activation sources for the time duration while deactivating the remaining number, M, of electric field activation sources in reverse order to thereby cause only ions having the predefined ion mobility or range of mobilities defined by the time duration to travel through the drift tube from the last drift tube segment to the first drift tube segment followed by sequentially activating each of the number, M, of electric field activation sources for the time duration while deactivating the remaining number, M, of electric field activation sources to thereby cause only ions having the predefined ion mobility or range of ion mobilities defined by the time duration to travel through the drift tube from the first drift tube segment to the last drift tube segment. Means may be provided for randomizing positions of the ions within the drift tube during each pass of ions from at least one of the first drift tube segment to the last drift tube segment and the last drift tube segment to the first drift tube segment.

The ion inlet of the first drift tube segment may comprise an ion gate. The instructions stored in the memory may further include instructions executable by the control circuit to control the ion gate to selectively allow entrance of ions generated by the ion source into the ion inlet of the first drift tube segment.

The ion source may comprise at least one ion separation instrument configured to separate ions in time as a function of one or more molecular characteristics. The at least one ion separation instrument may include at least one of a liquid chromatograph, a gas chromatograph, an ion mobility spectrometer, a mass spectrometer, and a capillary electrophoresis instrument.

The ion mobility spectrometer instrument may further comprise an ion detector configured to detect ions exiting the ion outlet of the last drift tube segment and produce corre-

sponding ion detection signals. The instructions stored in the memory may further include instructions executable by the control circuit to process the ion detection signals to determine ion mobility spectral information therefrom.

The predefined ion mobility or range of ion mobilities may be resonant with a fundamental frequency defined by the time duration. The instructions stored in the memory may further include instructions executable by the control circuit to control the number, M , of electric field activation sources to sweep the time duration between first and second predefined time durations to thereby cause ions within the drift tube that have at least one of ion mobilities defined by overtone frequencies of the time duration and ion mobilities resonant with fundamental frequencies of discrete time durations between the first and second time durations to travel through the drift tube.

A method of separating ions as a function of ion mobility in a drift tube partitioned into a plurality of cascaded drift tube segments each defining an ion inlet at one end and an ion outlet at an opposite end, with an ion elimination region defined between the ion outlet and an ion inlet of each adjacent drift tube segment, may comprise controlling an ion source to supply ions to the ion inlet of a first one of the plurality of drift tube segments, sequentially controlling electric fields in each of the plurality of drift tube segments and ion elimination regions for a time duration to cause only ions supplied by the ion source to the first one of the plurality of drift tube segments that have a predefined ion mobility or range of ion mobilities defined by the time duration to travel through the drift tube from the first one of the plurality of drift tube segments to a last one of the plurality of drift tube segments, to then, for a predefined number of times, sequentially control electric fields in each of the plurality of drift tube segments and ion elimination regions in reverse order to cause only ions having the predefined ion mobility or range of mobilities defined by the time duration to travel through the drift tube from the last one of the plurality of drift tube segments to the first one of the plurality of drift tube segments followed by sequentially controlling electric fields in each of the plurality of drift tube segments and ion elimination regions to cause only ions having the predefined ion mobility or range of ion mobilities defined by the time duration to travel through the drift tube from the first one of the plurality of drift tube segments to the last one of the plurality of drift tube segments, and randomizing positions of the ions within the drift tube during each pass of ions from at least one of the first one of the plurality of drift tube segments to the last one of the plurality of drift tube segments and the last one of the plurality of drift tube segments to the first one of the plurality of drift tube segments.

Randomizing positions of the ions within the drift tube may comprise trapping the ions for a trap period in an ion trap positioned within the drift tube during each pass of the ions. The trap period may be selected to allow ions trapped within the ion trap to randomize their positions relative to the ion trap. Alternatively or additionally, randomizing positions of the ions within the drift tube comprises trapping the ions for a trap period in a first ion trap positioned adjacent to the last one of the plurality of drift tube segments during each pass of the ions from the first one of the plurality of drift tube segments to the last one of the plurality of drift tube segments and trapping the ions for the trap period in a second ion trap positioned adjacent to the first one of the plurality of drift tube segments during each pass of the ions from the last one of the plurality of drift tube segments to the first one of the plurality of drift tube segments, wherein the trap period may be selected to allow ions trapped within the first and second ion

traps to randomize their positions relative to the first and second ion traps respectively. Alternatively or additionally, randomizing positions of the ions within the drift tube may comprise progressively diminishing magnitudes of the electric fields in a number of adjacent ones of the plurality of drift tube segments to cause the ions to randomize by bunching up in at least some of the number of adjacent ones of the plurality of drift tube segments in which the magnitudes of the electric fields are diminished. The number of adjacent ones of the plurality of drift tube segments may comprise a first subset of adjacent ones of the plurality of drift tube segments including the first one of the plurality of drift tube segments and a second subset of adjacent ones of the plurality of drift tube segments including the last one of the plurality of drift tube segments. Alternatively, the number of adjacent ones of the plurality of drift tube segments may include at least one of the first one of the plurality of drift tube segments and the last one of the plurality of drift tube segments.

The predefined ion mobility or range of ion mobilities may be resonant with a fundamental frequency defined by the time duration. The method may further comprise controlling the number, M , of electric field activation sources to sweep the time duration between first and second predefined time durations to thereby cause ions within the drift tube that have at least one of ion mobilities defined by overtone frequencies of the time duration and ion mobilities resonant with fundamental frequencies of discrete time durations between the first and second time durations to travel through the drift tube.

An ion mobility spectrometer instrument may comprise a linear drift tube partitioned into a plurality of cascaded drift tube segments, each defining an ion inlet at one end and an ion outlet at an opposite end, with an ion elimination region defined between the ion outlet and an ion inlet of each adjacent drift tube segment, an ion source coupled to the ion inlet of a first one of the plurality of cascaded drift tube segments, an ion trap positioned to receive therein ions traveling through the drift tube, a number, M , of electric field activation sources each operatively connected to one or more of the plurality of drift tube segments such that, when activated, each establishes a repulsive electric field in at least one of the first M ion elimination regions and in every following M th ion elimination region, and also establishes an electric drift field in all remaining ion elimination regions and in all of the plurality of cascaded drift tube segments, and a control circuit including a memory having instructions stored therein that are executable by the control circuit to, for a first predefined number of times, sequentially activate each of the number, M , of electric field activation sources for a time duration while deactivating the remaining number, M , of electric field activation sources to thereby cause only ions supplied by the ion source that have a predefined ion mobility or range of ion mobilities defined by the time duration to travel through the drift tube followed by controlling the ion trap to trap therein the ions traveling through the drift tube that have the predefined ion mobility or range of ion mobilities, and to then, for a second predefined number of times, control the ion trap to release the ions trapped therein, to sequentially activate each of the number, M , of electric field activation sources for the time duration while deactivating the remaining number, M , of electric field activation sources to cause the released ions having the predefined ion mobility or range of ion mobilities to travel from to one end of the linear drift tube, then back to the other end of the linear drift tube and back to the ion trap followed by controlling the ion trap to trap the ions therein for a trap period selected to allow ions trapped within the ion trap to randomize their positions relative to the ion trap, and to then control the ion trap to release the ions trapped therein to an ion detector.

The ion mobility spectrometer may further comprise a voltage supply operatively connected to the ion source and to the control circuit. The instructions stored in the memory may further include instructions executable by the control circuit to control the voltage source each of the first predefined number of times to cause the ion source to produce ions and supply the produced ions to the ion inlet of the first one of the plurality of drift tube segments.

The ion mobility spectrometer may further comprise a voltage supply operatively connected to the ion source and to the control circuit. The instructions stored in the memory may further include instructions executable by the control circuit to control the voltage source to cause the ion source to continuously produce ions and supply the produced ions to the ion inlet of the first one of the plurality of drift tube segments.

The ion detector may be configured to detect ions released from the first ion trap and produce corresponding ion detection signals. The instructions stored in the memory may further include instructions executable by the control circuit to process the ion detection signals to determine ion mobility spectral information therefrom.

The plurality of cascaded drift tube segments may comprise a last drift tube segment at an opposite end of the drift tube from the first drift tube segment. The ion trap may be coupled to the ion outlet of the last drift tube segment.

The predefined ion mobility or range of ion mobilities may be resonant with a fundamental frequency defined by the time duration. The instructions stored in the memory may further include instructions executable by the control circuit to control the number, M , of electric field activation sources during the first predefined time period and during the second predefined time period to sweep the time duration between first and second predefined time durations to thereby cause ions within the drift that have at least one of ion mobilities defined by overtone frequencies of the time duration and ion mobilities resonant with fundamental frequencies of discrete time durations between the first and second time durations to travel through the drift tube and to be trapped within the ion trap. In this embodiment, the ion mobility spectrometer may further comprise a voltage supply operatively connected to the ion source and to the control circuit, and the instructions stored in the memory may further include instructions executable by the control circuit to control the voltage source each of the first predefined number of times to cause the ion source to produce ions and supply the produced ions to the ion inlet of the first one of the plurality of drift tube segments. Alternatively, the instructions stored in the memory may include instructions executable by the control circuit to control the voltage source to cause the ion source to continuously produce ions and supply the produced ions to the ion inlet of the first one of the plurality of drift tube segments.

An ion mobility spectrometer instrument may comprise a linear drift tube, an ion source coupled to the ion inlet of the linear drift tube, a first ion trap positioned adjacent to the ion inlet of the linear drift tube, a second ion trap positioned adjacent to an ion outlet of the linear drift tube, the linear drift tube defining a single drift tube region between the first and second ion traps, and at least one electric field activation source operatively connected to the single drift tube region. The at least one electric field activation source may be controllable to establish an electric field in the single drift tube region in a first direction that causes ions supplied by the ion source to drift from the first ion trap toward the second ion trap and controllable to alternatively establish an electric field in the single drift tube region in a second direction that causes ions supplied by the ion source to drift from the second ion trap toward the first ion trap. A control circuit may include

a memory having instructions stored therein that are executable by the control circuit to execute a process a predefined number of times. The process may include activating the at least one electric field activation source for a time duration to establish an electric field in the first direction to cause only ions supplied by the ion source that have a predefined ion mobility or range of ion mobilities defined by the time duration to travel through the single drift tube region in the first direction toward the second ion trap followed by controlling the second ion trap to trap therein the ions that have the predefined ion mobility or range of ion mobilities, and then controlling the second ion trap to release the ions trapped therein and activate the at least one electric field activation source for the time duration to establish an electric field in the second direction to cause only ions supplied by the ion source that have the predefined ion mobility or range of ion mobilities defined by the time duration to travel through the single drift tube region in the second direction toward the first ion trap followed by controlling the first ion trap to trap therein the ions that have the predefined ion mobility or range of ion mobilities followed by controlling the first ion trap to release the ions trapped therein.

The instructions stored in the memory may further include instructions executable by the control circuit to control the first and second ion traps to trap ions therein for a trap period, the trap period selected to allow ions trapped within the first ion trap and the second ion trap to randomize their positions relative to the first and second ion trap respectively.

The ion mobility spectrometer instrument may further comprise an ion detector configured to detect ions exiting the linear drift tube. The instructions stored in the memory may further include instructions executable by the control circuit to control the second ion trap to release ions trapped therein toward the ion detector and to process the ion detection signals to determine ion mobility spectral information therefrom.

The predefined ion mobility or range of ion mobilities may be resonant with a fundamental frequency defined by the time duration. The instructions stored in the memory may further include instructions executable by the control circuit to control the at least one electric field activation source to sweep the time duration between first and second predefined time durations to thereby cause ions that have fundamental frequencies resonant with each of a number of discrete time durations between the first and second time durations to travel through the single drift tube region, and to execute the process the predefined number of times for each of the number of discrete time durations between the first and second predefined time durations.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a block diagram of one illustrative embodiment of an ion mobility spectrometer instrument.

FIG. 2 is a diagram of one illustrative embodiment of the drift tube and associated arrangement of the electric field activation sources of the ion mobility spectrometer of FIG. 1.

FIG. 3 is a timing diagram illustrating operation of the ion mobility spectrometer of FIGS. 1 and 2.

FIG. 4A is a diagram of one several cascaded sections of the drift tube illustrated in FIG. 2.

FIGS. 4B-4D illustrate alternate embodiments of the arrangement of the electric field activation sources relative to the drift tube of FIG. 4A.

FIG. 5 is a flowchart of one illustrative process for operating the ion mobility spectrometer of either of FIG. 1 or 3 as an

ion mobility filter operable to produce only ions having a selected mobility or range of mobilities from a continuous or discrete ion source.

FIG. 6 is a plot of ion intensity vs. drift time illustrating the drift time of ions of the sodiated monomer $[M+Na]^+$ form of the simple oligosaccharide isomer raffinose through one particular embodiment of the ion mobility spectrometer of FIG. 1.

FIG. 7 is a flowchart of one illustrative process for operating the ion mobility spectrometer of either of FIG. 1 or 3 by sweeping the pulse widths of the electric field activation sources over a range of pulse width durations.

FIG. 8 is a plot of ion intensity vs. frequency illustrating the result in the frequency domain of the process of FIG. 7 using a continuous source of raffinose ions.

FIG. 9 includes a number of plots of ion intensity vs. frequency illustrating results in the frequency domain of the process of FIG. 7 applied to ion mobility instruments having different phase numbers.

FIG. 10 includes a number of plots of ion intensity vs. frequency illustrating results in the frequency domain of the process of FIG. 5 applied to ion mobility instruments having different numbers of drift tube sections.

FIG. 11 includes a number of plots of ion intensity vs. frequency illustrating results in the frequency domain of the process of FIG. 7 applied to a raffinose sample, a melezitose sample and to a sample mixture of raffinose and melezitose.

FIG. 12A includes a number of plots of ion intensity vs. total drift time illustrating results in the time domain of the process of FIG. 5 applied to a raffinose/melezitose mixture using a cyclotron geometry ion mobility spectrometer.

FIG. 12B is a diagram of one illustrative embodiment of a cyclotron geometry ion mobility spectrometer used to generate the plots of FIG. 12A.

FIG. 13 is a block diagram of one illustrative embodiment of a cascaded ion mobility spectrometer instrument that employs some of the concepts illustrated and described with respect to FIGS. 1-12B.

FIG. 14 is a flowchart of one illustrative process for operating the ion mobility spectrometer of FIG. 12B by first pre-filling the drift tube with ions and then sequentially controlling the electric field activation sources to direct ions some number of revolutions around the drift tube in a manner that resolves only ions having a selected mobility or range of mobilities.

FIG. 15 is a flowchart of another illustrative process for operating the ion mobility spectrometer of FIG. 12B by sequentially controlling the electric field activation sources to direct ions having a selected mobility or range of mobilities around the drift tube while also periodically introducing new ions into the drift tube from the ion source, and then continuing to sequentially control the electric field activation sources to direct ions having the selected mobility or range of mobilities some number of revolutions around the drift tube without introducing new ions into the drift tube such that only ions within the drift tube having the selected mobility or range of mobilities are resolved.

FIGS. 16A-16L are successive or sequential block diagrams of one illustrative embodiment of the ion mobility spectrometer of FIG. 12B illustrating operation of the spectrometer during the part of the process illustrated in the flowchart of FIG. 15 in which the electric field activation sources are sequentially controlled to direct ions having a selected mobility or range of mobilities around the drift tube while also periodically introducing new ions into the drift tube from the ion source.

FIG. 17 is a block diagram of another illustrative embodiment of an ion mobility spectrometer instrument.

FIG. 18 is a block diagram of the ion mobility spectrometer of FIG. 1 illustrating one illustrative technique controlling electric fields within some of the drift tube segments adjacent to the ion entrance and ion exit ends when operating a linear drift tube ion mobility spectrometer to direct ions back and forth between the two ends of the drift tube in a manner that resolves only ions having a selected mobility or range of mobilities.

FIG. 19 is a block diagram of yet another illustrative embodiment of an ion mobility spectrometer instrument.

FIG. 20 is a flowchart of one illustrative process for operating the ion mobility spectrometer of FIG. 19 by sequentially controlling the electric field activation sources to direct ions back and forth between the ends of the drift tube in a manner that resolves only ions having a selected mobility or range of mobilities.

FIG. 21 is a block diagram of still another illustrative embodiment of an ion mobility spectrometer.

DESCRIPTION OF THE ILLUSTRATIVE EMBODIMENTS

For the purposes of promoting an understanding of the principles of the invention, reference will now be made to a number of illustrative embodiments shown in the attached drawings and specific language will be used to describe the same.

Referring to FIG. 1, a block diagram is shown of one illustrative embodiment of an ion mobility spectrometer instrument 10. In the illustrated embodiment, the ion mobility spectrometer instrument 10 includes an ion source 12 having an ion outlet that is couple to an ion inlet of a drift tube 14. An ion outlet of the drift tube 14 is coupled to an ion detector 16 having a signal output that is electrically connected to an input of a control circuit 18. The control circuit 18 includes a conventional memory unit 20, and further includes a conventional clock circuit 22 that may be controlled by the control circuit 18 in a conventional manner to produce periodic signals of desired frequency. Illustratively, a source of buffer gas 24 supplies buffer gas to the drift tube 14 in a conventional manner.

The control circuit 18 is electrically connected to a control input of an ion source voltage supply, V_{IS} , having a number, K, of outputs that are electrically connected to the ion source 12, where K may be any positive integer. The ion source 12 may be any conventional ion source that is configured to controllably produce ions from one or more samples. The ion source voltage supply, V_{IS} , may accordingly represent one or more voltage supplies configured to controllably produce, under the control of the control circuit 18 and/or manually controllable or programmable, one or more corresponding voltages for controlling operation of the ion source 12 in a conventional manner to produce ions. Illustratively, the ion source 12 may be configured to continuously produce ions, or may alternatively be configured to produce discrete packets of ions. Examples of such conventional ion sources include, but are not limited to, electrospray ion sources (ESI), ion sources using radiation source to desorb ions from a sample, e.g., matrix-assisted laser desorption ion sources (MALDI), ion sources that collect generated ions in an ion trap for subsequent release, and the like. Alternatively or additionally, the ion source 12 may be or include one or more conventional ion separation instruments configured to separate ions in time as a function of one or more molecular characteristics. Examples include, but are not limited to, a conventional liquid

or gas chromatograph, a conventional mass spectrometer, a conventional ion mobility spectrometer, a capillary electrophoresis instrument, or the like. In any case, ions produced by the ion source **12** exit an ion outlet of the ion source **12** and enter an ion inlet of the drift tube **14** of the ion mobility spectrometer instrument **10**.

The ion mobility spectrometer **10** further includes a number, M , of electric field activation sources, e.g., voltage sources, V_1 - V_M , where M may be any positive integer greater than 1. In the illustrated embodiment, the control circuit **18** includes a corresponding number of outputs, each of which is electrically connected to an input of a different one of the electric field activation sources, V_1 - V_M . In alternate embodiments, the control circuit **18** may include fewer outputs that are electrically connected to corresponding inputs of fewer of the electric field activation sources, V_1 - V_M . In such embodiments, some of which will be described in detail hereinafter, one or more of the electric field activation sources, V_1 - V_M , may be electrically connected to corresponding outputs of the control circuit **18** and one or more others of the electric field activation sources, V_1 - V_M , may be triggered by operation of an adjacent or other ones of the electric field activation sources, V_1 - V_M , and/or be programmed for specified operation. In any case, the outputs of the voltage sources V_1 - V_M are electrically connected to the drift tube **14** in a manner that will be fully described in detail hereinafter.

In the illustrated embodiment, the ion detector **16** is conventional and is configured to produce an ion intensity signal that is proportional to the number of ions that reach, and are detected by, the ion detector **16**. The ion intensity signal is supplied to the control circuit **18**, which then processes the ion intensity signal to produce ion mobility spectral information. The memory unit **20** has instructions stored therein that are executable by the control circuit **18** to control the operation of the various electric field activation sources, V_1 - V_M .

In the embodiment illustrated in FIG. 1, the drift tube **14** is partitioned into a plurality of cascaded drift tube segments beginning with a first drift tube segment positioned adjacent to the ion source **12** and defining the ion inlet of the drift tube **14**, and ending with an N th drift tube segment defining the ion outlet of the drift tube **14**. Ions generated by the ion source **12** enter the ion inlet of the drift tube **14**, and the electric field activation sources, V_1 - V_M , are operated such that the electric fields, i.e., drift fields, established in the various drift tube segments are modulated at a frequency that allows only ions having mobilities that are resonant with the operating conditions to drift through all of the various drift tube segments. In this way, the ion mobility spectrometer **10** operates as an ion mobility filter that filters out or away all ions except those having ion mobilities that are within a specified range of ion mobilities defined by the frequency of operation of the electric field activation sources, V_1 - V_M . Additionally, ions drift through the various drift tube segments at frequencies that are overtones of the frequency of operation of the electric field activation sources, V_1 - V_M . Thus, the ion mobility spectrometer **10** may be operated, as will be described in detail herein, to filter away all ions except those having ion mobilities that are resonant with a fundamental frequency, f_f , and/or associated overtone frequencies, of operation of the electric field activation sources, V_1 - V_M . Because of the ability to selectively transmit ions in different frequency regions, including those associated with higher overtones, the techniques described herein may be referred to as Overtone Mobility Spectrometry (OMS). In this document, the terms “harmonics” should be understood to include the fundamental frequency, f_f , and integer multiples of the fundamental fre-

quency, and the term “overtone” should be understood to include only the integer multiples of the fundamental frequency, f_f .

Referring now to FIG. 2, a diagram is shown of one illustrative embodiment of a portion of the drift tube **14** along with one illustrative arrangement of the electric field activation sources of the ion mobility spectrometer **10** of FIG. 1. In the illustrated embodiment, the drift tube **14** is partitioned into a number, N , of cascaded segments, S_1 - S_N , where N may be any positive integer greater than 2, and segments S_1 - S_5 are shown in FIG. 2. Each of the segments, e.g., S_1 - S_5 , is illustratively constructed of five concentric, electrically conductive rings, 30_1 - 30_5 , each separated by a concentric, electrically insulating ring 32_1 - 32_4 (illustrated in FIG. 2 for the segment S_1 only). The first electrically conductive ring, 30_1 , of each segment defines an ion inlet gate, G_I , to the segment, and the last electrically conductive ring, 30_5 , of each segment defines an ion outlet gate, G_O , of the segment. Illustratively, the first and last rings 30_1 and 30_5 contain mesh grids, e.g., 90% transmittance Ni mesh grid, although this disclosure contemplates embodiments which do not include one or both of the rings 30_1 and 30_5 . In any case, adjacent ones of the electrically conductive rings, 30_1 - 30_5 , are separated by one of the electrically insulating rings, 32_1 - 32_4 , and adjacent segments, S_1 - S_N , of the drift tube **14** are separated by a concentric, electrically insulating isolator ring **34**, e.g., Teflon®, a synthetic fluoropolymer resin. All of the rings, 30_1 - 30_5 , 32_1 - 32_4 and **34** are stacked together, sealed with O-rings and compressed using a number, e.g., eight, of threaded rods, e.g., nylon. The segments, S_1 - S_N , are then joined together to form the drift tube **14**.

In the illustrated embodiment, a resistor, R , is electrically connected between each of the electrically conductive rings in each drift tube segment, and a resistor R_E is connected between the ion outlet gate and ion inlet gate of each adjacent drift tube segment. The drift tube **14** of the ion mobility spectrometer instrument **10** is constructed with the electrically conductive rings 30_1 - 30_5 electrically insulated from each other and with the drift tube segments S_1 - S_N also electrically isolated from each other so that electric fields can be developed separately and independently in each of the segments S_1 - S_N and/or in groups of the segments S_1 - S_N . By applying suitable voltages across the drift tube segments and/or groups of drift tube segments, as will be described in greater detail hereinafter, uniform electric fields are illustratively established in each drift tube segment in a manner that transmits ions generated by the ion source **12** through the drift tube **14** and through the ion outlet of the last segment S_N .

The region between the ion inlet gate and the ion outlet gate of each drift tube segment defines an ion transmission region of distance, d_t , and the region between the ion outlet gate of one drift tube segment and the ion inlet gate of the next adjacent drift tube segment defines an ion elimination region of distance, d_e . Thus, for example, the drift tube segment S_1 has an ion transmission region of distance, $d_t(1)$ defined between G_{I1} and G_{O1} , and an ion elimination region of distance $d_e(1)$ defined between G_{O1} and G_{I2} .

In one example embodiment, the drift tube **14** is constructed of 21 identical drift tube segments as just described, with an ion focusing funnel (not shown) positioned approximately mid way between the ion inlet and the ion outlet of the drift tube **14**. In this example embodiment, the ion transmission region, d_t , and the ion elimination region, d_e , are together 5.84 cm in length, and the total length of the 22-section drift tube **14** is 128.5 cm from the ion inlet to the ion outlet of the drift tube **14**. Further details relating to this example construction of the drift tube **14**, including construction of the ion

focusing funnel, are provided in co-pending U.S. Patent Application Pub. No. US 2007/0114382 A2, the disclosure of which is incorporated herein by reference. It will be understood, however, that this disclosure contemplates other embodiments in which the drift tube **14** is constructed in accordance with other conventional techniques, portions or the entirety of which may be linear or non-linear. For example, the drift tube **14** may alternatively be provided in the form of a circular or cyclotron drift tube, and further details relating to some example circular or cyclotron drift tube arrangements are provided in co-pending PCT Publication No. WO 2008/028159 A2, filed Aug. 1, 2007, the disclosure of which is incorporated herein by reference. It will be understood, however, that in any such alternate configuration the drift tube will define a number of cascaded drift tube sections such that electric fields may be selectively and separately created in individual and/or groups of the drift tube sections.

In the embodiment illustrated in FIG. 2, one illustrative arrangement **40** of the electric field activation sources, V_1 - V_M , is shown that includes two electric field activation sources, V_1 and V_2 , electrically connected to the drift tube **14**. The control circuit **18** is illustratively configured to control operation of the electric field activation sources, V_1 and V_2 , e.g., in accordance with instructions stored in the memory **20** that are executable by the control circuit **18**, in an alternating fashion to generate electric fields within the drift tube segments, S_1 - S_N , which cause ions of a specified range of ion mobilities to drift through the drift tube **14**.

In the illustrated embodiment, the electric field activation sources V_1 and V_2 are both conventional DC voltage sources that are controllable by the control circuit **18** to produce a desired DC voltage across the + and - terminals. The + terminals of V_1 and V_2 are both electrically connected to the ion inlet gate, G_{I1} , of the first drift tube segment, S_1 . The + terminal of V_1 is further electrically connected to the ion inlet gates of the even-numbered drift tube segments, e.g., to the ion inlet gate, G_{I2} of the second drift tube segment, S_2 , the ion inlet gate, G_{I4} , of the fourth drift tube segment, S_4 , etc., and the + terminal of V_2 is further electrically connected to the ion inlet gates of the odd-numbered drift tube segments, e.g., to the ion inlet gate, G_{I3} of the third drift tube segment, S_3 , the ion inlet gate, G_{I5} , of the fifth drift tube segment, S_5 , etc. The - terminal of V_1 is electrically connected to the ion outlet gates of the odd-numbered drift tube segments, e.g., to the ion outlet gates, G_{O1} , G_{O3} , G_{O5} , etc. of the drift tube segments S_1 , S_3 , S_5 , etc., respectively. The - terminal of V_2 is electrically connected to the ion outlet gates of the even-numbered drift tube segments, e.g., to the ion outlet gates, G_{O2} , G_{O4} , G_{O6} , etc. of the drift tube segments S_2 , S_4 , S_6 , etc., respectively. With the exception of V_1 connected across the ion inlet and ion outlet gates, G_{I1} and G_{O1} of the first drift tube segment, S_1 , V_1 and V_2 are thus connected across the ion inlet and outlet gates of alternating, adjacent pairs of drift tube segments. For example, V_2 is electrically connected across S_1 and S_2 , e.g., between G_{I1} and G_{O2} , V_1 is electrically connected across S_2 and S_3 , e.g., between G_{I2} and G_{O3} , V_2 is electrically connected across S_3 and S_4 , e.g., between G_{I3} and G_{O4} , etc.

As illustrated in FIG. 2, the voltage sources, V_1 and V_2 , when activated, produce linear voltage gradients, VG_1 and VG_2 respectively, across the drift tube segments to which they are connected. Equal-valued resistors, R , are electrically connected across adjacent pairs of the electrically conductive rings, **30**₁-**30**₅, of each drift tube segment, S_1 - S_N , and equal-valued resistors, R_E , are connected between the ion outlet gates and ion inlet gates of adjacent pairs of drift tube segments. The value of R_E is selected relative to R (or vice versa) such that the linear voltage gradients, VG_1 and VG_2 , establish

corresponding, constant-valued electrical fields across the various drift tube segment pairs.

The control circuit **18** is configured to control operation of the voltage sources, V_1 and V_2 , by periodically switching one voltage source, V_1 , V_2 , on while the other voltage source, V_1 , V_2 , is off. This has the effect of alternately establishing a constant electric field across sequential, cascaded pairs of the drift tube segment, S_1 - S_N . This generally allows only ions having ion mobilities that match the switching frequency to traverse each cascaded pair of drift tube segments. The periodic switching between V_1 and V_2 also establishes a repulsive electric field, i.e., an electric field that is oriented to repel ions traveling in a direction toward the ion detector **16**, in the ion elimination regions, d_e , that follow each cascaded pair of drift tube segments. To illustrate this repulsive electric field, consider the case when V_1 is off and V_2 is on so that only the voltage gradients VG_2 of FIG. 2 exist. Ions entering the first drift tube segment S_1 will drift under the constant electric field established by VG_2 while V_2 is on. However, ions that reach G_{O2} while V_2 is still on will be filtered out by the repulsive electric field, e.g., reverse electric field, established between the high $+V_2$ potential at the ion inlet gate G_{I3} and the low $-V_2$ potential at the ion outlet gate G_{O2} . Generally, V_2 establishes, when activated, repulsive electric fields in the ion elimination regions d_e between the ion outlet gates of even-numbered drift tube segments and the ion inlet gates of the next sequential, odd-numbered drift tube segments, and V_1 likewise establishes, when activated, identical repulsive electric fields in the ion elimination regions d_e between the ion outlet gates of odd-numbered drift tube segments and the ion inlet gates of the next sequential, even-numbered drift tube segments. This periodic traversal of two drift tube segments and ion elimination in the activated ion elimination regions, d_e , causes only ions having ion mobilities that drift in the established electric fields at the rate defined by the V_1 , V_2 switching rate and overtones thereof to drift through the length of the drift tube **14** to the ion detector **16**. Generally, if the switching rate between V_1 and V_2 is constant, this switching rate defines a fundamental frequency, f_f , at which ions of a corresponding range of mobilities can travel progressively through the drift tube segments S_1 - S_N . Alternatively or additionally, if the switching rate is swept over a range of switching rates, ions having the corresponding range of ion mobilities will also travel progressively through the drift tube segments S_1 - S_N at overtone frequencies of the fundamental frequency, f_f .

Referring now to FIG. 3, a number of plots A-F are shown demonstrating the progression of ions through the first five segments, S_1 - S_5 of the drift tube **14** of FIGS. 1 and 2 when the voltage sources V_1 and V_2 are alternatively switched on and off. In the example illustrated in FIG. 5, the ion source **12** is configured to continually produce ions **50**. Plot A illustrates the condition when V_1 and V_2 are both initially off. Plot B illustrates the condition when V_1 is subsequently turned on while V_2 remains off, which establishes a constant-valued electric field, E_1 , in the ion transmission regions d_t of each of the drift tube segments, S_1 - S_5 , and also in the even-numbered ion elimination regions d_e (**2**) and d_e (**4**), and which establishes a repulsive electric field in the odd-numbered ion elimination regions d_e (**1**), d_e (**3**) and d_e (**5**). A portion **51** of the continually generated ions **50** drift through d_t (**1**) under the influence of the electric field E_1 toward d_t (**2**). However, ions that arrive at the ion elimination region d_e (**1**) before V_1 is switched off are filtered out of the ions **51** by the repulsive field established in the ion elimination region d_e (**1**) by V_1 . It will be understood that the voltage applied by V_1 across the first drift tube segment, S_1 , will be different than that applied across remaining pairs of the drift tube segments as illustrated in FIG. 2. Gen-

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erally, the voltage applied by V_1 across the first drift tube segment, S_1 , will be selected so as to establish an electric field, E_1 , in the ion transmission region $d_t(1)$ that is identical to the electric field E_1 established across various pairs of the remaining drift tube segments, S_2 - S_N .

Plot C illustrates the condition when V_1 is switched off and V_2 is switched on, which establishes a constant-valued electric field, E_2 ($E_2=E_1$), in the ion transmission regions d_t of each of the drift tube segments, S_1 - S_5 , and also in the odd-numbered ion elimination regions $d_e(1)$, $d_e(3)$ and $d_e(5)$, and which establishes a repulsive electric field in the even-numbered ion elimination regions $d_e(2)$ and $d_e(4)$. The portion of ions **51** in the $d_t(1)$ region continues to advance under the influence of the electric field E_2 through $d_t(2)$ toward $d_t(3)$, and another portion **52** of the continually generated ions **50** drifts through $d_t(1)$ under the influence of the electric field E_2 toward $d_t(2)$. Ions that arrive at the ion elimination region $d_e(2)$ before V_2 is switched off are filtered out of the ions **51** by the repulsive field established in the ion elimination region $d_e(2)$ by V_2 .

Plot D illustrates the condition when V_2 is switched off and V_1 is switched back on, which establishes the constant-valued electric field E_1 as described with respect to plot B. The portion of ions **51** in the $d_t(2)$ region continues to advance under the influence of the electric field E_1 through $d_t(3)$ toward $d_t(4)$, and another portion **53** of the continually generated ions **50** drifts through $d_t(1)$ under the influence of the electric field E_1 toward $d_t(2)$. However, the ions **52** that were previously in the $d_t(1)$ region are filtered away by the repulsive electric field established in the ion elimination region $d_e(1)$ and therefore do not advance to $d_t(2)$, and ions that arrive at the ion elimination regions $d_e(1)$ and $d_e(3)$ before V_1 is switched off are filtered out of the ions **53** and **51** respectively by the repulsive field established in the ion elimination regions $d_e(1)$ and $d_e(3)$ respectively.

Plot E illustrates the condition when V_1 is again switched off and V_2 is switched back on, which establishes the constant-valued electric field, E_2 described with respect to plot C. The portion of ions **51** in the $d_t(3)$ region continues to advance under the influence of the electric field E_2 through $d_t(4)$ toward $d_t(5)$, the portion of ions **53** in the $d_t(1)$ region continues to advance under the influence of the electric field E_2 through $d_t(2)$ toward $d_t(3)$, and yet another portion **54** of the continually generated ions **50** drifts through $d_t(1)$ under the influence of the electric field E_2 toward $d_t(2)$. Ions that arrive at the ion elimination regions $d_e(2)$ and $d_e(4)$ before V_2 is switched off are filtered out of the ions **53** and **51** respectively by the repulsive field established in the ion elimination regions $d_e(2)$ and $d_e(4)$ respectively.

Plot F illustrates the condition when V_2 is again switched off and V_1 is switched back on, which establishes the constant-valued electric field E_1 as described with respect to plot B. The portion of ions **51** in the $d_t(4)$ region continues to advance under the influence of the electric field E_1 through $d_t(5)$ toward the next drift tube segment (S_6), the portion of ions **53** in the $d_t(2)$ regions continues to advance under the influence of the electric field E_1 through $d_t(3)$ toward $d_t(4)$, and yet another portion **55** of the continually generated ions **50** drifts through $d_t(1)$ under the influence of the electric field E_1 toward $d_t(2)$. The ions **54** that were previously in the $d_t(1)$ region are filtered away by the repulsive electric field established in the ion elimination region $d_e(1)$ and therefore do not advance to $d_t(2)$, and ions that arrive at the ion elimination regions $d_e(3)$ and $d_e(5)$ before V_1 is switched off are filtered out of the ions **53** and **51** respectively by the repulsive fields established in the ion elimination regions $d_e(3)$ and $d_e(5)$ respectively.

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While the embodiment of the drift tube **14** of FIG. **2** was illustrated and described as including an arrangement **40** of electric field activation sources in the form of two DC voltage sources, V_1 and V_2 , it will be understood that this disclosure is not so limited and that embodiments are contemplated in which the arrangement of electric field activation sources includes more than two voltage sources. Referring now to FIGS. **4A-4D**, for example, a number of voltage gradient plots are shown, in relation to the first eight cascaded segments, S_1 - S_8 , of the drift tube **14**, that illustrate alternative embodiments in which the arrangement of electric field activation sources include additional voltage sources. As a reference, the voltage gradient plot **40** of FIG. **4B**, illustrates the embodiment just described in which the arrangement of electric field activation sources includes two voltage sources V_1 and V_2 connected and configured to produce the two illustrated voltage gradients VG_1 and VG_2 .

The voltage gradient plot **60** of FIG. **4C**, in contrast, illustrates an embodiment in which the arrangement of electric field activation sources includes three voltage sources, V_1 , V_2 and V_3 , each illustratively identical to the voltage sources V_1 and V_2 illustrated and described with respect to FIG. **2**. In the embodiment of FIG. **4C**, $+V_1$, $+V_2$ and $+V_3$ are all electrically connected to the ion inlet gate G_{I1} of the first drift tube segment, S_1 . The $+V_1$ is further electrically connected to the ion inlet gates G_{I2} , G_{I5} and G_{I8} , of the drift tube segments S_2 , S_5 and S_8 respectively, the $+V_2$ is further electrically connected to the ion inlet gates G_{I3} , and G_{I6} , of the drift tube segments S_3 and S_6 respectively, and the $+V_3$ is further electrically connected to the ion inlet gates G_{I4} , and G_{I7} , of the drift tube segments S_4 and S_7 respectively. The $-V_1$ is electrically connected to the ion outlet gates G_{O1} , G_{O4} and G_{O7} , the $-V_2$ is electrically connected to the ion outlet gates G_{O3} , G_{O5} and G_{O8} , and the $-V_3$ is electrically connected to the ion outlet gates G_{O2} and G_{O6} . In the three voltage source arrangement, the voltage sources V_1 - V_3 are thus electrically connected, in alternating fashion, across three consecutive drift tube segments with all three voltage sources electrically connected to the ion inlet grid G_{I1} of the first drift tube segment, S_1 , and then with V_1 electrically connected across S_1 , S_2 - S_4 , and S_5 - S_7 , with V_2 electrically connected across S_1 - S_2 , S_3 - S_5 and S_6 - S_8 and with V_3 electrically connected across S_1 - S_3 and S_4 - S_7 .

In operation, the control circuit **18** controls the voltage sources V_1 - V_3 by sequentially switching one voltage source on for a specified duration while maintaining the other two voltage sources in their off state for that duration. As illustrated in FIG. **4C**, for example, the control circuit **18** turns on V_1 for the specified duration while maintaining V_2 and V_3 in their off states, followed by turning off V_1 and turning on V_2 while maintaining V_3 in its off state for the specified duration, followed by turning off V_2 and turning on V_3 while maintaining V_1 in its off state for the specified duration. The control circuit **18** repeats the above process many times to cause ions having mobilities related to the voltage source switching frequency to drift through the various drift tube segments. It will be understood that the voltage applied by V_1 across the first drift tube segment, S_1 , will be different than that applied by V_1 across remaining triplets of the drift tube segments, and that the voltage applied by V_2 across the first two drift tube segments, S_1 - S_2 , will also be different than that applied by V_2 across remaining triplets of the drift tube segments. Generally, the voltage applied by V_1 across the first drift tube segment, S_1 , will be selected so as to establish an electric field, E_1 , in the ion transmission region $d_t(1)$ that is identical to the electric field E_1 established by V_1 across various triplets of the remaining drift tube segments, S_2 - S_N , and the voltage applied

by V_2 across the first two drift tube segment, S_1 - S_2 , will be selected so as to establish an electric field, E_2 , in the ion transmission region $d_t(1)$, ion elimination region $d_e(1)$ and ion transmission region $d_t(2)$ that is identical to the electric field E_2 established by V_2 across various triplets of the remaining drift tube segments, S_3 - S_N .

The voltage gradient plot **70** of FIG. **4D** illustrates an embodiment in which the arrangement of electric field activation sources includes four voltage sources, V_1 , V_2 , V_3 and V_4 , each illustratively identical to the voltage sources V_1 and V_2 illustrated and described with respect to FIG. **2**. In the embodiment of FIG. **4D**, $+V_1$, $+V_2$, $+V_3$ and $+V_4$ are all electrically connected to the ion inlet gate G_{I1} of the first drift tube segment, S_1 . The $+V_1$ is further electrically connected to the ion inlet gates G_{I2} and G_{I6} , of the drift tube segments S_2 and S_6 respectively, the $+V_2$ is further electrically connected to the ion inlet gates G_{I3} , and G_{I7} , of the drift tube segments S_3 and S_7 respectively, the $+V_3$ is further electrically connected to the ion inlet gates G_{I4} , and G_{I8} , of the drift tube segments S_4 and S_8 respectively, and the $+V_4$ is further electrically connected to the ion inlet gate G_{I5} of the drift tube segment S_5 . The $-V_1$ is electrically connected to the ion outlet gates G_{O1} and G_{O5} , the $-V_2$ is electrically connected to the ion outlet gates G_{O2} and G_{O6} , the $-V_3$ is electrically connected to the ion outlet gates G_{O3} and G_{O7} , and the $-V_4$ is electrically connected to the ion outlet gates G_{O4} and G_{O8} . In the four voltage source arrangement, the voltage sources V_1 - V_4 are thus electrically connected, in alternating fashion, across four consecutive drift tube segments with all four voltage sources electrically connected to the ion inlet grid G_{I1} of the first drift tube segment, S_1 , and then with V_1 electrically connected across S_1 , S_2 - S_5 , and S_6 - S_9 , with V_2 electrically connected across S_1 - S_2 and S_3 - S_6 , with V_3 electrically connected across S_1 - S_3 and S_4 - S_7 , and with V_4 electrically connected across S_1 - S_4 and S_5 - S_8 .

In operation, the control circuit **18** controls the voltage sources V_1 - V_4 by sequentially switching one voltage source on for a specified duration while maintaining the other three voltage sources in their off state for that duration. As illustrated in FIG. **4D**, for example, the control circuit **18** turns on V_1 for the specified duration while maintaining V_2 , V_3 and V_4 in their off states, followed by turning off V_1 and turning on V_2 while maintaining V_3 and V_4 in their off states for the specified duration, followed by turning off V_2 and turning on V_3 while maintaining V_1 and V_4 in their off states for the specified duration, followed by turning off V_3 and turning on V_4 while maintaining V_1 and V_2 in their off states for the specified duration. The control circuit **18** repeats the above process many times to cause ions having mobilities related to the voltage source switching frequency to drift through the various drift tube segments. It will be understood that the voltage applied by V_1 across the first drift tube segment, S_1 , will be different than that applied by V_1 across remaining quadruplets of the drift tube segments, the voltage applied by V_2 across the first two drift tube segments, S_1 - S_2 , will be different than that applied by V_2 across remaining quadruplets of the drift tube segments, and the voltage applied by V_3 across the first three drift tube segments, S_1 - S_3 , will be different than that applied by V_3 across remaining quadruplets of the drift tube segments. Generally, the voltage applied by V_1 across the first drift tube segment, S_1 , will be selected so as to establish an electric field, E_1 , in the ion transmission region $d_t(1)$ that is identical to the electric field E_1 established by V_1 across various quadruplets of the remaining drift tube segments, S_2 - S_N , the voltage applied by V_2 across the first two drift tube segment, S_1 - S_2 , will be selected so as to establish an electric field, E_2 , in the ion transmission region $d_t(1)$, ion

elimination region $d_e(1)$ and ion transmission region $d_t(2)$ that is identical to the electric field E_2 established by V_2 across various quadruplets of the remaining drift tube segments, S_3 - S_N , and the voltage applied by V_3 across the first three drift tube segment, S_1 - S_3 , will be selected so as to establish an electric field, E_3 , in the ion transmission regions $d_t(1)$, $d_t(2)$ and $d_t(3)$ and in the ion elimination regions $d_e(1)$ and $d_e(2)$ that is identical to the electric field E_3 established by V_3 across various quadruplets of the remaining drift tube segments, S_4 - S_N .

The number of electric field activation sources, e.g., voltage sources, used in any particular embodiment, and the manner in which they are electrically connected to the various drift tube segments to operate as described above, is referred to as the phase (ϕ) of the ion mobility spectrometer **10**. In the example of FIGS. **2**, **3** and **4B** in which two voltage sources V_1 and V_2 are used as described above, $\phi=2$ as indicated in the plot **40** of FIG. **4B**. In the example of FIG. **4C** in which three voltage sources V_1 , V_2 and V_3 are used as described above, $\phi=3$ as indicated in the plot **60** of FIG. **4C**. In the example of FIG. **4D** in which four voltage sources V_1 , V_2 , V_3 and V_4 are used as described above, $\phi=4$ as indicated in the plot **70** of FIG. **4D**. It will be noted from FIG. **3** that in a $\phi=2$ system, the fill rate of ions in the various drift tube segments S_1 - S_N , i.e., the duty cycle of the ion mobility spectrometer **10**, is 50%. It can be shown that in a $\phi=3$ system, the duty cycle of the ion mobility spectrometer is 66.67% and in a $\phi=4$ system, the duty cycle of the ion mobility spectrometer is 75%. A general expression for the duty cycle, d , of the ion mobility spectrometer **10** as a function of the phase, ϕ , is thus $d=1-(1/\phi)$.

Referring again to FIG. **3**, the electric fields in the drift tube **14** in a two-phase ($\phi=2$) ion mobility spectrometer **10** are established by two source V_1 and V_2 . The electric fields established in the drift tube **14** by activation of V_1 include an electric drift field E_1 , i.e., an electric field through which ions generated by the ion source drift toward the ion detector **16**, in each of the drift tube segments, i.e., in each of the ion transmission regions d_t , and also in the even-numbered ion elimination regions, $d_e(2)$, $d_e(4)$, etc., and also includes a repulsive electric field, i.e., an electric field that repels and filters away ions traveling in the direction of the electric drift field, in odd-numbered ion elimination regions, $d_e(1)$, $d_e(3)$, $d_e(5)$, etc. Similarly, the electric fields established in the drift tube **14** by activation of V_2 includes an electric drift field E_2 in each of the drift tube segments and also in the odd-numbered ion elimination regions, $d_e(1)$, $d_e(3)$, $d_e(5)$, etc., and also includes a repulsive electric field in even-numbered ion elimination regions, $d_e(2)$, $d_e(4)$, etc.

It can be shown that in three-phase systems ($\phi=3$) that include three electric field activation sources, V_1 - V_3 , such as that illustrated in FIG. **4C**, activation of V_1 establishes a repulsive electric field in the first ion elimination region, $d_e(1)$, and in every following 3rd ion elimination region, $d_e(4)$, $d_e(7)$, $d_e(10)$, etc., and also establishes an electric drift field, E_1 , in all remaining ion elimination regions and in all of the drift tube segments d_t . Activation of V_2 likewise establishes a repulsive electric field in the second ion elimination region, $d_e(2)$, and in every following 3rd ion elimination region, $d_e(5)$, $d_e(8)$, $d_e(11)$, etc., and also establishes an electric drift field, E_2 , in all remaining ion elimination regions and in all of the drift tube segments d_t . Activation of V_3 similarly establishes a repulsive electric field in the third ion elimination region, $d_e(3)$, and in every following 3rd ion elimination region, $d_e(6)$, $d_e(9)$, $d_e(12)$, etc., and also establishes an electric drift field, E_3 , in all remaining ion elimination regions and in all of the drift tube segments d_t .

It can also be shown that in four-phase systems ($\phi=4$) that include four electric field activation sources, V_1-V_4 , such as that illustrated in FIG. 4D, activation of V_1 establishes a repulsive electric field in the first ion elimination region, $d_e(1)$, and in every following 4th ion elimination region, $d_e(5)$, $d_e(9)$, $d_e(13)$, etc., and also establishes an electric drift field, E_1 , in all remaining ion elimination regions and in all of the drift tube segments d_r . Activation of V_2 likewise establishes a repulsive electric field in the second ion elimination region, $d_e(2)$, and in every following 4th ion elimination region, $d_e(6)$, $d_e(10)$, $d_e(14)$, etc., and also establishes an electric drift field, E_2 , in all remaining ion elimination regions and in all of the drift tube segments d_r . Activation of V_3 similarly establishes a repulsive electric field in the third ion elimination region, $d_e(3)$, and in every following 4th ion elimination region, $d_e(7)$, $d_e(11)$, $d_e(15)$, etc., and also establishes an electric drift field, E_3 , in all remaining ion elimination regions and in all of the drift tube segments d_r . Finally, activation of V_4 establishes a repulsive electric field in the fourth ion elimination region, $d_e(4)$, and in every following 4th ion elimination region, $d_e(8)$, $d_e(12)$, $d_e(16)$, etc., and also establishes an electric drift field, E_4 , in all remaining ion elimination regions and in all of the drift tube segments d_r .

From the foregoing examples, a generalized characterization can be made for an M-phase system, i.e., one that includes a number, M, of electric field activation sources, V_1-V_M . In such an M-phase system, the number, M, of electric field activation sources are each be operatively connected to one or more of the plurality of drift tube segments such that, when activated, each establishes a repulsive electric field in at least one of the first M ion elimination regions and in every following Mth ion elimination region, and also establishes an electric drift field in all remaining ion elimination regions and in all of the plurality of cascaded drift tube segments. In operation, the control circuit 18 sequentially activates each of the number, M, of electric field activation sources for a time duration while deactivating the remaining number, M, of electric field activation sources a number of times to thereby cause only ions generated by the ion source that have a predefined ion mobility or range of ion mobilities to traverse the drift tube 14.

Transmission of ions through the various drift tube segments S_1-S_N as just described is only possible if the mobilities of the ions are in resonance with the switching rates of the electric fields applied by the electric field activation sources regardless of the phase of the spectrometer 10. In other words, to transmit ions sequentially through the various drift tube segments S_1-S_N as just described, the ions must have mobilities that allow traversal exactly one drift tube segment in one field application duration. Ions with mobilities that are off resonance either traversing a drift tube segment too quickly or too slowly are eventually eliminated in one of the ion elimination regions d_e . The frequency at which the various electric field activation sources are switched on/off, i.e., the frequency at which the ions have resonant mobilities, is termed the fundamental frequency, f_p .

In the above description of the operation of the ion mobility spectrometer instrument 10, the control circuit 18 is described as being configured to control operation of the electric field activation sources V_1-V_M . Illustratively, the memory unit 20 has instructions stored therein that are executable by the control circuit 18 to control operation of the electric field activation sources V_1-V_M in this manner.

In one alternative embodiment, each of the electric field activation sources V_1-V_M may be programmable to produce, when triggered by an adjacent, e.g., lower-numbered, one of the electric field activation sources V_1-V_M , an electric field

activation pulse of desired duration. In this embodiment, each higher-numbered one of the electric field activation sources V_1-V_M may be programmable to be triggered for activation by deactivation of an adjacent lower-numbered one of the electric field activation sources V_1-V_M . Thus, deactivation of V_1 will trigger activation of V_2 , deactivation of V_2 will trigger activation of V_3 (or V_1 again), and so forth. In this embodiment, the control circuit 18 is configured to control operation of the electric field activation sources V_1-V_M only by activating the first one of the electric field activation sources V_1-V_M .

In another alternative embodiment, each of the electric field activation sources V_1-V_M may be programmable to produce, when triggered by the control circuit 18, an electric field activation pulse having desired duration. In this embodiment, the control circuit 18 controls activation times of each of the electric field activation sources V_1-V_M , and once activated each of the electric field activation sources V_1-V_M is operable to produce a pulse having time duration equal to a programmed pulse duration. In this embodiment, the control circuit 18 is configured to control operation of the electric field activation sources V_1-V_M only by activating at specified times each of the electric field activation sources V_1-V_M .

It will be understood that while the electric field activation sources, V_1-V_M were described as producing DC voltages of programmable duration this disclosure contemplates embodiments in which the electric field activation sources are configured to produce alternatively shaped electric field activation pulses. For example, such alternatively shaped electric field activation pulses may be linear or piece-wise linear pulse shapes, such as triangular or other linear or piece-wise linear shapes, or may be non-linear shapes such as sine-wave, Gaussian or other non-linear shapes. The corresponding electric fields applied in time-dependent fashion to the various segments S_1-S_N of the drift tube 14 as described above may thus be linearly, piece-wise linearly or non-linearly varying. Alternatively still, different ones and/or blocks of the electric field activation sources V_1-V_M may be activated for different durations. Those skilled in the art will recognize that, in general, any one or more of the segments S_1-S_N may be operated for a duration that is different than the duration of operation of any one or more of the remaining ones of the segments S_1-S_N , and that operation of the ion mobility instrument 10 in this manner will result in a multi-dimensional ion mobility spectrometer instrument, i.e., a drift tube having one or more segments in any location relative to the ion inlet and ion outlet that is/are tuned to pass therethrough only ions having a mobility or range of mobilities that is/are different than that/those of one or more of the remaining segments.

Referring now to FIG. 5, a flowchart is shown of one illustrative embodiment of a process 80 for operating the ion mobility spectrometer instrument 10 to act as an ion mobility filter by allowing travel through the drift tube 14 of only ions having a predefined mobility or range of mobilities as described hereinabove with respect to FIGS. 1-4D. The process 80 illustrated in FIG. 5 may be provided, in whole or in part, in the form of instructions that are stored in the memory unit 20 of the control circuit 18 and that are executable by the control circuit 18 to control the ion mobility spectrometer instrument 10 in accordance with the process 80. The process 80 begins at step 82 where the drift time, DT, through the drift tube 14 is determined for the sample component of interest. This may be done, for example, by first operating the ion drift tube 14 in a conventional manner to determine the drift time, DT, of the sample component of interest, although other conventional techniques may be used at step 82 to determine the drift time, DT, of the sample component of interest. For example, conventional ion mobility spectrometer configura-

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tions could be used to determine a drift time, or a drift time could be retrieved from literature, although in either case, instrument operating parameters used to determine such drift times, e.g., buffer gas pressure, operating temperature, drift tube length, etc., would have to be taken into account to determine corresponding operating parameters for those of the ion mobility spectrometer 10. Referring to FIG. 6, a plot 94 of ion intensity vs. drift time is shown illustrating the drift time of ions of the sodiated monomer $[M+Na]^+$ form of the simple oligosaccharide isomer raffinose through one particular embodiment of the ion mobility spectrometer 10. In this embodiment, the drift time, DT, of raffinose through the drift tube 14 is approximately 15.8 ms.

Following step 82, the pulse width, PW, of the number of electric field activation sources V_1-V_M used in the ion mobility spectrometer instrument 10 is computed at step 84. The pulse width, PW, is the duration of the electric field that will be applied by each of the electric field activation sources V_1-V_M to pass the sample component of interest, e.g., raffinose, through each segment. In order to pass the sample component of interest through a drift tube 14 having N segments, the pulse width, PW, must therefore satisfy the relationship $PW=DT/N$.

Following step 84, the shape of the pulse width is selected at step 86, and thereafter at step 88 the peak voltage of the electric field activation sources V_1-V_M is selected. The process 80 advances from step 88 to step 90, and simultaneously with step 90 the ion source voltage supply, V_{IS} , is controlled at step 92 in a manner that causes the ion source 12 to produce ions. The ions produced at step 92 may be produced continuously or may instead be produced discretely as described hereinabove. In any case, the control circuit 18 is operable at step 90 to control the electric field activation sources V_1-V_M , as described hereinabove, to sequentially apply electric fields having the selected shape, duration and peak field strength to the various drift tube segments, S_1-S_N as described hereinabove by example with reference to FIGS. 2-4D. Steps 90 and 92 may be repeated continuously or a finite number of times to thereby operate the ion mobility spectrometer instrument 10 as a continuous or discrete ion mobility filter. For the raffinose sample illustrated in FIG. 6, the pulse width, PW, of the electric field activation sources V_1-V_M in the ion mobility spectrometer instrument 10 of FIG. 1, in which the drift tube 14 is constructed of 20 drift tube segments, S_1-S_{20} , and one ion focusing filter positioned approximately mid way between the ion inlet and ion outlet of the drift tube 14, is approximately 500 microseconds, which corresponds to an electric field activation source switching frequency of approximately 2.0 kHz. It will be understood that steps 82-88 are not required to be executed in the illustrated order, and that one or more of these steps may alternatively be interchanged with one or more other of these steps.

In addition to operation of the ion mobility spectrometer instrument 10 as an ion mobility filter as illustrated and described herein, the ion mobility spectrometer instrument 10 may also be operated in a manner that transmits ions at overtone frequencies of the fundamental frequency, f_p , as described briefly above. Referring to FIG. 7, for example, a flowchart of an illustrative process 100 for operating the ion mobility spectrometer 10 by sweeping the pulse widths, PW, of the electric field activation sources, V_1-V_M , over a range of pulse width durations. In addition to producing a fundamental ion intensity peak that corresponds to ion intensity peak resulting from the process 80 of FIG. 5, the process 100 further produces overtone ion intensity peaks that may be analyzed in the frequency domain to reveal additional characteristics of the sample component of interest. The process

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100 illustrated in FIG. 7 may be provided, in whole or in part, in the form of instructions that are stored in the memory unit 20 of the control circuit 18 and that are executable by the control circuit 18 to control the ion mobility spectrometer instrument 10 in accordance with the process 100.

The process 100 begins at step 102 where initial and final pulse width durations, PW_I and PW_F respectively, and a ramp rate, R (or step size), are selected. Illustratively, the initial pulse width duration, PW_I , may be selected to be slightly longer than necessary to produce the fundamental ion intensity peak so that the resulting ion intensity vs. frequency spectrum begins approximately at the fundamental peak. Illustratively, the final pulse width duration, PW_F , may be selected to be a frequency beyond which no useful information is expected to occur, or beyond which no ion intensity information is sought. In any case, the ramp rate, R, and/or frequency step size between the initial and final pulse width durations, PW_I and PW_F , will typically be selected to provide sufficient time at each pulse width duration to extract useful information from the ion mobility spectrometer instrument 10. Such information can be of the form of ion collision cross sections, Ω , which can be derived from OMS measurements according to the following equation:

$$\Omega = \frac{(18\pi)^{1/2}}{16} \frac{ze}{(k_b T)^{1/2}} \left[\frac{1}{m_1} + \frac{1}{m_B} \right]^{1/2} \frac{E[\phi(h-1)+1] 760}{f(d_i + d_e)} \frac{T}{P} \frac{1}{273.2 N}$$

where ze is ion charge, k_b is Boltzmann's constant, P and T correspond to the buffer gas pressure and temperature respectively, N is the neutral number density, E is the electric field, f is the field application frequency, the quantity $\phi(h-1)+1$ is the harmonic number or overtone number, m_1 and m_B correspond to the mass of the ion and the mass of the buffer gas, respectively, and all other variables have been defined herein.

Following step 102, the shape of the pulse width is selected at step 104, and thereafter at step 106 the peak voltage of the electric field activation sources V_1-V_M is selected. The process 100 advances from step 106 to step 108, and simultaneously with step 108 the ion source voltage supply, V_{IS} , is controlled at step 110 in a manner that causes the ion source 12 to produce ions. The ions produced at step 110 may be produced continuously or may instead be produced discretely as described hereinabove, although if produced discretely a timing mechanism will typically be required to trigger new supplies of ions coincident with the changing of the pulse width durations. In any case, the control circuit 18 is operable at step 108 to control the electric field activation sources V_1-V_M , as described hereinabove, to apply electric fields having the selected shape and peak field strength to the drift tube segments, S_1-S_N while sweeping the pulse width duration, PW, between PW_I and PW_F at the selected ramp rate and/or step size. It will be understood that steps 102-106 are not required to be executed in the illustrated order, and that one or more of these steps may alternatively be interchanged with one or more other of these steps.

While not specifically illustrated in FIG. 7 as a step in the process 100, ion detection signals produced by the ion detector 16 may be processed by the control circuit 18 and converted to the frequency domain in a conventional manner for further analysis and/or observation. For the raffinose sample illustrated in FIG. 6, for example, sweeping the pulse width, PW, of the electric field activation sources V_1-V_M in the ion mobility spectrometer instrument 10 of FIG. 1 between approximately 10 milliseconds down to approximately 22 micro-seconds yields the ion intensity vs. frequency spectrum

112 illustrated in FIG. 8. Illustratively, the 3rd overtone produces the most highly resolved ion intensity peak.

Generally, the overtones produced by frequency sweeps of the type illustrated in FIG. 8 will be defined, at least in part, by the phase (ϕ) of the ion mobility spectrometer 100. Referring to FIG. 9, for example, a number of plots 120, 122, 124, 126 and 128 are shown of frequency spectrums of raffinose in which the phase, ϕ , of the ion mobility spectrometer 10 correspondingly increases. In all cases, the electric field activation sources, V_1 - V_M were configured to operate as described hereinabove with respect to FIGS. 2-4D. In the plot 120, $\phi=2$, and the associated frequency spectrum includes an ion peak at the fundamental frequency, f_β and additional peaks at the third and fifth overtones. In the plot 122, $\phi=3$, and the associated frequency spectrum includes an ion peak at the fundamental frequency, f_β and additional peaks at the fourth and seventh overtones. In the plots 124, 126 and 128, $\phi=4, 5$ and 6 respectively. The frequency spectrum 124 includes an ion peak at the fundamental frequency, f_β and additional peaks at the fifth, ninth and thirteenth overtones, the frequency spectrum 126 includes an ion peak at the fundamental frequency, f_β and additional peaks at the sixth, eleventh and sixteenth overtones, and the frequency spectrum 128 includes an ion peak at the fundamental frequency, f_β and additional peaks at the seventh, thirteenth and nineteenth overtones. It should be noted that as the phase of the ion mobility spectrometer 10 is increased, secondary overtones increasing appear between the fundamental peak, f_β and the first expected overtone. These secondary overtones correspond to intermediate harmonic frequencies, i.e., those between the overtone frequencies, and may carry additional ion information.

Generally, the overtones that should be expected to be observed in embodiments of the ion mobility spectrometer 10 operated with uniform, constant electric fields in the various drift tube segments, S_1 - S_N as described hereinabove, are given by the equation $H=\phi(h-1)+1$, $h=1, 2, 3, \dots$, where H is a harmonic number, ϕ is the phase of the ion mobility spectrometer 10, and h is an integer. Thus, for $\phi=2$, $H=1, 3, 5, 7, \dots$, for $\phi=3$, $H=1, 4, 7, 10, \dots$, for $\phi=4$, $H=1, 5, 9, 13, \dots$, for $\phi=5$, $H=1, 6, 11, 16, \dots$, and for $\phi=6$, $H=1, 7, 13, 19, \dots$, etc.

The resolving power, R, of the ion mobility spectrometer instrument 10 is defined by the equation $R_{OMS}=f/\Delta f$, where f is the frequency at which maximum ion intensity of transmitted and Δf is the width of the peak at half maximum. Generally, it is observed that the resolving power, R, of the ion mobility spectrometer instrument 10 increases with increasing overtone number, H. The resolving power, R, of the ion mobility spectrometer instrument 10 is also influenced by the total number, N, of drift tube segments, S_1 - S_N , used. Referring to FIG. 10, for example, a number of plots 130 are shown illustrating the shapes of fundamental-frequency, ion intensity peaks for a four-phase ($\phi=4$) ion mobility spectrometer instrument 10 in which the total number of drift tube segments, N, is varied between 11 and 43 as indicated on the left portion of FIG. 10. The plots 130 were generated from a sample of the sodiated monomer $[M+Na]^+$ form of the simple oligosaccharide isomer melezitose using the ion mobility instrument 10 illustrated and described herein. As illustrated in FIG. 10, whereas the peak intensities do not change significantly, the widths, Δf , of the peaks at half maximum decrease as N increases. For example, Δf_{11} , corresponding to the width of the N=11 peak at half maximum, is approximately 1600 Hz, whereas Δf_{43} , corresponding to the width of the N=43 peak at half maximum, is approximately 345 Hz. The ratio $f/\Delta f$, and thus, R_{OMS} , accordingly increases as the number, N, of drift tube segments S_1 - S_N increases.

In a conventional ion mobility spectrometer; that is to say, an ion mobility spectrometer in which a single electric field is applied across the length of the drift tube, the resolving power is generally understood to follow the relationship $R_{IMS}=\text{SQRT}[(E*e*L)/(16*k_b*T*\ln 2)]$, where E is the applied electric field, e is the elementary charge value, L is the length of the drift tube, k_b is Boltzmann's constant, and T is the temperature of the drift tube.

In the ion mobility instruments 10 illustrated and described herein, the overall resolving power, R_{OMS} , is a function of R_{IMS} and is also a function of the total number, n, of drift tube segments, S_1 - S_N , the phase number, ϕ , of the applied electric field and the harmonic number, m. Illustratively, R_{OMS} is given by the equations:

$$R_{OMS} = \frac{1}{1 - \left[1 - \frac{C}{R_{IMS}} \right] \left[\frac{mn - \left[\phi - 1 - \frac{l_e}{l_t + l_e} \right]}{mn} \right]}$$

or

$$R_{OMS} = \frac{1}{\frac{C}{R_{IMS}} \left[1 - \frac{\phi - 1 - \frac{l_e}{l_t + l_e}}{mn} \right] + \frac{\phi - 1 - \frac{l_e}{l_t + l_e}}{mn}}$$

where C is a constant and all other variables have been defined herein. It should be noted that the resolving power, R_{OMS} , generally increases with increasing n and also with increasing m, and the resolving power, R_{OMS} , decreases with increasing ϕ . It should also be noted that in the limit of high R_{IMS} , the first term in the denominator of the foregoing equation approaches zero and the foregoing equation reduces to $R_{OMS}=m*n/[\phi-1-I_e/(I_t+I_e)]$.

It can further be shown that the resolving power of any peak in an OMS distribution can be obtained by replacing the harmonic number, m, in the above equation with $(\phi q+1)$, and then by multiplying the entire equation by the quantity $(\phi/k+1)$, where k is an overtone series index having limits of 0 to $\phi-1$, and q is an overtone peak index having limits of 0 to infinity.

Referring now to FIG. 11, plots of ion intensity vs. frequency are shown to illustrate one implementation of the enhanced resolving power of the ion mobility spectrometer 10 at overtone frequencies. The plots of FIG. 11 are frequency-domain plots that were generated with a two-phase ($\phi=2$) configuration of the ion mobility instrument 10. In the plots of FIG. 11, only the overtone peaks 3 and 5 are shown along with the peak at the fundamental frequency, 1. The plot 140 represents a frequency-domain plot of raffinose, the plot 142 represents a frequency-domain plot of the sodiated monomer $[M+Na]^+$ form of the simple oligosaccharide isomer melezitose, and the plot 144 represents a frequency-domain plot of a 3:1 raffinose:melezitose mixture. The frequency spectrum of the plot 144 illustrates that whereas the raffinose and melezitose are indistinguishable at the fundamental frequency, they are partially resolved at the third overtone, 146₁ and 146₂, and are fully resolved at the fifth overtone, 148₁ and 148₂. The harmonic/overtone analysis described in this disclosure, e.g., the pulse width duration sweeping process 100 illustrated in FIG. 7, may therefore be used to accurately identify a sample component of interest, and/or to distinguish a sample component of interest from another sample component.

The raffinose and melezitose mixture can alternatively be resolved at or near their fundamental frequencies if allowed to

drift along a sufficiently long drift distance. This may be accomplished, for example, by employing the ion mobility spectrometer operating technique illustrated in FIG. 5 in an ion mobility spectrometer having a circular or so-called cyclotron geometry, as illustrated and described in co-pending PCT Publication No. WO 2008/028159 A2, filed Aug. 1, 2007, the disclosure of which has been incorporated herein by reference. Referring now to FIG. 12A, plots 150, 152 and 154 are shown of such an experiment in which raffinose and melezitose were separated in a circular or cyclotron geometry ion mobility spectrometer 160 having a cyclotron portion constructed such that the drift tube, made up of cascaded ion transmission sections (d_t) and ion elimination sections (d_e) as illustrated and described hereinabove with respect to FIGS. 2-4, defines a closed and continuous ion travel path.

Referring to FIG. 12B, one illustrative embodiment of such a cyclotron ion mobility spectrometer 160 is shown. In the illustrated embodiment, the drift tube is made up of four conventional ion funnels, F2-F5 joined at each end by curved drift tube segments D1-D4. Two of the curved drift tube segments D1 and D4 have Y-shaped geometries. In addition to forming one drift tube segment of the cyclotron portion of the drift tube, the segment D1 selectively direct ions generated by an ion source, e.g., an electrospray ion source, ESI, coupled to D1 via a funnel/gate arrangement, F1/G1, into the cyclotron portion via an ion entrance drift tube section. In addition to forming another drift tube segment of the cyclotron portion of the drift tube, the segment D4 selectively directs ions via an ion exit drift tube segment from the cyclotron portion and through a cascaded funnel, F6, and drift tube segment, D5 to an ion detector, DET. It will be understood that the embodiment of the cyclotron ion mobility spectrometer 160 shown in FIG. 12B is merely illustrative, and that the cyclotron portion of the spectrometer 160 may alternatively include more or fewer drift tube segments than the eight segments (D1-D4 and F2-F5) shown. It will further be understood that while the ion entrance drift tube segment is shown coupled between the ion source (ESI-F1/G1) and the drift tube segment D1, it may alternatively be coupled to a different one of the drift tube segments. Likewise, while the ion exit drift tube segment is shown coupled between the drift tube segment D4 and the funnel segment F6, it may alternatively be coupled to a different one of the drift tube segments. Moreover, while the ion entrance and exit drift tube segments are shown coupled to different ones of the drift tube segments, they may alternatively be coupled to a common one of the drift tube segments such that ions are admitted to and extracted from the same drift tube segment. It will further be understood that more or fewer drift tube segments and/or ion funnels may be positioned between the ion outlet of the ion exit drift tube segment of D4 and the ion detector, DET. In one embodiment, for example, the ion detector, DET, may be coupled directly to the ion outlet of the ion exit drift tube segment of D4, and in other embodiments any number of drift tube segments and/or ion funnels may be positioned between the ion exit drift tube segment of D4 and the ion detector, DET. In any case, the ion detector, DET, may be conventional and is configured to detect ions exiting the ion drift tube segment portion of D4 and produce corresponding ion detection signals. The memory of the control circuit illustratively includes instructions stored therein that are executable by the control circuit to process the ion detection signals in a conventional manner to determine ion mobility spectral information therefrom.

Although not specifically shown in FIG. 12B for ease of illustration and understanding, it will be understood that a number, M, of electric field activation sources are connected to the various drift tube sections of the cyclotron ion mobility

spectrometer 160, a voltage source, V_{IS} , is connected to the ion source (ESI-F1/G1), a source of buffer gas is fluidly coupled to the drift tube, and a control circuit is electrically connected to one or more of the M electric field activation sources, voltage source, V_{IS} and ion detector, all as illustrated and described herein with respect to FIGS. 1-4. The control circuit, as described hereinabove, illustratively includes a memory having instructions stored therein that are executable by the control circuit to control operation of the cyclotron ion mobility spectrometer 160. The various voltage sources and control circuitry, as illustrated and described above, are thus omitted from FIG. 12B for brevity. The number, M, may be any positive integer greater than 2, and general operation of the number, M, of electric field activation sources is illustrated and described herein with respect to FIGS. 1-4.

The ion source is illustrated in FIG. 12B as an electrospray ion source fluidly coupled to an ion funnel/gate, F1/G1, although the ion source may alternatively be or include any conventional ion source that may be controlled, via the voltage source, V_{IS} , by the control circuit according to instructions stored in the memory that are executable by the control circuit to selectively produce ions in a single, e.g., one-shot, periodic, e.g., pulsed, and/or continuous fashion as is known in the art. The ion gate, G1, of the ion source is illustratively positioned at an ion inlet of the ion entrance drift tube segment of D1 such that the ion source is coupled to the inlet of the ion entrance drift tube segment of D1, and an ion outlet of the ion entrance drift tube segment of D1 is coupled to the cyclotron portion of D1. The ion exit drift tube segment of D4 likewise has an ion inlet that is coupled to the cyclotron portion of D4, and an ion outlet coupled to the inlet of the ion funnel F6.

The drift tube of the cyclotron ion mobility spectrometer 160 illustrated in FIG. 12B is, like the embodiments illustrated in FIGS. 1-4, partitioned into multiple cascaded drift tube segments D1-D4 and F2-F5. In one embodiment, each of the drift tube segments D1-D4 and F2-F5 has an ion inlet at one end and an ion outlet at an opposite end, and an ion elimination region is defined between the ion outlet and the ion inlet of each adjacent drift tube segment as illustrated and described hereinabove with respect to FIGS. 1-4. The ion outlet of a last one of the drift tube segments, e.g., F5, is coupled to the ion inlet of the first one of the drift tube segments, e.g., D1, such that the drift tube defines therein a closed and continuous ion travel path which, in the illustrated embodiment, extends clockwise within D1-D4 and F2-F5. Illustratively, as just described, the ion elimination regions may be defined between the ion outlets and ion inlets of each of the drift tube segments D1-D4 and F2-F5, such as illustrated in FIG. 2, and in this embodiment, each of D1-D4 and F2-F5 is an ion transmission section, d_t , and the ion elimination regions, d_e , are defined between adjacent ones of D1-D4 and F2-F5. In alternative embodiments, the lengths of the funnel sections F2-F5 may be made shorter than the lengths of the drift tube sections D1-D4, and in this embodiment, the drift tube sections D1-D4 are the ion transmission sections, d_t , and the funnel sections F2-F5 are the ion elimination sections, d_e . In other alternative embodiments, the lengths of the drift tube sections D1-D4 may be made shorter than the lengths of the funnel sections F2-F5, and in this embodiment the funnel sections F2-F5 are the ion transmission sections, d_t , and the drift tube sections D1-D4 are the ion elimination sections.

An ion gate arrangement is positioned within the drift tube segment D4, and is configured to control ion travel through the cyclotron and ion exit drift tube portions of D4. The ion gate arrangement is generally responsive to one set of one or

more ion gate signals produced by the control circuit to direct ions moving through the drift tubes D1-D3 and F2-F5 through the cyclotron drift tube portion of D4 such that the ions may continue to travel around the cyclotron portion of the spectrometer 160 defined by D1-D4 and F2-F5 while also blocking the ions from entering the ion exit drift tube segment portion of D4 such that ions moving through the cyclotron drift tube segment portion of D4 cannot advance to the ion detector, DET. The ion gate arrangement is also generally responsive to another set of the one or more ion gate signals produced by the control circuit to direct ions moving through the drift tubes D1-D3 and F2-F5 through the ion exit drift tube segment portion of D4 while also blocking ions from moving completely through the drift tube segment portion of D4 such that the ions travelling around the cyclotron portion of the spectrometer 160 defined by D1-D4 and F2-F5 do not advance completely through the drift tube segment portion of D4 and instead advance through the ion exit drift tube segment portion of D4 to the ion detector, DET. The ion gate arrangement is thus responsive to the one set of one or more ion gate signals to direct ions traveling through the cyclotron portion of the spectrometer 160 to the next drift tube section, e.g., F5, in the cyclotron portion of the spectrometer 160, and to the other set of one or more ion gate signals to extract the ions traveling through the cyclotron portion of the spectrometer 160 by directing the ions through the ion exit drift tube section of D4 toward the ion detector, DET. Illustratively, the ion mobility spectrometer 160 includes one or more additional voltage sources electrically connected to the ion gate arrangement, and the control circuit is thus generally operable to control the ion gate arrangement to direct ions moving through, and or blocking ions from moving through, the ion gate arrangement by controlling operation of such voltage sources in a conventional manner. The one or more additional voltage sources may be conventional voltage sources included within, or in addition to, the number, M, of electric field activation sources. Illustratively, the memory of the control circuit has instructions stored therein that are executable by the control circuit to control operation of the ion gate arrangement just described by controlling operation of the one or more additional voltage sources.

In the embodiment illustrated in FIG. 12B, the ion gate arrangement just described is implemented in the form of two separate ion gates; G2a positioned in, or at the ion inlet of, the ion exit drift tube segment portion of D4, and G2b positioned in the cyclotron drift tube segment portion of D4. In this embodiment, the one set of the one or more ion gate signals described above may include a first ion gate signal to which the ion gate G2b is responsive to allow ions to pass therethrough and a second ion gate signal to which the ion gate G2a is responsive to block ions from passing therethrough, and the other set of the one or more ion gate signals described above may include a third ion gate signal to which the ion gate G2b is responsive to block ions from passing therethrough and a fourth ion gate signal to which the ion gate G2a is responsive to allow ions to pass therethrough. Those skilled in the art will recognize that the ion gate arrangement may include more or fewer ion gates variously positioned relative to D4 and controllable by the control circuit or other electronic controller to direct ions through the cyclotron drift tube segment portion of D4 while blocking ions from entering the ion exit drift tube segment portion of D4, and to alternatively direct ions through the ion exit drift tube segment portion of D4 while blocking ions from traveling completely through the cyclotron drift tube segment portion of D4.

In the embodiment illustrated in FIG. 12B, ions are introduced into the cyclotron portion (e.g., D1-D4 and F2-F5) of

the spectrometer 160 via control of the gate, G1, such that ions enter the cyclotron portion via the ion entrance drift tube segment portion of D1. With the ion gates G2a and G2b set that G2b allows ions to pass therethrough and G2a blocks ions from passing therethrough, ions are then directed around the cyclotron portion of the spectrometer 160 via sequential pulses applied by the number, M, of electric field activation sources to the various cyclotron sections D1-D4 and F2-F5 which create sequential electric fields in the cyclotron sections D1-D4 and F2-F5 at a desired frequency or pulse rate as described hereinabove with respect to FIG. 5 to thereby cause only ions supplied by the ion source that have a predefined ion mobility or range of ion mobilities defined by the frequency or pulse rate to travel through the cyclotron portion of the spectrometer 160. Ions may be so directed around the cyclotron portion of the spectrometer 160 any number of times, and can then be extracted from the cyclotron portion of the spectrometer 160 by controlling the ion gate G2b to block ions from passing therethrough and controlling the ion gate G2a to allow ions to pass therethrough to the ion detector, DET. The number, M, of electric field activation sources may include two or more sources as illustrated and described hereinabove with respect to FIGS. 1-4, and the electric fields created within the various drift tube segments D1-D4 and F2-F5 of the cyclotron portion of the spectrometer 160 by the number, M, of The electric field activation sources may be constant, linear, non-linear or have any desired shape or profile, also as described hereinabove. Illustratively, the electric fields created in F6 and D5 when extracting ions from the cyclotron portion of the spectrometer 160 are constant, although these fields may alternatively also be linear, non-linear or have any desired shape or profile.

Illustratively, the memory of the control circuit has instructions stored therein that are executable by the control circuit to control the ion source voltage source, V_{IS} , to produce ions, to control the ion gate arrangement to direct ions around the cyclotron portion of the spectrometer 160 while blocking ions from the ion detector, and to sequentially activate the number, M, of electric field activation sources for a predefined time duration while deactivating the remaining number, M, of electric field activation sources to thereby cause only ions supplied by the ion source that have a predefined ion mobility or range of ion mobilities defined by the predefined time duration, e.g., the activation frequency or pulse rate of the number, M, of electric field activation sources, to travel through the cyclotron portion of the spectrometer 160 and, after the ions have traveled around the cyclotron portion of the spectrometer 160 a selected number of times, to control the ion gate arrangement to draw ions moving through the cyclotron portion of the spectrometer 160 into the ion exit drift tube segment and toward the ion detector. As described hereinabove, the mobility or range of mobilities of ions resulting from operation of the spectrometer 160 as just described is/are resonant with a fundamental frequency, f_p , of operation of the electric field activation sources, V_1-V_M . Alternatively or additionally, as described hereinabove with respect to FIGS. 7-9, the instructions stored in the memory of the control circuit may include instructions that are executable by the control circuit to conduct OMS analysis, as this term has been defined hereinabove, by controlling the ion source voltage source, V_{IS} , and the number, M, of electric field activation sources to sweep the activation frequency or pulse rate of the number, M, of electric field activation sources over a predefined set of activation frequencies or pulse rates to thereby cause ions within the drift tube that have ion mobilities resonant with one or more overtones, e.g., harmonic frequencies, of operation of the electric field activation sources, V_1-V_M .

and/or that have ion mobilities resonant with fundamental frequencies of the activation frequencies or pulse rates, i.e., activation times, of the electric field activation sources, V_1-V_M , for each of the discrete activation frequencies or pulse rates over the predefined set of activation frequencies or pulse rates, to travel through the spectrometer 160.

Referring again to FIG. 12a, the plot 150 represents the raffinose, R, and melezitose, M, ion peaks after $1\frac{3}{4}$ cycles of ion travel through the cyclotron portion of the instrument 160. The plot 152 similarly represents the raffinose, R, and melezitose, M, ion peaks after $3\frac{3}{4}$ cycles, and the plot 154 represents the raffinose, R, and melezitose, M, ion peaks after $6\frac{3}{4}$ cycles. While $1\frac{3}{4}$ cycles is sufficient to isolate each of the raffinose and melezitose ions, it is evident from FIG. 12a that the two ion peaks separate further as the number of cycles increases.

Referring now to FIG. 14, a flowchart is shown illustrating a process 250 for operating the ion mobility spectrometer 160 of FIG. 12B to first pre-fill the cyclotron portion of the spectrometer 160 with ions generated by the ion source, and to then operate the spectrometer 160 as described herein to cause only ions supplied by the ion source that have a predefined ion mobility or range of ion mobilities defined by the activation frequency or pulse rate of the number, M, of electric field activation sources, to travel through the spectrometer 160 and/or to sweep the activation frequency or pulse rate of the number, M, of electric field activation sources over a predefined set of activation frequencies or pulse rates to thereby cause ions within the drift tube that have ion mobilities resonant with one or more overtone, e.g., harmonic, frequencies of operation of the electric field activation source, V_1-V_M , and/or that have ion mobilities resonant with fundamental frequencies of the activation frequencies or pulse rates, i.e., activation times, of the electric field activation sources, V_1-V_M , for each of the discrete activation frequencies or pulse rates over the predefined set of activation frequencies or pulse rates, to travel through the spectrometer 160. This process provides for a significant increase in sensitivity and resolution compared with operating the ion mobility spectrometer 160 with single pulses or packets of ions produced by the ion source as described above. Illustratively, the process 250 is stored in the memory 20 of the control circuit 18 in the form of instructions that are executable by the control circuit 18 to control operation of the ion mobility spectrometer 160. The process 250 begins at step 252 where the operational settings of the number, M, of electric field activation sources are defined, and a value of an integer, N, is set. In embodiments in which the spectrometer 160 will be operated to produce ions having a mobility or range of mobilities that is/are resonant with only a fundamental frequency, f_p , of operation of the electric field activation sources, V_1-V_M , step 252 may include, for example, the steps 82-88 of the process 80 of FIG. 5. In other embodiments in which the spectrometer 160 will be operated to produce ions having ion mobilities resonant with one or more overtones, e.g., harmonic frequencies, of operation of the electric field activation sources, V_1-V_M , step 252 may include, for example, the steps 102-106 of the process 100 of FIG. 7. In any case, the value of the integer, N, corresponds to the number of times ions will travel around the cyclotron portion of the drift tube defined by the ion mobility spectrometer 160.

Following step 252, the process 250 advances to step 254 where the control circuit 18 is operable to control the ion source, e.g., ES1-F1/G1, to produce ions and to open the ion gate G1, and to control the ion gate arrangement to open the ion gate G2b and close the ion gate, G2a. By opening the ion gate G1, ions generated by the ion source may thus enter the ion entrance drift tube portion of the drift tube segment D1.

By opening the ion gate G2b and closing the ion gate G2a, the generated ions will be confined to the cyclotron portion of the drift tube (D1-D4 and F2-F5) and will be blocked from advancing to the ion detector, DET, as described hereinabove. Thereafter at step 256, the control circuit 18 is operable to control the electric field activation sources, V_1-V_M , to allow ions produced by the ion source to fill the cyclotron portion of the drift tube, e.g., D1-D4 and F2-F5. In one embodiment, step 256 comprises controlling the electric field activation sources, V_1-V_M , in a conventional manner to allow ions of different mobilities to enter and advance through the cyclotron portion of the drift tube D1-D4 and F2-F5, i.e., to pass all ions generated by the ion source from each of the plurality of drift tube segments D1-D4 and F2-F5 to the next. This may be done, for example, by simultaneously and identically activating all of the electric field activation sources, V_1-V_M , such that a continuous, constant electric field is established in all of the ion transmission sections, d_r , and ion elimination sections, d_e , of each of the adjacent drift tube segments. Those skilled in the art will recognize other techniques for controlling the various electric field activation sources, V_1-V_M , such that ions generated by the ion source may enter and fill the cyclotron portion of the drift tube D1-D4 and F2-F5, and such other techniques are contemplated by this disclosure.

Following step 256, the process 250 advances to step 258 where the control circuit 18 is operable to control the ion source to stop producing ions and to close the ion gate G1 so that no new ions from the ion source enter the cyclotron portion of the drift tube. Thereafter at step 260, the control circuit 18 is operable to set a counter, L, equal to 1, and thereafter at step 262 the control circuit 18 is operable to control the electric field activation sources, V_1-V_M , to according to source settings, e.g., those determined at step 252, to direct ions one revolution around the cyclotron portion of the drift tube, i.e., one complete path about the closed cyclotron defined by D1-D4 and F2-F5. Illustratively, the control circuit 18 is operable at step 262 to control the electric field activation sources, V_1-V_M , by sequentially activating, as described hereinabove with respect to FIG. 5, one or more of the number, M, of electric field activation sources V_1-V_M for the time duration, i.e., pulse width for activation of the sources V_1-V_M as determined at step 252, while deactivating the remaining number, M, of electric field activation sources to thereby cause only ions within the drift tube (D1-D4 and F2-F5) that have a predefined ion mobility or range of ion mobilities defined by the time duration to travel through the drift tube. In this embodiment, ions having the predefined ion mobility or range of ion mobilities travel, under such control at step 262, one revolution around the drift tube defined by D1-D4 and F2-F5. Thereafter at step 264, the control circuit 18 is operable to determine whether the counter, L, is equal to the number N. If not, the process 250 advances to step 266 where the counter, L, is incremented by 1 and the process 250 then loops back to again execute step 262. If, at step 264, the control circuit 18 determines that $L=N$, then the ions have traveled around the cyclotron portion of the drift tube (D1-D4 and F2-F5) the selected number of times, N, and the process 250 advances to step 268.

At step 268, the control circuit 18 is operable to control the ion gate arrangement to close the ion gate G2b and open the ion gate G2a, and to control the electric field activation sources, V_1-V_M , thereafter at step 270 to sequentially direct ions in the cyclotron portion of the drift tube to the ion detector, DET. With the ion gate G2b closed and the ion gate G2a open, sequential operation of the electric field activation sources V_1-V_M in the manner just described with respect to step 262 is thus carried out at step 270, in addition to sequen-

tially activating electric fields within F6 and D5 in like manner, to sequentially direct the ions in the cyclotron portion of the drift tube that have the predefined ion mobilities or range of ion mobilities through the ion exit drift tube segment of D4, through F6 and D5, and to the ion detector, DET. Optionally, the process 250 may include an extra step 272, executed following step 270, in which the control circuit 18 is operable to execute steps 254-270 until the pulse width durations, i.e., the "time durations" of activations of the electric field activation sources, V_1 - V_{M^p} , have been swept through a range of pulse width durations between an initial pulse width duration, PW, and a final pulse width duration, PW_F . In embodiments which include step 272, step 252 will of course include a determination of PW_I and PW_F as illustrated in the process 100 of FIG. 7. Generally, PW_I and PW_F will be selected to produce one or more overtones, i.e., harmonic frequencies of which the predefined ion mobilities or range of ion mobilities are resonant, and/or to produce ions that have ion mobilities resonant with fundamental frequencies of the activation frequencies or pulse rates, i.e., activation times, of the electric field activation sources, V_1 - V_{M^p} , for each of the discrete activation frequencies or pulse rates over and between PW_I and PW_F , as described hereinabove.

Referring now to FIG. 15, a flowchart is shown illustrating another process 300 for operating the ion mobility spectrometer 160 of FIG. 12B to selectively add ions from the ion source to the cyclotron portion of the spectrometer 160 during each of a first number of revolutions of ions around the cyclotron portion of the drift tube of the ion mobility spectrometer 160 in which only ions that have a predefined ion mobility or range of ion mobilities sequentially advance through the cyclotron portion of the drift tube, and to then stop adding ions and operate the spectrometer 160 as described herein to cause only ions in the cyclotron portion of the drift tube that have the predefined ion mobility or range of ion mobilities defined by the activation frequency or pulse rate of the number, M, of electric field activation sources, to travel around the cyclotron portion of the drift tube a second number of times before being directed to the ion detector. Optionally, this process may also be done while also sweeping the activation frequency or pulse rate of the number, M, of electric field activation sources over a predefined set of activation frequencies or pulse rates to thereby cause ions within the drift tube that have ion mobilities resonant with one or more overtone, e.g., harmonic, frequencies of operation of the electric field activation source, V_1 - V_{M^p} , and/or to cause ions that have ion mobilities resonant with fundamental frequencies of the activation frequencies or pulse rates, i.e., activation times, of the electric field activation sources, V_1 - V_{M^p} , for each of a number of discrete activation frequencies over the predefined set of activation frequencies or pulse rates, to travel through the spectrometer 160. In any case, the process 300 is illustratively stored in the memory 20 of the control circuit 18 in the form of instructions that are executable by the control circuit 18 to control operation of the ion mobility spectrometer 160.

The process 300 begins at step 302 where the operational settings of the number, M, of electric field activation sources are defined, and values of two integers, N and M are set. In embodiments in which the spectrometer 160 will be operated to produce ions having a mobility or range of mobilities that is/are resonant with only a fundamental frequency, f_p , of operation of the electric field activation sources step 252 may include, for example, the steps 82-88 of the process 80 of FIG. 5. In other embodiments in which the spectrometer 160 will be operated to produce ions having ion mobilities resonant with one or more overtones, e.g., harmonic frequencies, of operation of the electric field activation sources step 252 may

include, for example, the steps 102-106 of the process 100 of FIG. 7. In any case, the integer M set at step 302 is different from, and should not be confused with, the number, M, of electric field activation sources.

Following step 302, the process 300 advances to step 304 where the control circuit 18 is operable to control the ion source, e.g., ES1-F1/G1, to produce ions and to control the ion gate arrangement to open the ion gate G2b and close the ion gate, G2a. By opening the ion gate G1, ions generated by the ion source may thus enter the ion entrance drift tube portion of the drift tube segment D1. By opening the ion gate G2b and closing the ion gate G2a, ions introduced into the spectrometer 160 via the ion source will be confined to the cyclotron portion of the drift tube and will be blocked from advancing to the ion detector, DET, as described hereinabove. Thereafter at step 306, the control circuit 18 is operable to set a counter, L, equal to 1.

Following step 306, the process 300 advances to step 308 where the control circuit 18 is operable to control the ion source to open the ion gate G1, and to control the electric field activation sources, V_1 - V_{M^p} , to according to source settings, e.g., those determined at step 302, to allow ions from the ion source to enter the first drift tube segment, e.g., D1, and to also advance ions already in the cyclotron portion of the drift tube to the next sequential drift tube segment(s). Thereafter at step 310, the control circuit 18 is operable to close the ion gate G1, and to control the electric field activation sources, V_1 - V_{M^p} , according to the source settings to advance ions in the cyclotron portion of the drift tube to the next sequential drift tube segment(s). Optionally, step 310 may also include controlling the ion source to stop producing ions and step 308 may include controlling the ion source to produce ions. In any case, following step 310 the process 300 advances to step 312 where the control circuit 18 determines whether the counter, L, is equal to the sum of the integer M and another integer P. If not, the process advances to step 314 where the counter, L, is incremented by 1 before again executing steps 308 and 310. If, at step 312, the control circuit 18 determines that $L=M+P$, the process 300 advances to step 316 where the control circuit 18 controls the ion source to stop producing ions and to reset the counter, L, equal to 1.

The sub-process of the process 300 between and including steps 302 and 316 controls the ion mobility spectrometer 160 as described hereinabove to sequentially advance only ions around the cyclotron portion of the drift tube having ion mobilities or range of ion mobilities defined by the activation pulse widths, i.e., time durations of activation, of the electric field activation sources. During this process ions generated by the ion source are also selectively added to the first drift tube segment, D1, during and throughout a selected number, M, of revolutions of the ions around the cyclotron portion of the drift tube (D1-D4 and F2-F5). This sub-process of the process 300 between and including steps 302 and 316 may be referred to herein as "selective enhancement." The integer P corresponds to the number of times steps 308 and 310 must be executed to sequentially fill and advance ions one revolution around the cyclotron portion of the drift tube, and the integer M corresponds to the number of times steps 308 and 310 must be executed to continue the process of sequentially filling and advancing ions one revolution around the cyclotron portion of the drift tube in order to direct the ions completely around the cyclotron portion of the drift tube a desired number of times while also selectively adding ions to the drift tube. The total number of revolutions, R, of the ions around the cyclotron portion of the drift tube when the "YES" branch of step 312 is satisfied will thus be $M/P+1$.

Referring now to FIGS. 16A-16L, the selective enhancement sub-process of the process 300 is graphically illustrated in the context of the various drift tube sections of the cyclotron ion mobility spectrometer 160 of FIG. 12B. It will be understood that in FIGS. 16A-16L the ion mobility spectrometer 160 is partitioned into eight cascaded drift tube segments D1-D4 and F2-F5 each having an ion transmission section, d_t , and an ion elimination region, d_e , between the ion outlet of the ion transmission section and the ion inlet of the ion transmission section of the next adjacent segment. Thus, D1 has an ion elimination region between the ion outlet of D1 and the ion inlet of F2, F2 has an ion elimination region between the ion outlet of F2 and the ion inlet of D2, etc. The ion elimination regions, d_e , are not specifically shown in FIGS. 16A-16L, although it will be understood that electric fields within these regions are established as described hereinabove with respect to FIGS. 1-4 under control of the plurality of electric field activation sources, V_1 - V_M . In alternative embodiments, as described hereinabove, the drift tube segments D1-D4 may be sized to serve as the ion transmission sections and the funnel segments F2-F5 may be sized smaller and serve as the ion elimination regions to D1-D4 respectively, or the funnel segments F2-F5 may be sized to serve as the ion transmission sections and the drift tube segments D1-D4 may be sized smaller and serve as the ion elimination regions to F2-F5 respectively. In any case, each sequential pair of FIGS. 16A-16L represent sequential snapshot of ions within the spectrometer 160 at the end of steps 308 and 310 respectively. Thus, for example, FIG. 16A represents a snapshot of ions within the spectrometer 160 at the end of the first execution of step 308, FIG. 16B represents a snapshot of ions within the spectrometer 160 at the end of the first execution of step 310, FIG. 16C represents a snapshot of ions within the spectrometer at the end of the second execution of step 308, etc.

Referring to FIG. 16A, the first execution of step 308 has occurred, and a group or packet of ions, 11, generated by the ion source 350 has moved through the ion inlet gate, G1, at the entrance of the ion entrance drift tube segment of D1, and has moved under the influence of an electric field established in the ion entrance drift tube segment of D1 toward the ion outlet of the ion transmission segment of D1. In FIG. 16B, the ion gate G1 has been closed, and the ion packet I1 has moved under the influence of an electric field established in D1/F2 toward the ion outlet of the ion transmission segment of F2.

In FIG. 16C, the ion packet I1 has moved under the influence of an electric field established in F2/D2 toward the ion outlet of the ion transmission segment of D2. At the same time, the ion gate G1 has been opened and another packet of ions, I2, generated by the ion source 350 has moved through the ion entrance drift tube segment of D1, and has moved under the influence of an electric field established in the ion entrance drift tube segment of D1 toward the ion outlet of the ion transmission segment of D1. In FIG. 16D, the ion gate G1 has been closed, and the ion packet I1 has moved under the influence of an electric field established in D2/F3 toward the ion outlet of the ion transmission segment of F3 and the ion packet I2 has moved under the influence of an electric field established in D1/F2 toward the ion outlet of the ion transmission segment of F2.

In FIG. 16E, the ion packet I1 has moved under the influence of an electric field established in F3/D3 toward the ion outlet of the ion transmission segment of D3, and the ion packet I2 has moved under the influence of an electric field established in F2/D2 toward the ion outlet of the ion transmission segment of D2. At the same time, the ion gate G1 has again been opened and another packet of ions, 13, generated by the ion source 350 has moved through the ion entrance drift

tube segment of D1, and has moved under the influence of an electric field established in the ion entrance drift tube segment of D1 toward the ion outlet of the ion transmission segment of D1. In FIG. 16F, the ion gate G1 has been closed, and the ion packet I1 has moved under the influence of an electric field established in D3/F4 toward the ion outlet of the ion transmission segment of F4, the ion packet I2 has moved under the influence of an electric field established in D2/F3 toward the ion outlet of the ion transmission segment of F3, and the ion packet I3 has moved under the influence of an electric field established in D1/F2 toward the ion outlet of the ion transmission segment of F2.

In FIG. 16G, the ion packet I1 has moved under the influence of an electric field established in F4/D4 toward the ion outlet of the ion transmission segment of D4 (since G2a is closed and G2b is open), the ion packet I2 has moved under the influence of an electric field established in F3/D3 toward the ion outlet of the ion transmission segment of D3 and the ion packet I3 has moved under the influence of an electric field established in F2/D2 toward the ion outlet of the ion transmission segment of D2. At the same time, the ion gate G1 has again been opened and another packet of ions, 14, generated by the ion source 350 has moved through the ion entrance drift tube segment of D1, and has moved under the influence of an electric field established in the ion entrance drift tube segment of D1 toward the ion outlet of the ion transmission segment of D1. In FIG. 16H, the ion gate G1 has been closed, and the ion packet I1 has moved under the influence of an electric field established in D4/F5 toward the ion outlet of the ion transmission segment of F5, the ion packet I2 has moved under the influence of an electric field established in D3/F4 toward the ion outlet of the ion transmission segment of F4, the ion packet I3 has moved under the influence of an electric field established in D2/F3 toward the ion outlet of the ion transmission segment of F3 and the ion packet I4 has moved under the influence of an electric field established in D1/F2 toward the ion outlet of the ion transmission segment of F2.

In FIG. 16I, the ion packet I1 has moved under the influence of an electric field established in the cyclotron portion of F5/D1 toward the ion outlet of the ion transmission segment of D1, the ion packet I2 has moved under the influence of an electric field established in F4/D4 toward the ion outlet of the ion transmission segment of D4, the ion packet I3 has moved under the influence of an electric field established in F3/D3 toward the ion outlet of the ion transmission segment of D3 and the ion packet I4 has moved under the influence of an electric field established in F2/D2 toward the ion outlet of the ion transmission segment of D2. At the same time, the ion gate G1 has again been opened and another packet of ions, 15, generated by the ion source 350 has moved through the ion entrance drift tube segment of D1, and has moved under the influence of an electric field established in the ion entrance drift tube segment of D1 toward the ion outlet of the ion transmission segment of D1. It will be observed in FIG. 16I that as ion packets move from D2 to D1, the widths of the ion packets I4-I1 respectively decrease. This decrease in ion packet width is intended to represent a filtering of ions according to ion mobility (determined by activation pulse width of the electric field activation sources) such that fewer ions are included in I1 than in I2, fewer ions are included in I2 than in I3, etc. The ions in ion packet I1 are thus more highly resolved than those in I2, etc. because the illustrated ion mobility filtering process sequentially eliminates more ions having ion mobility or range of ion mobilities outside of that defined by the activation pulse width, i.e., the time duration of activation, of the electric field activation sources, V_1 - V_M as

the ions sequentially move through the various drift tube segments of the cyclotron portion of the ion mobility instrument **160**.

In FIG. **16J**, the ion gate **G1** has been closed, and the ion packets **I1** and **I5** have together moved under the influence of an electric field established in **D1/F2** toward the ion outlet of the ion transmission segment of **F2** such that ion packets **I1** and **I5** are now combined in **F2**. The ion packet **I2** has also moved under the influence of an electric field established in **D4/F5** toward the ion outlet of the ion transmission segment of **F5**, the ion packet **I3** has moved under the influence of an electric field established in **D3/F4** toward the ion outlet of the ion transmission segment of **F4** and the ion packet **I4** has moved under the influence of an electric field established in **D2/F3** toward the ion outlet of the ion transmission segment of **F3**.

In FIG. **16K**, the ion packet **I2** has moved under the influence of an electric field established in the cyclotron portion of **F5/D1** toward the ion outlet of the ion transmission segment of **D1**, the ion packet **I3** has moved under the influence of an electric field established in **F4/D4** toward the ion outlet of the ion transmission segment of **D4**, the ion packet **I4** has moved under the influence of an electric field established in **F3/D3** toward the ion outlet of the ion transmission segment of **D3** and the combination of ion packets **I1** and **I5** have moved under the influence of an electric field established in **F2/D2** toward the ion outlet of the ion transmission segment of **D2**. At the same time, the ion gate **G1** has again been opened and another packet of ions, **I6**, generated by the ion source **350** has moved through the ion entrance drift tube segment of **D1**, and has moved under the influence of an electric field established in the ion entrance drift tube segment of **D1** toward the ion outlet of the ion transmission segment of **D1**. In FIG. **16L**, the ion gate **G1** has been closed, and the ion packets **I2** and **I6** have together moved under the influence of an electric field established in **D1/F2** toward the ion outlet of the ion transmission segment of **F2** such that ion packets **I2** and **I6** are now combined in **F2**. The ion packet **I3** has also moved under the influence of an electric field established in **D4/F5** toward the ion outlet of the ion transmission segment of **F5**, the ion packet **I4** has moved under the influence of an electric field established in **D3/F4** toward the ion outlet of the ion transmission segment of **F4** and the combination of ion packets **I1** and **I5** has moved under the influence of an electric field established in **D2/F3** toward the ion outlet of the ion transmission segment of **F3**.

Referring again to FIG. **15**, the sub-process carried out by steps **302-316** of the process **300** and illustrated in FIGS. **16A-16L** can be executed any number of times to selectively add ions to individual packets of ions circulating through the various drift tube segments **D1-D4** and **F2-F5** of the ion mobility spectrometer **160**. As illustrated in FIGS. **16A-16H**, the loop defined by steps **308-314** is executed four times to complete one revolution of ions around the cyclotron portion (**D1-D4** and **F2-F5**) of the ion mobility spectrometer **160**. Thus, "P" at step **312** is equal to four in the illustrated embodiment, and the counter value "M" is therefore selected such that the total desired number of revolutions, R, of ions around the cyclotron portion of the ion mobility spectrometer **160** during the selective enhancement sub-process of steps **302-316**, i.e., during which ions from the ion source **350** are selectively added to ions already circulating through the cyclotron portion of the spectrometer **160**, must satisfy the relation $R=M/P+1$ as described above.

It will be understood that the ion mobility spectrometer **160** may be controlled and operated using similar yet alternate techniques to perform the selective enhancement process just

illustrated and described with respect to FIGS. **16A-16L**. For example, the spectrometer **160** may be alternatively operated such that ions from the ion source **350** fill the **D1** and **F2** regions during one field application setting. Next the fields would switch such that ions from **F2** would move into the **D2** region while ions from the source **350** would be shut off. Application of the next field would see the transmission of the ions with resonant mobilities into the **F3** region. At the same time, ions from the ion source **350** would be allowed to fill the **D1** and **F2** regions again. Completion of another two field application periods would yield ions in the **F4** and **F3** regions with a filling of the **D1** and **F2** regions. Yet another two application periods would result in ions in the **F5**, **F4**, and **F3** regions as well as a filling of the **D1** and **F2** regions. With the addition of two more application periods the first ion packet would reach the **F2** region again having completed a full cycle around the cyclotron portion of the drift tube (**D1-D4** and **F2-F5**). During this time, ions from the source would be allowed into the **D1** and **F2** region combining with this ion packet. Another cycle would see the filtering of these added ions according to resonant mobilities. Ions could be added to each successive packet for a desired amount of time or a desired number of cycles around the cyclotron portion of the drift tube (**D1-D4** and **F2-F5**). Alternatively still, the process just described could be modified to move ions around the cyclotron portion of the spectrometer **160** using longer ion transmission regions. For example, the spectrometer **160** may be alternatively operated such that ions from the ion source **350** fill the **D1** and **F2** regions during one field application setting. The ion source may then be shut off and an electric field may be activated in the **D1/F2/D2/F3** region to move ions into the **D2/F3** region, etc. Ions may thus be moved through the cyclotron portion of the spectrometer **160** by propagating two regions worth of ions around the cyclotron portion using fewer field applications to complete each traversal of the cyclotron portion of the spectrometer **160**.

As described hereinabove, the design of the cyclotron portion of the drift can be altered from that described above such that the **D** regions comprise the ion transmission regions, d_n , and the **F** regions comprise the ion elimination regions, d_e , or such that the **F** regions comprise the ion transmission regions, d_n , and the **D** regions comprise the ion elimination regions, d_e . Those skilled in the art will recognize that the selective enhancement sub-process just described comprising steps **302-316** may be easily modified to be performed using such an alternate design of the cyclotron portion of the drift tube (**D1-D4** and **F2-F5**), and that any such modifications to steps **302-316** would be a mere mechanical step for a skilled artisan.

Referring again to FIG. **15**, the process **300** advances from step **316** to steps **318-326**, and optional also to step **328**. Steps **318-328** are identical to steps **262-272** illustrated and described hereinabove with respect to FIG. **14**, in which the control circuit **18** is operable to control the electric field activation sources, V_1-V_M , and the ion gates **G2a** and **G2b** to cause the ions within the cyclotron portion of the ion mobility spectrometer **160** to travel around the cyclotron drift tube "N" times prior to directing the ions to the ion detector, DET, where N may be any positive integer. Optionally, step **328** may be included to perform overtone analysis, as this process is described above, using the combination of the selective enhancement sub-process described above followed by controlling the spectrometer **160** to circulate the post-selectively enhanced ions in the cyclotron drift tube N times prior to directing the ions toward the ion detector, DET.

Mixtures may alternatively be resolved over long distances in linear drift tubes, e.g., of the type illustrated in FIGS. **1-4**,

at or near their fundamental frequencies by controlling the electric field activation sources, V_1-V_M , in a manner that directs ions back and forth between the ends of the drift tube. More specifically, ions entering the ion inlet of the drift tube **14** are directed by the electric field activation sources, V_1-V_M , toward the ion outlet of the drift tube **14** by selectively controlling the activation times and pulse widths of the electric field activation sources as described hereinabove with respect to FIGS. 1-5. In this embodiment, prior to reaching the ion outlet, e.g., at or near the last drift tube segment, the control circuit **18** may control the electric field activation sources, V_1-V_M , to reverse the direction of the sequentially applied electric fields to the cascaded drift tube segments such that the ions reverse direction and move linearly toward the ion inlet of the drift tube **14**. As before, the duration of the pulse widths, PW, would determine the range of ion mobilities of the ions traversing the drift tube **14**. In any case, this may be repeated any number of times to allow the ions to drift any desired distance. After drifting the desired distance, a gate at the ion outlet of the drift tube **14** may be activated to allow the ions to exit the ion outlet of the drift tube **14** and be detected by an ion detector positioned to detect ions exiting the drift tube.

Running the drift separation in a back and forth manner as just described can be limited in that ions that limit resolving power, e.g., those with slightly mismatched mobilities, may not be eliminated as they move back to their initial positions on all even passes (i.e., the 2nd, 4th, 6th, etc. pass through the drift tube). This limitation may be overcome by, for example, randomizing positions of the ions in the drift tube during each pass of ions from the first drift tube segment to the last and/or during each pass of ions from the last drift tube segment to the first.

Referring now to FIG. 17, one illustrative embodiment of an ion mobility spectrometer **400** is shown having a linear drift tube **14'** that is configured to randomize ion positions during each such pass of ions. The drift tube **14'** is identical to the drift tube **14** illustrated and described hereinabove with respect to FIGS. 1-4 except that a conventional ion trap **402** is positioned between two adjacent ones of the number, N, of cascaded drift tube segments, e.g., between the ion outlet of the third ion elimination region, $d_e(3)$ and the ion inlet of the fourth ion transmission region, $d_t(4)$. All other features of the drift tube **14'** are identical to the drift tube **14** illustrated and described hereinabove, and all other components of the ion mobility spectrometer **400** are identical to correspondingly numbered components of the ion mobility spectrometer **10** illustrated and described hereinabove. The primary purpose of the ion trap **402** in the spectrometer **400** is to trap ions of the desired mobility during each pass of ions from the first drift tube segment to the last and/or during each pass of ions from the last drift tube segment to the first to thereby randomize the positions of the ions during each such pass. In this regard, the memory **20** of the processor **18** has, in this embodiment, instructions stored therein that are executable by the processor **18** to control the ion trap, e.g., via a suitable voltage source or voltage sources, which may or may not be, or be part of, one or more of the electric field activation sources, V_1-V_M , to trap ions therein during each pass of ions from the first drift tube segment to the last and/or during each pass of ions from the last drift tube segment to the first for a trap period selected to allow ions trapped within the ion trap **402** to randomize their positions relative to the ion trap **402** and thereby randomize their positions relative to the drift tube **14'**. During the trap period, ions will thus randomize their positions, causing a greater mismatch in timing for a population of undesired ions, e.g., those with slightly off-resonance mobilities. This

will lead to more effective elimination of these undesired ions. It will be understood that the ion trap **402** illustrated in FIG. 17 may be alternatively positioned anywhere along its length, i.e., at either end or between any two adjacent drift tube segments. Alternatively or additionally, the drift tube **14'** may include two or more such ion traps **402** positioned anywhere along its length. In one specific embodiment, for example, one such ion trap **402** is positioned at one end of the drift tube **14'** and another such ion trap **402** is positioned at an opposite end of the drift tube **14'**. In this embodiment, the control circuit controls each ion trap to trap ions therein during each pass of ions from one end of the drift tube to the other.

Referring now to FIG. 18, the ion mobility spectrometer **10** of FIG. 1 is shown alternatively configured to randomize ion positions during each such pass of ions. In particular, the instructions stored in the memory **20** include, in the embodiment illustrated in FIG. 18, instructions that are executable by the control circuit **18** to control the strengths, i.e., i.e., the magnitudes, of the electric fields established by the electric field activation sources, V_1-V_M , in a number of adjacent drift tube segments. More specifically, the electric fields in a number of adjacent drift tube segments are progressively diminished to cause the ions to randomize their positions relative to the drift tube **14** by bunching up in one or more of the number of adjacent drift tube segments. In the embodiment illustrated in FIG. 18, for example, the control circuit **18** is configured to control the electric field activation sources, V_1-V_M , to cause the magnitudes of the electric fields E_1-E_4 in the four adjacent drift tube segments at each end of the drift tube to diminish such that $E_1 > E_2 > E_3 > E_4$. In alternative embodiments, the number of adjacent drift tube segments in which the electric fields are diminished in magnitude may be more or fewer, may comprise any number of such adjacent drift tube segments at either or both ends of the drift tube **14**, or may comprise any number of such adjacent drift tube segments between the two ends of the drift tube **14**.

The back-and-forth mobility separation in the segmented drift tube as just describe with respect to FIGS. 17 and 18 may alternatively or additionally be used for OMS modes of operation as described hereinabove with respect to FIG. 7. This allows the use of overtone frequencies as a means of mobility selection. Additionally, such a device could incorporate ion trapping on either end to allow for selective enrichment of a mobility region prior to mobility selection refinement with the back-and-forth cycling of ions. Here, ions from a continuous or pulsed source can pass through a linear drift tube in either direction and those with resonant frequencies can be trapped in an ion trap positioned in the drift tube. After selective filling for a predetermined time period, i.e., as described hereinabove with respect to FIGS. 16A-16L, the ions would then be cycled back-and-forth through the linear drift tube a number of times to obtain greater resolution (isolation of ions of a given mobility). Referring to FIG. 19, one illustrative embodiment of such an ion mobility spectrometer **500** is shown in which an ion trap **502** is positioned at the end of the linear drift tube **14''**, which is otherwise identical to the drift tube **14** of FIGS. 1-4. The remaining components of the spectrometer **500** are likewise identical to like-numbered components of the spectrometer **10** of FIGS. 1-4 except that the memory includes instructions stored therein that are executable by the control circuit **18** to control and operate the spectrometer **500** to selectively fill the drift tube **14''** for a predefined time period or number of back and forth cycles, and to thereafter cycle the ions back and forth a desired number of times as generally described hereinabove with respect to FIGS. 15-16L.

Referring now to FIG. 20, a flowchart is shown of one illustrative embodiment of a process 600 for operating the linear drift tube 14" of FIG. 19 as just described. Illustratively, the process 600 is stored in the memory 20 of the control circuit 18 in the form of instructions that are executable by the processor 18 to control operation of the spectrometer 500. The process 600 begins at step 602 where the operational settings of the number, M, of electric field activation sources are defined, and a value of an integer, N, (and optionally M) is set. In embodiments in which the spectrometer 500 will be operated to produce ions having a mobility or range of mobilities that is/are resonant with only a fundamental frequency, f_f , of operation of the electric field activation sources, V_1 - V_M , step 602 may include, for example, the steps 82-88 of the process 80 of FIG. 5. In other embodiments in which the spectrometer 500 will be operated to produce ions having ion mobilities resonant with one or more overtones, e.g., harmonic frequencies, of operation of the electric field activation sources, V_1 - V_M , step 602 may include, for example, the steps 102-106 of the process 100 of FIG. 7.

Following step 602, the process 600 advances to step 604 where the control circuit 18 is operable in one embodiment to reset a timer, e.g., set a timer value, T, to zero (or to another arbitrary value), and in an alternate embodiment to set a counter value, K, equal to 1. Thereafter at step 606, the control circuit 18 is operable to control the ion source 12 to generate ions, and thereafter at step 608 the control circuit 18 is operable to control the electric field activation sources, V_1 - V_M , according to the source settings determined at step 602 to sequentially advance ions sequentially through the drift tube segments toward the last drift tube segment, i.e., toward the ion trap 502. The ions advance through the drift tube at step 608 will, of course, have ion mobilities or ranges of ion mobilities that are resonant with the activation time, i.e., time duration of activation, of the electric field activation sources V_1 - V_M as illustrated and described hereinabove. Thereafter at step 610, the control circuit 18 is operable to control the ion trap 502 to trap ions advanced through the drift tube 14" to the ion trap 502. Thereafter at step 612, the control circuit 18 is operable to determine whether the timer has reached a predefined time period, T_p , since being reset, or to determine whether the value of the counter, K, has reached the value M which was optionally set at step 602. In some embodiments, the ion source 12 is controlled at step 606 to continuously generate ions, and in other embodiments the ion source 12 is controlled at step 606 to generate discrete packets or pulses of ions. In either case, a timer or a counter may be used to control the amount of time that ions are collected in the ion trap 502 or the number of passes in which ions are advanced into the ion trap via the drift tube 14". If a timer is used, step 612 loops back to step 606 (or to step 608 in the case of continuous generation of ions) until $T > T_p$. If a counter is used, step 612 advances to step 614 to increment K, and to then loop back to step 606 (or to step 608 in the case of continuous generation of ions) until $K = M$, where $M =$ the number of times ions are advanced through the drift tube 14" into the ion trap 502. In either case, the "YES" branch of step 612 advances to step 616 where the control circuit 18 is operable to stop producing ions and to set a counter value, L, equal to 1.

Following step 616, the process 600 advances to step 618 where the control circuit 18 controls the ion trap 502 and the electric field activation sources, V_1 - V_M , to according to source settings, e.g., those determined at step 602, to sequentially advance ions in the ion trap 502 in a reverse direction toward the first drift segment of the drift tube 14", i.e., to the $d_1(1)$. When the ions are determined at step 620 by the control circuit 18 to be in the first drift tube segment (e.g., as a

function of time after being released from the ion trap 502 at step 618), the process advances to step 622, and otherwise loops back to step 618 until step 620 is satisfied. At step 622, the control circuit 18 controls the electric field activation sources, V_1 - V_M , to according to source settings, e.g., those determined at step 602, to sequentially advance ions in the ion trap 502 in a forward direction from the first drift tube segment, $d_1(1)$ toward last drift tube segment, i.e., the ion trap 502. Thereafter at step 624, the control circuit 18 is operable to control the ion trap 502 to trap therein ions passing through the last drift tube segment for a time period, T_T , where T_T is a trapping time period that allows the ions to randomize as described hereinabove with respect to FIG. 17. Thereafter at step 626, the control circuit 18 is operable to determine whether the counter, L, is equal to the number N. If not, the process 600 advances to step 628 where the counter, L, is incremented by 1 and the process 600 then loops back to again execute step 618. If, at step 626, the control circuit 18 determines that $L = N$, then the ions have traversed the linear drift tube 14" the desired number of times, and the process 600 advances to step 630 where the control circuit 18 is operable to control the ion trap 502 to direct ions trapped therein to the ion detector 16. Optionally, the process 600 may include an extra step 632, executed following step 630, in which the control circuit 18 is operable to execute steps 604-630 until the pulse width durations, i.e., the "time durations" of activations of the electric field activation sources, V_1 - V_M , have been swept through a range of pulse width durations between an initial pulse width duration, PW_I and a final pulse width duration, PW_F . In embodiments which include step 632, step 602 will of course include a determination of PW_I and PW_F as illustrated in the process 100 of FIG. 7. Generally, PW_I and PW_F will be selected to produce one or more overtones, i.e., harmonic frequencies of which the predefined ion mobilities or range of ion mobilities are resonant, and/or to produce ions that have ion mobilities resonant with fundamental frequencies of the activation frequencies or pulse rates, i.e., activation times, of the electric field activation sources, V_1 - V_M , for each of the discrete activation frequencies or pulse rates over and between PW_I and PW_F , as described hereinabove.

While the spectrometer 500 illustrated in FIG. 19 is illustrated with the ion trap 502 located at one end of the drift tube 14", it will be understood that the ion trap 502 may alternatively be positioned at the opposite end of the drift tube 14" or between the two ends of the drift tube 14". Alternatively or additionally, any number of ion traps may be positioned in the drift tube 14", e.g., one at each end, for the purpose of trapping and randomizing positions of the ions trapped therein as illustrated and described with respect to FIG. 17, and/or the magnitudes of the electric fields of a number of adjacent ones of the drift tube segments may be sequentially diminished to enhance or achieve this result as illustrated and described with respect to FIG. 18. In such case or cases, the ion trap 502 may, need not, be controlled in as described for the purpose of randomizing ions trapped therein.

In any of the linear or cyclotron configurations of the ion mobility spectrometer illustrated and described herein, a non-destructive detector, e.g., rather than an ion counting detector 16, could be used that is configured to measure the image charge many times at a specified position within drift tube. Ion distributions could then be recorded as the frequency that ions pass the non-destructive detector. A conventional frequency transformation, e.g., Fourier transform, could then be used to back-calculate ion mobility.

Referring now to FIG. 21, yet another embodiment of an ion mobility spectrometer 600 is shown. In the illustrated embodiment, some of the illustrated components are identical

to those described hereinabove, and like reference numbers are therefore used to identify like components. In FIG. 21, the drift tube 602 includes a single drift tube segment of length L positioned between two ion traps 604 and 606. The ion trap 604 is positioned adjacent to the inlet of the single drift tube segment 602, and the ion trap 606 is positioned adjacent to the ion outlet of the single drift tube segment 602. At least one drift tube voltage source, V_{DT} , is electrically connected between the control circuit 18 and the single drift tube segment 602, and is controllable in a conventional manner to establish an electric field in the single drift tube region 602 in one direction that causes ions supplied by the ion source 12 to drift from the ion trap 604 toward the ion trap 606, and to alternatively establish an electric drift field in the single drift tube region 602 in an opposite direction that causes ions to drift from the ion trap 606 toward the ion trap 604. An ion trap voltage source, V_{IT1} , is electrically connected between the control circuit 18 and the ion trap 604, and another ion trap voltage source, V_{IT2} , is electrically connected between the control circuit 18 and the ion trap 606.

The memory 20 illustratively includes instructions stored therein that are executable by the control circuit 18 to execute a process a predefined number of times. The process illustratively includes activating the at least one electric field activation source, V_{DT} , for a time duration to establish an electric field in the one direction to cause only ions supplied by the ion source 12 that have a predefined ion mobility or range of ion mobilities defined by the time duration to travel through the single drift tube region 602 in the direction from the ion trap 604 toward the second ion trap 606 followed by controlling the ion trap 606 to trap therein the ions that have the predefined ion mobility or range of ion mobilities. The ion trap 606 is then controlled to release the ions trapped therein and the control circuit 18 then activates the at least one electric field activation source, V_{DT} , for the time duration to establish an electric field in the opposite direction to cause only ions that have the predefined ion mobility or range of ion mobilities defined by the time duration to travel through the single drift tube region 602 in the direction from the ion trap 606 toward the ion trap 604 followed by controlling the ion trap 604 to trap therein the ions that have the predefined ion mobility or range of ion mobilities followed by controlling the ion trap 604 to release the ions trapped therein. This process may be performed any number of times to thereby cause ions to traverse the single drift tube region 602 any such number of times. The control circuit 18 may then control the ion trap 606 to release ions trapped therein toward the ion detector 16 and to process the ion detection signals produced by the ion detector to determine ion mobility spectral information therefrom. The ion source 12 may be controlled in a pulsed fashion to produce discrete packets of ions or may alternatively be controlled to continuously produce ions. The instructions stored in the memory 20 may further include instructions executable by the control circuit 18 to control the ion traps 604 and 606 to trap ions therein for a trap period. The trap period is illustratively selected to allow ions trapped within the ion trap 604 and within the ion trap 606 to randomize their positions relative to the respective ion trap 604/606.

The spectrometer 600 may alternatively be operated in the OMS mode illustrated and described hereinabove. For example, the instructions stored in the memory 20 may further include instructions executable by the control circuit 18 to control the at least one electric field activation source, V_{DT} , to sweep the time duration between first and second predefined time durations to thereby cause ions that have fundamental frequencies resonant with each of a number of discrete time durations between the first and second time durations to

travel through the single drift tube region 602, and to execute the process the predefined number of times for each of the number of discrete time durations between the first and second predefined time durations.

Referring now to FIG. 13, a block diagram of one illustrative embodiment of a cascaded ion mobility spectrometer instrument 170 is shown that employs some of the concepts illustrated and described hereinabove with respect to FIGS. 1-12B. In the illustrated embodiment, the instrument 170 includes an ion source 12 having an ion outlet coupled to an ion inlet of a first ion mobility spectrometer (IMS1). An ion outlet of IMS1 is coupled to an ion inlet of a second ion mobility spectrometer (IMS2) having an ion outlet that is coupled to an ion detector 16. The IMS1 has an axial length of L1 and the IMS2 has an axial length of L2. A control circuit 180 includes a memory unit 182, and is electrically connected to a control input of an ion source voltage supply, V_{IS} , having an output that is electrically connected to the ion source 12. The instrument 170 further includes a plurality of electric field activation sources, V_1-V_Q , that are electrically connected between the control circuit 180 and IMS1 and IMS2, where Q may be any integer greater than 1. Illustratively, a subset of the electric field activation sources, V_1-V_p , are dedicated to IMS1, and another subset, $V_{p+1}-V_Q$ are dedicated to IMS2. Alternatively, $V_{p+1}-V_Q$ may be omitted, and V_1-V_p may be used for both of IMS1 and IMS2. In any case, each of the foregoing components may be as described hereinabove with respect to the embodiment of FIG. 1. In one illustrative embodiment, the instrument 170 is operable just as described hereinabove with respect to any of FIGS. 1-12B, except that the ions are resolved over an effective drift tube length of L1+L2 rather than over the length of a single drift tube, such that IMS1 and IMS2 together form a single ion mobility spectrometer.

The ion mobility spectrometer instrument 170 of FIG. 13 may further include at least one additional voltage source, V_F , which may be controlled by the control circuit 180 to produce one or more voltages that control one or more ion fragmentation units or other conventional device for inducing structural changes in ions within IMS1, IMS2 and/or positioned between IMS1 and IMS2. In embodiments in which the drift tubes of IMS1 and IMS2 are constructed according to the teachings of co-pending U.S. Patent Application Pub. No. US 2007/0114382, for example, an ion activation region of the type described therein may be positioned at the end of any one or more ion funnels that form IMS1 and/or IMS2. Alternatively, IMS1 and/or IMS2 may be modified in other embodiments to include one or more conventional structural change inducing devices or stages, e.g., one or more ion fragmentation stages, ion conformational change stages, and/or other conventional structural change inducing devices or stages, therein or interposed between IMS1 and IMS2. For example, such a structural change inducing device may be positioned between IMS1 and IMS2, and the ion mobility spectrometer 170 may be operated as described hereinabove to conduct fundamental frequency and/or overtone frequency analysis with IMS1, to then induce structural changes in ions emerging from IMS1, and to then conduct fundamental frequency and/or overtone frequency analysis with IMS2 on the ions in which structural changes were induced. Alternatively or additionally, the fragmented ions may be mobility filtered in a conventional manner prior to entering IMS2. Alternatively or additionally still, such fragmented and mobility-selected ions may be further fragmented and possibly further mobility selected any number of times prior to entrance into IMS2.

IMS1 may further include an operating condition selection unit 190, and IMS2 may likewise include an operating con-

dition selection unit **200**. The operating condition selection units **190** and **200** may be manually controlled via respective manual controls **194** and **204**, and/or may be automatically controlled by the control circuit **180** via suitable electrical control lines **192** and **202** respectively. The operating condition selection units **190** and **200** are block diagram components that may represent conventional structures that control any one or more of the operating temperature of IMS1 and/or IMS2, the operating pressure of IMS1 and/or IMS2, the chemical make up and/or flow rate of gas, e.g., buffer gas, supplied to the ion pathway of IMS1 and/or IMS2, and the like. In the operation of the ion mobility spectrometer instrument **170**, such as described hereinabove, IMS1 and IMS2 may be operated as described hereinabove and further with any one or more of, or with any combination of, the same or different drift tube lengths, L1 and L2, the same or different electrical field strengths applied by the electric field activation sources V_1-V_Q , the same or different pulse shapes applied by the electric field activation sources V_1-V_Q , the same or different pulse width durations, PW, applied by the electric field activation sources V_1-V_Q , the same or different operating temperatures (e.g., T1 for IMS1 and T2 for IMS2), the same or different operating pressures, (e.g., P1 for IMS1 and P2 for IMS2), with the ions passing through IMS1 and IMS2 exposed to the same or different gasses (Gas1 for IMS1 and Gas2 for IMS2), or with ion fragmentation occurring within or between IMS1 and IMS2. Further details relating to some of these operational scenarios or modes are provided in U.S. Pat. No. 7,077,904, the disclosure of which is incorporated herein by reference.

It will be understood that the ion mobility spectrometer instrument illustrated in FIG. **13** and described herein represents only an example multiple drift tube instrument, and that the instrument may alternatively include any number of IMS units or drift tubes. Alternatively still, the IMS drift tubes in such an arrangement need not be linear, and the instrument **170** illustrated in FIG. **13** may include any number of non-linear IMS drift tube, such as two or more circular drift tubes of the type described in co-pending PCT Publication No. WO 2008/028159 A2, filed Aug. 1, 2007, the disclosure of which has been incorporated herein by reference.

While the invention has been illustrated and described in detail in the foregoing drawings and description, the same is to be considered as illustrative and not restrictive in character, it being understood that only illustrative embodiments thereof have been shown and described and that all changes and modifications that come within the spirit of the invention are desired to be protected.

What is claimed is:

1. An ion mobility spectrometer instrument comprising:

a drift tube partitioned into a plurality of cascaded drift tube segments, each defining an ion inlet gate at one end, an ion outlet gate at an opposite end and a first distance between the ion inlet gate and the ion outlet gate, with an ion elimination region defining a second distance between the ion outlet gate of each drift tube segment and the ion inlet gate of the next adjacent drift tube segment, the ion outlet gate of a last one of the drift tube segments coupled by a last ion elimination region to the ion inlet gate of a first one of the drift tube segments such that the drift tube defines therein a closed and continuous ion travel path,

an ion source,

an ion entrance drift tube segment having an ion inlet coupled to the ion source and an ion outlet coupled to one of the plurality of cascaded drift tube segments,

an ion exit drift tube segment having an ion inlet coupled to the one or another one of the plurality of drift tube segments, and an ion outlet,

an ion gate arrangement responsive to a first set of one or more ion gate signals to direct ions moving through the drift tube through the one or another one of the plurality of cascaded drift tube segments while blocking the ions from entering the ion exit drift tube segment, and to a second set of one or more ion gate signals to direct the ions moving through the drift tube into the ion exit drift tube segment while blocking the ions from moving through the one or another one of the plurality of cascaded drift tube segments,

a number, M, of electric field activation sources each operatively connected to one or more of the plurality of drift tube segments such that, when activated, each establishes a repulsive electric field in at least one of the first M ion elimination regions and in every following Mth ion elimination region, and also establishes an electric drift field in all remaining ion elimination regions and in all of the plurality of cascaded drift tube segments, and

a control circuit including a memory having instructions stored therein that are executable by the control circuit to produce the first set of one or more ion gate signals and sequentially activate each of the number, M, of electric field activation sources for a time duration while deactivating the remaining number, M, of electric field activation sources to thereby cause only ions supplied by the ion source that have a predefined ion mobility or range of ion mobilities defined by the time duration to travel through the drift tube, and after the ions have traveled around the drift tube a selected number of times to produce the second set of one or more ion gate signals to draw ions moving through the drift tube out of the drift tube and into the ion exit drift tube segment where the ions exit via the ion mobility spectrometer via the ion outlet of the ion exit drift tube segment.

2. The ion mobility spectrometer of claim **1** further comprising an ion detector configured to detect ions exiting the ion exit drift tube segment and produce corresponding ion detection signals,

wherein the instructions stored in the memory further include instructions executable by the control circuit to process the ion detection signals to determine ion mobility spectral information therefrom.

3. The ion mobility spectrometer of claim **1** wherein the ion gate arrangement comprises:

a first ion gate positioned in the one or another one of the plurality of cascaded drift tube segments, and

a second ion gate positioned in or at the ion inlet of the ion exit drift tube segment,

wherein the first set of one or more ion gate signals comprises a first ion gate signal to which the first ion gate is responsive to allow ions to pass therethrough and a second ion gate signal to which the second ion gate is responsive to block ions from passing therethrough,

and wherein the second set of one or more ion gate signals comprises a third ion gate signal to which the first ion gate is responsive to block ions from passing therethrough and a fourth ion gate signal to which the second ion gate is responsive to allow ions to pass therethrough.

4. The ion mobility spectrometer of claim **1** further comprising a voltage supply operatively connected to the ion source and to the control circuit,

wherein the instructions stored in the memory further include instructions executable by the control circuit to

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control the voltage source to thereby selectively cause the ion source to produce ions and to selectively supply produced ions to the ion entrance drift tube segment.

5. The ion mobility spectrometer of claim 1 wherein the instructions stored in the memory further include instructions executable by the control circuit to produce the first set of one or more ion gate signals, to control the ion source to produce ions and control the number, M, of electric field activation sources in a manner that allows ions produced by the ion source to enter and fill each of the plurality of drift tube segments, to then control the ion source to stop producing ions and sequentially activate each of the number, M, of electric field activation sources for the time duration while deactivating the remaining number, M, of electric field activation sources to thereby cause only ions within the drift tube that have the predefined ion mobility or range of ion mobilities defined by the time duration to travel through the drift tube, and after the ions have traveled around the drift tube a selected number of times to produce the second set of one or more ion gate signals and control the number, M, of electric field activation sources to draw ions moving through the drift tube out of the drift tube and into the ion exit drift tube segment.

6. The ion mobility spectrometer of claim 5 wherein the instructions stored in the memory further include instructions executable by the control circuit to control the number, M, of electric field activation sources in the manner that allows ions produced by the ion source to enter and fill each of the plurality of drift tube segments by controlling the number, M, of electric field activation sources to pass all ions generated by the ion source from each of the plurality of drift tube segments to the next adjacent drift tube segment.

7. The ion mobility spectrometer of claim 5 wherein the predefined ion mobility or range of ion mobilities is resonant with a fundamental frequency defined by the time duration, and wherein the instructions stored in the memory further include instructions executable by the control circuit to control the number, M, of electric field activation sources to sweep the time duration between first and second predefined time durations to thereby cause ions within the drift tube that have at least one of ion mobilities defined by overtone frequencies of the time duration and ion mobilities resonant with fundamental frequencies of discrete time durations between the first and second time durations to travel through the drift tube.

8. The ion mobility spectrometer of claim 5 further comprising a voltage supply operatively connected to the ion source and to the control circuit,

wherein the instructions stored in the memory further include instructions executable by the control circuit to control the ion source to produce ions by controlling the voltage source to cause the ion source to produce ions and to supply the produced ions to the ion entrance drift tube segment, and to control the ion source to stop producing ions by controlling the voltage source to cause the ion source to stop producing ions.

9. The ion mobility spectrometer of claim 5 wherein the ion gate arrangement comprises:

a first ion gate positioned in the one or another one of the plurality of cascaded drift tube segments, and
a second ion gate positioned in or at the ion inlet of the ion exit drift tube segment,

wherein the first set of one or more ion gate signals comprises a first ion gate signal to which the first ion gate is responsive to allow ions to pass therethrough and a second ion gate signal to which the second ion gate is responsive to block ions from passing therethrough,

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and wherein the second set of one or more ion gate signals comprises a third ion gate signal to which the first ion gate is responsive to block ions from passing therethrough and a fourth ion gate signal to which the second ion gate is responsive to allow ions to pass therethrough.

10. The ion mobility spectrometer of claim 5 further comprising an ion detector configured to detect ions exiting the ion exit drift tube segment and produce corresponding ion detection signals,

wherein the instructions stored in the memory further include instructions executable by the control circuit to process the ion detection signals to determine ion mobility spectral information therefrom.

11. The ion mobility spectrometer of claim 1 wherein the ion outlet of the ion entrance drift tube segment is coupled to a first one of the plurality of drift tube segments,

and wherein the instructions stored in the memory further include instructions executable by the control circuit to produce the first set of the one or more gate signals, and to then control the ion source and the number, M, of electric field activation sources to alternately (a) supply ions to the first one of the plurality of cascaded drift tube segments via the ion entrance drift tube segment while also advancing ions in even-numbered ones of the plurality of drift tube segments to next adjacent odd-numbered ones of the plurality of drift tube segments and blocking advancement of ions in odd-numbered ones of the plurality of drift tube segments to next adjacent even-numbered ones of the plurality of drift tube segments, and (b) stop the supply of ions to the first one of the plurality of cascaded drift tube segments via the ion entrance drift tube segment while also advancing ions in odd-numbered ones of the plurality of drift tube segments to next adjacent even-numbered ones of the plurality of drift tube segments and blocking advancement of ions in even-numbered ones of the plurality of drift tube segments to next adjacent odd-numbered ones of the plurality of drift tube segments, a first number of times to thereby sequentially add ions selectively produced by the ion source to every other one of the plurality of drift tube segments.

12. The ion mobility spectrometer of claim 11 wherein the instructions stored in the memory further include instructions that are executable by the control circuit to, after ions selectively produced by the ion source have been added to every other one of the plurality of drift tube segments the first number of times, control the ion source to stop producing ions and sequentially activate each of the number, M, of electric field activation sources for the time duration while deactivating the remaining number, M, of electric field activation sources to thereby cause only ions within the drift tube that have the predefined ion mobility or range of ion mobilities defined by the time duration to travel through the drift tube, and after the ions have traveled around the drift tube a second number of times to produce the second set of the one or more ion gate signals to draw ions moving through the drift tube out of the drift tube and into the ion exit drift tube segment.

13. The ion mobility spectrometer of claim 12 further comprising a voltage supply operatively connected to the ion source and to the control circuit,

wherein the instructions stored in the memory further include instructions executable by the control circuit to control the ion source to produce ions by controlling the voltage source to cause the ion source to produce ions and to supply the produced ions to the ion entrance drift tube segment, and to control the ion source to stop pro-

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ducing ions by controlling the voltage source to cause the ion source to stop producing ions.

14. The ion mobility spectrometer of claim 12 wherein the ion gate arrangement comprises:

a first ion gate positioned in the one or another one of the plurality of cascaded drift tube segments, and

a second ion gate positioned in or at the ion inlet of the ion exit drift tube segment,

wherein the first set of one or more ion gate signals comprises a first ion gate signal to which the first ion gate is

responsive to allow ions to pass therethrough and a second ion gate signal to which the second ion gate is

responsive to block ions from passing therethrough,

and wherein the second set of one or more ion gate signals comprises a third ion gate signal to which the first ion

gate is responsive to block ions from passing there-

through and a fourth ion gate signal to which the second

ion gate is responsive to allow ions to pass therethrough.

15. The ion mobility spectrometer of claim 12 further comprising an ion detector configured to detect ions exiting the ion exit drift tube segment and produce corresponding ion detection signals,

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wherein the instructions stored in the memory further include instructions executable by the control circuit to process the ion detection signals to determine ion mobility spectral information therefrom.

16. The ion mobility spectrometer of claim 12 wherein the predefined ion mobility or range of ion mobilities are resonant with a fundamental frequency defined by the time duration,

and wherein the instructions stored in the memory further include instructions executable by the control circuit to

control the number, M, of electric field activation sources to sweep the time duration between first and

second predefined time durations to thereby cause ions within the drift tube that have at least one of ion mobili-

ties defined by overtone frequencies of the time duration and ion mobilities resonant with fundamental frequen-

cies of discrete time durations between the first and second time durations to travel through the drift tube.

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