CLAIMS

WHAT IS CLAIMED IS:

1. A method for sample purification, comprising:

(a) loading into a fluidic device

(i) a tissue sample comprising lysed solid tissue, wherein said lysed solid tissue comprises nucleic acids and a contaminant,

(ii) a trailing electrolyte buffer comprising first trailing electrolyte ions with an effective mobility having a magnitude lower than a magnitude of an effective mobility of said nucleic acids, and

(iii) a leading electrolyte buffer comprising first leading electrolyte ions, with a second effective mobility, wherein said second effective mobility has a magnitude greater than said magnitude of said effective mobility of said nucleic acids; and

(b) applying an electric field within said fluidic device to conduct isotachophoresis with said first trailing electrolyte ions, said nucleic acids, and said first leading electrolyte ions, thereby purifying said nucleic acids from said contaminant in said tissue sample.

2. The method of claim 1, wherein said effective mobility of said first trailing electrolyte ions has a magnitude greater than a magnitude of an effective mobility of said contaminant.

3. The method of claim 1, wherein said fluidic device is a microfluidic chip and said tissue sample, said trailing electrolyte buffer and said leading electrolyte buffer are loaded into a first zone of said microfluidic chip.

4. The method of any one of claims 1-3, further comprising in said first zone of said microfluidic chip, conducting on said tissue sample at least one sample preparation procedure selected from the group consisting of (1) removing embedding material, (2) disrupting tissue, (3) lysing cells, (4) de-crosslinking said nucleic acids, (5) digesting proteins, and (6) digesting said nucleic acids.

5. The method of any one of claims 1-4, wherein said isotachophoresis is conducted in a second zone of said microfluidic chip, wherein said second zone is separate from and fluidically connected to said first zone.

6. The method of any one of claims 1-5, wherein said solid tissue is derived from a solid organ.

7. The method of any one of claims 1-6, wherein said lysed solid tissue comprises a chemical fixative.

8. The method of claim 7, wherein said chemical fixative is formalin.

9. The method of claim 8, wherein said solid tissue is formalin fixed paraffin embedded tissue (FFPE).

10. The method of any one of claims 1-9, wherein said lysed solid tissue comprises urea or thiourea.

11. The method of any one of claims 1-10, further comprising disrupting cell-cell junctions, extracellular matrix, or connective tissue in order to obtain said lysed solid tissue.

12. The method of any one of claims 1-10, wherein said lysed solid tissue comprises solid particles.

13. The method of any one of claims 1-12, wherein said nucleic acids comprise dispersed or solvated nucleic acids.

14. The method of any one of claims 1-13, wherein said contaminant is selected from the group consisting of crosslinked nucleic acids, embedding material, tissue debris, fixation chemicals, proteins, inhibitors, and combinations thereof.

15. The method of any one of claims 1-14, wherein said contaminant comprises crosslinked nucleic acids.

16. The method of any one of claims 1-15,, wherein said tissue sample is combined with said trailing electrolyte buffer prior to said loading.

17. The method of any one of claims 1-16, wherein said tissue sample is combined with said leading electrolyte buffer prior to said loading.

18. The method of any one of claims 1-17, wherein said loading of said leading electrolyte buffer is conducted prior to said loading of said tissue sample.

19. The method of any one of claims 1-18, wherein said solid tissue is lysed in said leading electrolyte buffer prior to said loading of said tissue sample.

20. The method of any one of claims 1-19, wherein said solid tissue is lysed in said trailing electrolyte buffer prior to said loading of said tissue sample.

21. The method of any one of claims 4-20, wherein said sample preparation procedure comprises, prior to said applying of said electric field, removing embedding material by incubating said tissue sample in said fluidic device at a temperature of at least about 37 °C for a duration of at least about 1 minute.

22. The method of claim 21, wherein said temperature is from about 40 °C to about 80 °C.

23. The method of claim 21, wherein said duration is from about 1 minute to about 120 minutes.

24. The method of any one of claims 4-23, wherein said sample preparation procedure comprises disrupting tissue or lysing cells by applying mechanical stress to said tissue sample.

25. The method of any one of claims 4-24, wherein said sample preparation procedure comprises disrupting tissue or lysing cells by applying heat to said tissue sample.

26. The method of any one of claims 4-25, wherein said applying heat results in a temperature of said tissue sample within a range of from about 30 °C to about 80 °C.

27. The method of any one of claims 4-26, wherein said sample preparation procedure comprises disrupting tissue or lysing cells by contacting said tissue sample with a solution with pH of at least 10 or by proteolytically digesting said tissue sample.

28. The method of claim 27, wherein said proteolytic digestion is conducted at a temperature greater than about 25 °C.

29. The method of any one of claims 4-28, wherein said sample preparation procedure comprises disrupting tissue or lysing cells by applying at least one surfactant to said tissue sample.

30. The method of any one of claims 4-29, wherein said sample preparation procedure comprises disrupting tissue or lysing cells by applying a solution comprising urea to said tissue or cell sample.

31. The method of claim 30, wherein said solution further comprises thiourea.

32. The method of claim 31, wherein a concentration of said urea in said solution is within a range of from about 4 M to about 9 M and a concentration of said thiourea in said solution is in a range of from about 0.5 M to about 3.5 M.

33. The method of claim 31, wherein a concentration of said urea in said solution is from about 6.5 M to about 7.5 M and a concentration of said thiourea in said solution is from about 1.5 M to about 2.5 M.

34. The method of any one of claims 4-33, wherein said sample preparation procedure comprises de-crosslinking said nucleic acids by digesting crosslinking proteins with proteinase K.

35. The method of any one of claims 4-34, wherein said sample preparation procedure comprises digesting said nucleic acids with DNase or RNase.

36. The method of any one of claims 1-35, further comprising eluting an output solution comprising said purified nucleic acids from an outlet reservoir of said fluidic device.

37. The method of claim 36, wherein a concentration of said purified nucleic acids in said output solution is at least about two-fold higher than a concentration of said nucleic acids in said tissue sample.

38. The method of claim 36, wherein said tissue sample and said purified nucleic acids in said output solution comprise crosslinked nucleic acids and a concentration of said crosslinked nucleic acids in said output solution is at least about two-fold lower than a concentration of said crosslinked nucleic acids in said tissue sample.

39. The method of claim 36, wherein said contaminant is present in said output solution at a concentration that is at least two-fold less than a concentration of said contaminant in said tissue sample.

40. The method of any one of claims 1-39, wherein said first trailing electrolyte ions comprise caproic acid.

41. The method of any one of claims 1-40, wherein said first leading electrolyte ions comprise chloride.

42. The method of any one of claims 1-41, wherein said trailing electrolyte buffer comprises second trailing electrolyte ions having a different effective mobility than said first trailing electrolyte ions.

43. The method of claim 42, wherein said second trailing electrolyte ions comprise HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid) or MOPS (3-(*N*-morpholino)propanesulfonic acid).

44. The method of claim 42, wherein said second trailing electrolyte ions comprise HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid) and said first trailing electrolyte ions comprise caproic acid.

45. The method of claim 42, wherein said second trailing electrolyte ions comprise MOPS (3-(*N*-morpholino)propanesulfonic acid) and said first trailing electrolyte ions comprise caproic acid.

46. The method of claim 42, wherein said second trailing electrolyte ions comprise HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid) and said first trailing electrolyte ions comprise MOPS.

47. The method of any one of claims 1-46, wherein said trailing electrolyte buffer comprises second trailing electrolyte ions with a second effective mobility, wherein said second effective mobility has a magnitude about the same as or lower than said magnitude of said effective mobility of said contaminant.

48. The method of any one of claims 1-47, wherein said tissue sample loaded into said fluidic device has a volume of at least 50 µl.

49. The method of any one of claims 1-48, further comprising in said first zone of said microfluidic chip, conducting on said tissue sample a first sample processing procedure, and in a second zone of said microfluidic chip, conducting on said tissue sample an enzymatic reaction.

50. The method of claim 49, wherein said first sample processing procedure comprises removal of embedding material, disruption of tissue, or cell lysis, and said enzymatic reaction comprises de-crosslinking said nucleic acids, digesting proteins, or digesting nucleic acids.

51. The method of claim 49, wherein said first zone and said second zone each are each heated to a temperature above 37 °C.

52. The method of claim 49, wherein said first zone is heated to a temperature of about 60°C to 100 °C during said first sample processing procedure and wherein said second zone is heated to a temperature of 40°C to 60 °C.

53. A method for simultaneously purifying nucleic acids from at least two different samples comprising:

(a) loading into a first channel of a microfluidic chip (i) a first sample comprising first nucleic acids and a first contaminant, (ii) a first trailing electrolyte buffer comprising first trailing ions, wherein a magnitude of an effective mobility of said first trailing ions is less than a magnitude of an effective mobility of said first nucleic acids, and (iii) a first leading electrolyte buffer comprising first leading ions, wherein a magnitude of an effective mobility of said first leading ions is greater than said magnitude of said effective mobility of said first nucleic acids;

(b) loading into a second channel of said microfluidic chip (i) a second sample comprising second nucleic acids and a second contaminant, (ii) a second trailing electrolyte buffer comprising second trailing ions, wherein a magnitude of said second trailing ions is less than a magnitude of an effective mobility of said second nucleic acids, and (iii) a second leading electrolyte buffer comprising second leading ions, wherein a magnitude of an effective mobility of said second leading ions is greater than said magnitude of said effective mobility of said second nucleic acids; and

(c) applying a first electric field within said microfluidic chip to conduct isotachophoresis in said first channel with said first trailing ions, said first nucleic acids, and said first leading ions, and applying a second electric field to conduct isotachophoresis in said second channel with said second trailing ions, said second nucleic acids, and said second leading ions, thereby simultaneously purifying said first nucleic acids from said first contaminant and said second nucleic acids from said second contaminant.

54. The method of claim 53, wherein said first sample and said second sample are different sample types.

55. The method of claim 53, wherein said first nucleic acids and said second nucleic acids are different types or lengths of nucleic acids.

56. The method of any one of claims 1- 53, wherein said first trailing electrolyte buffer or said first leading electrolyte buffer further comprises a lysis agent or a tissue disruption agent.

57. The method of claim 56, wherein said lysis agent or said tissue disruption agent comprises one or more agents selected from the group consisting of a solution with pH greater than about 12, a proteinase, urea, thiourea, and a surfactant.

58. The method of any one of claims 53-57, wherein said first sample comprises lysed solid tissue.

59. The method of claim 58, wherein said second sample comprises lysed cells.

60. The method of any one of claims 53-59, wherein said first sample does not contact said second sample during said conducting of isotachophoresis.

61. The method of any one of claims 53-60, further comprising loading into a third channel of said microfluidic chip (i) a third sample comprising third nucleic acids and a third contaminant, (ii) a third trailing electrolyte buffer comprising third trailing ions, wherein a magnitude of an effective mobility of said third trailing ions is less than a magnitude of an effective mobility of said third nucleic acids, and (iii) a third leading electrolyte buffer comprising third leading ions, wherein a magnitude of an effective mobility of said third leading ions is greater than said magnitude of said effective mobility of said third nucleic acids, wherein said electric field is applied within said microfluidic chip to conduct said isotachophoresis in said third channel with said third trailing ions, said third nucleic acids, and said third leading ions, thereby simultaneously purifying said first nucleic acids from said first contaminant, said second nucleic acids from said second contaminant and said third nucleic acids from said third contaminant.

62. The method of any one of claims 53-61, wherein said first and second electric fields are generated from a single electrode pair.

63. The method of any one of claims 53-62, wherein said first and second electric fields are generated from different electrode pairs.

64. The method of claim 63, wherein said first and second channels are coupled to independent sensors.

65. The method of claim 64, wherein feedback from said independent sensors is used to independently control said first and second electric fields.

66. The method of claim 64, wherein said independent sensors detect voltage and said feedback is used to control current within said first and second channels.

67. The method of any one of claims 1-66, wherein said nucleic acids comprise DNA.

68. The method of any one of claims 1-66, wherein said nucleic acids comprise RNA.

69. A method for sample purification, comprising:

(a) loading onto a fluidic device

(i) a sample comprising fixed cells, fixed tissue, or embedded tissue, wherein said sample comprise nucleic acids,

(ii) a trailing electrolyte buffer comprising trailing electrolytes, wherein said trailing electrolytes have a lower effective mobility than said nucleic acids, and

(iii) a leading electrolyte buffer comprising leading electrolytes, wherein said leading electrolytes have a higher effective mobility than said nucleic acids; and

(b) applying an electric field on said fluidic device to conduct isotachophoresis with said trailing electrolytes, said nucleic acids, and said leading electrolytes, thereby purifying said nucleic acids from a contaminant in said sample.

70. The method of claim 69, wherein said contaminant is selected from the group consisting of crosslinked nucleic acids, embedding material, fixation chemicals, enzymes, and inhibitors.

71. The method of claim 69, wherein said sample comprises said fixed cells, said fixed tissue, or both said fixed cells and said fixed tissue.

72. The method of claim 69, wherein said sample is formalin-fixed.

73. The method of claim 69, wherein said sample comprises said embedded tissue.

74. The method of claim 69, wherein said sample comprises said tissue embedded in paraffin.

75. The method of claim 69, wherein said sample is a formalin-fixed paraffin-embedded (FFPE) tissue sample.

76. The method of claim 69 wherein said sample comprises a tissue biopsy.

77. The method of claim 75, wherein said sample is a dissected formalin-fixed paraffin-embedded (FFPE) sample.

78. The method of claim 69, further comprising comparing a characteristic of said nucleic acids to nucleic acids from other samples, wherein said characteristic is an expression level, a nucleic acid sequence, a molecular weight, nucleic acid integrity, nucleic acid purity or nucleic acid strandedness.

79. The method of claim 69, wherein said sample is a tumor sample.

80. The method of claim 69, wherein said trailing electrolyte buffer has a pH of greater than about 7.

81. The method of claim 69, further comprising, prior to said applying said electric field, incubating said tissue sample in said fluidic device at a temperature of at least about 37 °C for a duration of at least about 1 minute.

82. The method of claim 81, wherein said temperature is from about 40 °C to about 80 °C.

83. The method of claim 81, wherein said duration is from about 1 minute to about 120 minutes.

84. The method of claim 60, wherein said leading electrolyte buffer comprises proteinase K.

85. The method of claim 84, further comprising removing protein crosslinks from said nucleic acids using said proteinase K.

86. The method of claim 60, further comprising, after said applying said electric field, removing protein crosslinks from said nucleic acids using heat.

87. The method of claim 60, further comprising eluting an output solution comprising said purified nucleic acids from an outlet reservoir of said fluidic device.

88. The method of claim 87, wherein a concentration of said purified nucleic acids in said output solution is at least about two-fold higher than a concentration of said nucleic acids in said tissue sample.

89. The method of claim 87, wherein a concentration of said crosslinked nucleic acids in said output solution is at least about two-fold lower than a concentration of said crosslinked nucleic acids in said tissue sample.

90. The method of claim 87, wherein said output solution has a volume equal to or less than about 50 μL.

91. The method of claim 60, wherein said tissue sample has a mass of at least about 1 ng.

92. The method of claim 60, wherein said tissue sample has a volume greater than 25 μL.

93. The method of claim 60, wherein said trailing electrolytes have a higher effective mobility than said contaminant.

94. The method of claim 60, wherein said trailing electrolytes comprise (i) first ions, wherein said first ions have a higher effective mobility magnitude than said contaminant, and (ii) second ions, wherein said second ions have an effective mobility magnitude about the same as or lower than said contaminant.

95. The method of claim 60, wherein said conducting isotachophoresis quenches a pH of said tissue sample to about 7.5.

96. The method of claim 60, further comprising, prior to said loading, conducting de-paraffinization on said sample.

97. The method of claim 60, further comprising detecting a concentration of said nucleic acids.

98. The method of claim 88, wherein said concentration is less than or equal to about 1 picogram per microliter (pg/μL).

99. A method for sample purification, comprising:

(a) loading into a fluidic device

(i) a tissue sample comprising lysed solid tissue and nucleic acids,

(ii) a trailing electrolyte buffer, said trailing electrolyte buffer comprising trailing electrolyte ions with a first effective mobility, wherein said first effective mobility has a magnitude lower than a magnitude of an effective mobility of said nucleic acids,

(iii) a first leading electrolyte buffer in a first leading electrolyte reservoir, said first leading electrolyte buffer comprising first leading electrolyte ions with a second effective mobility, wherein said second effective mobility has a magnitude greater than said magnitude of said effective mobility of said nucleic acids, and

(iv) a second leading electrolyte buffer in a second leading electrolyte reservoir, said second leading electrolyte buffer comprising second leading electrolyte ions with a third effective mobility, wherein said third effective mobility has a magnitude greater than said magnitude of said effective mobility of said nucleic acids,

wherein said first leading electrolyte buffer is different from said second leading electrolyte buffer;

(b) first conducting isotachophoresis with said trailing electrolyte ions, said nucleic acids, and said first leading electrolyte ions, thereby purifying said nucleic acids from said contaminant in said tissue sample; and

(c) second conducting isotachophoresis with said trailing electrolyte ions, said nucleic acids, and said second leading electrolyte ions.

100. The method of claim 99, wherein said second conducting isotachophoresis comprises changing an applied current from a first channel to a second channel.

101. The method of claim 99 or 100, wherein said first leading electrolyte ions are the same as said second leading electrolyte ions, and wherein a concentration of said first leading electrolyte ions in said first leading electrolyte buffer is different from a concentration of said second leading electrolyte ions in said second leading electrolyte buffer.

102. The method of claim 99, 100, or 101, wherein said second effective mobility has a magnitude greater than said magnitude of said third effective mobility.

103. The method of any one of claims 99-102, wherein said first leading electrolyte ions are different from said second leading electrolyte ions.

104. The method of any one of claims 99-103, wherein said first leading electrolyte ions are the same as said second leading electrolyte ions, and wherein a concentration of said first leading electrolyte ions in said first leading electrolyte buffer is the same as a concentration of said second leading electrolyte ions in said second leading electrolyte buffer, and wherein said first leading electrolyte buffer comprises third leading electrolyte ions.

105. The method of any one of claims 99-104, wherein said first leading electrolyte ions are the same as said second leading electrolyte ions, and wherein a concentration of said first leading electrolyte ions in said first leading electrolyte buffer is the same as a concentration of said second leading electrolyte ions in said second leading electrolyte buffer, and wherein said second leading electrolyte buffer comprises third leading electrolyte ions.

106. The method of any one of claims 99-105, further comprising collecting said nucleic acids in said second leading electrolyte reservoir and removing said nucleic acids from said second leading electrolyte reservoir.

107. The method of any one of claims 99-106, wherein said first conducting isotachophoresis and said second conducting isotachophoresis are performed by applying a single electric field.

108. The method of any one of claims 99-107, wherein said first conducting isotachophoresis and said second conducting isotachophoresis are performed by applying more than one electric field.

109. The method of any one of claims 99-108, wherein the concentration of said second leading electrolyte ions in said second leading electrolyte buffer is less than 50 mM.

110. The method of any one of claims 99-108, wherein said second leading electrolyte buffer comprises 50 mM Tris HCl.

111. A microfluidic device comprising:

(a) a first isotachophoresis region in a microfluidic chip comprising:

i. a first sample reservoir in fluid communication with a first fluidic channel,
ii. a first buffer reservoir in fluid communication with said first fluidic channel, and
iii. a second buffer reservoir in fluid communication with said first channel; and

(b) a second isotachophoresis region in said microfluidic chip comprising:

i. a second sample reservoir in fluid communication with a second fluidic channel,
ii. a third buffer reservoir in fluid communication with said second fluidic channel, and
iii. a fourth buffer reservoir in fluid communication with said second channel,

wherein said first isotachophoresis region is not in fluid communication with said second isotachophoresis region and wherein said microfluidic device is configured to independently control a first electric circuit that applies current to said first isotachophoresis region and a second electric circuit that applies current to said second isotachophoresis region.

112. The microfluidic device of claim 111, wherein a leakage rate between said first and second isotachophoresis zones is less than 1 µl per hour.

113. The microfluidic device of claim 111 or 112, wherein current leakage between said first and second regions is less than 1 uA.

114. The microfluidic device of claim 111, 112, or 113, wherein an impedance is greater than 1 megaOhm.

115. The microfluidic device of any one of the preceding claims, wherein said first fluidic channel holds a liquid volume greater than 100 µl.

116. The microfluidic device of any one of the preceding claims,wherein said first fluidic channel is separated from said second fluidic channel by a distance that is at least 5-fold less than a width of said first channel.

117. The microfluidic device of any one of the preceding claims,wherein said microfluidic device is configured to control said first electric circuit simultaneously with said second electric circuit and independently of said second electric circuit.

118. The microfluidic device of any one of the preceding claims, further comprising an elution reservoir in fluid communication to said first channel, wherein a temperature sensor is situated within 5 mm of said elution reservoir.

119. A method, comprising:

(a) providing an electrokinetic fluidic device comprising a sample input reservoir in fluid communication with a channel;

(b) loading a sample volume into said sample input reservoir;

(c) moving at least 50% of said sample volume from said sample input reservoir to said channel, without adding additional volume to said sample input reservoir; and

(d) applying an ionic current through said channel.

120. The method of claim 119, wherein said moving is conducted with aid of gravity.

121. The method of claim 119 or 120, wherein said ionic current does not substantially pass through said channel.

122. The method of claim 119, 120 or 121, wherein said at least 50% of said sample volume comprises at least 80% of said sample volume.

123. The method of any one of the preceding claims wherein said sample volume comprises nucleic acids.

124. The method of any one of the preceding claims, wherein said sample volume comprises a tissue sample or a formalin-fixed paraffin-embedded (FFPE) sample.

125. The method of any one of the preceding claims, wherein said applying an ionic current comprises conducting isotachophoresis.

126. The method of any one of the preceding claims, wherein a total sample volume loaded into said sample input reservoir is less than or equal to an internal volume of said input reservoir.

127. The method of any one of the preceding claims, wherein said sample input reservoir comprises a top region connected to a bottom region via a tapered region, wherein said top region has a first diameter and said bottom region has a second diameter, wherein said first diameter is at least two- fold longer than said second diameter in order to facilitate said moving at least 50% of said sample volume from said sample input reservoir to said channel.

128. The method of any one of the preceding claims, wherein said sample volume loaded in said sample input reservoir is at least 25 μl.

129. A microfluidic chip comprising:

a first sample input reservoir, wherein said first sample input reservoir comprises a top region connected to a bottom region via a tapered region, wherein said top region has a first inner hydraulic diameter and said bottom region has a second inner hydraulic diameter, wherein said first inner hydraulic diameter is at least 2- fold greater than said second inner hydraulic diameter and wherein said first sample input reservoir is in fluid communication with a first channel;

a first buffer reservoir in fluid communication with said first channel, wherein said first sample reservoir is configured so that a free surface of a liquid in said first sample reservoir has a negligible buffer head height difference relative to a liquid in said first buffer reservoir; and

a second buffer reservoir in fluid communication with said first channel.

130. The microfluidic chip of claim 129, wherein said first inner hydraulic diameter is within a range of about 1 mm to about 15 mm.

131. The microfluidic chip of claim 129 or claim 130, wherein said second inner hydraulic diameter is a range of about 0.5 mm to about 5 mm.

132. The microfluidic chip of any one of the preceding claims, wherein said first sample reservoir is configured to hold a sample volume of at least 100 µl.

133. The microfluidic chip of any one of the preceding claims, wherein said microfluidic chip is configured to move at least 50% of said sample volume from said first sample reservoir to said first channel when a vacuum is applied thereto.

134. The microfluidic chip of any one of the preceding claims, wherein said microfluidic chip is configured to conduct isotachophoresis on a sample that enters said first channel.

135. A method of extracting nucleic acids, comprising:

(a) exposing a biological sample comprising cells or tissue to a solution comprising urea or thiourea, thereby lysing said cells or tissue within said biological sample and producing a cellular lysate;

(b) introducing said cellular lysate into a device; and

(c) performing isotachophoresis with said device in order to isolate nucleic acids from said cellular lysate.

136. The method of any one of the preceding claims, further comprising digesting said sample with proteinase K.

137. The method of any one of the preceding claims, wherein said solution comprises urea and thiourea.

138. The method of any one of the preceding claims, wherein said solution comprises a ratio of urea to thiourea of about 2 to 1.

139. The method of any one of the preceding claims, wherein a concentration of said urea in said solution is from about 4 M to about 9 M and a concentration of said thiourea in said solution is from about 0.5 M to about 3.5 M.

140. The method of any one of the preceding claims, wherein a concentration of said urea in said solution is from about 6.5 M to about 7.5 M and a concentration of said thiourea in said solution is from about 1.5 M to about 2.5 M.

141. The method of any one of the preceding claims, wherein said solution comprises trailing electrolyte ions or leading electrolyte ions or both trailing electrolyte ions and leading electrolyte ions.

142. A method of purifying high molecular weight nucleic acids from a tissue sample, comprising:

(a) loading into a fluidic device:

(i) a cellular sample comprising genomic DNA and a contaminant, wherein said cellular sample is contacted with a lysis buffer prior to or after said loading of said cellular sample into said fluidic device,

(ii) a trailing electrolyte buffer, said trailing electrolyte buffer comprising trailing electrolyte ions with a first effective mobility, wherein said first effective mobility has a magnitude lower than a magnitude of an effective mobility of said high molecular weight nucleic acids and a magnitude greater than a magnitude of said contaminant, and

(iii) a first leading electrolyte buffer, said first leading electrolyte buffer comprising first leading electrolyte ions with a second effective mobility, wherein said second effective mobility has a magnitude greater than said magnitude of said effective mobility of said high molecular weight nucleic acids;

(b) conducting isotachophoresis with said trailing electrolyte ions, said high molecular weight nucleic acids, and said first leading electrolyte ions, thereby separating said high molecular weight nucleic acids from said contaminant and enriching said high molecular weight nucleic acids in an isotachophoresis zone; and

(c) eluting said genomic DNA into a solution in an output reservoir, wherein greater than 50% of the mass of nucleic acids within said solution are greater than 30 kilobases.

143. The method of claim 142, wherein said lysis buffer does not comprise an alkaline buffer.

144. The method of any one of the preceding claims, wherein said lysis buffer comprises octylphenol ethoxylate.

145. The method of any one of the preceding claims, wherein greater than 50% of the mass of nucleic acids within said solution are greater than 50 kilobases.

146. A method of conducting isotachophoresis, comprising:

(a) providing a fluidic device comprising a first channel in fluid communication with a sample input reservoir comprising a tissue sample comprising lysed solid tissue, a first buffer reservoir comprising a first leading electrolyte buffer, and a second buffer reservoir comprising a trailing electrolyte buffer;

(b) contacting a first electrode to said first leading electrolyte buffer in said first buffer reservoir;

(c) contacting a second electrode to said trailing electrolyte buffer in said second buffer reservoir; and

(d) applying an electric field within said fluidic device to conduct isotachophoresis, wherein said isotachophoresis occurs without direct contact between said tissue sample and said first and second electrodes.

147. The method of claim 146, wherein said fluidic device further comprises a third buffer reservoir in fluid communication with said first channel and said first buffer reservoir, said third buffer reservoir comprising a lower concentration of said first leading electrolyte buffer than said first buffer reservoir.

148. The method of any one of the preceding claims, wherein said third buffer reservoir and said first buffer reservoir are connected by a second channel comprising one or more capillary barriers to limit pressure-driven flow within said second channel and between said third buffer reservoir and said first buffer reservoir.

149. The method of any one of the preceding claims, wherein said fluidic device further comprises an elution reservoir.

150. The method of any one of the preceding claims, wherein said elution reservoir is in fluid communication with a fourth buffer reservoir.

151. A microfluidic system, said microfluidic system comprising:

(a) a microfluidic chip comprising a first channel and a first reservoir in fluid communication with said first channel, wherein said first channel and said first reservoir meet at a first junction; and

(b) a mechanical member comprising a first tooth, wherein said mechanical member is configured to apply mechanical pressure to said first channel via said first tooth in order to at least partially close said first channel by plastic deformation of at least one wall of said first channel and increase fluid resistance between said first channel and said first reservoir.

152. The microfluidic system of claim 151, wherein said microfluidic chip further comprises a second reservoir in fluid communication with said first reservoir and a second channel connecting said first reservoir and said second reservoir, and wherein said mechanical member further comprises a second tooth configured to apply mechanical pressure to said second channel in order to plastically close said second channel and prevent fluid communication between said first reservoir and said second reservoir.

153. The microfluidic system of any one of the preceding claims, wherein said first tooth is configured to deliver mechanical pressure to said first junction in order to close said first channel by plastic deformation of at least one wall of said first channel.

154. The microfluidic system of any one of the preceding claims, wherein said first tooth is configured to heat said first channel.

155. The microfluidic system of any one of the preceding claims, wherein said mechanical member comprises a material with a Young's modulus of elasticity greater than a Young's modulus of elasticity of said first channel.

156. The microfluidic system of any one of the preceding claims, wherein said microfluidic system is configured to perform isotachophoresis.

157. The microfluidic system of any one of the preceding claims, wherein said first tooth is thermally coupled to a heating element.

158. The microfluidic system of any one of the preceding claims, wherein said first tooth is heated to a temperature greater than the glass transition temperature of said at least one wall of said first channel.

159. A method of completing a process in a fluidic system comprising using said microfluidic system of claim 151 to at least partially close said first channel by plastic deformation, thereby increasing resistance to fluid flow between said first channel and said first reservoir.

160. The method of claim 159, wherein said first tooth of said mechanical member applies a force of at least 0.25 lbs to said first channel.

161. The method of claim 159 wherein said process in said fluidic system is isotachophoresis.

162. A method of performing isotachophoresis on a sample comprising nucleic acids comprising:

(a) loading said sample comprising nucleic acids into a first reservoir of a microfluidic chip;

(b) loading a trailing electrolyte buffer into a second reservoir of said microfluidic chip, wherein said trailing electrolyte buffer comprises first trailing electrolyte ions with an effective mobility having a magnitude lower than a magnitude of an effective mobility of said nucleic acids;

(c) loading a leading electrolyte buffer into a third reservoir of said microfluidic chip, wherein said third reservoir comprises first leading electrolyte ions with a second effective mobility, wherein said second effective mobility has a magnitude greater than said magnitude of said effective mobility of said nucleic acids;

(d) applying an electric field within said microfluidic chip to conduct isotachophoresis with said first trailing electrolyte ions, said nucleic acids, and said first leading

electrolyte ions, thereby confining said nucleic acids, or a portion thereof, to an isotachophoresis zone; and

(e) using a temperature sensor to sense a temperature change in or near said isotachophoresis zone, wherein feedback from said temperature sensor is used to control said electric field.

163. The method of claim 162, wherein said control of said electric field results in positioning of said nucleic acids, or portion thereof, in an elution reservoir or region of said microfluidic chip.

164. The method of claim 162 or 163, wherein said temperature sensor is located within at most 8 mm of said elution reservoir.

165. The method of claim 162, 163, or 164, wherein said temperature change is within a range of about 0.2 ºC to 5 ºC.

166. The method of any one of the preceding claims, wherein said applied electric field causes said leading electrolyte and said trailing electrolyte to meet at an isotachophoresis interface and said temperature sensor senses said isotachophoresis interface.

167. A microfluidic device comprising:

(a) a first isotachophoresis region in a microfluidic chip comprising:

i. a first sample reservoir in fluid communication with a first fluidic channel;
ii. a first, a second, and a third buffer reservoir in fluid communication with said first fluidic channel, wherein said first and second buffer reservoirs are separated by a capillary barrier; and
iii. an elution reservoir in fluid communication with said first fluidic channel;

(b) a sensor configured to detect a temperature change in said first fluidic channel within said first isotachophoresis region; and

(c) an apparatus positioned to supply electrical current within said first channel within said first isotachophoresis region.

168. The microfluidic device of claim 167, further comprising a controller configured to trigger a reduction or elimination of said electrical current when said sensor receives a thermal signal.

169. The microfluidic device of claim 167 or 168, wherein said temperature change is an increase in temperature within a range of about 0.2 ºC to 5 ºC.

170. The microfluidic device of any one of the preceding claims, wherein said microfluidic device is further configured to isolate a sample of nucleic acids in said elution reservoir after said sensor detects a change in temperature.

171. The microfluidic device of any one of the preceding claims, wherein said sensing of said nucleic acids is performed with a sensor located within at most 8 mm of said elution reservoir.

172. The microfluidic device of any one of the preceding claims, wherein said first channel comprises a single sensor.

173. A kit comprising:

(a) said microfluidic device of claim 111, said microfluidic device of claim 167, or said microfluidic chip of claim 129;

(b) a trailing electrolyte buffer comprising trailing electrolytes; and

(c) a leading electrolyte buffer comprising leading electrolytes.

174. The kit of claim 173, wherein said trailing electrolyte buffer comprises a mixture of at least two electrolytes with different effective mobilities.

175. The kit of claim 174, wherein said mixture comprises (i) a first electrolyte that has a lower effective mobility magnitude than a nucleic acid and a higher effective mobility magnitude than a contaminant, and (ii) a second electrolyte which has a lower effective mobility magnitude than said contaminant.

176. The kit of claim 175, wherein said first electrolyte comprises caproic acid.

177. The kit of claim 175 or 176, wherein said second electrolyte comprises HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid).

178. The kit of any one of claims 175-177, wherein said kit further comprises sample buffer, wherein said sample buffer comprises leading electrolyte buffer, trailing electrolyte buffer, or urea in any combination.

179. The kit of any one of claims 178, wherein said kit further comprises sample buffer comprising urea and thiourea.