into a mass spectrometer is characterized by a less than a 0.1% standard error fluctuation in total mass spectrometric signal intensity.

[0013] In yet another aspect, disclosed herein is a method for providing stable electrospray ionization performance comprising: a) providing a microfluidic chip comprising a substrate, wherein the substrate comprises: (i) a fluid channel having a distal end that is in fluid communication with an electrospray ionization orifice, and (ii) a gas channel having a distal end that is in fluid communication with a gas outlet orifice; b) flowing a solution through the fluid channel; c) flowing a gas through the gas channel; and d) controlling a flow rate of the gas and a flow rate of the solution such that a ratio of volumetric flow rates for the gas and solution ranges from 1000:1 to 1,000,000:1 or a ratio of flow velocity for the gas at the gas outlet orifice and flow velocity for the solution at the electrospray ionization orifice ranges from 100:1 to 1,000,000:1. In some embodiments, the ratio of volumetric flow rates for the gas and solution ranges from 10,000:1 to 1,000,000:1. In some embodiments, the ratio of volumetric flow rates for the gas and solution ranges from 10,000:1 to 500,000:1, and more particularly from 10,000:1 to 300,000:1.

[0014] In some embodiments, the flow of solution is controlled by pressure, gravity, an electrokinetic force, or any combination thereof. In some embodiments, the flow of gas is provided by a compressed gas source. In some embodiments, the volumetric flow rate for the solution is less than 25 µL/min. In some embodiments, the microfluidic chip comprises two or more gas channels, each comprising a distal end that is in fluid communication with a gas outlet orifice, and wherein the two or more gas outlet orifices are disposed symmetrically about and adjacent to the electrospray ionization orifice. In some embodiments, the electrospray ionization orifice is disposed on an edge or corner of the substrate. In some embodiments, the one or more gas outlet orifices are disclosed adjacent to the electrospray ionization orifice on an edge of the substrate. In some embodiments, an electrospray ionization performance achieved when the microfluidic chip is configured to introduce a sample into a mass spectrometer is characterized by a less than a 1.0% standard error fluctuation in total mass spectrometric signal intensity. In some embodiments, an electrospray ionization performance when the microfluidic chip is configured to introduce a sample into a mass spectrometer is characterized by a less than a 0.1% standard error fluctuation in total mass spectrometric signal intensity.

[0015] ~~In another aspect,~~There is disclosed ~~herein is~~ a method for providing stable electrospray ionization performance comprising: a) providing a microfluidic chip comprising a substrate, wherein the substrate comprises: (i) a fluid channel having a distal end that is in fluid communication with an electrospray ionization orifice, and (ii) a gas channel having a distal end that is in fluid communication with a gas outlet orifice; b) flowing a solution through the fluid channel; c) flowing a gas through the gas channel; and d) controlling a flow rate of the gas and a flow rate of the solution

CLAIMS

WHAT IS CLAIMED IS:

1. A microfluidic chip comprising:

a) a substrate, wherein the substrate comprises:

i) a fluid channel comprising a distal end that is in fluid communication with an electrospray ionization orifice; and

ii) a gas channel comprising a distal end that is in fluid communication with a gas outlet orifice disposed adjacent to the electrospray ionization orifice;

wherein an angle between the distal end of the fluid channel and the distal end of the gas channel ranges from about 0 degrees to about 30 degrees.

~~2. The microfluidic chip of claim 1, wherein the electrospray ionization orifice is disposed on an edge or corner or tip of the substrate.~~

~~3~~2. The microfluidic chip of claim ~~2~~1, wherein the gas outlet orifice is disposed an edge of the substrate adjacent to the electrospray ionization orifice.

~~4. The microfluidic chip of any one of claims 1 to 3, wherein the substrate comprises two or more gas channels, each of which comprises a distal end that is in fluid communication with a gas outlet orifice.~~

~~5~~3. The microfluidic chip of claim ~~4~~2, wherein the substrate comprises two or more gas outlet orifices ~~are~~ disposed adjacent to and symmetrically about the electrospray ionization orifice.

~~6~~4. The microfluidic chip of any one of claims 1 to ~~5~~3, wherein the angle ranges from about 10 degrees to about 20 degrees.

~~7. The microfluidic chip of any one of claims 1 to 5, wherein the angle is about 15 ± 5 degrees.~~

~~8~~5. The microfluidic chip of any one of claims 1 to ~~7~~4, wherein the gas outlet orifice is configured to perform nebulization of a solution expelled from the electrospray ionization orifice.

~~9~~6. The microfluidic chip of any one of claims 1 to ~~8~~5, wherein the microfluidic device comprises three or more gas channels each comprising a gas outlet orifice disposed adjacent to the electrospray ionization orifice, and ~~.~~

~~10. The microfluidic chip of claim 9,~~ wherein at least one of the three or more gas channels are disposed within the substrate, and at least one of the three or more gas channels are disposed within an auxiliary component of the microfluidic chip that is positioned adjacent to the substrate such that the at least one gas channels are not located within a same plane as the substrate.

~~11~~7. The microfluidic chip of claim ~~10~~96, wherein the at least one of the three or more gas channels disposed within the auxiliary component are positioned such that:

(a) their gas outlet orifices lie in a plane that is substantially perpendicular to that of the substrate and are positioned symmetrically about and adjacent to the electrospray ionization orifice~~.~~, or

~~12. The microfluidic chip of claim 11, wherein the at least one of the three or more gas channels that are disposed within the auxiliary component are positioned such that~~

(b) their gas outlet orifices lie in one or more planes that are rotated relative to that of the substrate and are positioned in a radially-symmetric pairwise manner about and adjacent to the electrospray ionization orifice.

~~13. The microfluidic chip of any one of claims 1 to 12, wherein the fluid channel comprises a separation channel.~~

~~14~~8. The microfluidic chip of any one of claims 1 to ~~13~~7, wherein the microfluidic chip is configured to perform an isoelectric focusing or electrophoretic separation of a sample comprising a mixture of analytes in the fluid channel.

~~15~~9. The microfluidic chip of any one of claims 1 to ~~14~~8, wherein the fluid channel has one or more of the following dimensions:

(a) a width ranging from about 20 µm to about 600 µm~~.~~

~~16. The microfluidic chip of any one of claims 1 to 15, wherein the fluid channel has,~~

(b) a depth ranging from about 10 µm to about 100 µm~~.~~, ~~and~~or

~~17. The microfluidic chip of any one of claims 1 to 16, wherein the fluid channel has~~

(c) a length ranging from about 0.25 cm to about 30 cm and/or

the gas channel has one or more of the following dimensions:

(a) ~~a~~ width ranging from about 20 µm to about 200 µm~~.~~,

~~21. The microfluidic chip of any one of claims 1 to 20, wherein the gas channel has~~(b) a depth ranging from about 10 µm to about 100 µm, or~~.~~

~~22. The microfluidic chip of any one of claims 1 to 21, wherein the gas channel has~~(c) a length ranging from about 0.2 cm to about 20 cm.

10. The microfluidic chip of any one of claims 1 to 9, wherein the electrospray ionization orifice has a maximum cross-sectional dimension ranging from about 10 µm to about 100 µm.

~~23. The microfluidic chip of any one of claims 1 to 22, wherein the gas outlet orifice has a substantially square, rectangular, circular, ovoid, or lozenge-shaped cross-section.~~

11. The microfluidic chip of any one of claims 1 to 10, wherein the gas outlet orifice has a maximum cross-sectional dimension ranging from about 10 µm to about 50 µm.

12. The microfluidic chip of any one of claims 1 to 11, wherein the gas outlet orifice is disposed within 100 µm, ~~of the electrospray ionization orifice.~~

~~26. The microfluidic chip of any one of claims 1 to 25, wherein the gas outlet orifice is disposed within~~ 50 µm, or ~~of the electrospray ionization orifice.~~

~~27. The microfluidic chip of any one of claims 1 to 26, wherein the gas outlet orifice is disposed~~ within 15 µm of the electrospray ionization orifice.

~~28. The microfluidic chip of any one of claims 1 to 27, wherein the substrate is fabricated from glass, silicon, a polymer, or any combination thereof.~~

~~29~~13. A microfluidic chip comprising:

a) a substrate, wherein the substrate comprises:

i) two or more gas channels of different lengths, each configured to deliver a gas to a gas outlet orifice;

wherein a dimension of at least one of the two or more gas channels is adjusted along a portion of its length so that each of the two or more gas channels has about the same hydrodynamic flow resistance.

~~30~~14. The microfluidic chip of claim ~~29~~13, wherein a cross-sectional area of at least one of the two or more gas channels is adjusted along a portion of its length.

~~31~~15. The microfluidic chip of claim ~~29~~ 13 or claim ~~30~~14, wherein a ~~minimum~~ difference in length of the two or more gas channels ranges from about 1 cm to about 10 cm.

~~32. The microfluidic chip of any one of claims 29 to 31, wherein a maximum difference in length of the two or more gas channels ranges from about 1 cm to about 10 cm.~~

~~33~~16. The microfluidic chip of any one of claims ~~29~~ 13 to ~~32~~15, wherein the substrate further comprises a fluid channel comprising a distal end that is in fluid communication with an electrospray ionization orifice.

~~34~~17. The microfluidic chip of claim ~~33~~16, wherein the two or more gas outlet orifices are disposed symmetrically about and adjacent to the electrospray ionization orifice and are configured to perform nebulization of a solution expelled from the electrospray ionization orifice.

~~35~~18. The microfluidic chip of ~~any one of claims 33 to 34~~claim 16 or claim 17, wherein the electrospray ionization orifice is disposed on an edge or corner of the substrate and ~~.~~

~~36. The microfluidic chip of claim 35, wherein~~ the two or more gas outlet orifices are disposed on an edge of the substrate adjacent to the electrospray ionization orifice.

~~37. The microfluidic chip of any one of claims 29 to 36, wherein the fluid channel comprises a separation channel.~~

~~38~~19. The microfluidic chip of any one of claims ~~29~~ 13 to ~~37~~18, wherein the microfluidic chip is configured to perform isoelectric focusing or electrophoretic separations.

~~39~~20. The microfluidic chip of any one of claims ~~29~~ 13 to ~~38~~19, wherein the gas is a nebulizer gas ~~.~~

~~40. The microfluidic chip of claim 39, wherein the nebulizer gas comprises~~ comprising air, nitrogen, oxygen, nitrous oxide, fluorourethane, helium, argon, methanol, or any combination thereof.

~~41~~21. The microfluidic chip of any one of claims ~~35~~ 13 to ~~40~~20, further comprising a hydrophobic coating on at least a portion of an edge of the substrate or corner of the substrate on which the electrospray ionization orifice is disposed.

~~42~~22. A microfluidic chip comprising:

a) a substrate, wherein the substrate comprises:

i) a fluid channel comprising a proximal end that is in fluid communication with a fluid inlet port and a distal end that is in fluid communication with an electrospray ionization orifice; and

ii) at least two gas channels, each comprising a proximal end that is in fluid communication with a gas inlet port and a distal end in fluid communication with a gas outlet orifice;

wherein the at least one fluid inlet port and the at least two gas inlet ports are disposed along a first edge of the substrate.

~~43~~23. The microfluidic chip of claim ~~42~~22, wherein the electrospray ionization orifice is positioned on a second edge of the substrate~~.~~

~~44. The microfluidic chip of claim 43, wherein the electrospray ionization orifice is positioned~~ or on a corner of the substrate that does not comprise the first edge.

~~45~~24. The microfluidic chip ~~of any one of claims 42 to 44~~claim 22 or claim 23, wherein the substrate is less than about 2.0 mm thick.

~~46~~25. The microfluidic chip of any one of claims ~~42 to 45~~22 to 24, wherein the fluid channel comprises a separation channel configured to perform an electrophoretic separation~~.~~

~~47. The microfluidic chip of any one of claims 42 to 45, wherein the fluid channel comprises a separation channel configured to perform~~ or an isoelectric focusing separation.

~~48~~26. The microfluidic chip of any one of claims ~~46~~ 22 to ~~47~~25, wherein the substrate comprises a first separation channel and a second separation channel, wherein a distal end of the first separation channel is in fluid communication with a proximal end of the second separation channel, ~~and~~ wherein a distal end of the second separation channel is in fluid communication with the electrospray ionization orifice, and ~~.~~

~~49. The microfluidic chip of claim 48,~~ wherein the first separation channel is configured to perform a chromatographic separation, and wherein the second separation channel is configured to perform an electrophoretic separation or ~~.~~

~~50. The microfluidic chip of claim 48, wherein the first separation channel is configured to perform a chromatographic separation, and wherein the second separation channel is configured to perform~~ an isoelectric focusing separation.

~~51~~27. The microfluidic chip of any one of claims ~~42~~ 22 to ~~50~~26, wherein the fluid channel comprises a separation channel configured to perform isoelectric focusing separation of a sample comprising a mixture of analytes, and the substrate further comprises a mobilization electrolyte channel that is in

fluid communication with a distal end of the separation channel and is configured to provide electrophoretic introduction of a mobilization electrolyte at the distal end of the separation channel.

~~52~~28. A method for performing electrospray ionization from a microfluidic chip comprising:

a) providing a microfluidic chip comprising a substrate, wherein the substrate comprises:

i) at least one fluid channel comprising a distal end that is in fluid communication with an electrospray ionization orifice; and

ii) at least one gas channel configured to deliver a gas to a gas outlet orifice that is adjacent to the electrospray ionization orifice;

b) flowing a solution through the at least one fluid channel such that the solution is expelled from the electrospray ionization orifice; and

c) flowing a gas through the at least one gas channel such that the gas is expelled from the gas outlet orifice;

wherein a temperature of the substrate is controlled by a temperature of the gas flowing through the at least one gas channel.

~~53~~29. The method of claim ~~52~~28, wherein the temperature of the gas ranges from about 4 ^{o}C to about 100°C, and ~~.~~

~~54. The method of claim 52 or claim 53, wherein~~ the temperature of the substrate ranges from about 10 ^{o}C to about 50 ^{o}C.

~~55. The method of any one of claims 52 to 54, wherein the average temperature of the substrate is held at 30 ± 5 ^{o}C.~~

~~56. The method of any one of claims 52 to 55, wherein the at least one fluid channel comprises a separation channel.~~

~~57~~30. The method of claim 28 or claim ~~56~~29, wherein the separation channel is configured to perform an isoelectric focusing separation ~~of a sample comprising a mixture of analytes.~~

~~58. The method of claim 56, wherein the separation channel is configured to perform~~ or an electrophoretic separation of a sample comprising a mixture of analytes.

~~59~~31. The method of any one of claims ~~52 to 58~~28 to 30, wherein an electrospray ionization performance ~~achieved~~, when the microfluidic chip is configured to introduce a sample into a mass

spectrometer, is characterized by a less than a 1.0% ~~standard error fluctuation in total mass spectrometric signal intensity.~~

~~60. The method of any one of claims 52 to 59, wherein an electrospray ionization performance when the microfluidic chip is configured to introduce a sample into a mass spectrometer is characterized~~or by a less than a 0.1% standard error fluctuation in total mass spectrometric signal intensity.

~~61~~32. A method for providing stable electrospray ionization performance comprising:

a) providing a microfluidic chip comprising a substrate, wherein the substrate comprises: (i) a fluid channel having a distal end that is in fluid communication with an electrospray ionization orifice, and (ii) a gas channel having a distal end that is in fluid communication with a gas outlet orifice;

b) flowing a solution through the fluid channel;

c) flowing a gas through the gas channel; and

d) controlling a flow rate of the gas and a flow rate of the solution such that a ratio of volumetric flow rates for the gas and solution ranges from 1000:1 to 1,000,000:1 or a ratio of flow velocity for the gas at the gas outlet orifice and flow velocity for the solution at the electrospray ionization orifice ranges from 100:1 to 1,000,000:1.~~.~~

~~62. The method of claim 61, wherein the ratio of volumetric flow rates for the gas and solution ranges from 10,000:1 to 500,000:1.~~

~~63~~33. The method of claim ~~61 or claim 62~~32, wherein the flow of solution is controlled by pressure, gravity, an electrokinetic force, or any combination thereof~~.~~

~~64. The method of any one of claims 61 to 63,~~ and wherein the flow of gas is provided by a compressed gas source.

~~65~~34. The method of ~~any one of claims 61 to 64~~claim 32 or 33, wherein the volumetric flow rate for the solution is less than 25 µL/min.

~~66~~35. The method of any one of claims ~~61 to 65~~32 to 34, wherein the microfluidic chip comprises two or more gas channels, each comprising a distal end that is in fluid communication with a gas outlet orifice, and wherein the two or more gas outlet orifices are disposed symmetrically about and adjacent to the electrospray ionization orifice.

~~67~~36. The method of any one of claims ~~61 to 66~~32 to 35, wherein the electrospray ionization orifice is disposed on an edge or corner of the substrate and ~~.~~

~~68. The method of claim 67,~~ wherein the one or more gas outlet orifices are disclosed adjacent to the electrospray ionization orifice on an edge of the substrate.

~~69~~37. The method of any one of claims ~~61 to 68~~32 to 36, wherein an electrospray ionization performance, ~~achieved~~ when the microfluidic chip is configured to introduce a sample into a mass spectrometer, is characterized by a less than a 1.0% ~~standard error fluctuation in total mass spectrometric signal intensity.~~

~~70. The method of any one of claims 61 to 69, wherein an electrospray ionization performance when the microfluidic chip is configured to introduce a sample into a mass spectrometer is characterized~~or by a less than a 0.1% standard error fluctuation in total mass spectrometric signal intensity.

~~71. A method for providing stable electrospray ionization performance comprising:~~

~~a) providing a microfluidic chip comprising a substrate, wherein the substrate comprises: (i) a fluid channel having a distal end that is in fluid communication with an electrospray ionization orifice, and (ii) a gas channel having a distal end that is in fluid communication with a gas outlet orifice;~~

~~b) flowing a solution through the fluid channel;~~

~~c) flowing a gas through the gas channel; and~~

~~d) controlling a flow rate of the gas and a flow rate of the solution such that a ratio of flow velocity for the gas at the gas outlet orifice and flow velocity for the solution at the electrospray ionization orifice ranges from 100:1 to 1,000,000:1.~~

~~72~~38. The method of any one of claims ~~71~~32 to 37, wherein the ratio of flow velocity for the gas at the gas outlet orifice and flow velocity for the solution at the electrospray ionization orifice ranges from 500:1 to 5,000:1 or ~~.~~

~~73. The method of claim 71 or claim 72, wherein the ratio of flow velocity for the gas at the gas outlet orifice and flow velocity for the solution at the electrospray ionization orifice ranges~~ from 1,000:1 to 3,000:1.

~~74~~39. A microfluidic cartridge comprising:

a) a microfluidic chip comprising at least one fluid port and at least two gas ports disposed on an edge of the microfluidic chip; and

b) a microfluidic cartridge component that is in fluid communication with the microfluidic chip and is configured to encompass at least a portion of the microfluidic chip, the microfluidic cartridge component comprising at least one fluid port and at least two gas ports that align with the at least one fluid port and at least two gas ports of the microfluidic chip.

~~75~~40. The microfluidic cartridge of claim ~~74~~39, further comprising one or more elastomeric components disposed between the edge of the microfluidic chip and a surface of the cartridge; and wherein the one or more elastomeric components form a substantially leak-proof seal between the at least one fluid port and at least two gas ports of the microfluidic chip and the at least one fluid port and at least two gas ports of the microfluidic cartridge component upon application of force.

~~76~~41. The microfluidic cartridge of claim ~~74~~ 39 or claim ~~75~~40, wherein the edge of the microfluidic chip is less than about 2.0 mm thick.

~~77. The microfluidic cartridge of any one of claims 74 to 76, wherein the edge of the microfluidic chip is about 1 ± 0.4 mm thick.~~

~~78~~42. A system comprising:

a) a microfluidic cartridge comprising two or more fluid ports and configured to be removeable from the system; and

b) an instrument comprising two or more fluid interconnects;

wherein each of the two or more fluid interconnects is configured to provide a substantially leak-proof fluid coupling between a fluid line of the instrument and a fluid port of the microfluidic cartridge upon application of force to an assembly comprising the two or more fluid interconnects and the two or more fluid ports of the microfluidic cartridge, and

wherein the substantially leak-proof fluid couplings are maintained when a relative fluid pressure within two of the two or more fluid lines varies by a factor of at least 10-fold.

~~79~~43. The system of claim ~~78~~42, wherein the substantially leak-proof fluid couplings are maintained when the relative fluid pressure within two of the two or more fluid lines varies by a factor of at least 100-fold.

~~80~~44. The system of claim ~~78~~ 42 or claim ~~79~~43, wherein each of the two or more fluid interconnects comprises an independently spring-loaded fitting.

~~81~~45. The system of claim ~~80~~44, wherein the independently spring-loaded fittings comprise a flat face-sealing fitting that mates with a fluid port comprising a hole in the microfluidic cartridge.

~~82. The microfluidic chip of any one of claims 1 to 8, wherein the microfluidic device comprises three or more gas channels each comprising a gas outlet orifice disposed immediately adjacent to the electrospray ionization orifice.~~

~~83. The microfluidic chip of claim 82, wherein at least one of the three or more gas channels are disposed within the substrate, and at least one of the three or more gas channels are disposed within an auxiliary component of the microfluidic chip that is positioned immediately adjacent to the substrate such that the at least one gas channels are not located within a same plane as the substrate.~~

~~84. The microfluidic chip of claim 83, wherein the at least one of the three or more gas channels disposed within the auxiliary component are positioned such that their gas outlet orifices lie in a plane that is substantially perpendicular to that of the substrate and are positioned symmetrically about and immediately adjacent to the electrospray ionization orifice.~~

~~85. The microfluidic chip of claim 84, wherein the at least one of the three or more gas channels that are disposed within the auxiliary component are positioned such that their gas outlet orifices lie in one or more planes that are rotated relative to that of the substrate and are positioned in a radially-symmetric pairwise manner about and immediately adjacent to the electrospray ionization orifice.~~

~~86~~46. The microfluidic chip of claim ~~47~~25 or 26, wherein isoelectric focusing is performed while flowing a fluid from the fluid inlet port through the separation channel.

~~87. The microfluidic chip of claim 48, wherein electrospray ionization is performed while flowing a fluid from the fluid inlet port through the first and second separation channels.~~