

REDUCED PRESSURE FAIMS AND DUAL ION SOURCE**CROSS REFERENCE**

[0001] This application claims the benefit of U.S. Provisional Application No. 63/592,198, filed on October 22, 2023, and U.S. Provisional Application No. 63/644,411, filed on May 8, 2024, both which are incorporated herein by reference in their entirety.

BACKGROUND

[0002] Mass spectrometry offers a rich analysis mass-to-charge ratios of e.g., the one or more molecules of a biological sample, enabling precision identification or screening capabilities for a given molecular target. However, mass spectrometry analysis of an ionized biological sample is a time intensive process, taking anywhere from 20-40 minutes for analyzing a single sample. There exists an unmet need for an improved system capable of reducing the time required for mass spectrometry analysis of biological samples without sacrificing the resolution of measurements. Moreover, there is a need for improved mass spectrometry devices with improved detection, sensitivity, accuracy and/or precision, particularly when analyzing complex biological samples.

SUMMARY

[0003] Aspects of the disclosure describe an ion manifold comprising: an ion manifold inlet; an ion repeller manifold; a first ion optic configured to receive a flux of ions through the ion manifold inlet; and a second ion optic configured to receive an output of the flux of ions through the first ion optic, wherein the second ion optic comprises a plurality of outputs that split the flux of ions into a plurality of ion streams.

[0004] Provided herein are ion manifolds comprising: (a) an orthogonal ion manifold inlet; (b) a first ion optic configured to receive a flux of ions through the ion manifold inlet, wherein the ion inlet is inside the first ion optic; and (c) a second ion optic configured to receive an output of the flux of ions through the first ion optic, wherein the second ion optic comprises a plurality of outputs that split the flux of ions into a plurality of ion streams. Further provided are ion manifolds wherein the first ion optic and the second ion optic comprises one or more electrical conductor segments, wherein the one or more electrical conductor segments comprise one or more through holes. Further provided are ion manifolds wherein the one or more electrical conductor segments are independently controllable. Further provided are ion manifolds wherein the one or more electrical conductor segments energized with RF and/or DC voltage. Further provided are ion manifolds wherein the first ion optic and the second ion optic each comprise an electrodynamic ion funnel. Further provided are ion manifolds wherein the first ion optic and the second ion optic each independently comprise a different pressure. Further provided are ion

manifolds wherein the ion manifold further comprises an in-line ion inlet. Further provided are ion manifolds wherein the method further comprises providing a calibrant ion flux into the first ion optic via an in-line ion manifold inlet. Further provided are ion manifolds wherein the flux of ions from the orthogonal ion inlet and the flux of ions from the in-line ion manifold inlet are offset by 1-5 mm. Further provided are ion manifolds wherein the ion manifold further comprises an ion repeller manifold that is (i) positioned such that an axis along a normal vector of a surface of ion repeller manifold is orthogonal to a central axis of the ion manifold inlet, and (ii) is configured to direct a path of the flux of ions into the first ion optic. Further provided are ion manifolds wherein the inline manifold inlet penetrates through the ion repeller manifold. Further provided are ion manifolds wherein the ion repeller manifold comprises a segmented plate, wherein the ion repeller manifold is configured to allow differing voltages. Further provided are ion manifolds wherein the repeller, the ion manifold inlet, and the first ion optic are contained at least partially within a first chamber. Further provided are ion manifolds wherein the second ion optic is contained at least partially in a second chamber, different than the first chamber. Further provided are ion manifolds wherein a reduced-pressure FAIMS (high field asymmetric waveform ion mobility spectrometer) device is configured to receive ions from the first ion optic and selectively output ions to the second ion optic. Further provided are ion manifolds wherein a reduced-pressure FAIMS (high field asymmetric waveform ion mobility spectrometer) device is configured to receive ions from the first ion optic and selectively output multiply charged ions to the second ion optic as compared to singly charged ions.

[0005] Provided herein are methods comprising: generating a plurality of ion streams, the method comprising: (a) providing an ion flux to an orthogonal ion manifold inlet of an ion manifold, the ion manifold comprising: (i) the orthogonal ion manifold inlet; (ii) a first ion optic configured to receive the ion flux through the ion manifold inlet, wherein the ion inlet is inside the first ion optic; and (iii) a second ion optic configured to receive an output of the ion flux through the first ion optic, wherein the second ion optic comprises a plurality of outputs; and (b) generating the plurality of ion streams from the plurality of outputs of the second ion optic when the ion flux traverses through the second ion optic. Further provided are methods wherein the first ion optic and the second ion optic comprises one or more electrical conductor segments, wherein the one or more electrical conductor segments comprise one or more through holes. Further provided are methods wherein the one or more electrical conductor segments are independently controllable. Further provided are methods wherein the one or more electrical conductor segments energized with RF and/or DC voltage. Further provided are methods wherein the first ion optic and the second ion optic each comprise an electrodynamic ion funnel. Further provided are methods wherein the first ion optic and the second ion optic each

independently comprise a different pressure. Further provided are methods wherein the ion manifold further comprises an in-line ion inlet. Further provided are methods wherein the method further comprises providing a calibrant ion flux into the first ion optic via an in-line ion manifold inlet. Further provided are methods wherein the flux of ions from the orthogonal ion inlet and the flux of ions from the in-line ion manifold inlet are offset by 1-5 mm. Further provided are methods wherein the ion manifold further comprises an ion repeller manifold that is (i) positioned such that an axis along a normal vector of a surface of ion repeller manifold is orthogonal to a central axis of the ion manifold inlet, and (ii) is configured to direct a path of the flux of ions into the first ion optic. Further provided are methods wherein the inline manifold inlet penetrates through the ion repeller manifold. Further provided are methods wherein the ion repeller manifold comprises a segmented plate, wherein the ion repeller manifold is configured to allow differing voltages. Further provided are methods wherein the repeller, the ion manifold inlet, and the first ion optic are contained at least partially within a first chamber. Further provided are methods wherein the second ion optic is contained at least partially in a second chamber, different than the first chamber. Further provided are methods wherein a reduced-pressure FAIMS (high field asymmetric waveform ion mobility spectrometer) device is configured to receive ions from the first ion optic and selectively output ions to the second ion optic. Further provided are methods wherein a reduced-pressure FAIMS (high field asymmetric waveform ion mobility spectrometer) device is configured to receive ions from the first ion optic and selectively output multiply charged ions to the second ion optic as compared to singly charged ions.

[0006] Provided herein are ion mobility devices comprising: a first substrate plate comprising: a coplanar first outer electrode and second outer electrode; and a first separation electrode; and a second substrate plate comprising: a coplanar third outer electrode and fourth outer electrode; and a second separation electrode; wherein the first substrate plate and the second substrate plate are substantially parallel. Further provided herein are ion mobility devices wherein the distance between the first plate and the second plate is 4 to 12 mm. Further provided herein are ion mobility devices wherein the first outer electrode, the second outer electrode, the third outer electrode, and the fourth outer electrode are configured as RF confining electrodes to confine the ion beam to the center of the device. Further provided herein are ion mobility devices wherein the region surrounding the first separation electrode and the second separation electrode has a pressure of no more than 20 torr. Further provided herein are ion mobility devices wherein the device comprises guard rail electrodes in each side of the device. Further provided herein are ion mobility devices wherein the guard rail electrodes comprise a DC gradient. Further provided herein are ion mobility devices wherein a voltage is applied to the first separation electrode.

Further provided herein are ion mobility devices wherein a FAIMS separation voltage is applied to the first separation electrode. Further provided herein are ion mobility devices wherein a FAIMS separation voltage is applied to only the first separation electrode. Further provided herein are ion mobility devices wherein a FAIMS separation voltage of at least 800V is applied to at least one separation electrode. Further provided herein are ion mobility devices wherein a FAIMS separation voltage of at least 2000V is applied to at least one separation electrode. Further provided herein are ion mobility devices wherein a FAIMS separation voltage of at least 2000V is applied to at least one separation electrode, and the region surrounding the first separation electrode and the second separation electrode has a pressure of about 20 torr. Further provided herein are ion mobility devices wherein the ion manifold comprises a device disclosed herein.

[0007] Provided herein are methods of spatially separating ions comprising: providing an ion flux to an ion mobility device described herein; applying a high voltage RF waveform to the separation electrodes; applying an ion confining waveform to the outer electrodes; and selecting transmitting ions based on mobility to generate a mobility-selected ion stream.

[0008] Provided herein are reduced-pressure field asymmetric ion mobility devices comprising: an enclosed mobility chamber having an ion inlet and an ion outlet disposed at opposite ends and configured to be filled with an inert gas at a pressure of less than atmospheric pressure; at least one inner electrode disposed longitudinally between the ion inlet and the ion outlet of the enclosed mobility chamber; at least one outer electrode disposed longitudinally between the ion inlet and the ion outlet of the enclosed mobility chamber, the outer electrode being disposed such that the inner electrode is at least partially enclosed within the outer electrode; and one or more power supplies configured deliver a waveform to the inner electrode or the outer electrode, the waveform being configured to differentially deflect ions having different ion mobilities based on interaction of the ions with the waveform and the inert gas, wherein the differential deflection is configured to selectively remove ions having mobilities that correspond to singly charged species prior to said species reaching the ion outlet, wherein the inner electrode and the outer electrode are substantially planar. Further provided herein are reduced-pressure field asymmetric ion mobility devices wherein the one or more power supplies provide a waveform comprising at least two sinusoids which are phase-shifted with respect to each other. Further provided herein are reduced-pressure field asymmetric ion mobility devices wherein the waveform is delivered to the outer electrode. Further provided herein are reduced-pressure field asymmetric ion mobility devices wherein the outer electrode comprises at least two ion outlets. Further provided herein are reduced-pressure field asymmetric ion mobility devices wherein the reduced-pressure field asymmetric ion mobility device further comprises one or more sets of ion

optics configured to guide ions into the ion inlet, out of the ion outlet, or a combination thereof. Further provided herein are reduced-pressure field asymmetric ion mobility devices wherein multiply charged ions are transmitted from the ion inlet to the ion outlet in less than about 100 milliseconds (e.g., less than about 50 ms, 25 ms, 10 ms, 5 ms, or 3 ms). Further provided herein are reduced-pressure field asymmetric ion mobility devices wherein the electrodes are configured to be independently controllable. Further provided herein are reduced-pressure field asymmetric ion mobility devices wherein the electrodes are positioned at or near the outputs.

[0009] Provided herein are methods of separating singly charged ions from multiply charged ions, the method comprising: (a) providing an ion flux to an ion inlet of a reduced-pressure field asymmetric ion mobility device, the reduced-pressure field asymmetric ion mobility device comprising: an enclosed mobility chamber having the ion inlet and an ion outlet disposed at opposite ends and configured to be filled with an inert gas at a pressure of less than atmospheric pressure; at least one inner electrode disposed longitudinally between the ion inlet and the ion outlet of the enclosed mobility chamber; at least one outer electrode disposed longitudinally between the ion inlet and the ion outlet of the enclosed mobility chamber; and one or more power supplies configured deliver a waveform to the inner electrode or the outer electrode, the waveform being configured to differentially deflect ions having different ion mobilities based on interaction of the ions with the waveform and the inert gas, wherein the differential deflection is configured to selectively remove ions having mobilities that correspond to singly charged species prior to said species reaching the ion outlet; (b) applying the waveform using the one or more power supplies to thereby substantially prevent ions of the ion flux having mobilities that correspond to singly charged species from reaching the ion outlet of the reduced-pressure field asymmetric ion mobility device; and (c) obtaining a multiply charged ion population at the ion outlet of the reduced-pressure field asymmetric ion mobility device which is enriched for ions that correspond to multiply charged species. Further provided herein are methods wherein the one or more power supplies provide a waveform comprising at least two sinusoids which are phase-shifted with respect to each other. Further provided herein are methods wherein the waveform is delivered to the outer electrode. Further provided herein are methods wherein the outer electrode comprises at least two ion outlets. Further provided herein are methods further comprising one or more sets of ion optics configured to guide ions into the ion inlet, out of the ion outlet, or a combination thereof. Further provided herein are methods wherein multiply charged ions are transmitted from the ion inlet to the ion outlet in less than about 100 milliseconds (e.g., less than about 50 ms, 25 ms, 10 ms, 5 ms, or 3 ms). Further provided herein are methods wherein the electrodes are configured to be independently controllable. Further provided herein are methods wherein the electrodes are positioned at or near the outputs.

[0010] Additional aspects and advantages of the present disclosure will become readily apparent to those skilled in this art from the following detailed description, wherein only illustrative embodiments of the present disclosure are shown and described. As will be realized, the present disclosure is capable of other and different embodiments, and its several details are capable of modifications in various obvious respects, all without departing from the disclosure. Accordingly, the drawings and description are to be regarded as illustrative in nature, and not as restrictive.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings (also “Figure” and “FIG.” herein), of which:

[0012] **FIG. 1.** shows an example schematic for an ion manifold, as described in some embodiments herein.

[0013] **FIG. 2** shows an example schematic of the first ion optic and the second ion optic, as described in some embodiments herein.

[0014] **FIG. 3** shows an example computer system that is programmed or otherwise configured to implement methods provided herein, as described in some embodiments herein.

[0015] **FIG. 4** shows an example workflow diagram for a method of generating a plurality of ion streams, as described in some embodiments herein.

[0016] **FIG. 5A** shows an example of a planar FAIMS (high field asymmetric waveform ion mobility spectrometry) configuration, as described in some embodiments herein, showing top and bottom PCBs (printed circuit boards).

[0017] **FIG. 5B** shows an example of a planar FAIMS configuration, as described in some embodiments herein, showing FAIMS and RF polarities.

[0018] **FIG. 6** shows an example cross-section view schematic of a FAIMS configuration with top and bottom PCBs, as described in some embodiments herein.

[0019] **FIG. 7** shows another example schematic of a FAIMS configuration, as described in some embodiments herein.

[0020] **FIG. 8** shows an example schematic of a FAIMS configuration with a separation segmented electrode, as described in some embodiments herein.

[0021] **FIG. 9A** shows an example front-view schematic of a device configuration comprising an assembly of FAIMS, as described in some embodiments herein.

[0022] **FIG. 9B** shows an example front-view schematic of a device configuration comprising an assembly of FAIMS with shared electrodes, as described in some embodiments herein.

[0023] **FIG. 10** shows an example workflow diagram for a front-end interface, as described in some embodiments herein.

[0024] **FIG. 11** shows an example high-level schematic of a planar FAIMS configuration, as described in some embodiments herein.

[0025] **FIG. 12A** shows an isometric top-view of a FAIMS front-end interface, as described in some embodiments herein.

[0026] **FIG. 12B** shows an isometric top-view of a FAIMS front-end interface, as described in some embodiments herein.

[0027] **FIG. 12C** shows a top-view of a FAIMS front-end interface, as described in some embodiments herein;

[0028] **FIG. 12D** shows a bottom-view of a FAIMS front-end interface, as described in some embodiments herein.

[0029] **FIG. 12E** shows a side-view of a FAIMS front-end interface, as described in some embodiments herein.

[0030] **FIG. 12F** shows a side-view of a FAIMS front-end interface, as described in some embodiments herein.

[0031] **FIG. 12G** shows a cross-section side-view of a FAIMS front-end interface comprising a planar FAIMS configuration, as described in some embodiments herein.

[0032] **FIG. 12H** shows an exploded isometric top view of a FAIMS front-end interface comprising a planar FAIMS configuration, as described in some embodiments herein.

[0033] **FIG. 13A** shows isometric top view of a device comprising a FAIMS front-end interface coupled to a TWIMS (traveling-wave ion mobility spectrometry) interface, as described in some embodiments herein.

[0034] **FIG. 13B** shows isometric top-view of a device comprising a FAIMS front-end interface coupled to a TWIMS (traveling-wave ion mobility spectrometry) interface, as described in some embodiments herein.

[0035] **FIG. 13C** shows a top-view of a device comprising a FAIMS front-end interface coupled to a TWIMS (traveling-wave ion mobility spectrometry) interface, as described in some embodiments herein.

[0036] **FIG. 13D** shows a bottom-view of a device comprising a FAIMS front-end interface coupled to a TWIMS (traveling-wave ion mobility spectrometry) interface, as described in some embodiments herein.

[0037] **FIG. 13E** shows a side-view of a device comprising a FAIMS front-end interface coupled to a TWIMS (traveling-wave ion mobility spectrometry) interface, as described in some embodiments herein.

[0038] **FIG. 13F** shows a back-view of a device comprising a FAIMS front-end interface coupled to a TWIMS (traveling-wave ion mobility spectrometry) interface, as described in some embodiments herein.

[0039] **FIG. 13G** shows a cross-section side-view of a device comprising a FAIMS front-end interface coupled to a TWIMS (traveling-wave ion mobility spectrometry) interface, as described in some embodiments herein.

[0040] **FIG. 13H** shows an isometric exploded view of a device comprising a FAIMS front-end interface coupled to a TWIMS (traveling-wave ion mobility spectrometry) interface, as described in some embodiments herein.

[0041] **FIG. 14A** shows an example configuration for a FAIMS device.

[0042] **FIG. 14B** shows the results of ion isolation with and without a FAIMS device. With the FAIMS device off, major ions include 621.57, 1221.25, 1521.10, and 1820.95 m/z. With the FAIMS device turned on (CV 5 volts) major ions were 921.41 and 621.57.

[0043] **FIG. 14C** shows a graph of resolution with experiments with the FAIMS device on (CV 6.5V or off).

[0044] **FIG. 14D** shows a graph of ions measured using a CV ramp. Ramping the CV allows to filter as a function of their masses. The high mass transmission was greater than an average QTOF6600. Varying the CV selectively transmitted ions based on their masses, higher masses for lower CV and lower masses for greater CV.

[0045] **FIG. 14E** shows a graph of CV ramping and mass dependency, with intensity (cps) plotted against CV (volts).

[0046] **FIG. 14F** shows a graph of CV ramping and mass dependency, with relative intensity (percent) plotted against CV (volts).

[0047] **FIG. 14G** shows a graph of CV vs. ion populations. Varying the CV allows to discriminate ions based on their charged state. Here, lower CV favored the singly charged ions over the doubly charged. The opposite was observed for greater CVs.

[0048] **FIG. 14H** shows a graph of Multi Charged Ions, zoomed window of m/z 900 to m/z 930.

[0049] **FIG. 15** shows a schematic of an example device described herein having an orthogonal ion manifold inlet, in-line ion manifold inlet, repeller plate, reduced pressure FAIMS, ion funnel, and 4-way split ion outlet.

[0050] **FIG. 16** shows an image of a pair of DC guardrails for use on each side of a FAIMS device described herein.

DETAILED DESCRIPTION

[0051] While various embodiments of the disclosure have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions can occur to those skilled in the art without departing from the disclosure. It should be understood that various alternatives to the embodiments of the disclosure described herein can be employed. The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described.

[0052] In some embodiments, the disclosure describes an ion manifold configured for multiplex detection of one or more ion streams (e.g., derived from a biological sample) with one or more mass spectrometer-based sensors. The disclosure describes, in some embodiments, an ion manifold configured to receive a stream of ions and to divide or split the stream of ions to a plurality of streams of ions. In some cases, a first stream of ions split from e.g., an input stream of ions, may be detected with a first mass spectrometer sensor and a second stream of ions split from the input stream of ions may be detected with a second mass spectrometer. By splitting or dividing an input stream of ions, the time of analysis of the input stream of mass spectrometry may be reduced by at least about 5 seconds, 15 seconds, 20 seconds, 30 seconds, 1 minute, 5 minutes, 10 minutes, 20 minutes, 30 minutes, or least about 1 hour. In some case, parallel analysis may provide improved detection, sensitivity, accuracy, and/or precision relative to non-multiplexed methods using the same analysis time.

Example Ion Manifolds

[0053] In some embodiments, **FIG. 1** shows an ion manifold **100**, comprising an ion manifold inlet **106**, an ion repeller manifold **104**, a first ion optic **116**, a second ion optic **118**, a port **130**, or any combination thereof. In some embodiments, the first ion optic **116** is configured to receive a flux of ions **132** through the ion manifold inlet **106**. In some embodiments, a second ion optic **118** is configured to receive an output of the flux of ions through the first ion optic **116**. In some embodiments, the second ion optic **118** comprises a plurality of outputs **114** that split or divide the flux of ions into a plurality of ion streams. In some embodiments, the first ion optic **116**, the second ion optic **118**, or a combination thereof, are configured to output one or more ion streams of ions comprising a range of mass/charge. For example, the second ion optic may be configured to output ions within a range including about 400 to about 900 mass/charge. In some embodiments, the second ion optic is configured to transmit at least 50% (e.g., at least 60%, at least 70%, at least 80%, at least 90%, or at least 95%) of the ions received in the second ion optic. In some embodiments, the first ion optic **116** and the second ion optic **118** comprise an ion funnel. In some embodiments, the first ion optic **116** and the second ion optic **118**

comprise one or more electrical conductor segments **124**. In some embodiments, the one or more electrical conductor segments **124** may comprise a printed circuit board (PCB). In some embodiments, the ion manifold inlet **106** may comprise a heated ion manifold inlet. In some embodiments, the ion manifold inlet **106** comprises a slotted capillary. In some embodiments, the slotted capillary may comprise a rectangular cross-sectional geometry **107**. In some cases, the rectangular cross-sectional geometry **107** of the slotted capillary provides efficient ionization of one or more molecules of a sample to improve the accuracy of the ion manifold's analysis and detection of one or more molecules or molecule signatures. In some embodiments, the ion manifold inlet **106** comprises a circular or oval cross-sectional geometry. In some embodiments, the capillary comprises at least one dimension that is less than about 250 microns, less than about 150 microns, or less than about 100 microns. In some embodiments, the capillary comprises at least one dimensions that is less than 250 microns and at least one dimension that is greater than 1 mm. In some embodiments, the capillary comprises at least one dimensions that is less than 150 microns and at least one dimension that is greater than 2 mm.

[0054] In some embodiments, the ion repeller manifold **104**, ion manifold inlet **106**, or the first ion optic **116** are contained at least partially within a first chamber **110**. In some embodiments, the second ion optic **118** is contained at least partially in a second chamber **112**, different than the first chamber **110**. In some embodiments, the first chamber **110** comprises a first pressure and the second chamber **112** comprises a second pressure, where the first pressure is higher than the second pressure. In some embodiments, the first chamber **110** comprises a first pressure and the second chamber **112** comprises a second pressure, where the first pressure is lower than the second pressure. In some embodiments, the first chamber **110** comprises a pressure of at least about 8 torr. In some embodiments, the second chamber **112** comprises a pressure of at least about 2 torr. In some embodiments, the second chamber **112** comprises a pressure of no more than about 6 torr. In some embodiments, the flux of ions **132** is provided to the ion manifold inlet **106** by electrospray ionization from a multi-emitter array. In some embodiments, the multi-emitter array can be a microfluidic multi-emitter with five or more emitters. In some embodiments, the ion repeller manifold **104** comprises a segmented plate with one or more segments (**105, 108, 109**). In some embodiments, the ion repeller manifold **104** is configured to allow for different voltages that can improve the efficiency of delivering ions into the ion funnel. In some embodiments, the segmented plate (**105, 108, 109**) comprises at least about 2 segments or at least about 3 segments. In some embodiments, the central axis of the first ion optic and the second ion optic **128** is orthogonal to a central axis of the ion manifold inlet **130**. In some embodiments, the central axis of the ion manifold inlet **130** is orthogonal to an axis normal to the surface of the ion repeller manifold **128**. In some embodiments, a first electrode segment **105**

of the ion repeller manifold may output a lower voltage than an adjacent second electrode segment **108** of the ion repeller manifold **104**. In some embodiments, the ion repeller manifold **104** comprises a voltage gradient across a longitudinal length of the ion repeller manifold **104**. In some embodiments, the ion manifold **100** comprises a port **102** fluidically coupled to the ion manifold **100**, wherein the port **102** is configured to pressurize the first chamber **110**, the second chamber **112**, or a combination thereof. In some embodiments, the central axis of the port **130** is co-linear with a central axis of the ion manifold inlet **130**. Although the devised purpose of the port **102** is to pressurize the first chamber **110**, the second chamber **112**, or a combination of the two, it has the unexpected benefit of improving signal and reducing noise by removing the solvent of a flux of ions **132** provided to the ion manifold inlet. In some embodiments, the first ion optic **116** or the second ion optic **118** comprise a linear DC gradient provided by the one or more electrical conductor segments **124** across a longitudinal length of the first ion optic **116** or the second ion optic **118**. In some embodiments, one or more electrical conductor segments **124** of the first ion optic **116** or the second ion optic **118** comprises up to about 4 direct current (DC) conductance limits. In some embodiments, a first electrical conductor segment of the one or more electrical conductor segments **124** provides a first signal with a first phase and a second electrical conductor segment of the one or more electrical conductor segments **124** provides a second signal with an anti-phase of the first phase.

[0055] While **FIG. 1** depicts ion manifold **100** with ion manifold inlet **106** configured such that ion flux **132** enters ion manifold **100** in a direction orthogonal to linear axis **128**, the ion manifold inlet **106** may be configured such that ion flux **132** enters parallel to linear axis **128**. In such cases, ion repeller manifold **104** may be omitted and the ion manifold inlet **106**

[0056] The skilled person, guided by the teachings of the present application, will appreciate that other components may be included in ion manifold **100**. For example, additional ports may be included to provide different vacuum pressures, pressure sensors, electrical feedthroughs, and the like may be included. In some embodiments, the ion manifold may include a FAIMS device between the first ion optic and the second optic as disclosed herein.

[0057] In some embodiments, the first ion optic **116** or the second ion optic **118**, comprise one or more electrical conductor segments **124**, as shown in **FIG. 2**. In some embodiments, the one or more electrical conductor segments **124** may comprise one or more through holes **126**. In some embodiments, the one or more through holes **126** may comprise a circular, oval, polygonal, or square shape, as shown in **FIG. 2**. In some embodiments, the one or more electrical conductor segments **124** may comprise a center to center spacing of at least about 1 millimeter (mm). In some embodiments, the one or more through holes are provided along a linear axis **128** on a surface of the one or more electrical conductor segments **124**. In some

embodiments, the positioning of two or more through holes is symmetric. In some embodiments, the two or more through holes of the one or more electrical conductor segments are adjacent or in contact with each other, as shown in **FIG. 2**. In some embodiments, a first electrical conductor segment **124** comprises a first dimension of a through hole and an adjacent second electrical conductor segment **124** comprises a second dimension smaller than the first dimension. In some cases, one or more electrical conductor segments **124** may form an inner geometry of the first ion optic **122** and second ion optic **123**. In some cases, the inner geometry of the first ion optic **122** and second ion optic **123** may comprise one or more segments. In some cases, the one or more segments of the inner geometry may comprise a linear no slope segment, a linear positive slope segment, linear negative slope segment, or any combination thereof, as shown in **FIG. 2**. In some cases, the one or more electrical conductor segments **124** may split or divide a stream of ions, as described elsewhere herein, into a plurality of streams of ions. By splitting a stream of ions into a plurality of streams of ions, multiplex detection, and further processing of individual ion populations, e.g., ions within a given mass-to-charge ratio band may be isolated, measured, or analyzed. The effect of said ion stream multiplexing and detection shortens the time required otherwise to detect molecules of the ion stream. Thus, additional components may receive the divided ion flux from the second ion optic. For example, two or more of the ion fluxes output from the second ion optic may each be operable coupled to different mass analyzers (e.g., different time-of-flight mass analyzer).

[0058] In some embodiments, the one or more electrical conductor segments **124** may output a voltage of about 0 V to about 500 V. In some embodiments, the one or more electrical conductor segments may output a voltage of about 0 V to about 20 V, about 0 V to about 40 V, about 0 V to about 50 V, about 0 V to about 100 V, about 0 V to about 150 V, about 0 V to about 300 V, about 0 V to about 500 V, about 20 V to about 40 V, about 20 V to about 50 V, about 20 V to about 100 V, about 20 V to about 150 V, about 20 V to about 300 V, about 20 V to about 500 V, about 40 V to about 50 V, about 40 V to about 100 V, about 40 V to about 150 V, about 40 V to about 300 V, about 40 V to about 500 V, about 50 V to about 100 V, about 50 V to about 150 V, about 50 V to about 300 V, about 50 V to about 500 V, about 100 V to about 150 V, about 100 V to about 300 V, about 100 V to about 500 V, about 150 V to about 300 V, about 150 V to about 500 V, or about 300 V to about 500 V. In some embodiments, the one or more electrical conductor segments may output a voltage of about 0 V, about 20 V, about 40 V, about 50 V, about 100 V, about 150 V, about 300 V, or about 500 V. In some embodiments, the one or more electrical conductor segments may output a voltage of at least about 0 V, about 20 V, about 40 V, about 50 V, about 100 V, about 150 V, or about 300 V. In some embodiments, the one or

more electrical conductor segments may output a voltage of at most about 20 V, about 40 V, about 50 V, about 100 V, about 150 V, about 300 V, or about 500 V.

[0059] In some embodiments, the one or more electrical conductor segments **124** may output a current of about 0 μA to about 100 μA . In some embodiments, the one or more electrical conductor segments **124** may output a current of about 0 μA to about 10 μA , about 0 μA to about 20 μA , about 0 μA to about 40 μA , about 0 μA to about 50 μA , about 0 μA to about 80 μA , about 0 μA to about 100 μA , about 10 μA to about 20 μA , about 10 μA to about 40 μA , about 10 μA to about 50 μA , about 10 μA to about 80 μA , about 10 μA to about 100 μA , about 20 μA to about 40 μA , about 20 μA to about 50 μA , about 20 μA to about 80 μA , about 20 μA to about 100 μA , about 40 μA to about 50 μA , about 40 μA to about 80 μA , about 40 μA to about 100 μA , about 50 μA to about 80 μA , about 50 μA to about 100 μA , or about 80 μA to about 100 μA . In some embodiments, the one or more electrical conductor segments **124** may output a current of about 0 μA , about 10 μA , about 20 μA , about 40 μA , about 50 μA , about 80 μA , or about 100 μA . In some embodiments, the one or more electrical conductor segments **124** may output a current of at least about 0 μA , about 10 μA , about 20 μA , about 40 μA , about 50 μA , or about 80 μA . In some embodiments, the one or more electrical conductor segments **124** may output a current of at most about 10 μA , about 20 μA , about 40 μA , about 50 μA , about 80 μA , or about 100 μA .

[0060] In some embodiments, the flux of ions is generated through electrospray ionization by applying a voltage of about 0 kV to about 5 kV. In some embodiments, the flux of ions is generated through electrospray ionization by applying a voltage of about 0.5 kV, about 1 kV, about 1.5 kV, about 2 kV, about 2.5 kV, about 3 kV, about 3.5 kV, about 4 kV, about 4.5 kV, or about 5 kV. In some embodiments, the flux of ions is generated through electrospray ionization by applying a voltage of at least about 0.5 kV, about 1 kV, about 1.5 kV, about 2 kV, about 2.5 kV, about 3 kV, about 3.5 kV, about 4 kV, or about 4.5 kV. In some embodiments, the flux of ions is generated through electrospray ionization by applying a voltage of at most about 0.5 kV, about 1 kV, about 1.5 kV, about 2 kV, about 2.5 kV, about 3 kV, about 3.5 kV, about 4 kV, about 4.5 kV, or about 5 kV.

[0061] In some embodiments, the flux of ions is generated through electrospray ionization by utilizing a current of about 0 μA to about 100 μA . In some embodiments, the flux of ions is generated through electrospray ionization by utilizing a current of about 0 μA to about 10 μA , about 0 μA to about 20 μA , about 0 μA to about 40 μA , about 0 μA to about 50 μA , about 0 μA to about 80 μA , about 0 μA to about 100 μA , about 10 μA to about 20 μA , about 10 μA to about 40 μA , about 10 μA to about 50 μA , about 10 μA to about 80 μA , about 10 μA to about 100 μA , about 20 μA to about 40 μA , about 20 μA to about 50 μA , about 20 μA to about 80 μA , about

20 μA to about 100 μA , about 40 μA to about 50 μA , about 40 μA to about 80 μA , about 40 μA to about 100 μA , about 50 μA to about 80 μA , about 50 μA to about 100 μA , or about 80 μA to about 100 μA . In some embodiments, the flux of ions is generated through electrospray ionization by utilizing a current of about 0 μA , about 10 μA , about 20 μA , about 40 μA , about 50 μA , about 80 μA , or about 100 μA . In some embodiments, the flux of ions is generated through electrospray ionization by utilizing a current of at least about 0 μA , about 10 μA , about 20 μA , about 40 μA , about 50 μA , or about 80 μA . In some embodiments, the flux of ions is generated through electrospray ionization by utilizing a current of at most about 10 μA , about 20 μA , about 40 μA , about 50 μA , about 80 μA , or about 100 μA .

[0062] In some embodiments, the ion repeller manifold **104** has a DC bias for each segment (**105, 108, 109**) of about 0 V to about 500 V. In some embodiments, the ion repeller manifold **104** has a DC bias for each segment (**105, 108, 109**) of about 0 V to about 20 V, about 0 V to about 40 V, about 0 V to about 50 V, about 0 V to about 100 V, about 0 V to about 150 V, about 0 V to about 300 V, about 0 V to about 500 V, about 20 V to about 40 V, about 20 V to about 50 V, about 20 V to about 100 V, about 20 V to about 150 V, about 20 V to about 300 V, about 20 V to about 500 V, about 40 V to about 50 V, about 40 V to about 100 V, about 40 V to about 150 V, about 40 V to about 300 V, about 40 V to about 500 V, about 50 V to about 100 V, about 50 V to about 150 V, about 50 V to about 300 V, about 50 V to about 500 V, about 100 V to about 150 V, about 100 V to about 300 V, about 100 V to about 500 V, about 150 V to about 300 V, about 150 V to about 500 V, or about 300 V to about 500 V. In some embodiments, the ion repeller manifold **104** has a DC bias for each segment (**105, 108, 109**) of about 0 V, about 20 V, about 40 V, about 50 V, about 100 V, about 150 V, about 300 V, or about 500 V. In some embodiments, the ion repeller manifold **104** has a DC bias for each segment (**105, 108, 109**) of at least about 0 V, about 20 V, about 40 V, about 50 V, about 100 V, about 150 V, or about 300 V. In some embodiments, the ion repeller manifold **104** has a DC bias for each segment (**105, 108, 109**) of at most about 20 V, about 40 V, about 50 V, about 100 V, about 150 V, about 300 V, or about 500 V.

[0063] In some embodiments, the ion repeller manifold **104** utilizes a current for each segment (**105, 108, 109**) of about 0 μA to about 100 μA . In some embodiments, the ion repeller manifold **104** utilizes a current for each segment (**105, 108, 109**) of about 0 μA to about 10 μA , about 0 μA to about 20 μA , about 0 μA to about 40 μA , about 0 μA to about 50 μA , about 0 μA to about 80 μA , about 0 μA to about 100 μA , about 10 μA to about 20 μA , about 10 μA to about 40 μA , about 10 μA to about 50 μA , about 10 μA to about 80 μA , about 10 μA to about 100 μA , about 20 μA to about 40 μA , about 20 μA to about 50 μA , about 20 μA to about 80 μA , about 20 μA to about 100 μA , about 40 μA to about 50 μA , about 40 μA to about 80 μA , about 40 μA to

about 100 μA , about 50 μA to about 80 μA , about 50 μA to about 100 μA , or about 80 μA to about 100 μA . In some embodiments, the ion repeller manifold **104** utilizes a current for each segment (**105, 108, 109**) of about 0 μA , about 10 μA , about 20 μA , about 40 μA , about 50 μA , about 80 μA , or about 100 μA . In some embodiments, the ion repeller manifold **104** utilizes a current for each segment (**105, 108, 109**) of at least about 0 μA , about 10 μA , about 20 μA , about 40 μA , about 50 μA , or about 80 μA . In some embodiments, the ion repeller manifold **104** utilizes a current for each segment (**105, 108, 109**) of at most about 10 μA , about 20 μA , about 40 μA , about 50 μA , about 80 μA , or about 100 μA .

[0064] In some embodiments, the heated ion manifold inlet has a DC voltage bias of about 0 V to about 500 V. In some embodiments, the heated ion manifold inlet has a DC voltage bias of about 0 V to about 20 V, about 0 V to about 40 V, about 0 V to about 50 V, about 0 V to about 100 V, about 0 V to about 150 V, about 0 V to about 300 V, about 0 V to about 500 V, about 20 V to about 40 V, about 20 V to about 50 V, about 20 V to about 100 V, about 20 V to about 150 V, about 20 V to about 300 V, about 20 V to about 500 V, about 40 V to about 50 V, about 40 V to about 100 V, about 40 V to about 150 V, about 40 V to about 300 V, about 40 V to about 500 V, about 50 V to about 100 V, about 50 V to about 150 V, about 50 V to about 300 V, about 50 V to about 500 V, about 100 V to about 150 V, about 100 V to about 300 V, about 100 V to about 500 V, about 150 V to about 300 V, about 150 V to about 500 V, or about 300 V to about 500 V. In some embodiments, the heated ion manifold inlet has a DC voltage bias of about 0 V, about 20 V, about 40 V, about 50 V, about 100 V, about 150 V, about 300 V, or about 500 V. In some embodiments, the heated ion manifold inlet has a DC voltage bias of at least about 0 V, about 20 V, about 40 V, about 50 V, about 100 V, about 150 V, or about 300 V. In some embodiments, the heated ion manifold inlet has a DC voltage bias of at most about 20 V, about 40 V, about 50 V, about 100 V, about 150 V, about 300 V, or about 500 V.

[0065] In some embodiments, the heated ion manifold inlet utilizes a current of about 0 μA to about 100 μA . In some embodiments, the heated ion manifold inlet utilizes a current of about 0 μA to about 10 μA , about 0 μA to about 20 μA , about 0 μA to about 40 μA , about 0 μA to about 50 μA , about 0 μA to about 80 μA , about 0 μA to about 100 μA , about 10 μA to about 20 μA , about 10 μA to about 40 μA , about 10 μA to about 50 μA , about 10 μA to about 80 μA , about 10 μA to about 100 μA , about 20 μA to about 40 μA , about 20 μA to about 50 μA , about 20 μA to about 80 μA , about 20 μA to about 100 μA , about 40 μA to about 50 μA , about 40 μA to about 80 μA , about 40 μA to about 100 μA , about 50 μA to about 80 μA , about 50 μA to about 100 μA , or about 80 μA to about 100 μA . In some embodiments, the heated ion manifold inlet utilizes a current of about 0 μA , about 10 μA , about 20 μA , about 40 μA , about 50 μA , about 80 μA , or about 100 μA . In some embodiments, the heated ion manifold inlet utilizes a current of at

least about 0 μA , about 10 μA , about 20 μA , about 40 μA , about 50 μA , or about 80 μA . In some embodiments, the heated ion manifold inlet utilizes a current of at most about 10 μA , about 20 μA , about 40 μA , about 50 μA , about 80 μA , or about 100 μA .

[0066] In some embodiments, the first ion optic **116** and the second ion optic **118** have RF phase and anti-phase have a peak-to-peak voltage of about 10 Vp-p to about 200 Vp-p. In some embodiments, the first ion optic **116** and the second ion optic **118** have RF phase and anti-phase have a peak-to-peak voltage of about 10 Vp-p to about 20 Vp-p, about 10 Vp-p to about 40 Vp-p, about 10 Vp-p to about 50 Vp-p, about 10 Vp-p to about 100 Vp-p, about 10 Vp-p to about 200 Vp-p, about 20 Vp-p to about 40 Vp-p, about 20 Vp-p to about 50 Vp-p, about 20 Vp-p to about 100 Vp-p, about 20 Vp-p to about 200 Vp-p, about 40 Vp-p to about 50 Vp-p, about 40 Vp-p to about 100 Vp-p, about 40 Vp-p to about 200 Vp-p, about 50 Vp-p to about 100 Vp-p, about 50 Vp-p to about 200 Vp-p, or about 100 Vp-p to about 200 Vp-p. In some embodiments, the first ion optic **116** and the second ion optic **118** have RF phase and anti-phase have a peak-to-peak voltage of about 10 Vp-p, about 20 Vp-p, about 40 Vp-p, about 50 Vp-p, about 100 Vp-p, or about 200 Vp-p. In some embodiments, the first ion optic **116** and the second ion optic **118** have RF phase and anti-phase have a peak-to-peak voltage of at least about 10 Vp-p, about 20 Vp-p, about 40 Vp-p, about 50 Vp-p, or about 100 Vp-p. In some embodiments, the first ion optic **116** and the second ion optic **118** have RF phase and anti-phase have a peak-to-peak voltage of at most about 20 Vp-p, about 40 Vp-p, about 50 Vp-p, about 100 Vp-p, or about 200 Vp-p.

[0067] In some embodiments, the first ion optic **116** and the second ion optic **118** utilize a DC voltage of about 0 V to about 500 V. In some embodiments, the first ion optic **116** and the second ion optic **118** utilize a DC voltage of about 0 V to about 20 V, about 0 V to about 40 V, about 0 V to about 50 V, about 0 V to about 100 V, about 0 V to about 150 V, about 0 V to about 300 V, about 0 V to about 500 V, about 20 V to about 40 V, about 20 V to about 50 V, about 20 V to about 100 V, about 20 V to about 150 V, about 20 V to about 300 V, about 20 V to about 500 V, about 40 V to about 50 V, about 40 V to about 100 V, about 40 V to about 150 V, about 40 V to about 300 V, about 40 V to about 500 V, about 50 V to about 100 V, about 50 V to about 150 V, about 50 V to about 300 V, about 50 V to about 500 V, about 100 V to about 150 V, about 100 V to about 300 V, about 100 V to about 500 V, about 150 V to about 300 V, about 150 V to about 500 V, or about 300 V to about 500 V. In some embodiments, the first ion optic **116** and the second ion optic **118** utilize a DC voltage of about 0 V, about 20 V, about 40 V, about 50 V, about 100 V, about 150 V, about 300 V, or about 500 V. In some embodiments, the first ion optic **116** and the second ion optic **118** utilize a DC voltage of at least about 0 V, about 20 V, about 40 V, about 50 V, about 100 V, about 150 V, or about 300 V. In some

embodiments, the first ion optic **116** and the second ion optic **118** utilize a DC voltage of at most about 20 V, about 40 V, about 50 V, about 100 V, about 150 V, about 300 V, or about 500 V.

[0068] In some embodiments, the first ion optic **116** and the second ion optic **118** utilize a current of about 0 μA to about 100 μA . In some embodiments, the first ion optic **116** and the second ion optic **118** utilize a current of about 0 μA to about 10 μA , about 0 μA to about 20 μA , about 0 μA to about 40 μA , about 0 μA to about 50 μA , about 0 μA to about 80 μA , about 0 μA to about 100 μA , about 10 μA to about 20 μA , about 10 μA to about 40 μA , about 10 μA to about 50 μA , about 10 μA to about 80 μA , about 10 μA to about 100 μA , about 20 μA to about 40 μA , about 20 μA to about 50 μA , about 20 μA to about 80 μA , about 20 μA to about 100 μA , about 40 μA to about 50 μA , about 40 μA to about 80 μA , about 40 μA to about 100 μA , about 50 μA to about 80 μA , about 50 μA to about 100 μA , or about 80 μA to about 100 μA . In some embodiments, the first ion optic **116** and the second ion optic **118** utilize a current of about 0 μA , about 10 μA , about 20 μA , about 40 μA , about 50 μA , about 80 μA , or about 100 μA . In some embodiments, the first ion optic **116** and the second ion optic **118** utilize a current of at least about 0 μA , about 10 μA , about 20 μA , about 40 μA , about 50 μA , or about 80 μA . In some embodiments, the first ion optic **116** and the second ion optic **118** utilize a current of at most about 10 μA , about 20 μA , about 40 μA , about 50 μA , about 80 μA , or about 100 μA .

[0069] In some embodiments, the first ion optic **116** or the second ion optic **118** is configured to selectively transmit ions having mass from about 400 m/z to 900 m/z. For example, the dimensions of the ion optic and applied voltages can be configured to selective transmit a desired mass range while selecting removing other mass ranges. In some embodiments, a third ion optic may be included between the first ion optic **116** and the second ion optic **118**, where the third ion optic is configured to selectively transmit ions having mass from about 400 m/z to 900 m/z. In some embodiments, the first ion optic or second ion optic do not selectively transmit ions.

[0070] In some embodiments, a device provided herein comprises the configuration shown in **FIG. 14**. In this configuration, a high-Pressure ion funnel can be replaced with an RF confining FAIMS with a 90-degree bend radius to connect with the orthogonal inlet and a straight section to connect with the inline inlet.

Example Methods

[0071] In some embodiments, the disclosure describes a method of generating a plurality of ion streams **400**, as seen in **FIG. 4**. In some embodiments, the method comprises providing an ion flux **132** to an ion manifold inlet **106** of an ion manifold **100**, where the ion manifold comprises: an ion manifold inlet; an optional ion repeller manifold **104**; a first ion optic **116** configured to receive the ion flux through the ion manifold inlet **106**; and a second ion optic **118** configured to

receive an output of the ion flux through the first ion optic, where the second ion optic **118** comprises a plurality of outputs (**114**) **401**; and generating the plurality of ion streams from the plurality of outputs of the second ion optic when ion flux traverses through the second ion optic (**118**) **402**. In some embodiments, a central axis of the ion manifold inlet **130** is orthogonal to the central axis of the first ion optic **128** or a central axis of the second ion optic **128**. In some cases, a central axis of the first ion optic **128** and a central axis of the second ion optic **128** are co-linear. In some cases, the ion manifold further comprises a port **102**, configured to pressurize the ion manifold **100**. In some cases, the ion manifold **100** comprises a first chamber **110** and a second chamber **112**. In some embodiments, the first chamber **110** comprises a first pressure and the second chamber **112** comprises a second pressure, where the first pressure is higher than the second pressure. In some embodiments, the first chamber **110** comprises a first pressure and the second chamber **112** comprises a second pressure, where the first pressure is lower than the second pressure. In some embodiments, the first ion optic **116** and the second ion optic **118** comprise an ion funnel. In some embodiments, the first ion optic **116** and the second ion optic **118** may comprise one or more electrical conductor segments **124**. In some embodiments, the one or more electrical conductor segments **124** may comprise a printed circuit board. In some embodiments, the ion manifold inlet **106** may comprise a heated ion manifold inlet. In some embodiments, the ion manifold inlet **106** comprises a slotted capillary. In some embodiments, the slotted capillary may comprise a rectangular cross-sectional geometry **107**. In some embodiments, the ion manifold inlet **106** comprises a circular or oval cross-sectional geometry. In some embodiments, the ion repeller manifold **104**, ion manifold inlet **106**, or the first ion optic **116** are contained at least partially within first chamber **110**. In some embodiments, first chamber **110** comprises a pressure of at least about 8 torr (e.g., about 8 torr to about 12 torr). In some embodiments, the second ion optic **118** is contained at least partially in a second chamber **112**, different than the first chamber **110**. In some embodiments, the second chamber **112** comprises a pressure of at least about 1 torr (e.g., about 1 torr to about 3 torr). In some embodiments, the flux of ions **132** is provided to the ion manifold inlet **106** by electrospray ionization from a multi-emitter array. In some embodiments, the ion repeller manifold **104** comprises a segmented plate (**105**, **108**, **109**) comprising one or more segments. In some embodiments, the segmented plate (**105**, **108**, **109**) comprises at least about 2 segments or at least about 3 segments. In some embodiments, the central axis of the first ion optic **128** or the second ion optic **128** is orthogonal to a central axis of the ion manifold inlet **130**. In some embodiments, the central axis of the ion manifold inlet **130** is orthogonal to an axis normal to the surface of the ion repeller manifold **128**. In some embodiments, a first electrode segment **105** of the ion repeller manifold comprises a lower voltage than an adjacent second electrode

segment **108** of the ion repeller manifold **104**. In some embodiments, the ion repeller manifold **104** comprises a voltage gradient across a longitudinal length of the ion repeller manifold **104**. In some embodiments, the ion manifold **100** comprises a port **102** fluidically coupled to the ion manifold **100**, wherein the port **102** is configured to pressurize the first chamber **110**, the second chamber **112**, or a combination thereof. In some embodiments, the central axis of port **130** is co-linear with a central axis of the ion manifold inlet **130**. Although the devised purpose of the port **102** is to pressurize the first chamber **110**, the second chamber **112**, or a combination of the two, it has the unexpected benefit of improving signal and reducing noise by removing solvent in the ion stream provided from the ion manifold inlet. In some embodiments, the first ion optic **116** or the second ion optic **118** comprise a linear DC gradient provided by the one or more electrical conductor segments **124** across a longitudinal length of the first ion optic or the second ion optic. In some embodiments, one or more electrical conductor segments **124** of the first ion optic **116** or the second ion optic **118** comprises up to 4 DC conductance limits. In some embodiments, the first electrical conductor segment of the one or more electrical conductor segments **124** provides a first signal with a first phase and a second electrical conductor segment of the one or more electrical conductor segments **124** provides a second signal with an anti-phase of the first phase.

[0072] In some embodiments, the first ion optic **116** or the second ion optic **118**, comprise one or more electrical conductor segments **124**, as shown in **FIG. 2**. In some embodiments, the one or more electrical conductor segments **124** may comprise one or more through holes **126**. In some embodiments, the one or more through holes **126** may comprise a circular, oval, polygonal, or square shape, as shown in **FIG. 2**. In some embodiments, the one or more electrical conductor segments **124** may comprise a center to center spacing of at least about 1mm. In some embodiments, the one or more through holes are provided along a linear axis **128** on a surface of the one or more electrical conductor segments **124**. In some embodiments, the two or more through holes of the one or more electrical conductor segments are adjacent or in contact with each other, as shown in **FIG. 2**. In some embodiments, a first electrical conductor segment **124** comprises a first diameter of a through hole and an adjacent second electrical conductor segment **124** comprises a second diameter smaller than the first diameter. In some cases, one or more electrical conductor segments **124** may form an inner geometry of the first ion optic **122** and second ion optic **123**. In some cases, the inner geometry of the first ion optic **122** and second ion optic **123** may comprise one or more segments. In some cases, the one or more segments of the inner geometry may comprise a linear no slope segment, and a linear positive or linear negative slope segment, as shown in **FIG. 2**. In some cases, the one or more electrical conductor segments **124** may split or divide a stream of ions, as described elsewhere herein, into a plurality of streams of ions.

[0073] In some embodiments, the electrospray ionization may originate from one supply. In some embodiments, the electrospray ionization utilizes a voltage adjustable from about 0 kV to about 5 kV. In some embodiments, the electrospray ionization is static. In some embodiments, the electrospray ionization has a 100 μ A maximum current. In some embodiments, the electrospray ionization comprises an accuracy or reliability within at least about 1% of a performance parameter of the electrospray ionizer. In some cases, accuracy may be measured or determined by evaluating signal intensity of the ions generated by the electrospray ionization compared with an expected value or standard signal intensity of ions generated by electrospray ionization. In some instances, accuracy of the electrospray ionization may be measured by comparing observed mass to charge values of the ions generated by electrospray ionization compared to known reference compound mass to charge ratios generated by electrospray ionization. In some embodiments, the electrospray ionization has voltage read-back. In some embodiments, the electrospray ionization has current read-back. In some embodiments, the electrospray ionization has over current shutdown.

[0074] In some embodiments, the ion repeller manifold **104** has a DC bias for each segment (**105, 108, 109**) of about 0 V to about 500 V. In some embodiments, the ion repeller manifold **104** is static but adjustable. In some embodiments, the ion repeller manifold **104** has a 0.1% accuracy. In some embodiments, the ion repeller manifold **104** has voltage read-back. In some embodiments, the ion repeller manifold **104** has voltage error shutdown.

[0075] In some embodiments, the heated ion manifold inlet has a DC voltage bias adjustable between about 0 V to about 500 V. In some embodiments, the heated ion manifold inlet has a maximum current of 100 μ A. In some embodiments, the heated ion manifold inlet has voltage readback. In some embodiments, the heated ion manifold inlet has voltage error shutdown. In some embodiments, the heated ion manifold inlet has resistive heaters operating at 50 W. In some embodiments, the heated ion manifold inlet has TC temperature monitoring and control. In some embodiments, the heated ion manifold inlet has 1% temperature control accuracy. In some embodiments, the heated ion manifold inlet has a nominal temperature of about 180 °C.

[0076] In some embodiments, funnel RF is generated with a resonant circuit, and the coil in the RF head resonates against the capacitance of the funnel. In some embodiments, phase to phase RF voltage is different under 5%. In some embodiments, RF output levels have read-backs and are level controlled. In some embodiments, the DC gradient across the funnel is done with two resistive dividers, one for each RF phase, with each resistor having a resistance of about 500K. In some embodiments, each plate is capacitively coupled to its RF bus. In some embodiments, the coupling capacitor is large relative to the funnel plate to plate capacitance.

[0077] In some embodiments, the first ion optic 116 and the second ion optic 118 comprise an adjustable DC voltage range from about 0 V to about 500 V. In some embodiments, the first ion optic 116 and the second ion optic 118 have 0.1% accuracy. In some embodiments, the first ion optic 116 and the second ion optic 118 have a maximum current of 100 μ A. In some embodiments, the first ion optic 116 and the second ion optic 118 have voltage read-back and error detection. In some embodiments, the first ion optic 116 and the second ion optic 118 have DC in, DC out, and a DC conductance limit. In some embodiments, the second ion optic 118 has four total DC conductance limits. In some embodiments, the DC conductance limit voltages of the second ion optic 118 are dynamic. In some embodiments, the first ion optic 116 and the second ion optic 118 have RF phase and anti-phase have a peak-to-peak voltage of about 10 V_{p-p} to about 200 V_{p-p}.

Example Ion Mobility Spectrometry Processes

[0078] Methods and mass spectrometers described herein can utilize one or more ion mobility devices within the ion optics of a mass spectrometer to discriminate between and/or separate analyte ions and background ions within an ion flux prior to analysis with one or more mass analyzer. Ion mobility systems can include Field asymmetric ion mobility spectrometry devices (FAIMS), traveling-wave ion mobility spectrometry devices (TWIMS), trapped ion mobility spectrometry devices (TIMS), drift-tube ion mobility spectrometry devices (DT-IMS), and/or combinations thereof. In some embodiments, the methods and mass spectrometers include both FAIMS and TWIMS.

[0079] Combining FAIMS with TWIMS or another secondary ion mobility separation device can reduce or eliminate the need for a high resolution FAIMS separation. A reduced resolution requirement allows for operation of FAIMS at reduced pressure which reduces loss of ion flux usually associated with ion-neutral collisions and/or ion-ion recombination. In some instances, FAIMS can be used as a filter. For example, a set of conditions can be applied to pass a selected class of ions, ions outside the transmission conditions (e.g., non-selected ions) are removed. A FAIMS device can operate at reduced pressure, for example, between 1-4 Torr with enough resolution to separate between two aggregate class of ions, for example, a separation between singly charged chemical background species and multiply charged peptide ions. Singly charged ions can be removed, reducing the total ion flux, and enriching for multiply charged ions that can be passed to downstream analysis, preserving the ions of interest and enhancing the performance of the subsequent TWIMS separation, which can be used to improve utilization of the mass analyzer, by separating peptides in time. In some cases, the traveling-wave ion mobility device comprises a plurality of RF electrodes and guard electrodes disposed within a vacuum system configured to maintain a pressure within the traveling-wave ion mobility device which is

less than the pressure of the inert gas within the enclosed mobility chamber of the reduced-pressure field asymmetric ion mobility device. In some embodiments, a high pressure ion funnel in a device configuration provided herein is replaced with a FAIMS device.

[0080] In some embodiments, the present disclosure provides implementations for high-field asymmetric-waveform ion mobility spectrometry (FAIMS). At a high level, FAIMS may include separating or characterizing ions by differences in their mobility in high and low electric fields. In practice, FAIMS may enable ion filtering and increasing separation in mass spectrometry analysis.

[0081] High Field Asymmetric Waveform Ion Mobility Spectrometry (FAIMS) can separate gas-phase ions at atmospheric pressure. In FAIMS, the ions can be introduced into a mobility region ("FAIMS region") across which a radio frequency (rf) waveform, the magnitude of which is referred to as dispersion voltage (DV), is applied such that the ions are alternately subjected to high and low electric fields. The waveform can be asymmetric; for example, the high field may be applied for one time unit followed by an opposite-polarity low field of half of the high field component applied for twice as long. For example, the RF voltage can be a sum of two separate RF voltages, where one RF voltage is a sine function, and another is the same sine function, but phase shifted by $\pi/2$. The result is a bi-sinusoidal waveform having a low and high period with a 3:1 ratio of duration. Other ratios are possible. The field-dependent change in the mobility of the ions causes the ions to drift towards the walls of the separation region. Since the dependence of ion mobility on electric field strength can be ion specific, a separation of different types of ions one from the other and can be referred to as FAIMS separation. In order to transmit an ion of interest through FAIMS, an appropriate direct current compensation voltage (CV) can be applied to compensate for the drift of the ion of interest toward the analyzer wall. By varying the CV, different ions can be selectively transmitted through the FAIMS device (or selectively removed). Described herein are novel FAIMS devices which are capable of producing such separations at less than atmospheric pressure without significant loss of ion flux, resulting in high ion transmission.

[0082] These high-voltage asymmetric waveforms may be at radio frequency (RF). Ions may migrate towards one of the two electrodes based on the ratio of the high-field and low-field mobility of each ion. Accordingly, ions with mobilities outside a certain range may not pass through a FAIMS device, which ions with mobilities inside the certain range may pass through the FAIMS device. FAIMS can be achieved in some instances using a bi-sinusoidal waveform (e.g., V_{pp} 1000V, CV -60V to 0V, 2MHz). In some instances, a flyback transformer waveform is used in the methods described herein.

[0083] In some cases, one or more power supplies provide a waveform comprising a sinusoidal waveform, a square waveform, a triangular waveform, a sawtooth waveform, or combinations of one or more thereof. In some cases, one or more power supplies provide a waveform comprising at least two waveforms which are phase-shifted with respect to each other. In some cases, a phase-shift between waveforms is about 30° to about 120° (e.g., about 30°, about 45°, about 60°, about 90°, or about 120°). In some cases, the at least two waveforms are sinusoids. In some cases, the at least two waveforms have different amplitudes.

[0084] A frequency of any of the waveforms used herein may independently be 100 kHz to about 2 MHz (e.g., about 100 kHz, about 500 kHz, about 750 kHz, about 1 MHz, about 1.5 MHz, or about 2 MHz). In some embodiments, the frequency is about 100 kHz to about 1,000 kHz. In some embodiments, the frequency is about 100 kHz to about 200 kHz, about 100 kHz to about 300 kHz, about 100 kHz to about 400 kHz, about 100 kHz to about 500 kHz, about 100 kHz to about 750 kHz, about 100 kHz to about 1,000 kHz, about 200 kHz to about 300 kHz, about 200 kHz to about 400 kHz, about 200 kHz to about 500 kHz, about 200 kHz to about 750 kHz, about 200 kHz to about 1,000 kHz, about 300 kHz to about 400 kHz, about 300 kHz to about 500 kHz, about 300 kHz to about 750 kHz, about 300 kHz to about 1,000 kHz, about 400 kHz to about 500 kHz, about 400 kHz to about 750 kHz, about 400 kHz to about 1,000 kHz, about 500 kHz to about 750 kHz, about 500 kHz to about 1,000 kHz, or about 750 kHz to about 1,000 kHz. In some embodiments, the frequency is about 100 kHz, about 200 kHz, about 300 kHz, about 400 kHz, about 500 kHz, about 750 kHz, or about 1,000 kHz. In some embodiments, the frequency is at least about 100 kHz, about 200 kHz, about 300 kHz, about 400 kHz, about 500 kHz, or about 750 kHz. In some embodiments, the frequency is at most about 200 kHz, about 300 kHz, about 400 kHz, about 500 kHz, about 750 kHz, or about 1,000 kHz. In some embodiments, the frequency is about 1 MHz to about 2 MHz. In some embodiments, the frequency is about 1 MHz to about 1.25 MHz, about 1 MHz to about 1.5 MHz, about 1 MHz to about 1.75 MHz, about 1 MHz to about 2 MHz, about 1.25 MHz to about 1.5 MHz, about 1.25 MHz to about 1.75 MHz, about 1.25 MHz to about 2 MHz, about 1.5 MHz to about 1.75 MHz, about 1.5 MHz to about 2 MHz, or about 1.75 MHz to about 2 MHz. In some embodiments, the frequency is about 1 MHz, about 1.25 MHz, about 1.5 MHz, about 1.75 MHz, or about 2 MHz. In some embodiments, the frequency is at least about 1 MHz, about 1.25 MHz, about 1.5 MHz, or about 1.75 MHz. In some embodiments, the frequency is at most about 1.25 MHz, about 1.5 MHz, about 1.75 MHz, or about 2 MHz.

[0085] An absolute value of the maximum amplitude of any of the waveforms used may be about 100 V to about 2000 V (e.g., about 250 V to about 1750 V, about 500 V to about 1500 V, about 750 V to about 1000 V, about 100 V, about 300 V, about 500V, about 700 V, about 800

V, about 1000V, about 1500 V, or about 2000 V). In some instances a voltage used for FAIM herein is 200-3000, 200-2000, 500-2000, 750-3000, 1000-3000, 750-2000 or 1000-2000 V. In some instances the voltage used for FAIMS herein is at least 250, 300, 500, 600, 750, 800, 900, 1000, 1200, 1500, 1700, 2000, or at least 2500 V.

[0086] A reduced-pressure field asymmetric ion mobility device of any may comprise an overall duty cycle of the waveform delivered by the one or more power supplies is about 5% to about 90% (e.g., about 5%, about 10%, about 20%, about 30%, about 50%, or about 90%). In some embodiments, the duty cycle is about 5 % to about 90 %. In some embodiments, the duty cycle is about 5 % to about 10 %, about 5 % to about 20 %, about 5 % to about 30 %, about 5 % to about 50 %, about 5 % to about 60 %, about 5 % to about 80 %, about 5 % to about 90 %, about 10 % to about 20 %, about 10 % to about 30 %, about 10 % to about 50 %, about 10 % to about 60 %, about 10 % to about 80 %, about 10 % to about 90 %, about 20 % to about 30 %, about 20 % to about 50 %, about 20 % to about 60 %, about 20 % to about 80 %, about 20 % to about 90 %, about 30 % to about 50 %, about 30 % to about 60 %, about 30 % to about 80 %, about 30 % to about 90 %, about 50 % to about 60 %, about 50 % to about 80 %, about 50 % to about 90 %, about 60 % to about 80 %, about 60 % to about 90 %, or about 80 % to about 90 %. In some embodiments, the duty cycle is about 5 %, about 10 %, about 20 %, about 30 %, about 50 %, about 60 %, about 80 %, or about 90 %. In some embodiments, the duty cycle is at least about 5 %, about 10 %, about 20 %, about 30 %, about 50 %, about 60 %, or about 80 %. In some embodiments, the duty cycle is at most about 10 %, about 20 %, about 30 %, about 50 %, about 60 %, about 80 %, or about 90 %.

[0087] Waveforms used in devices and methods described herein may each be delivered or otherwise applied independently to the inner electrode or the outer electrode.

[0088] Ion inlets and ion outlets of this disclosure can be aligned with axes which are substantially perpendicular to each other. In some cases, ion inlets are aligned along a first axis and the ion outlet is aligned along a second axis, the first and second axes being aligned substantially parallel to each other.

[0089] In some cases, the ion inlet is aligned along a first axis and the ion outlet is aligned along a second axis, the first and second axes being aligned such that the first axis and the second axis form an angle of about 40° to about 120° at their intersection (e.g., about 45°, about 60°, about 75°, about 100°, or about 120°). In some cases, the inert gas used is nitrogen, helium, or argon. In some cases, the reduced-pressure field asymmetric ion mobility device is configured for transmission of ions having m/z values of about 400 to about 900. In some cases, the reduced-pressure field asymmetric ion mobility device is configured for transmission of ions having m/z values greater than about 400 m/z. In some cases, the reduced-pressure field asymmetric ion

mobility device is configured to remove ions having m/z values less than about 350 m/z . In some cases, an ion inlet extends generally parallel to a direction of ion movement between the inner electrode and the outer electrode. In some cases, an ion inlet extends at angle to a direction of ion movement between the inner electrode and the outer electrode, wherein the angle is about 20° to about 70° (e.g., about 30° to about 60° , or about 40° to about 50°). In some cases, an ion outlet extends generally parallel to a direction of ion movement between the inner electrode and the outer electrode. In some cases, an ion outlet extends at angle to a direction of ion movement between the inner electrode and the outer electrode, wherein the angle is about 60° to about 120° (e.g., about 70° to about 110° , about 80° to about 90°). In some cases, an ion inlet and the ion outlet are substantially aligned along a common axis.

[0090] Reduced-pressure field asymmetric ion mobility devices of the disclosure may be configured to remove at least about 80% of singly charged ions (e.g., at least about 85%, at least about 90%, at least about 95%, at least about 98%, or at least about 99%). In some cases, at least about 80% of singly charged ions are removed within the first 50% of the distance between the inlet and the outlet.

[0091] In some embodiments, a singly charged ion current passing through FAIMS devices of the disclosure is reduced or redirected to an alternate outlet of the device by about 50 % to about 99.5 %. In some embodiments, a singly charged ion current passing through FAIMS devices of the disclosure is reduced or redirected to an alternate outlet of the device by about 50 % to about 60 %, about 50 % to about 70 %, about 50 % to about 80 %, about 50 % to about 95 %, about 50 % to about 90 %, about 50 % to about 95 %, about 50 % to about 99 %, about 50 % to about 99.5 %, about 60 % to about 70 %, about 60 % to about 80 %, about 60 % to about 95 %, about 60 % to about 90 %, about 60 % to about 95 %, about 60 % to about 99 %, about 60 % to about 99.5 %, about 70 % to about 80 %, about 70 % to about 95 %, about 70 % to about 90 %, about 70 % to about 95 %, about 70 % to about 99 %, about 70 % to about 99.5 %, about 80 % to about 95 %, about 80 % to about 90 %, about 80 % to about 95 %, about 80 % to about 99 %, about 80 % to about 99.5 %, about 95 % to about 90 %, about 95 % to about 95 %, about 95 % to about 99 %, about 95 % to about 99.5 %, about 90 % to about 95 %, about 90 % to about 99 %, about 90 % to about 99.5 %, about 95 % to about 99 %, about 95 % to about 99.5 %, or about 99 % to about 99.5 %. In some embodiments, a singly charged ion current passing through FAIMS devices of the disclosure is reduced or redirected to an alternate outlet of the device by about 50 %, about 60 %, about 70 %, about 80 %, about 95 %, about 90 %, about 95 %, about 99 %, or about 99.5 %. In some embodiments, a singly charged ion current passing through FAIMS devices of the disclosure is reduced or redirected to an alternate outlet of the device by at least about 50 %, about 60 %, about 70 %, about 80 %, about 95 %, about 90 %, about 95 %, about 99 %, or about 99.5 %.

or about 99 %. In some embodiments, a singly charged ion current passing through FAIMS devices of the disclosure is reduced or redirected to an alternate outlet of the device by at most about 60 %, about 70 %, about 80 %, about 95 %, about 90 %, about 95 %, about 99 %, or about 99.5 %.

[0092] FAIMS devices of the disclosure may be configured to resolve singly charged ions from multiply charged ions in a radial direction about the central axis of the enclosed mobility chamber. In some cases, a radial resolution of multiply charged species from singly charged species is at least about 2 mm on average (e.g., at least 2 mm, at least 5 mm, at least 10 mm, at least 12 mm, or at least 20 mm) when measured at the ion outlet.

[0093] In some cases, reduced-pressure field asymmetric ion mobility devices comprises one or more sets of ion optics configured to guide ions into the ion inlet, out of the ion outlet, or a combination thereof. The one or more sets of ion optics may each independently comprise: one or more ion funnels, one or more DC lenses, or combinations of two or more thereof. In some cases, the one or more sets of ion optics are configured to guide ions from the ion outlet into a traveling-wave ion mobility device.

[0094] In some cases, an average ion transmission efficiency of multiply-charged ions from the ion inlet to the ion outlet is at least about 50% (e.g., at least about 50%, at least about 70%, at least about 80%, at least about 90%, or at least about 95%). In some cases, an average ion transmission efficiency of singly-charged ions from the ion inlet to the ion outlet is no more than about 50%, (e.g., no more than about 50%, no more than about 30%, no more than about 10%, no more than about 5%, or no more than about 1%).

[0095] In some cases, multiply charged ions are transmitted from the ion inlet to the ion outlet in less than about 100 milliseconds (e.g., less than about 50 ms, 25 ms, 10 ms, 5 ms, or 3 ms). In some cases, multiply charged ions are transmitted from the ion inlet to the ion outlet in about 0.1 ms to about 10 ms, about 0.5 ms to about 5 ms, or about 1 ms to about 3 ms. In some cases, a pressure of the gas at the inlet is about 0.1 torr to about 10 torr greater than a pressure of the gas at the outlet (e.g., about 0.5 torr to about 8, about 1 torr to about 5 torr, or about 1 torr to about 3 torr).

[0096] In some cases, the differential deflection is configured to selectively remove ions having mobilities that correspond to singly charged species have a mass of about 400 Da or less (e.g., about 300 Da or less, about 200 Da or less, or about 100 Da or less). In some cases, the singly charged species are solvents used for electrospray ionization of a sample. In some cases, about 5%-50%, about 10%-40%, or about 20%-35% of the ions are selectively removed by the ion mobility device. In some cases, gas moves through the ion mobility device at a velocity of about 10 m/s to about 300 m/s, or about 50 m/s to about 200 m/s. In some cases, the ion mobility

device includes a gradient DC bias to move ions and does not include gas flow as disclosed further below.

[0097] In some embodiments, FAIMS may be used as a separation operation with mass spectrometric analysis. FAIMS may, for example, allow for improved detection of peptides in complex samples, filtering out “chemical noise,” filtering out interfering ions and selecting charge states for analysis, etc. In some embodiments, FAIMS may be used to select for ions that are of low abundance in a sample that otherwise may not be analyzed (e.g., because of limitations in duty cycles of mass spectrometers). For example, by selectively removing more abundant ions, FAIMS may assist in distinguishing between ions with similar mass to charge ratios and preventing a more abundant ion from masking the presence of a less abundant ion.

[0098] In some embodiments, FAIMS devices comprise one or more guardrail electrodes charged with either RF or DC to assist with ion confinement. An example of DC guard rails is shown in **FIG. 15**.

[0099] **FIG. 10** shows an example workflow diagram **1000** for a front-end interface. Specifically, **FIG. 10** shows an example of how FAIMS may be integrated into one or more of the implementations for ion manifolds disclosed herein. The workflow diagram **1000** may include electrospray ionization at **1010**, ion funneling at **1020**, application of FAIMS at **1030**, and split ion funneling at **1040**.

[0100] The workflow diagram **1000** may begin, in some embodiments, with the electrospray ionization (ESI) at **1010**. For example, ESI may use electrical energy to assist the transfer of ions from solution into the gaseous phase before the ions are subjected to mass spectrometric analysis. The electrical energy may include a high voltage applied over a liquid to produce an aerosol. The ESI at **1010** may include a soft ionization technique used for production of gas phase ions (e.g., with minimal to no fragmentation). In some embodiments, this electrospray at **1010** may be the same as or similar to one or more of the techniques for electrospray disclosed herein.

[0101] In some embodiments, the ESI at **1010** may provide a plurality of ions to an ion funnel at **1020**. The ion funnel may focus a stream of ions. For example, the ion funnel may focus the stream of ions using one or more electrodes (e.g., stacked ring electrodes) of decreasing inner diameter. In some embodiments, the ion funnel may focus and transmit ions efficiently to areas lower pressure. This may help to address certain challenges arising from ESI in which ions may be created at atmospheric pressure, but may be analyzed at lower pressures, resulting in ion loss by a phenomenon of joule expansion or free-jet expansion. The focusing and transmitting of ions by the ion funnel may help to offset the expansion of ion clouds that limits the amount of ions that reach the detector. While the workflow diagram **1000** is illustrated with the ion funnel at

1020, before FAIMS at **1030**, in some embodiments, in addition or in alternative, an ion funnel may be positioned after the FAIMS at **1030**. In some embodiments, this ion funnel at **1020** may be the same as or similar to the one or more ion funnels disclosed herein. In some embodiments, the ion funnel may be operated at a pressure of at least 8 torr (e.g., about 8 torr to about 12 torr). **[0102]** In some embodiments, the ion funnel at **1020** may transmit a focused stream of ions into the FAIMS at **1030**. In some embodiments, the FAIMS at **1030** may be a FAIMS device. For example, the FAIMS device may be a planar FAIMS device as disclosed herein. In another example, the FAIMS device may be a non-planar FAIMS device (e.g., having a curved or round structure), such as that described in PCT/US2024/027512, which is incorporated by reference in its entirety. Some examples of planar FAIMS devices are illustrated herein at **FIGs. 5A-8**. In some embodiments, an ion funnel may be integrated into the FAIMS device at **1030** in addition or in alternative to external ion funnels (e.g., the ion filter at **1020** or the split ion funnel at **1040**). In some embodiments, at **1030**, the FAIMS device may separate ions from the ion stream on the basis of their differential mobility in an asymmetric (e.g., oscillating) electric field. Accordingly, the FAIMS at **1030** may output a filtered ion stream.

[0103] In some embodiments, the filtered ion stream from the FAIMS at **1030** may be input into a split ion funnel at **1040**. The split ion funnel may, for example, have certain similarities to the ion funnel of **1020**. In some embodiments, the split ion funnel may split the filtered ion stream into a plurality of filtered ion streams. This split ion funnel at **1040** may perform a splitting operation that may be the same as or similar to one or more of the splitting techniques disclosed herein. Operations may be performed on each of the filtered ion streams in the plurality of filtered ion streams. For example, the operations may be the same for at least two of (or e.g., each of) the plurality of filtered ion streams. In another example, the operations may be the different for at least two of (or e.g., each of) the plurality of filtered ion streams. In enabling the operations to be applied to the plurality of filtered ion streams, multiplexing may be enabled. For example, multiplexed mass spectrometry may be performed by performing mass spectrometry separately (and, e.g., at least partially overlapping in time) with one or more of the plurality of filtered ion streams. This multiplexing may enable quicker and more efficient (with respect to, e.g., time, computing resources, network traffic, materials, etc.) mass spectrometry analysis. The multiplexing may also enable improved detection, sensitivity, precision, and/or accuracy.

[0104] In some embodiments, a first set of ion optics comprises a field asymmetric waveform ion mobility spectrometry device and a traveling wave ion mobility spectrometry device (TWIMS) or a trapped ion mobility spectrometry device (TIMS). In some embodiments, the field asymmetric waveform ion mobility spectrometry device is upstream of the traveling wave ion mobility spectrometry device (TWIMS) or the trapped ion mobility spectrometry device

(TIMS). In some embodiments, the field asymmetric waveform ion mobility spectrometry device is designed to operate at less than atmospheric pressure (e.g., less than 100 torr, less than 50 torr, less than 20 torr, less than 10 torr, or less than 5 torr). In some embodiments, the field asymmetric waveform ion mobility spectrometry device is designed to operate at about 3 to about 8 torr. In some embodiments, the field asymmetric waveform ion mobility spectrometry device is designed to operate at about 4 to about 6 torr. In some embodiments, the field asymmetric waveform ion mobility spectrometry device is configured to preferentially remove ions with a +1 net charge. In some embodiments, the second set of ion optics further comprising at least one collision cell and at least one upstream mass filter corresponding to each of the at least one mass analyzers. In some embodiments, the second set of ion optics comprises a second collision cell and/or a second mass filter corresponding to each of the at least one mass analyzers.

Example Reduced-pressure Planar Ion Mobility Spectrometry Implementations

[0105] **FIG. 5A** shows an example of a planar FAIMS (high field asymmetric waveform ion mobility spectrometry) configuration (front view) **501** and **FIG. 5B** shows an example of a planar FAIMS configuration (back view) **502** showing FAIMS and RF (outer electrode) polarities for electrodes on upper and lower substrate plates. **FIG. 5A** illustrates a front view as seen from the flow of ions entering the device. **FIG. 5B** illustrates a back view as seen from the flow of ions leaving the device. The top PCB **503a** comprises outer electrodes **505a** and **505b**. The bottom PCB **503b** comprises outer electrodes **506a** and **506b**. In **FIG. 5B**, the top PCB **503a** comprises a top RF+ electrode **505a**, a top FAIMS+ separation electrode **507a**, and a top RF- electrode **505b**. The bottom PCB **503b** comprises a top RF- electrode **506a**, a top FAIMS- separation electrode **507b**, and a top RF+ electrode **506b**. In some embodiments, the outer electrodes may together be configured to function as a quadrupole to guide ion through the planar FAIMS. Electrodes may be constructed from any suitable materials commonly used in the art. In some instances, electrodes comprise gold plated copper.

[0106] **FIG. 6** shows an example top view schematic of one planar substrate used in a FAIMS configuration **600**. A second planar substrate with the same design may be placed above the first planar substrate (e.g., as depicted in **FIGS. 5A** and **5B**). The directional flow of ions is shown as **605**. In some embodiments, the FAIMS may operate with a fluid (e.g., inert gas) flow across the FAIMS. For example, as illustrated in **FIG. 6**, fluid may flow from left to right. The fluid may flow across one or more substrate plates **620**. In some embodiments, the one or more substrate plates comprise PCBs (boards). In some instances, the substrate plates have attachment points **601/602** to a device chassis. In some instances, attachment points **601** and **602** are staggered for the top substrate plate and bottom substrate plate. The substrate plates may run at least some of

the length of the FAIMS region **603**. As illustrated, the FAIMS region may not run the full length of the device. For example, the FAIMS region may be located with space from the left side of the device, as illustrated. This space may enable a runway for ions to, for example, slow down before entering the FAIMS region. In some embodiments, the FAIMS region may be operated at reduced pressurized. For example, the FAIMS region may operate with a low pressure (e.g., about 5 torr). In some embodiments, the FAIMS region may be defined as the region within the quadrupole. The quadrupole may be driven by one or more outer electrodes. In addition or in alternative, the quadrupole may be driven by SD electrodes as guardrails. The FAIMS region may comprise an inner electrode **625**. The substrate plates in some instances are at least partially surrounded or integrated with one or more ion funnels (See **FIGS. 1-2, 10**).

[0107] In some embodiments, the FAIMS may include one or more substrate plates of length (longest linear dimension) about 10 mm to about 1,000 mm. In some embodiments, the FAIMS may include one or more substrate plates of length about 10 mm to about 50 mm, about 10 mm to about 100 mm, about 10 mm to about 150 mm, about 10 mm to about 200 mm, about 10 mm to about 250 mm, about 10 mm to about 300 mm, about 10 mm to about 350 mm, about 10 mm to about 400 mm, about 10 mm to about 450 mm, about 10 mm to about 500 mm, about 10 mm to about 1,000 mm, about 50 mm to about 100 mm, about 50 mm to about 150 mm, about 50 mm to about 200 mm, about 50 mm to about 250 mm, about 50 mm to about 300 mm, about 50 mm to about 350 mm, about 50 mm to about 400 mm, about 50 mm to about 450 mm, about 50 mm to about 500 mm, about 50 mm to about 1,000 mm, about 100 mm to about 150 mm, about 100 mm to about 200 mm, about 100 mm to about 250 mm, about 100 mm to about 300 mm, about 100 mm to about 350 mm, about 100 mm to about 400 mm, about 100 mm to about 450 mm, about 100 mm to about 500 mm, about 100 mm to about 1,000 mm, about 150 mm to about 200 mm, about 150 mm to about 250 mm, about 150 mm to about 300 mm, about 150 mm to about 350 mm, about 150 mm to about 400 mm, about 150 mm to about 450 mm, about 150 mm to about 500 mm, about 150 mm to about 1,000 mm, about 200 mm to about 250 mm, about 200 mm to about 300 mm, about 200 mm to about 350 mm, about 200 mm to about 400 mm, about 200 mm to about 450 mm, about 200 mm to about 500 mm, about 200 mm to about 1,000 mm, about 250 mm to about 300 mm, about 250 mm to about 350 mm, about 250 mm to about 400 mm, about 250 mm to about 450 mm, about 250 mm to about 500 mm, about 250 mm to about 1,000 mm, about 300 mm to about 350 mm, about 300 mm to about 400 mm, about 300 mm to about 450 mm, about 300 mm to about 500 mm, about 300 mm to about 1,000 mm, about 350 mm to about 400 mm, about 350 mm to about 450 mm, about 350 mm to about 500 mm, about 350 mm to about 1,000 mm, about 400 mm to about 450 mm, about 400 mm to about 500 mm, about 400 mm to about 1,000 mm, about 450 mm to about 500 mm, about 450 mm to about

1,000 mm, or about 500 mm to about 1,000 mm. In some embodiments, the FAIMS may include one or more substrate plates of length about 10 mm, about 50 mm, about 100 mm, about 150 mm, about 200 mm, about 250 mm, about 300 mm, about 350 mm, about 400 mm, about 450 mm, about 500 mm, or about 1,000 mm. In some embodiments, the FAIMS may include one or more substrate plates of length at least about 10 mm, about 50 mm, about 100 mm, about 150 mm, about 200 mm, about 250 mm, about 300 mm, about 350 mm, about 400 mm, about 450 mm, or about 500 mm. In some embodiments, the FAIMS may include one or more substrate plates of length at most about 50 mm, about 100 mm, about 150 mm, about 200 mm, about 250 mm, about 300 mm, about 350 mm, about 400 mm, about 450 mm, about 500 mm, or about 1,000 mm.

[0108] In some embodiments, the FAIMS comprises a first substrate plate and a second substrate plate. In some instances the distance between the first plate and the second plate is 0.1 to 20 mm, 0.3 to 20 mm, 0.5 to 20 mm, 1 to 20 mm, 2 to 20 mm, 5 to 20 mm, 0.5 to 10 mm, 0.1 to 10 mm, 0.5 to 12 mm, 3 to 10 mm, 4 to 8 mm, 5 to 10 mm, or 5 to 10 mm. In some instances the distance between the first plate and the second plate is no more than 0.1, 0.2, 0.3, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, or no more than 20 mm. In some instances the distance between the first plate and the second plate is at least 0.1, 0.2, 0.3, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, or at least 20 mm. In some instances the distance between the first plate and the second plate is about 0.1, 0.2, 0.3, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, or about 20 mm.

[0109] In some embodiments, the FAIMS may have a pressure of about 0.1 torr to about 100 torr. In some embodiments, the FAIMS may have a pressure of about 0.1 torr to about 0.5 torr, about 0.1 torr to about 1 torr, about 0.1 torr to about 2 torr, about 0.1 torr to about 4 torr, about 0.1 torr to about 6 torr, about 0.1 torr to about 8 torr, about 0.1 torr to about 10 torr, about 0.1 torr to about 15 torr, about 0.1 torr to about 20 torr, about 0.1 torr to about 40 torr, about 0.1 torr to about 100 torr, about 0.5 torr to about 1 torr, about 0.5 torr to about 2 torr, about 0.5 torr to about 4 torr, about 0.5 torr to about 6 torr, about 0.5 torr to about 8 torr, about 0.5 torr to about 10 torr, about 0.5 torr to about 15 torr, about 0.5 torr to about 20 torr, about 0.5 torr to about 40 torr, about 0.5 torr to about 100 torr, about 1 torr to about 2 torr, about 1 torr to about 4 torr, about 1 torr to about 6 torr, about 1 torr to about 8 torr, about 1 torr to about 10 torr, about 1 torr to about 15 torr, about 1 torr to about 20 torr, about 1 torr to about 40 torr, about 1 torr to about 100 torr, about 2 torr to about 4 torr, about 2 torr to about 6 torr, about 2 torr to about 8 torr, about 2 torr to about 10 torr, about 2 torr to about 15 torr, about 2 torr to about 20 torr, about 2 torr to about 40 torr, about 2 torr to about 100 torr, about 4 torr to about 6 torr, about 4 torr to about 8 torr, about 4 torr to about 10 torr, about 4 torr to about 15 torr, about 4 torr to about 20 torr, about 4 torr to about 40 torr, about 4 torr to about 100 torr, about 6 torr to about 8 torr,

about 6 torr to about 10 torr, about 6 torr to about 15 torr, about 6 torr to about 20 torr, about 6 torr to about 40 torr, about 6 torr to about 100 torr, about 8 torr to about 10 torr, about 8 torr to about 15 torr, about 8 torr to about 20 torr, about 8 torr to about 40 torr, about 8 torr to about 100 torr, about 10 torr to about 15 torr, about 10 torr to about 20 torr, about 10 torr to about 40 torr, about 10 torr to about 100 torr, about 15 torr to about 20 torr, about 15 torr to about 40 torr, about 15 torr to about 100 torr, about 20 torr to about 40 torr, about 20 torr to about 100 torr, or about 40 torr to about 100 torr. In some embodiments, the FAIMS may have a pressure of about 0.1 torr, about 0.5 torr, about 1 torr, about 2 torr, about 4 torr, about 6 torr, about 8 torr, about 10 torr, about 15 torr, about 20 torr, about 40 torr, or about 100 torr. In some embodiments, the FAIMS may have a pressure of at least about 0.1 torr, about 0.5 torr, about 1 torr, about 2 torr, about 4 torr, about 6 torr, about 8 torr, about 10 torr, about 15 torr, about 20 torr, or about 40 torr. In some embodiments, the FAIMS may have a pressure of at most about 0.5 torr, about 1 torr, about 2 torr, about 4 torr, about 6 torr, about 8 torr, about 10 torr, about 15 torr, about 20 torr, about 40 torr, or about 100 torr.

[0110] The length of the FAIMS region (e.g., the length of the FAIMs region **603**) is at least about 10 mm, at least about 50 mm, at least about 100 mm, or at least about 150 mm. In some embodiments, the length of the FAIMS region is no more than about 750 mm, no more than about 500 mm, no more than about 400 mm, no more than about 300 mm. In some embodiments, the length of the FAIMS region is about 100 mm to about 400 mm.

[0111] **FIG. 7** shows an example top view schematic of a FAIMS configuration **700** where the FAIMS region **603** and FAIMS electrode **507a** runs approximately the entire length of the device.

[0112] **FIG. 8** shows an example top view schematic of a FAIMS configuration **800** where the FAIMS region **603** runs approximately the entire length of the device (longest linear dimension), and utilizes a separation segmented electrode (comprising segments **801**, **802**, etc.). Any number of segments may be utilized for the FAIMS electrode, such as at least 2, 3, 4, 6, 8, 12, 16, 20, 24, or at least 32 segments. In some instances, the FAIMS electrode comprises no more than 2, 3, 4, 6, 8, 12, 16, 20, 24, or no more than 32 segments. In some instances, the FAIMS electrode comprises 2-32, 2-24, 2-16, 2-8, 4-32, 4-16, 4-12, 8-32, 8-24, 8-16, or 12-32 segments. The segments in some instances overlay a DC gradient to drive ions through the FAIMS region. In some embodiments, the segments overlay a DC gradient to drive ions through the FAIMS region without gas flow. In some instances, the segments are positioned in a serpentine pattern to increase distance while minimizing device size.

[0113] The skilled person, guided by the teachings of the present application, will appreciate that various features of the planar FAIMs disclosed herein may be combined. For example,

FAIMs configuration **600** may be modified to include segmented electrodes to drive ions without gas flow.

[0114] **FIG. 9A** shows an example front view schematic of a FAIMS configuration **900**. A stack of PCBs **905** is integrated into a single assembly. An exit ion funnel is shown as **901**. PCBs **905** in some instances are double sided (comprise electrodes on both top and bottom sides of a single board). Any number of substrate plates may be integrated into an assembly such as 2, 3, 4, 5, 6, 8, 10, 12, 15, 20, 30, or more. Substrate plates in some instances arranged in a one-dimensional array (e.g., 1x2, 1x3, 1x4, and the like) or a two-dimensional array (e.g., 2x2, 2x3, 3x2, 2x4, 3x3, 4x4, or 2x5 configuration and the like). Substrate plates may be PCB, but other suitable materials may be used. **FIG. 9B** shows an example front view schematic of a FAIMS configuration **903**. In some instances, adjacent outer electrodes (**904a/904b**) are shared between FAIMS devices.

[0115] **FIG. 11** illustrates a schematic view of a device configuration **1100** comprising an ion funnel **1020**, a planar FAIMs **1030**, an ion funnel **1035**, a split ion funnel **1040**, and split ion output **1050**. A portion of the planar FAIMs device may be disposed within the second ion funnel as shown, or the planar FAIMs device may be spaced apart from the second ion funnel. In some embodiments, ion funnel **1035** may be a rectangular ion funnel having rectangular cross-sections of openings to funnel ions.

[0116] **FIGS. 12A-12H** depict a front end ion manifold **1200** described herein comprising an ion inlet **1206**. Ports may be present in one or more chambers of the device, such as ports for sensors **1201a-c** (monitor conditions such as pressure, temperature, or other conditions), electrical connections **1203a-b**, vacuum ports **1204a-b**, an ion inlet **1206**, and one or more (e.g., splitter) ion outlets **1205**. **FIG. 12G** shows a cross-section view of a device configuration **1200** described herein comprising an ion inlet, an ion funnel chamber **1020**, a FAIMS chamber **1030** (with an ion funnel **1035**), and a split ions funnel chamber **1040**. Ions flow from left to right. The cross-section is taken along plane 7 as depicted in **FIG. 12C**. Ports may be present in one or more chambers of the device, such as ports for sensors **1201a-c** (monitor conditions such as pressure, temperature, or other condition), electrical connections **1203**, vacuum ports **1204**, an ion inlet, and one or more (e.g., splitter) ion outlets **1205**. The FAIMs chamber **1030** comprises a planar FAIMS with top **503a** and bottom **503b** PCBs, and an ion funnel **1035**. The front end device **1200** also comprises first ion funnel **116** and split ion funnel **118**.

[0117] **FIGS. 13A-13H** depict a device **1300** comprising both the front end device **1200** and TWIMs (traveling-wave ion mobility) device **1301**. In some instances, the front end device comprises a FAIMS interface of **FIGS. 12A-12H**. **FIG. 13G** shows a cross-section along plane **14** as depicted in **FIG. 13C**. TWIMs device **1301** includes substrates **1305** (e.g., PCB boards)

with electrodes separating ions based on ion mobility using travelling waves. Each output from the split ion funnel (e.g., ion outlets **1205** depicted in **FIG. 12G**) may feed into separate regions of TWIMs device for ion mobility separation before exiting TWIMs outlets **1310**. In instances where the split ion funnel has four outlets, additional substrates may be included for ion mobility separation before exiting optional TWIMs outlets **1315**. As disclosed herein, in some embodiments, two or more of the of the TWIMs outlets may be operably coupled to different mass analyzers for multiplex analysis.

[0118] In some embodiments plates sued with a FAIMS configuration may be flexible. Flexibility of supports described herein (e.g., circuit boards) may be measured using Young's modulus. Young's modulus measures the resistance of a material to elastic (recoverable) deformation under load. A listing of Young's modulus for stiffness of example materials described herein is provided as follows: nylon (3 GPa), nitrocellulose (1.5 GPa), polypropylene (2 GPa), silicon (150 GPa), polystyrene (3 GPa), agarose (1-10 GPa), polyacrylamide (1-10 GPa), polydimethylsiloxane (PDMS) (1-10 GPa). Solid supports described herein can have a Young's moduli from 1 to 500, 1 to 40, 1 to 10, 1 to 5, or 3 to 11 GPa. Solid supports described herein can have a Young's moduli of about 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 20, 25, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250, 400, 500 GPa, or more. As the relationship between flexibility and stiffness are inverse to each other, a flexible material has a low Young's modulus and changes its shape considerably under load. In some cases flexibility of supports refers to a support which is capably of maintaining structural integrity of a substrate of the support when bent (compared to a planar substrate) according to a radius of curvature of not less than 100, 50, 30, 20, 10, or 5 mm.

[0119] The skilled person, guided by the teaching of the present application, will appreciate that that split ion funnels disclosed herein may be arranged at various locations relative to the other components. For example, the split ion funnel may be positioned before the FAIMs device such that each output of the split ion funnel may be operably coupled to different FAIMs devices (e.g., 4 outlets feed into 4 separate FAIMs devices). As another example, the split ion funnel **118** can have independently controllable electrodes positioned at or near each of the outputs **114**. This allows adjusting the voltages at each output to control the relative flow of ions between the outputs. The voltages could be adjusted to have about the same ion flux for each output; alternatively, the voltages could be adjusted bias more ion flux toward certain outputs. In some cases, this can be dynamically controlled during operation of the device. As another example, the split ion funnel may receive ion mobility separated ions from the TWIMs device. This has the advantage of only using one TWIMs device. Other configurations are possible and within the scope of the present application.

Example Computer Systems

[0120] The present disclosure provides computer systems that are programmed to implement methods of the disclosure. **FIG. 3** shows a computer system **201** that is programmed or otherwise configured to implement the methods and systems described herein. The computer system **201** can be an electronic device of a user or a computer system that is remotely located with respect to the electronic device. The electronic device can be a mobile electronic device

[0121] The computer system **201** includes a central processing unit (CPU, also "processor" and "computer processor" herein) **205**, which can be a single core or multi core processor, or a plurality of processors for parallel processing. The computer system **201** also includes memory or memory location **210** (e.g., random-access memory, read-only memory, flash memory), electronic storage unit **215** (e.g., hard disk), communication interface **220** (e.g., network adapter) for communicating with one or more other systems, and peripheral devices **225**, such as cache, other memory, data storage or electronic display adapters. The memory **210**, storage unit **215**, interface **220** and peripheral devices **225** are in communication with the CPU **205** through a communication bus (solid lines), such as a motherboard. The storage unit **215** can be a data storage unit (or data repository) for storing data. The computer system **201** can be operatively coupled to a computer network ("network") **230** with the aid of the communication interface **220**. The network **230** can be the Internet, an internet or extranet, or an intranet or extranet that is in communication with the Internet. The network **230** in some cases is a telecommunication or data network. The network **230** can include one or more computer servers, which can enable distributed computing, such as cloud computing. The network **230**, in some cases with the aid of the computer system **201**, can implement a peer-to-peer network, which may enable devices coupled to the computer system **201** to behave as a client or a server.

[0122] The CPU **205** can execute a sequence of machine-readable instructions, which can be embodied in a program or software. The instructions may be stored in a memory location, such as the memory **210**. The instructions can be directed to the CPU **205**, which can subsequently program or otherwise configure the CPU **205** to implement methods of the present disclosure. Examples of operations performed by the CPU **205** can include fetch, decode, execute, and writeback.

[0123] The CPU **205** can be part of a circuit, such as an integrated circuit. One or more other components of the system **201** can be included in the circuit. In some cases, the circuit is an application specific integrated circuit (ASIC).

[0124] The storage unit **215** can store files, such as drivers, libraries and saved programs. The storage unit **215** can store user data, e.g., user preferences and user programs. The computer system **201** in some cases can include one or more additional data storage units that are external to

the computer system **201**, such as located on a remote server that is in communication with the computer system **201** through an intranet or the Internet.

[0125] The computer system **201** can communicate with one or more remote computer systems through the network **230**. For instance, the computer system **201** can communicate with a remote computer system of a user. Examples of remote computer systems include personal computers (e.g., portable PC), slate or tablet PC's (e.g., Apple® iPad, Samsung® Galaxy Tab), telephones, Smart phones (e.g., Apple® iPhone, Android-enabled device, Blackberry®), or personal digital assistants. The user can access the computer system **201** via the network **230**.

[0126] Methods as described herein can be implemented by way of machine (e.g., computer processor) executable code stored on an electronic storage location of the computer system **201**, such as, for example, on the memory **210** or electronic storage unit **215**. The machine executable or machine-readable code can be provided in the form of software. During use, the code can be executed by the processor **205**. In some cases, the code can be retrieved from the storage unit **215** and stored on the memory **210** for ready access by the processor **205**. In some situations, the electronic storage unit **215** can be precluded, and machine-executable instructions are stored on memory **210**.

[0127] The code can be pre-compiled and configured for use with a machine having a processor adapted to execute the code or can be compiled during runtime. The code can be supplied in a programming language that can be selected to enable the code to execute in a pre-compiled or as-compiled fashion.

[0128] Aspects of the systems and methods provided herein, such as the computer system **201**, can be embodied in programming. Various aspects of the technology may be thought of as "products" or "articles of manufacture" typically in the form of machine (or processor) executable code or associated data that is carried on or embodied in a type of machine-readable medium. Machine-executable code can be stored on an electronic storage unit, such as memory (e.g., read-only memory, random-access memory, flash memory) or a hard disk. "Storage" type media can include any or all of the tangible memory of the computers, processors or the like, or associated modules thereof, such as various semiconductor memories, tape drives, disk drives and the like, which may provide non-transitory storage at any time for the software programming. All or portions of the software may at times be communicated through the Internet or various other telecommunication networks. Such communications, for example, may enable loading of the software from one computer or processor into another, for example, from a management server or host computer into the computer platform of an application server. Thus, another type of media that may bear the software elements includes optical, electrical, and electromagnetic waves, such as used across physical interfaces between local devices, through wired and optical landline

networks and over various air-links. The physical elements that carry such waves, such as wired or wireless links, optical links, or the like, also may be considered as media bearing the software. As used herein, unless restricted to non-transitory, tangible "storage" media, terms such as computer or machine "readable medium" refer to any medium that participates in providing instructions to a processor for execution.

[0129] Hence, a machine-readable medium, such as computer-executable code, may take many forms, including but not limited to, a tangible storage medium, a carrier wave medium or physical transmission medium. Non-volatile storage media include, for example, optical or magnetic disks, such as any of the storage devices in any computer(s) or the like, such as may be used to implement the databases, etc. shown in the drawings. Volatile storage media include dynamic memory, such as main memory of such a computer platform. Tangible transmission media include coaxial cables; copper wire and fiber optics, including the wires that comprise a bus within a computer system. Carrier-wave transmission media may take the form of electric or electromagnetic signals, or acoustic or light waves such as those generated during radio frequency (RF) and infrared (IR) data communications. Common forms of computer-readable media therefore include for example: a floppy disk, a flexible disk, hard disk, magnetic tape, any other magnetic medium, a CD-ROM, DVD or DVD-ROM, any other optical medium, punch cards paper tape, any other physical storage medium with patterns of holes, a RAM, a ROM, a PROM and EPROM, a FLASH-EPROM, any other memory chip or cartridge, a carrier wave transporting data or instructions, cables or links transporting such a carrier wave, or any other medium from which a computer may read programming code or data. Many of these forms of computer readable media may be involved in carrying one or more sequences of one or more instructions to a processor for execution.

[0130] The computer system **201** can include or be in communication with an electronic display **235** that comprises a user interface (UI) **240** for providing, for example, selection of ion manifold injection parameters. Examples of UI's include, without limitation, a graphical user interface (GUI) and web-based user interface.

[0131] Methods and systems of the present disclosure can be implemented by way of one or more algorithms. An algorithm can be implemented by way of software upon execution by the central processing unit **205**.

EMBODIMENTS

[0132] The following are exemplary embodiments of the disclosure herein:

Embodiment 1. An ion manifold comprising:

(a) an ion manifold inlet;

- (b) a first ion optic configured to receive a flux of ions through the ion manifold inlet; and
- (c) a second ion optic configured to receive an output of the flux of ions through the first ion optic, wherein the second ion optic comprises a plurality of outputs that split the flux of ions into a plurality of ion streams.

Embodiment 2. A method of generating a plurality of ion streams, the method comprising:

- (a) providing an ion flux to an ion manifold inlet of an ion manifold, the ion manifold comprising:
 - i. the ion manifold inlet;
 - ii. a first ion optic configured to receive the ion flux through the ion manifold inlet; and
 - iii. a second ion optic configured to receive an output of the ion flux through the first ion optic, wherein the second ion optic comprises a plurality of outputs; and
- (b) generating the plurality of ion streams from the plurality of outputs of the second ion optic when the ion flux traverses through the second ion optic.

Embodiment 3. The ion manifold or method of any of the preceding embodiments, wherein the first ion optic and the second ion optic comprise an ion funnel.

Embodiment 4. The ion manifold or method of any of the preceding embodiments, wherein the first ion optic and the second ion optic comprises one or more electrical conductor segments.

Embodiment 5. The ion manifold or method of any of the preceding embodiments, wherein the one or more electrical conductor segments comprise one or more through holes.

Embodiment 6. The ion manifold or method of any of the preceding embodiments, wherein the one or more through holes comprise a circular, oval, polygonal, or square shape.

Embodiment 7. The ion manifold or method of any of the preceding embodiments, wherein the one or more electrical conductor segments comprise a printed circuit board.

Embodiment 8. The ion manifold or method of any of the preceding embodiments, wherein the one or more electrical conductor segments comprise a center to center spacing of at least about 1mm.

Embodiment 9. The ion manifold or method of any of the preceding embodiments, wherein the one or more through holes are provided along a linear axis on a surface of the one or more electrical conductor segments.

- Embodiment 10. The ion manifold or method of any of the preceding embodiments, wherein the two or more through holes of the one or more electrical conductor segments are adjacent or in contact with each other.
- Embodiment 11. The ion manifold or method of any of the preceding embodiments, wherein the ion manifold inlet comprises a heated ion manifold inlet.
- Embodiment 12. The ion manifold or method of any of the preceding embodiments, wherein the ion manifold inlet comprises a slotted capillary.
- Embodiment 13. The ion manifold or method of any of the preceding embodiments, wherein the slotted capillary comprises a rectangular cross-sectional geometry.
- Embodiment 14. The ion manifold or method of any of the preceding embodiments, wherein the ion manifold inlet comprises a circular or oval cross-sectional geometry.
- Embodiment 15. The ion manifold or method of any of the preceding embodiments, wherein the repeller, ion manifold inlet, and first ion optic are contained at least partially within a first chamber.
- Embodiment 16. The ion manifold or method of any of the preceding embodiments, wherein the first chamber comprises a pressure of at least about 8 torr (e.g., about 8 torr to about 12 torr).
- Embodiment 17. The ion manifold or method of any of the preceding embodiments, wherein the second ion optic is contained at least partially in a second chamber, different than the first chamber.
- Embodiment 18. The ion manifold or method of any of the preceding embodiments, wherein the second chamber comprises a pressure of at least about 1 torr (e.g., about 1 torr to about 3 torr).
- Embodiment 19. The ion manifold or method of any of the preceding embodiments, wherein the first chamber comprises a first pressure and the second chamber comprises a second pressure, and wherein the first pressure is higher than the second pressure.
- Embodiment 20. The ion manifold or method of any of the preceding embodiments, wherein the flux of ions is provided to the ion manifold inlet by electrospray ionization from a multi-emitter array.
- Embodiment 21. The ion manifold or method of any one of the preceding embodiments, wherein the ion manifold further comprises an ion repeller manifold that is (i) positioned such that an axis along a normal vector of a surface of ion repeller manifold is orthogonal to a central axis of the ion manifold inlet, and (ii) is configured to direct a path of the flux of ions into the first ion optic.

- Embodiment 22. The ion manifold or method of any of the preceding embodiments, wherein the ion repeller manifold comprises a segmented plate, optionally comprising at least about 2 segments or at least about 3 segments.
- Embodiment 23. The segmented ion repeller manifold of embodiment 22, wherein the segmented ion repeller is configured to allow for differing voltages to improve the efficiency of the delivery of ions into the ion funnel.
- Embodiment 24. The ion manifold or method of any of the preceding embodiments, wherein a central axis of the first ion optic and the second ion optic is orthogonal to a central axis of the ion manifold inlet.
- Embodiment 25. The ion manifold or method of any of the preceding embodiments, wherein a central axis of the ion manifold inlet is orthogonal to an axis normal to a surface of the ion repeller manifold.
- Embodiment 26. The ion manifold or method of any of the preceding embodiments, wherein a first electrode segment of the ion repeller manifold comprises a lower voltage than an adjacent second electrode segment of the ion repeller manifold.
- Embodiment 27. The ion manifold or method of any of the preceding embodiments, wherein the ion repeller manifold comprises a voltage gradient across a longitudinal length of the ion repeller manifold.
- Embodiment 28. The ion manifold or method of any of the preceding embodiments, wherein the ion manifold comprises a port fluidically coupled to the ion manifold, wherein the port is configured to pressurize the first chamber, the second chamber, or a combination thereof.
- Embodiment 29. The ion manifold or method of any of the preceding embodiments, wherein a central axis of the port is co-linear with a central axis of the ion manifold inlet.
- Embodiment 30. The ion manifold or method of any of the preceding embodiments, wherein the first ion optic or the second ion optic comprise a linear DC gradient provided by the one or more electrical conductor segments across a longitudinal length of the first ion optic or the second ion optic.
- Embodiment 31. The ion manifold or method of any of the preceding embodiments, wherein the one or more electrical conductor segments of the first ion optic or the second ion optic comprises up to 4 DC conductance limits.
- Embodiment 32. The ion manifold or method of any of the preceding embodiments, wherein a first electrical conductor segment of the one or more electrical conductor segments provides a first signal with a first phase and a second electrical conductor

segment of the one or more electrical conductor segments provides a second signal with an anti-phase of the first phase.

Embodiment 33. The ion manifold or method of any of the preceding embodiments, wherein the first ion optic, the second ion optic, or a combination thereof, are configured to output one or more ion streams of the ions flux provided at the ion manifold inlet in the range of about 400 to about 900 mass/charge.

Embodiment 34. The ion manifold or method of any of the preceding embodiments, wherein a reduced-pressure FAIMS (high field asymmetric waveform ion mobility spectrometer) device is configured to receive ions from the first ion optic and selectively output ion to the second ion optic.

Embodiment 35. The ion manifold or method of embodiment 34, wherein the reduced-pressure FAIMS device is a planar FAIMs device comprising two substrates having outer electrodes and a separation electrode.

Embodiment 36. An ion mobility device comprising:

- a. a first substrate plate comprising:
 - i. a coplanar first outer electrode and second outer electrode; and
 - ii. a first separation electrode; and
- b. a second substrate plate comprising:
 - i. a coplanar third outer electrode and fourth outer electrode; and
 - ii. a second separation electrode;

wherein the first substrate plate and the second substrate plate are substantially parallel.

Embodiment 37. The device of embodiment 36, wherein the device further comprises an inlet configured for gas flow.

Embodiment 38. The device of embodiment 36 or 37, wherein the longest linear dimension of the first substrate plate and the second plate is 100-300 mm.

Embodiment 39. The device of any one of embodiments 36-38, wherein the distance between the first plate and the second plate is 0.5 to 12 mm.

Embodiment 40. The device of any one of embodiments 36-38, wherein the distance between the first plate and the second plate is about 6 mm.

Embodiment 41. The device of any one of embodiments 36-40, wherein the region surrounding the first separation electrode and the second separation electrode has a pressure of no more than 20 torr.

Embodiment 42. The device of any one of embodiments 36-40, wherein the region surrounding the first separation electrode and the second separation electrode has a pressure of 5-15 torr.

- Embodiment 43. The device of any one of embodiments 36-42, wherein a portion of either the first separation electrode or the second separation electrode is at least partially surrounded by an ion funnel.
- Embodiment 44. The device of embodiment 43, wherein the ion funnel comprises a rectangular ion funnel (RIF).
- Embodiment 45. The device of any one of embodiments 36-44, wherein the longest linear dimension of the separation electrodes is shorter than the longest linear dimension of the outer electrodes.
- Embodiment 46. The device of embodiment 45, wherein the separation electrodes are positioned distal from an ion flow relative to the outer electrodes.
- Embodiment 47. The device of any one of embodiments 36-46, wherein the separation electrode is segmented.
- Embodiment 48. The device of embodiment 47, wherein at least a portion of the segments are independently addressable.
- Embodiment 49. The device of embodiment 47 or 48, wherein the separation electrode comprises at least 2 segments (e.g., 2-40 segments).
- Embodiment 50. The device of embodiment 47 or 48, wherein the segments are in arranged a substantially linear configuration.
- Embodiment 51. The device of embodiment 47 or 48, wherein the segments are arranged in a serpentine configuration.
- Embodiment 52. The device of any one of embodiments 36-51, wherein the substrate plate comprises a printed circuit board (PCB).
- Embodiment 53. The device of any one of embodiments 36-52, wherein the substrate plate further comprises electrodes configured to provide ion mobility separation using traveling wave ion mobility spectrometry (TWIMS) or a trapped ion mobility spectrometry (TIMS).
- Embodiment 54. A device assembly comprising a plurality of ion mobility devices of any one of embodiments 36-53.
- Embodiment 55. The device assembly of embodiment 54, wherein two or more adjacent outer electrodes are shared on the substrate plate.
- Embodiment 56. The device assembly of embodiment 54 or 55, wherein the device assembly comprises a 2x1, 1x2, 2x2, 2x3, 3x2, 2x4, 3x3, 4x4, or 2x5 arrangement of ion mobility devices (rows x columns).
- Embodiment 57. The device assembly of any one of embodiments 54-56, wherein the device assembly comprises at least 4 ion mobility devices.

Embodiment 58. The ion manifold or method of any one of embodiments 1-34, wherein the ion manifold or method comprises a device of any one of embodiments 36-57.

Embodiment 59. The ion manifold or method of embodiment 59, wherein the device of any one of embodiments 36-57 is attached between the first ion optic and the second ion optic.

Embodiment 60. The ion manifold or method of embodiment 58 or 59, wherein the pressure in the ion funnel of the first ion optic is higher than the pressure in the ion mobility device.

Embodiment 61. A method of separating ions comprising:

- a. providing an ion flux to an ion mobility device of any one of embodiments 36-57;
- b. applying a high voltage RF waveform to the separation electrodes;
- c. applying an ion confining waveform to the outer electrodes;
- d. selecting transmitting ions based on mobility to generate a mobility-selected ion

stream.

Embodiment 62. The method of embodiment 61, wherein the RF waveform comprises a flyback transformer waveform.

Embodiment 63. The method of embodiments 62 or 63, wherein a carrier gas is flowed into an inlet of the ion mobility device.

Embodiment 64. The method of embodiments 62 or 63, wherein the separation electrodes are segmented and comprise a DC gradient.

Embodiment 65. A reduced-pressure field asymmetric ion mobility device comprising:

- iii. an enclosed mobility chamber having an ion inlet and an ion outlet disposed at opposite ends and configured to be filled with an inert gas at a pressure of less than atmospheric pressure;
- iv. at least one inner electrode disposed longitudinally between the ion inlet and the ion outlet of the enclosed mobility chamber;
- v. at least one outer electrode disposed longitudinally between the ion inlet and the ion outlet of the enclosed mobility chamber, the outer electrode being disposed such that the inner electrode is at least partially enclosed within the outer electrode; and
- vi. one or more power supplies configured deliver a waveform to the inner electrode or the outer electrode, the waveform being configured to differentially deflect ions having different ion mobilities based on interaction of the ions with the waveform and the inert gas, wherein the

differential deflection is configured to selectively remove ions having mobilities that correspond to singly charged species prior to said species reaching the ion outlet, wherein the inner electrode and the outer electrode are substantially planar.

Embodiment 66. A method of separating singly charged ions from multiply charged ions, the method comprising:

- e. providing an ion flux to an ion inlet of a reduced-pressure field asymmetric ion mobility device, the reduced-pressure field asymmetric ion mobility device comprising:
 - 1. an enclosed mobility chamber having the ion inlet and an ion outlet disposed at opposite ends and configured to be filled with an inert gas at a pressure of less than atmospheric pressure;
 - 2. at least one inner electrode disposed longitudinally between the ion inlet and the ion outlet of the enclosed mobility chamber;
 - 3. at least one outer electrode disposed longitudinally between the ion inlet and the ion outlet of the enclosed mobility chamber; and
 - 4. one or more power supplies configured deliver a waveform to the inner electrode or the outer electrode, the waveform being configured to differentially deflect ions having different ion mobilities based on interaction of the ions with the waveform and the inert gas, wherein the differential deflection is configured to selectively remove ions having mobilities that correspond to singly charged species prior to said species reaching the ion outlet;
- f. applying the waveform using the one or more power supplies to thereby substantially prevent ions of the ion flux having mobilities that correspond to singly charged species from reaching the ion outlet of the reduced-pressure field asymmetric ion mobility device; and
- g. obtaining a multiply charged ion population at the ion outlet of the reduced-pressure field asymmetric ion mobility device which is enriched for ions that correspond to multiply charged species.

Embodiment 67. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the pressure of the gas is less than about 700 torr (e.g., less than about 100 torr, less than about 10 torr, or less than about 5 torr).

Embodiment 68. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein a distance between the ion inlet and the ion outlet is about 10 mm to about 700 mm (e.g., about 100 mm to about 500 mm., about 200 mm to about 400 mm, or about 250 mm to about 350 mm).

Embodiment 69. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein a distance from a central axis of the enclosed mobility chamber to an outer surface of the at least one outer electrode is about 7 mm to about 50 mm (e.g., about 10 mm to about 40 mm, or about 15 mm to about 25 mm).

Embodiment 70. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein a distance from a central axis of the enclosed mobility chamber to an outer surface of the at least one inner electrode is about 0.2 mm to about 20 mm (e.g., about 1 mm to about 15 mm, or about 3 mm to about 10 mm).

Embodiment 71. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein a distance from an outer surface of the at least one inner electrode to an inner surface of the at least one outer electrode is about 5 mm to about 40 mm (e.g., about 5 mm to about 30 mm, about 8 mm to about 20 mm, or about 10 mm to about 15 mm).

Embodiment 72. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the one or more power supplies provide a waveform comprising a sinusoidal waveform, a square waveform, a triangular waveform, a sawtooth waveform, or combinations of one or more thereof.

Embodiment 73. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the one or more power supplies provide a waveform comprising at least two sinusoids which are phase-shifted with respect to each other.

Embodiment 74. The method or the reduced-pressure field asymmetric ion mobility device of embodiment 73, wherein the phase shift is about 30° to about 120° (e.g., about 30°, about 45°, about 60°, about 90°, or about 120°).

Embodiment 75. The method or the reduced-pressure field asymmetric ion mobility device of any one of embodiments 73-74, wherein a frequency of at least one of the at least two sinusoids is about 100 kHz to about 2 MHz (e.g., about 100 kHz, about 500 kHz, about 750 kHz, about 1 MHz, about 1.5 MHz, or about 2 MHz).

Embodiment 76. The method or the reduced-pressure field asymmetric ion mobility device of any one of embodiments 73-75, wherein an absolute value of the maximum amplitude of the waveform is about 100 V to about 2000 V (e.g., about 250 V to about 1750 V, about 500 V to about 1500 V, about 750 V to about 1000 V, about 100 V, about 300 V, about 500V, about 700 V, about 1000V, about 1500 V, or about 2000 V).

Embodiment 77. The method or the reduced-pressure field asymmetric ion mobility device of any one of the preceding embodiments, wherein an overall duty cycle of the waveform delivered by the one or more power supplies is about 5% to about 90% (e.g., about 5%, about 10%, about 20%, about 30%, about 50%, or about 90%).

Embodiment 78. The method or the reduced-pressure field asymmetric ion mobility device of any one of the preceding embodiments, wherein the waveform is delivered to the inner electrode.

Embodiment 79. The method or the reduced-pressure field asymmetric ion mobility device of any one of embodiments 65-77, wherein the waveform is delivered to the outer electrode.

Embodiment 80. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the ion inlet extends generally parallel to a direction of ion movement between the inner electrode and the outer electrode.

Embodiment 81. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the ion inlet extends at angle to a direction of ion movement between the inner electrode and the outer electrode, wherein the angle is about 20° to about 70° (e.g., about 30° to about 60°, or about 40° to about 50°).

Embodiment 82. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the ion outlet extends generally parallel to a direction of ion movement between the inner electrode and the outer electrode.

Embodiment 83. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the ion outlet extends at angle to a direction of ion movement between the inner electrode and the outer electrode, wherein

the angle is about 60° to about 120° (e.g., about 70° to about 110°, about 80° to about 90°).

Embodiment 84. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the ion inlet and the ion outlet are substantially aligned along a common axis.

Embodiment 85. The method or the reduced-pressure field asymmetric ion mobility device of any of embodiments 65-79, wherein the ion inlet and the ion outlet are aligned with axes which are substantially perpendicular to each other.

Embodiment 86. The method or the reduced-pressure field asymmetric ion mobility device of any of embodiments 65-79, wherein the ion inlet is aligned along a first axis and the ion outlet is aligned along a second axis, the first and second axes being aligned substantially parallel to each other.

Embodiment 87. The method or the reduced-pressure field asymmetric ion mobility device of any of embodiments 65-79, wherein the ion inlet is aligned along a first axis and the ion outlet is aligned along a second axis, the first and second axes being aligned such that the first axis and the second axis form an angle of about 40° to about 120° at their intersection (e.g., about 45°, about 60°, about 75°, about 100°, or about 120°).

Embodiment 88. The method or the reduced-pressure field asymmetric ion mobility device of any one of embodiments 65-87, wherein the at least one outlet is operably coupled to at least one ion optic.

Embodiment 89. The method or the reduced-pressure field asymmetric ion mobility device of any one of embodiments 65-88, wherein the outer electrode comprises at least two ion outlets.

Embodiment 90. The method or the reduced-pressure field asymmetric ion mobility device of embodiment 89, wherein the at least two ion outlets are operably coupled to a common ion optic.

Embodiment 91. The method or the reduced-pressure field asymmetric ion mobility device of embodiment 89 or 90, wherein the at least two ion outlets are independently operably coupled to different common ion optics.

Embodiment 92. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the inert gas is nitrogen, helium, or argon.

Embodiment 93. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the reduced-pressure field asymmetric ion mobility device is configured for transmission of ions having m/z values of about 400 to about 900.

Embodiment 94. The method or the reduced-pressure field asymmetric ion mobility device of any of embodiments 68-93, wherein the reduced-pressure field asymmetric ion mobility device is configured to remove at least about 80% of singly charged ions within the first 50% of the distance between the inlet and the outlet (e.g., at least about 85%, at least about 90%, at least about 95%, at least about 98%, or at least about 99%).

Embodiment 95. The method or the reduced-pressure field asymmetric ion mobility device of any of embodiments 70-93, wherein the reduced-pressure field asymmetric ion mobility device is configured to resolve singly charged ions from multiply charged ions in a radial direction about the central axis of the enclosed mobility chamber.

Embodiment 96. The method or the reduced-pressure field asymmetric ion mobility device of embodiment 95, wherein the radial resolution of multiply charged species from singly charged species is at least about 2 mm on average (e.g., at least 2 mm, at least 5 mm, at least 10 mm, at least 12 mm, or at least 20 mm) when measured at the ion outlet.

Embodiment 97. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the reduced-pressure field asymmetric ion mobility device further comprises one or more sets of ion optics configured to guide ions into the ion inlet, out of the ion outlet, or a combination thereof.

Embodiment 98. The method or the reduced-pressure field asymmetric ion mobility device of embodiment 97, wherein the one or more sets of ion optics each independently comprise: one or more ion funnels, one or more DC lenses, or combinations of two or more thereof.

Embodiment 99. The method or the reduced-pressure field asymmetric ion mobility device of embodiment 98, wherein the one or more sets of ion optics are configured to guide ions from the ion outlet into a traveling-wave ion mobility device.

Embodiment 100. The method or the reduced-pressure field asymmetric ion mobility device of embodiment 99, wherein the traveling-wave ion mobility device comprises a plurality of RF electrodes and guard electrodes disposed within a vacuum system configured to maintain a pressure within the traveling-wave ion mobility device which is less than the

pressure of the inert gas within the enclosed mobility chamber of the reduced-pressure field asymmetric ion mobility device.

Embodiment 101. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein an average ion transmission efficiency of multiply-charged ions from the ion inlet to the ion outlet is at least about 50% (e.g., at least about 50%, at least about 70%, at least about 80%, at least about 90%, or at least about 95%).

Embodiment 102. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein an average ion transmission efficiency of singly-charged ions from the ion inlet to the ion outlet is no more than about 50%, (e.g., no more than about 50%, no more than about 30%, no more than about 10%, no more than about 5%, or no more than about 1%).

Embodiment 103. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein multiply charged ions are transmitted from the ion inlet to the ion outlet in less than about 100 milliseconds (e.g., less than about 50 ms, 25 ms, 10 ms, 5 ms, or 3 ms).

Embodiment 104. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein multiply charged ions are transmitted from the ion inlet to the ion outlet in about 0.1 ms to about 10 ms, about 0.5 ms to about 5 ms, or about 1 ms to about 3 ms.

Embodiment 105. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein a pressure of the gas at the inlet is about 0.1 torr to about 10 torr greater than a pressure of the gas at the outlet (e.g., about 0.5 torr to about 8, about 1 torr to about 5 torr, or about 1 torr to about 3 torr).

Embodiment 106. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the differential deflection is configured to selectively remove ions having mobilities that correspond to singly charged species have a mass of about 400 Da or less (e.g., about 300 Da or less, about 200 Da or less, or about 100 Da or less). The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the singly charged species are solvents used for electrospray ionization of a sample.

Embodiment 107. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein about 5%-50%, about 10%-40%, or about 20%-35% of the ions are selectively removed by the ion mobility device.

Embodiment 108. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding embodiments, wherein the gas moves through the ion mobility device at a velocity of about 10 m/s to about 300 m/s, or about 50 m/s to about 200 m/s.

EXAMPLES

Example 1: Generating a plurality of ion streams with an orthogonal injection ion manifold

[0133] An ion manifold, as described elsewhere herein, is used to generate a plurality of ion streams from an input stream of ions of a biological sample. The biological sample is prepared for ionization by purifying and concentrating the biological sample to remove salts, buffers, or contaminants that may interfere with the ionization process. Once the biological sample is purified and concentrated, the biological sample is digested or broken down to produce analyte molecules (e.g., protein peptides) suitable for ionization and analysis by the one or more mass spectrometers. The digested or broken biological sample is then mixed with a solvent (e.g., water-acetonitrile mixtures) to enhance solubility of analyte molecules and promote ionization. The biological sample in solvent is then ionized by electrospray ionization and provided to an ion manifold inlet of the ion manifold, described elsewhere herein. In some cases, liquid chromatography can be performed to separate the sample before ionization. The stream of ions flowing into the ion manifold interact with an ion repeller manifold positioned such that an axis along a normal vector of a surface of ion repeller manifold is orthogonal to a central axis of the ion manifold inlet. The stream of ions is pushed or repelled by the ion repeller manifold moving, shift or directing a path of the stream of ions into a first ion optic and a second ion optic, as described elsewhere herein, where the central axis of the first ion optic and the second ion optic is also orthogonal to the central axis of the ion manifold inlet. As the stream of ions exit the second ion optic, the stream of ions is split or divided into a plurality of ion streams based on at least the one or more through hole geometry features of one or more electrical conductor segments of the second ion optic. The plurality of ion streams exiting the second ion optic are then directed or provided to one or more mass spectrometer sensors to analyze the biological sample analytes.

Example 2: Generating a plurality of ion streams with an orthogonal injection ion manifold

[0134] Following the general procedure of Example 1, the stream of ions is pushed or repelled by the ion repeller manifold moving, shift or directing a path of the stream of ions into a first ion optic, a FAIMS device (e.g., planar FAIMS device), and a second ion optic, as described elsewhere herein, where the central axis of the first ion optic and the second ion optic is also orthogonal to the central axis of the ion manifold inlet. As the stream of ions exit the second ion optic, the stream of ions is split or divided into a plurality of ion streams based on at least the one or more through hole geometry features of one or more electrical conductor segments of the second ion optic. The plurality of ion streams exiting the second ion optic are then directed or provided to one or more ion mobility devices operably coupled to mass analyzers to analyze the biological sample analytes

Example 3: Use of a planer FAIMS devices with QToF 6600

[0135] A device was constructed as shown in FIG. 14, having a Front End Configuration:

Spray → Axial Capillary → Funnel → FAIMS → 6 mm Orifice Lens → QToF 6600.

[0136] Samples Sciex PPG calibration Mix, Sciex “Electrospray” Mix, and Sciex ESI Mix were analyzed using this configuration. Two models of FAIMS were tested: (1) FAIMS + Side RF (6 mm Orifice between FAIMS and 6600 Qjet) and (2) FAIMS + DC Gradient (6 mm Orifice between FAIMS and 6600 Qjet). Side RF vs. Side DC refers to RF or DC guard rails for confinement, respectively. Pressure parameters are shown in **Table 1**.

Table 1

Meas. Pressures for Best Ion Transmission	Funnel Pressure (Torr)	FAIMS Pressure (Torr)	Qjet Pressure (Torr)
FAIMS + Side RF	25 to 30	4 to 5	1.5 to 2
FAIMS + Side DC	10.5	6.2	2.2

[0137] The side DC, used to accelerate the ion in the FAIMS, provided an improvement with very small voltage applied (a maximum of 10 volts across the resistors). For an optimum ion transmission in this experiment, the pressure in the ion funnel was lower.

[0138] The following FAIMS conditions were used with sample AG Mix, and m/z isolation was examined: Frequency = 750 kHz, Vp-p = 650 volts, (4 mm gap between FAIMS Electrodes, ~1.65 kv/cm), and CV = 6.5 volts to isolate m/z 922. Results are shown in **FIGS. 14B-14C**. Notably, 30,000 FWHM was maintained both with and without the FAIMS electrodes turned on.

[0139] Ion transmission vs. CV was measured using sample PPG mix (**FIG. 14D**). Ramping the CV allowed for filtering as a function of ion masses. The high mass transmission was excellent and greater than an average QTOF6600. Varying the CV selectively transmitted ions based on their masses, with higher masses for lower CV and lower masses for greater CV. **FIGS. 14E-14F**. Vary the CV also allowed for discrimination of ions based on their charged state. Here, lower CV favored the singly charged ions over the doubly charged ions. The opposite was observed for greater CVs. **FIG. 14G**.

[0140] Multi charged ions were also examined between 900 m/z to 930 m/z. (**FIG. 14H**). Data was collected using PPG mix and a Vp-p at 350 volts only (because of arcing at greater values). Increasing the CV allowed for discrimination of m/z 907 (singly charged) from the doubly charged ions around m/z 927. Increasing the RF amplitude is expected to further improve ion discrimination.

Example 4: Planar FAIMS+TWIMS

[0141] The general methods of Example 3 are followed, with modification: a TWIMS device is added between the FAIMS device and the mass analyzer.

Example 5: Reduced pressure FAIMS

[0142] The general methods of Example 3 are followed, with modification: the device is configured as shown in **FIG. 15** wherein a high pressure ion funnel is replaced with a reduced pressure FAIMS device.

CERTAIN DEFINITIONS AND ADDITIONAL CONSIDERATIONS

[0143] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which this disclosure belongs. All patents and publications referred to herein are incorporated by reference.

[0144] Whenever the term “at least,” “greater than,” or “greater than or equal to” precedes the first numerical value in a series of two or more numerical values, the term “at least,” “greater than” or “greater than or equal to” applies to each of the numerical values in that series of numerical values. For example, greater than or equal to 1, 2, or 3 is equivalent to greater than or equal to 1, greater than or equal to 2, or greater than or equal to 3.

[0145] Whenever the term “no more than,” “less than,” or “less than or equal to” precedes the first numerical value in a series of two or more numerical values, the term “no more than,” “less than,” or “less than or equal to” applies to each of the numerical values in that series of numerical values. For example, less than or equal to 3, 2, or 1 is equivalent to less than or equal to 3, less than or equal to 2, or less than or equal to 1.

[0146] Certain inventive embodiments herein contemplate numerical ranges. When ranges are present, the ranges include the range endpoints. Additionally, every sub range and value within the range is present as if explicitly written out.

[0147] The term “about” or “approximately” may mean within an acceptable error range for the particular value, which will depend in part on how the value is measured or determined, e.g., the limitations of the measurement system. For example, “about” may mean within 1 or more than 1 standard deviation, per the practice in the art. Alternatively, “about” may mean a range of up to 20%, up to 10%, up to 5%, or up to 1% of a given value. Where particular values are described in the application and claims, unless otherwise stated the term “about” meaning within an acceptable error range for the particular value may be assumed.

[0148] As used herein, “or” is intended to mean an “inclusive or” or what is also known as a “logical OR,” wherein when used as a logic statement, the expression “A or B” is true if either A or B is true, or if both A and B are true, and when used as a list of elements, the expression “A, B or C” is intended to include all combinations of the elements recited in the expression, for example, any of the elements selected from the group consisting of A, B, C, (A, B), (A, C), (B, C), and (A, B, C); and so on if additional elements are listed. As such, any reference to “or” herein is intended to encompass “and/or” unless otherwise stated.

[0149] It will be understood that when an element such as a layer, region, or substrate is referred to as being “on” or extending “onto” another element, it may be directly on or extend directly onto the other element or intervening elements may also be present. In contrast, when an element is referred to as being “directly on” or extending “directly onto” another element, there are no intervening elements present. Likewise, it will be understood that when an element such as a layer, region, or substrate is referred to as being “over” or extending “over” another element, it may be directly over or extend directly over the other element or intervening elements may also be present. In contrast, when an element is referred to as being “directly over” or extending “directly over” another element, there are no intervening elements present. It will also be understood that when an element is referred to as being “connected” or “coupled” to another element, it may be directly connected or coupled to the other element or intervening elements may be present. In contrast, when an element is referred to as being “directly connected” or “directly coupled” to another element, there are no intervening elements present.

[0150] Relative terms such as “below” or “above” or “upper” or “lower” or “horizontal” or “vertical” may be used herein to describe a relationship of one element, layer, or region to another element, layer, or region as illustrated in the Figures. It will be understood that these terms and those discussed above are intended to encompass different orientations of the device in addition to the orientation depicted in the Figures.

[0151] It will be understood that, although the terms “first,” “second,” “third,” etc. may be used herein to describe various elements, these elements should not be limited by these terms. These terms are only used to distinguish one element from another. For example, a first element may be termed a second element, and, similarly, a second element may be termed a first element, without departing from the scope of the present disclosure.

[0152] As used herein, “ion optic” generally refers to any device or combination of devices that are capable of directing the path of an ion flux in a controlled manner. Non-limiting examples include AC or DC lenses, quadrupoles, collision cells and the like.

[0153] As used herein, “mass analyzer” generally refers to a device which is capable of determining a mass to charge ratio and an intensity or a number of counts per second of one or more ions arriving at a detector comprised within the analyzer.

[0154] The term “molecule” refers to biological components that may be involved in corona formation, including, but not limited to, for example, proteins, polypeptides, polysaccharides, a sugar, a lipid, a lipoprotein, a metabolite, an oligonucleotide, metabolome or combination thereof. It is contemplated that the biomolecule coronas of distinct particles may contain some of the same biomolecules, may contain distinct biomolecules with regard to the other sensor elements, or may differ in level or quantity, type or conformation of the biomolecule that binds to each sensor element. In one embodiment, the biomolecule is selected from the group of proteins, nucleic acids, lipids, and metabolomes.

[0155] “ion manifolds” described herein are devices which can direct an ion flux entering through an inlet to a plurality of outlets in a configurable manner, by, e.g., dividing an ion flux between selected outlets of the ion manifold. Ion manifolds can comprise a series of ion optics to guide or divide a stream of ions.

[0156] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

[0157] Although the steps of the methods as described and claimed herein show or describe each of the methods or sets of operations in accordance with embodiments, a person of ordinary skill in the art will recognize many variations based on the teaching described herein. The steps may be completed in a different order. Steps may be added or omitted. Some of the steps may

comprise sub-steps. Many of the steps may be repeated as often as beneficial. One or more steps may be conducted simultaneously.

[0158] One or more of the steps of each of the methods or sets of operations may be performed with circuitry as described herein, for example, one or more of the processor or logic circuitry such as programmable array logic for a field programmable gate array. The circuitry may be programmed to provide one or more of the steps of each of the methods or sets of operations and the program may comprise program instructions stored on a computer readable memory or programmed steps of the logic circuitry such as the programmable array logic or the field programmable gate array, for example.

[0159] Throughout this specification, plural instances may implement components, operations, or structures described as a single instance. Although individual operations of one or more methods are illustrated and described as separate operations, one or more of the individual operations may be performed concurrently, and nothing requires that the operations be performed in the order illustrated. Structures and functionality presented as separate components in example configurations may be implemented as a combined structure or component. Similarly, structures and functionality presented as a single component may be implemented as separate components. These and other variations, modifications, additions, and improvements fall within the scope of the subject matter herein.

[0160] Additionally, certain embodiments are disclosed herein as including logic or a number of routines, subroutines, applications, or instructions. These may constitute either software (e.g., code embodied on a machine-readable medium) or hardware. In hardware, the routines, etc., are tangible units capable of performing certain operations and may be configured or arranged in a certain manner. In example embodiments, one or more computer systems (e.g., a standalone, client or server computer system) or one or more hardware modules of a computer system (e.g., a processor or a group of processors) may be configured by software (e.g., an application or application portion) as a hardware module that operates to perform certain operations as disclosed herein.

[0161] In various embodiments, a hardware module may be implemented mechanically or electronically. For example, a hardware module may comprise dedicated circuitry or logic that is permanently configured (e.g., as a special-purpose processor, such as a field programmable gate array (FPGA) or an application-specific integrated circuit (ASIC) to perform certain operations. A hardware module may also comprise programmable logic or circuitry (e.g., as encompassed within a general-purpose processor or other programmable processor) that is temporarily configured by software to perform certain operations. It will be appreciated that the decision to implement a hardware module mechanically, in dedicated and permanently configured circuitry,

or in temporarily configured circuitry (e.g., configured by software) may be driven by cost and time considerations.

[0162] Accordingly, hardware modules may encompass a tangible entity, be that an entity that is physically constructed, permanently configured (e.g., hardwired), or temporarily configured (e.g., programmed) to operate in a certain manner or to perform certain operations disclosed herein. Considering embodiments in which hardware modules are temporarily configured (e.g., programmed), each of the hardware modules need not be configured or instantiated at any one instance in time. For example, where the hardware modules comprise a general-purpose processor configured using software, the general-purpose processor may be configured as respective different hardware modules at different times. Software may accordingly configure processor, for example, to constitute a particular hardware module at one instance of time and to constitute a different hardware module at a different instance of time.

[0163] Hardware modules may provide information to, and receive information from, other hardware modules. Accordingly, the described hardware modules may be regarded as being communicatively coupled. Where multiple of such hardware modules exist contemporaneously, communications may be achieved through signal transmission (e.g., over appropriate circuits and buses) that connect the hardware modules. In embodiments in which multiple hardware modules are configured or instantiated at different times, communications between such hardware modules may be achieved, for example, through the storage and retrieval of information in memory structures to which the multiple hardware modules have access. For example, one hardware module may perform an operation and store the output of that operation in a memory device to which it is communicatively coupled. A further hardware module may then, at a later time, access the memory device to retrieve and process the stored output. Hardware modules may also initiate communications with input or output devices, and may operate on a resource (e.g., a collection of information). Elements that are described as being coupled and or connected may refer to two or more elements that may be (e.g., direct physical contact) or may not be (e.g., electrically connected, communicatively coupled, etc.) in direct contact with each other, but yet still cooperate or interact with each other.

[0164] The various operations of example methods disclosed herein may be performed, at least partially, by one or more processors that are temporarily configured (e.g., by software) or permanently configured to perform the relevant operations. Whether temporarily or permanently configured, such processors may constitute processor-implemented modules that operate to perform one or more operations or functions. The modules referred to herein may, in some example embodiments, comprise processor-implemented modules.

[0165] Similarly, the methods or routines disclosed herein may be at least partially processor-implemented. For example, at least some of the operations of a method may be performed by one or more processors or processor-implemented hardware modules. The performance of certain operations may be distributed among the one or more processors, not only residing within a single machine, but deployed across a number of machines. In some example embodiments, the processor or processors may be located in a single location (e.g., within a home environment, an office environment or as a server farm), while in other embodiments the processors may be distributed across a number of locations.

[0166] The performance of certain operations may be distributed among the one or more processors, not only residing within a single machine, but deployed across a number of machines. In some example embodiments, the one or more processors or processor-implemented modules may be located in a single geographic location (e.g., within a home environment, an office environment, or a server farm). In other example embodiments, the one or more processors or processor-implemented modules may be distributed across a number of geographic locations.

CLAIMS

WHAT IS CLAIMED IS:

1. An ion manifold comprising:
 - (a) an orthogonal ion manifold inlet;
 - (b) a first ion optic configured to receive a flux of ions through the ion manifold inlet, wherein the ion inlet is inside the first ion optic; and
 - (c) a second ion optic configured to receive an output of the flux of ions through the first ion optic, wherein the second ion optic comprises a plurality of outputs that split the flux of ions into a plurality of ion streams.
2. A method of generating a plurality of ion streams, the method comprising:
 - (a) providing an ion flux to an orthogonal ion manifold inlet of an ion manifold, the ion manifold comprising:
 - (i) the orthogonal ion manifold inlet;
 - (ii) a first ion optic configured to receive the ion flux through the ion manifold inlet, wherein the ion inlet is inside the first ion optic; and
 - (iii) a second ion optic configured to receive an output of the ion flux through the first ion optic, wherein the second ion optic comprises a plurality of outputs; and
 - (b) generating the plurality of ion streams from the plurality of outputs of the second ion optic when the ion flux traverses through the second ion optic.
3. The ion manifold or method of any of the preceding claims, wherein the first ion optic and the second ion optic comprises one or more electrical conductor segments, wherein the one or more electrical conductor segments comprise one or more through holes.
4. The ion manifold or method of any of the preceding claims, wherein the one or more electrical conductor segments are independently controllable.
5. The ion manifold or method of any of the preceding claims, wherein the one or more electrical conductor segments energized with RF and/or DC voltage.
6. The ion manifold or method of any of the preceding claims, wherein the first ion optic and the second ion optic each comprise an electrodynamic ion funnel.
7. The ion manifold or method of any of the preceding claims, wherein the first ion optic and the second ion optic each independently comprise a different pressure.
8. The ion manifold of any of the preceding claims, wherein the ion manifold further comprises an in-line ion inlet.
9. The method of any of the preceding claims, wherein the method further comprises providing a calibrant ion flux into the first ion optic via an in-line ion manifold inlet.

10. The ion manifold or method of any one of the preceding claims, wherein the flux of ions from the orthogonal ion inlet and the flux of ions from the in-line ion manifold inlet are offset by 1-5 mm.
11. The ion manifold or method of any one of the preceding claims, wherein the ion manifold further comprises an ion repeller manifold that is (i) positioned such that an axis along a normal vector of a surface of ion repeller manifold is orthogonal to a central axis of the ion manifold inlet, and (ii) is configured to direct a path of the flux of ions into the first ion optic.
12. The ion manifold or method of any one of the preceding claims, wherein the inline manifold inlet penetrates through the ion repeller manifold.
13. The ion manifold or method of any of the preceding claims, wherein the ion repeller manifold comprises a segmented plate, wherein the ion repeller manifold is configured to allow differing voltages.
14. The ion manifold or method of any of the preceding claims, wherein the repeller, the ion manifold inlet, and the first ion optic are contained at least partially within a first chamber.
15. The ion manifold or method of any of the preceding claims, wherein the second ion optic is contained at least partially in a second chamber, different than the first chamber.
16. The ion manifold or method of any of the preceding claims, wherein a reduced-pressure FAIMS (high field asymmetric waveform ion mobility spectrometer) device is configured to receive ions from the first ion optic and selectively output ions to the second ion optic.
17. The ion manifold or method of any of the preceding claims, wherein a reduced-pressure FAIMS (high field asymmetric waveform ion mobility spectrometer) device is configured to receive ions from the first ion optic and selectively output multiply charged ions to the second ion optic as compared to singly charged ions.
18. An ion mobility device comprising:
 - (a) a first substrate plate comprising:
 - i. a coplanar first outer electrode and second outer electrode; and
 - ii. a first separation electrode; and
 - (b) a second substrate plate comprising:
 - i. a coplanar third outer electrode and fourth outer electrode; and
 - ii. a second separation electrode;wherein the first substrate plate and the second substrate plate are substantially parallel.
19. The device of claim 18, wherein the distance between the first plate and the second plate is 4 to 12 mm.

20. The device of claim 18, wherein the first outer electrode, the second outer electrode, the third outer electrode, and the fourth outer electrode are configured as RF confining electrodes to confine the ion beam to the center of the device.
21. The device of any one of claims 18-20, wherein the region surrounding the first separation electrode and the second separation electrode has a pressure of no more than 20 torr.
22. The device of any one of claims 18-20, wherein the device comprises guard rail electrodes in each side of the device.
23. The device of claim 22, wherein the guard rail electrodes comprise a DC gradient.
24. The device of claim 18, wherein a voltage is applied to the first separation electrode.
25. The device of claim 18, wherein a FAIMS separation voltage is applied to the first separation electrode.
26. The device of claim 18, wherein a FAIMS separation voltage is applied to only the first separation electrode.
27. The device of any one of claims 18-26, wherein a FAIMS separation voltage of at least 800V is applied to at least one separation electrode.
28. The device of any one of claims 18-26, wherein a FAIMS separation voltage of at least 2000V is applied to at least one separation electrode.
29. The device of any one of claims 18-26, wherein a FAIMS separation voltage of at least 2000V is applied to at least one separation electrode, and the region surrounding the first separation electrode and the second separation electrode has a pressure of about 20 torr.
30. The ion manifold or method of any one of claims 1-17, wherein the ion manifold or method comprises a device of any one of claims 18-24.
31. A method of spatially separating ions comprising:
- (a) providing an ion flux to an ion mobility device of any of the preceding claims;
 - (b) applying a high voltage RF waveform to the separation electrodes;
 - (c) applying an ion confining waveform to the outer electrodes; and
 - (d) selecting transmitting ions based on mobility to generate a mobility-selected ion stream.
32. A reduced-pressure field asymmetric ion mobility device comprising:
- an enclosed mobility chamber having an ion inlet and an ion outlet disposed at opposite ends and configured to be filled with an inert gas at a pressure of less than atmospheric pressure;
 - at least one inner electrode disposed longitudinally between the ion inlet and the ion outlet of the enclosed mobility chamber;

at least one outer electrode disposed longitudinally between the ion inlet and the ion outlet of the enclosed mobility chamber, the outer electrode being disposed such that the inner electrode is at least partially enclosed within the outer electrode; and

one or more power supplies configured deliver a waveform to the inner electrode or the outer electrode, the waveform being configured to differentially deflect ions having different ion mobilities based on interaction of the ions with the waveform and the inert gas, wherein the differential deflection is configured to selectively remove ions having mobilities that correspond to singly charged species prior to said species reaching the ion outlet, wherein the inner electrode and the outer electrode are substantially planar.

33. A method of separating singly charged ions from multiply charged ions, the method comprising:

(a) providing an ion flux to an ion inlet of a reduced-pressure field asymmetric ion mobility device, the reduced-pressure field asymmetric ion mobility device comprising:

an enclosed mobility chamber having the ion inlet and an ion outlet disposed at opposite ends and configured to be filled with an inert gas at a pressure of less than atmospheric pressure;

at least one inner electrode disposed longitudinally between the ion inlet and the ion outlet of the enclosed mobility chamber;

at least one outer electrode disposed longitudinally between the ion inlet and the ion outlet of the enclosed mobility chamber; and

one or more power supplies configured deliver a waveform to the inner electrode or the outer electrode, the waveform being configured to differentially deflect ions having different ion mobilities based on interaction of the ions with the waveform and the inert gas, wherein the differential deflection is configured to selectively remove ions having mobilities that correspond to singly charged species prior to said species reaching the ion outlet;

(b) applying the waveform using the one or more power supplies to thereby substantially prevent ions of the ion flux having mobilities that correspond to singly charged species from reaching the ion outlet of the reduced-pressure field asymmetric ion mobility device; and

(c) obtaining a multiply charged ion population at the ion outlet of the reduced-pressure field asymmetric ion mobility device which is enriched for ions that correspond to multiply charged species.

34. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding claims, wherein the one or more power supplies provide a waveform comprising at least two sinusoids which are phase-shifted with respect to each other.

35. The method or the reduced-pressure field asymmetric ion mobility device of any one of claims 32-34, wherein the waveform is delivered to the outer electrode.

36. The method or the reduced-pressure field asymmetric ion mobility device of any one of claims 32-35, wherein the outer electrode comprises at least two ion outlets.

37. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding claims, wherein the reduced-pressure field asymmetric ion mobility device further comprises one or more sets of ion optics configured to guide ions into the ion inlet, out of the ion outlet, or a combination thereof.

38. The method or the reduced-pressure field asymmetric ion mobility device of any of the preceding claims, wherein multiply charged ions are transmitted from the ion inlet to the ion outlet in less than about 100 milliseconds (e.g., less than about 50 ms, 25 ms, 10 ms, 5 ms, or 3 ms).

39. The method or the reduced-pressure field asymmetric ion mobility device of any one of the preceding claims, wherein the electrodes are configured to be independently controllable.

40. The method or the reduced-pressure field asymmetric ion mobility device of any one of the preceding claims, wherein the electrodes are positioned at or near the outputs.