CLAIMS

What is claimed is:

1. An electroporation cartridge, comprising:

an electroporation chamber defined by an elongate body;

a first electrode disposed at a proximal end of the electroporation chamber; and

a second electrode disposed at an opposite, distal end of the electroporation chamber, wherein at least one of the first electrode or the second electrode is moveable between a capped position for electroporation and an uncapped position for loading a sample and/or the electroporation cartridge is configurable between sealed and unsealed states.

2. The electroporation cartridge of claim 1, wherein the elongate body is made of or includes one or more of a non-conductive plastic, glass, or ceramic and is configured to receive a cell-containing liquid to be electroporated within the electroporation chamber defined by the elongate body.

3. The electroporation cartridge of claim 2, wherein the electroporation chamber is made of or comprises glass and/or ceramic.

4. The electroporation cartridge of claim 2 or claim 3, wherein the electroporation chamber is made of or comprises polycarbonate or other non-conductive irradiation-stable plastic.

5. The electroporation cartridge of any one of claims 1–4, wherein at least a portion of the electroporation chamber is tapered between the first electrode and the second electrode.

6. The electroporation cartridge of claim 5, wherein the tapered portion of the electroporation chamber does not substantially interfere with generation of a uniform electric field between the first and second electrodes.

7. The electroporation cartridge of any one of claims 1–6, wherein the electroporation chamber comprises a uniform cross section along a length of the reaction chamber.

8. The electroporation cartridge of claim 7, wherein the uniform cross section extends an entire length of the electroporation chamber between the first and second electrodes such that the electroporation cartridge is configured to produce a uniform electric field within the electroporation chamber disposed between the first and second electrodes.

9. The electroporation cartridge of claim 7 or claim 8, wherein the electroporation chamber comprises a cylindrical cavity and the uniform cross section comprises a circle.

10. The electroporation cartridge of any one of claims 1–7, further comprising a proximal sidewall defined between a proximal opening of the elongate body and an inflection point of the sidewall defining the electroporation chamber, wherein the proximal sidewall narrows from a first diameter defined by the proximal opening to a second, smaller diameter defined at a position distal to the inflection point.

11. The electroporation cartridge of any one of claims 1–10, wherein the first electrode comprises a bulbous extension having a substantially flat distal surface.

12. The electroporation cartridge of any one of claims 1–10, wherein the first electrode comprises a bulbous extension having a distal surface with a convex or angled contour.

13. The electroporation cartridge of claim 11 or claim 12, wherein the bulbous extension is separated from a base portion of the first electrode by a narrow stem.

14. The electroporation cartridge of any one of claims 11–13, wherein the bulbous extension is operable to displace one or more bubbles associated with a cell-containing liquid to be electroporated within the electroporation chamber upon securing the first electrode within the electroporation chamber.

15. The electroporation cartridge of any one of claims 1–14, further comprising a sealing member disposed between the first electrode and a proximal surface of the elongate body, the

sealing member operable to form a fluid tight connection between the first electrode and the elongate body.

16. The electroporation cartridge of claim 15, wherein the first electrode comprises a first electrode flange and the elongate body comprises a proximal body flange, the proximal body flange oriented in a plane substantially parallel to the first electrode flange, the sealing member being disposed between the first electrode flange and the proximal body flange, forming the fluid tight connection therebetween.

17. The electroporation cartridge of any one of claims 1–16, wherein the first electrode is operable to configure the electroporation cartridge between sealed and unsealed states.

18. The electroporation cartridge of claim 17, wherein the first electrode is operable to configure the electroporation cartridge between sealed and unsealed states without an additional removable cap piece.

19. The electroporation cartridge of claim 17 or claim 18, wherein the first electrode is a removable cap.

20. The electroporation cartridge of any one of claims 1–17, further comprising a removable cap secured to the first electrode, the removable cap comprising a coupling member for selectively securing the first electrode to the elongate body.

21. The electroporation cartridge of any one of claims 1–20, wherein a diameter of a proximal end of the second electrode is substantially equal to a cross section of the electroporation chamber.

22. The electroporation cartridge of any one of claims 1–21, wherein the second electrode comprises a protruding portion that extends into the electroporation chamber from a distal end of the elongate body.

23. The electroporation cartridge of claim 22, wherein a circumference of the protruding portion comprises a complementary shape of an inner surface of the elongate body defining the electroporation chamber.

24. The electroporation cartridge of any claim 22 or claim 23, wherein the second electrode additionally comprises a first sealing member disposed between the second electrode and a distal surface of the elongate body, the first sealing member operable to form a fluid tight connection between the second electrode and the distal surface of the elongate body.

25. The electroporation cartridge of claim 24, wherein the second electrode comprises an electrode flange and the elongate body comprises a distal body flange, the distal body flange oriented in a plane substantially parallel to the electrode flange, the sealing member being disposed between the electrode flange and the distal body flange, forming the fluid tight connection therebetween.

26. The electroporation cartridge of any one of claims 22–25, wherein the second electrode additionally comprises a second sealing member disposed about the protruding portion of the second electrode and positioned distal to the proximal surface of the second electrode, the second sealing member operable to form a fluid tight connection between the protruding portion and an inner surface of the elongate body defining the electroporation chamber.

27. The electroporation cartridge of any one of claims 22–26, wherein the proximal surface of the second electrode comprises a flat, uniform surface.

28. The electroporation cartridge of any one of claims 22–27, wherein the proximal surface of the second electrode is orthogonal to a longitudinal axis of the electroporation chamber.

29. The electroporation cartridge of any one of claims 1–28, further comprising a fixing pin associated with the second electrode and configured to secure the second electrode to the elongate body.

30. The electroporation cartridge of claim 29, wherein the second electrode defines a channel configured in size and shape to receive the fixing pin, the channel being aligned with a pair of apertures defined by the sidewall of the elongate body and configured to receive the fixing pin, thereby securing the second electrode at a fixed position relative to the elongate body.

31. The electroporation cartridge of claim 30, wherein the channel is formed through a central region of the protruding portion of the second electrode distal to the first sealing member and/or second sealing member.

32. The electroporation cartridge of any one of claims 1–31, wherein a volume of the electroporation chamber is less than about 5 mL, preferably less than about 3mL, more preferably less than about 1 mL or between about 100 μL – 1 mL.

33. The electroporation cartridge of any one of claims 1–32, further comprising a volume reducing sleeve configured in size and shape to fit within the electroporation chamber.

34. The electroporation cartridge of claim 33, wherein the volume reducing sleeve defines a secondary electroporation chamber having a smaller volume than the electroporation chamber.

35. The electroporation cartridge of claim 33 or claim 34, wherein the volume reducing sleeve comprises a distal opening configured to interface with the second electrode when secured within the electroporation chamber.

36. The electroporation cartridge of any one of claims 33–35, wherein the volume reducing sleeve comprises air vents disposed adjacent to the proximal end of the volume reducing sleeve that are configured to allow air to pass therethrough during introduction or extraction of the volume reducing sleeve with the electroporation chamber, thereby preventing formation of a vacuum between the secondary electroporation chamber and the electroporation chamber, thereby allowing the electroporated cell-containing fluid to fill the secondary electroporation chamber upon introduction of the volume reducing sleeve and to exit the secondary electroporation chamber upon introduction upon extraction of the volume reducing sleeve.

37. The electroporation cartridge of any one of claims 33–36, wherein the volume reducing sleeve includes a radial sealing member configured to secure the volume reducing sleeve within the electroporation chamber.

38. The electroporation cartridge of claim 37, wherein the radial sealing member forms a fluid tight seal with the sidewall defining the electroporation chamber to prevent leakage of cell containing fluid within the secondary electroporation chamber through the distal opening of the volume reducing sleeve.

39. The electroporation cartridge of any one of claims 33–38, wherein the first electrode is configured to selectively associate with and form a fluid tight seal with the volume reducing sleeve.

40. The electroporation cartridge of any one of claims 33–39, wherein a space is defined between an outer surface of the volume reducing sleeve and the inner sidewall of the elongate body, forming a fluid overfill space configured to receive a volume of overfill displaced by the first electrode upon sealing the electroporation chamber.

41. The electroporation cartridge of any one of claims 1–40, further comprising a fluid overfill space associated with a proximal region of the electroporation chamber and configured to receive a volume of overfill displaced by the first electrode upon sealing the electroporation chamber.

42. The electroporation cartridge of any one of claims 1–41, further comprising one or more springs longitudinally disposed on a proximal side of the elongate body and configured to situate the first electrode a distance away from the electroporation chamber in the uncapped position.

43. The electroporation cartridge of claim 42, wherein the electroporation cartridge being in the capped position configures the one or more springs to be compressed and the first electrode to be disposed within the electrode chamber and operable to electroporate a cell-containing fluid disposed therein.

44. The electroporation cartridge of any one of claims 1–43, wherein the electroporation cartridge comprises a flow-through electroporation cartridge.

45. The electroporation cartridge of claim 44, further comprising a port associated with the first electrode, the port defining a lumen within the first electrode such that the lumen is fluidically connected to the electroporation chamber.

46. The electroporation cartridge of claim 44, further comprising a port associated with a proximal portion of the elongate body, the port configured to exhaust displaced air from the electroporation chamber when the electroporation chamber is being filled and/or introduce filtered or purified air into the electroporation chamber when the electroporation chamber is being drained.

47. The electroporation cartridge of any one of claims 44–46, further comprising a chamber inlet and a chamber outlet, each of the chamber inlet and chamber outlet being fluidically connected to the electroporation chamber.

48. The electroporation cartridge of claim 47, wherein one or more of the chamber inlet or chamber outlet is disposed above a proximal surface of the second electrode.

49. The electroporation cartridge of claim 47 or claim 48, wherein a lumen of the chamber inlet and/or chamber outlet is substantially parallel to the proximal surface of the second electrode.

50. The electroporation cartridge of any one of claims 47–49, wherein one or more of the chamber inlet or chamber outlet is associated with a plug and/or valve to control an inward flow of cell-containing fluid to be electroporated within the electroporation chamber and/or to control an outward flow of electroporated cell-containing fluid from the electroporation chamber.

51. The electroporation cartridge of any one of claims 44–50, further comprising a fluid overfill space associated with the first electrode and/or the elongate body, the fluid overfill space configured to receive a volume of overfill displaced from the electroporation chamber when filling the electroporation chamber.

52. The electroporation cartridge of any one of claims 44–50, further comprising a fluid overfill space associated with a sealing cap, the fluid overfill space configured to receive a volume of overfill displaced from the electroporation chamber when sealing the electroporation chamber with the sealing cap.

53. An electroporation system configured to provide flow-through electroporation of a sample, the electroporation system comprising:
a modular casing having a plurality of compartments for holding and arranging a plurality of electroporation system components, the electroporation system components including:
one or more pumps configured for moving the sample through the system;
an electroporation compartment configured to receive a flow-through electroporation cartridge configured for holding a sub-volume of the sample within an electroporation chamber for electroporation of the sub-volume; and
tubing having an inlet end and an outlet end, the tubing being routed through the casing so as to fluidically connect the plurality of electroporation system components.

54. The electroporation system of claim 53, further comprising a bag compartment configured for receiving and supporting an input bag and/or output bag.

55. The electroporation system of claim 54, wherein the bag compartment comprises an insert that is slidably connected to the bag compartment so as to be capable of being selectively drawn out from the casing or enclosed within the casing.

56. The electroporation system of claim 55, wherein the bag compartment comprises one or more magnetic latches for holding the bag compartment in an enclosed position within the casing.

57. The electroporation system of any one of claims 53–56, further comprising a cooling module in thermal contact with the electroporation chamber and configured to regulate the temperature of the electroporation chamber.

58. The electroporation system of claim 57, wherein the cooling module comprises a ceramic block.

59. The electroporation system of claim 57 or 58, wherein the cooling module is cooled via thermoelectric cooling.

60. The electroporation system of any one of claims 53–59, further comprising a mixer reservoir disposed downstream of the inlet and upstream of the electroporation cartridge, the mixer reservoir comprising a mixing element configured to provide mixing to a portion of the sample contained within the mixing reservoir.

61. The electroporation system of claim 60, wherein the mixing element comprises a mixing blade.

62. The electroporation system of claim 60 or 61, wherein the mixer reservoir includes a mixer magnet assembly mechanically coupled to the mixing element, the mixer magnet assembly being disposed so as not to contact the portion of the sample contained within the mixer reservoir.

63. The electroporation system of claim 62, further comprising a mixer driver having a magnet magnetically coupled to the mixer magnet assembly and configured to indirectly drive rotation of the mixer magnet assembly via magnetic connection to the mixer magnetic assembly.

64. The electroporation system of claim 62 or 63, wherein the mixer reservoir comprises a cover, and wherein the mixer magnet assembly is disposed at or near the cover.

65. The electroporation system of any one of claims 60–64, further comprising a sample input assembly configured to aid in transfer of sample between an input and the mixer reservoir, the sample input assembly including a main section of tubing disposed between the input and the mixer reservoir, and an intermediate section of tubing pneumatically coupled to the main section of tubing and extending therefrom to a terminal end having access to air, the intermediate section

thereby allowing passage of air into the main section of tubing upon sufficient pressure drop in the main section of tubing.

66. The electroporation system of claim 65, wherein the terminal end of the intermediate section couples to an air reservoir that has a variable volume, and wherein the sample input assembly is configured to detect a threshold reduction of the variable volume to thereby determine that the sample has been moved into the mixer reservoir.

67. The electroporation system of claim 66, wherein the sample input sensor assembly comprises a syringe having a barrel and a plunger disposed within the barrel, the variable volume being defined by the position of the plunger within the barrel and the threshold reduction of the variable volume being detected as a result of movement of the plunger.

68. The electroporation system of any one of claims 53–67, further comprising a chamber sealing assembly operatively coupled to the electroporation chamber and configured to regulate pressure within the electroporation chamber during electroporation and thereby limit bubble formation.

69. The electroporation system of claim 68, wherein the chamber sealing assembly comprises one or more linear actuators configured to advance plungers toward or retract plungers away from the electroporation chamber to thereby regulate pressure within the electroporation chamber.

70. The electroporation system of any one of claims 53–69, further comprising a pre-cooling assembly disposed upstream of the electroporation chamber and configured for cooling a sub-volume of the sample prior to electroporation of the sub-volume.

71. The electroporation system of claim 70, wherein the pre-cooling assembly comprises a cooling block and a section of tubing disposed within or adjacent to the cooling block.

72. The electroporation system of claim 70 or 71, wherein the cooling block of the pre-cooling assembly is cooled via thermoelectric cooling.

73. The electroporation system of any one of claims 70–72, wherein the pre-cooling assembly comprises a flexible biasing element that biases the cooling block against the section of tubing disposed adjacent the cooling block.

74. The electroporation system of any one of claims 53–73, further comprising at least one flow sensor, wherein the at least one flow sensor is disposed between the mixer reservoir and the electroporation chamber.

75. The electroporation system of claim 74, wherein the flow sensor is an ultrasonic sensor.

76. The electroporation system of claim 74 or 75, the flow sensor comprising an actuatable trigger that when actuated, positions a corresponding section of tubing within the flow sensor for detection of flow through the section of tubing.

77. The electroporation system of any one of claims 53–76, further comprising one or more flow indicators that route a corresponding section of tubing to a position on an exterior of the casing to enable visualization of flow through the section of tubing.

78. The electroporation system of any one of claims 53–77, wherein the casing includes one or more handles.

79. The electroporation system of claim 78, wherein the one or more handles include a handle having a catch configured to engage with an instrument panel to attach the instrument panel to the casing.

80. The electroporation system of any one of claims 53–79, further comprising an electroporation cartridge attachment feature coupled to the electroporation cartridge, the attachment feature including a flexible biasing element that biases the electroporation cartridge toward a cooling module integrated within the casing.

81. The electroporation system of any one of claims 53–80, further comprising a capping mechanism configured to engage with the electroporation cartridge, wherein the electroporation cartridge comprises a first electrode and a second electrode, each disposed at opposite ends of an electroporation chamber, wherein at least one of the first electrode or second electrode is engageable with the capping mechanism and is moveable between a capped position for electroporation and an uncapped position for venting as a result of actuation of the capping mechanism.

82. The electroporation system of claim 81, wherein the electroporation cartridge comprises a spring mechanism that allows for overtravel of the capping mechanism relative to displacement of the electrode moved as a result of actuation of the capping mechanism.

83. The electroporation system of any one of claims 53–81, wherein the electroporation chamber comprises a chamber inlet and a chamber outlet, wherein the chamber outlet is coupled to an outlet plunger moveable between an advanced position that prevents outflow of the sub-volume from the electroporation chamber and a retracted position that allows outflow of the sub-volume from the electroporation chamber.

84. The electroporation system of any one of claims 53–83, wherein the electroporation cartridge comprises one or more bellows structures each configured to encase a moveable component of the electroporation chamber.

85. The electroporation system of any one of claims 53–84, wherein the electroporation chamber comprises the flow-through electroporation cartridge as in any one of claims 44–52.

86. The electroporation system of any one of claims 53–85, further comprising an electroporation assembly electrically coupled to the electroporation chamber, the electroporation assembly comprising a conductivity sensor for measuring conductivity across the electroporation chamber, the electroporation assembly being communicatively coupled to a controller having one or more processors and one or more hardware storage devices.

87. The electroporation system of claim 86, wherein the one or more hardware storage devices have stored thereon computer-executable instructions that when executed by the one or more processors configure the controller to perform at least the following:
determine, by way of the conductivity sensor, the conductivity of the sub-volume within the electroporation chamber;
based on the determined conductivity, determine a voltage drop across the electroporation chamber; and
charge a capacitor, which is in an electroporation circuit with the electroporation chamber, to a voltage level above the determined voltage drop across the electroporation chamber to compensate for other voltage drops between the capacitor and the electroporation chamber.

88. The electroporation system of claim 86 or 87, wherein the one or more hardware storage devices have stored thereon computer-executable instructions that when executed by the one or more processors configure the controller to perform at least the following:
determine, by way of the conductivity sensor, the conductivity of the sub-volume within the electroporation chamber;
determine a predicted temperature increase of the sub-volume based on the determined conductivity, an intended pulse voltage, and an intended pulse duration; and
if the predicted temperature increase leads to a temperature of the sub-volume that is greater than a predetermined threshold temperature, perform one or more of:
send an ark risk alert,
withdraw the sample sub-volume to preserve the sample sub-volume, and/or
tune cooling accordingly to decrease temperature of the electroporation chamber.

89. The electroporation system of claim 88, wherein the computer-executable instructions further configure the controller to determine an initial temperature of the sub-volume within the electroporation chamber by correlating the determined conductivity to a temperature.

90. The electroporation system of any one of claim 86–89, wherein the one or more hardware storage devices have stored thereon computer-executable instructions that when executed by the one or more processors configure the controller to perform at least the following:

determine, by way of the conductivity sensor, the conductivity of the sub-volume within the electroporation chamber; and

if the determined conductivity falls below a pre-determined threshold indicative of the presence of one or more bubbles within the electroporation chamber, to drain the sub-volume from the electroporation chamber.

91. The electroporation system of any one of claims 53–90, further comprising a controller having one or more processors and one or more hardware storage devices, wherein the one or more hardware storage devices have stored thereon computer-executable instructions that when executed by the one or more processors configure the controller to iteratively ramp charger voltage based on a previous input voltage and a corresponding previous measured actual voltage applied to the electroporation chamber.

92. The electroporation system of any one of claims 74–91, further comprising a controller having one or more processors and one or more hardware storage devices, wherein the one or more hardware storage devices have stored thereon computer-executable instructions that when executed by the one or more processors configure the controller to determine a step volume to be moved by the system between each electroporation event, the calibration being carried out by performing at least the following:

determine a number, N, of revolutions of a drive pump required to move a sample volume sufficient to fill the tubing disposed between the flow sensor and the electroporation chamber, as well as fully filling the electroporation chamber, the number, N, representing the volume between the flow sensor and the outlet of the electroporation chamber;

cause the electroporation chamber to be drained;

cause the drive pump to reverse the sample by a fixed number, k, of revolutions to a point upstream of the flow sensor, the fixed number, k, representing the volume between the point upstream of the flow sensor and the inlet of the electroporation chamber;

determine a number, x, of revolutions of the drive pump required to move the sample from the point upstream of the flow sensor to the flow sensor, the number, x, representing the volume between the point upstream of the flow sensor and the flow sensor, and the number, $(k - x)$,

representing the volume between the flow sensor and the inlet of the electroporation chamber; and

determine the volume between the inlet and outlet of the electroporation chamber as $N - (k - x)$, and set this volume as the step volume.

93. The electroporation system of any one of claims 53–92, further comprising a safety door configured to mechanically open the electroporation circuit to prevent voltage discharge while the safety door is open.

94. The electroporation system of any one of claims 53–93, wherein the capacitor circuit comprises one or more discharge resistors so as to discharge the capacitor when the capacitor circuit is not electrically connected to the electroporation cartridge.

95. The electroporation system of any one of claims 74–91, further comprising a controller having one or more processors and one or more hardware storage devices, wherein the one or more hardware storage devices have stored thereon computer-executable instructions that when executed by the one or more processors configure the controller to determine a step volume to be moved by the system between each electroporation event, the calibration being carried out by performing at least the following:

perform a first fill of the electroporation chamber by monitoring a drop in the electrical resistance of a sample fluid in the electroporation chamber during the first fill from several thousand ohms to a stable value in the range of from about 600-800 ohms, stopping the first fill when the stable value of resistance is reached;

gross filling the electroporation chamber for the second fill based on a calculated value, such as N_{rev} from the peristaltic pump;

measuring the electrical resistance after capping the top electrode after the second fill;

if the electrical resistance is within the stable value range determine from the first fill, then the second fill is complete and one can proceed to electroporate the sample;

if the electrical resistance is not within the stable value range determine from the first fill, then uncap the top electrode and fine fill by an additional n_{rev} amount;

measuring the electrical resistance after capping the top electrode after the fine fill;

if the electrical resistance is within the stable value range as determined from the first fill, then the second fill is complete and one can proceed to electroporate the sample;
if not repeat the fine fill and measuring the electrical resistance steps above till the electrical resistance is within the stable value range as determined from the first fill,
subsequent fills (third fill, fourth fill and so on) are done for pump revolutions of $N_{rev} + n_{rev}$ x (where x is equal to the number of tries of the fine fill).

96. The system of claim 95, wherein the stable value of electrical resistance is about 700 ohms.

97. The system of claim 95, wherein the step of gross filling the electroporation chamber for the second fill is further based on calculations using one or more parameters such as the inner tube diameter of tubing, the number of rollers of the pump, the diameter of the electroporation chamber, and/or the height of the electroporation chamber.