those that can do so in a manner that reduces the likelihood of contamination and/or arcing caused by bubble formation within the processed cell-containing fluid.

BRIEF SUMMARY

[0011] Implementations of the present disclosure solve one or more of the foregoing or other problems in the art with systems, devices, and methods for electroporating a cell-containing fluid. The terms "cell-containing fluid" and "sample" are used interchangeably herein.

[0012] In particular, one exemplary embodiment includes an electroporation cartridge having 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. 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 for a single use or automated batch processing and/or the electroporation cartridge is configurable between sealed and unsealed states. The electroporation cartridge further includes a fluid overfill space associated with a proximal region of the electroporation chamber and configured to receive a volume of overfill displaced upon sealing the electroporation chamber.

[0013] In one aspect, an elongate body of the disclosure can comprise, be made of or include one or more of a non-conductive plastic, a glass, and/or a ceramic and is configured to receive a cell-containing liquid to be electroporated within the electroporation chamber defined by the elongate body. For example, an electroporation chamber of the disclosure can comprise, be made of or includes a glass and/or a ceramic. As an additional example, the electroporation chamber can comprise, be made of or include polycarbonate and/or other non-conductive irradiation-stable plastic.

[0014] In one aspect, at least a portion of an electroporation chamber of the disclosure is tapered between the first electrode and the second electrode. When present, the tapered portion of the electroporation chamber does not substantially interfere with generation of a uniform electric field between the first and second electrodes.

[0015] Additionally or alternatively, an electroporation chamber of the disclosure has a uniform cross section along a length of the reaction chamber. The uniform cross section can, in some instances, extend 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. For example, an electroporation chamber of the disclosure can be a cylindrical cavity defined by the elongate body such that the uniform cross section is a circle.

fluidically connected to the electroporation chamber. One or more of the chamber inlet or chamber outlet can be disposed above a proximal surface of the second electrode and/or a lumen of the chamber inlet and/or chamber outlet can be substantially parallel to the proximal surface of the second electrode. Additionally, or alternatively, one or more of the chamber inlet or chamber outlet can be 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.

[0033] Electroporation cartridges disclosed herein can include a fluid overfill space associated with the first electrode and/or the elongate body that is configured to receive a volume of overfill displaced from the electroporation chamber when filling the electroporation chamber and/or when sealing the electroporation chamber with the sealing cap.

[0034] An exemplary electroporation system configured to provide flow-through electroporation of a sample includes a modular casing having a plurality of compartments for holding and arranging a plurality of electroporation system components. An electroporation system of the disclosure can include one or more pumps configured for moving a sample through the system, and an electroporation compartment configured to receive the electroporation cartridge as described, electroporation cartridge configured for holding a sub-volume of the sample within an electroporation chamber for electroporation of the sub-volume. An electroporation system of the disclosure can further include 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.

[0035] In one aspect, an electroporation system of the disclosure includes a bag compartment configured for receiving and supporting an input bag and/or output bag. A bag compartment can include 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 and may include one or more magnetic latches for holding the bag compartment in an enclosed position within the casing. In one aspect, an electroporation system includes one or more hooks on which to hang one or more bags outside of the casing.

[0036] In one aspect, an electroporation system of the disclosure includes one or more features for regulating the temperature of the sample via cooling and/or heating (*e.g.*, according to a predetermined target temperature). For example, an electroporation system can include a cooling module in thermal contact with the electroporation chamber and configured to regulate the

CLAIMS

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;

a second electrode disposed at an opposite, distal end of the electroporation chamber, wherein at least one of the first electrode or 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; and

a fluid overfill space associated with a proximal region of the electroporation chamber and configured to receive a volume of overfill displaced upon sealing the electroporation chamber.

2. The electroporation cartridge of claim 1, wherein at least a portion of the electroporation chamber is tapered between the first electrode and the second electrode.

3. The electroporation cartridge of claim 1 or claim 2, wherein the electroporation chamber comprises a uniform cross section along a length of the reaction chamber.

4. The electroporation cartridge of any one of claims 1–3, 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.

5. The electroporation cartridge of any one of claims 1–4, wherein the first electrode comprises a bulbous extension having a substantially flat distal surface, or wherein the first electrode comprises a bulbous extension having a distal surface with a convex or angled contour.

6. The electroporation cartridge of any one of claims 1–5, wherein the first electrode is operable to configure the electroporation cartridge between sealed and unsealed states without an additional removable cap piece, or wherein the first electrode is a removable cap.

7. The electroporation cartridge of any one of claims 1-6, wherein a proximal surface of the second electrode comprises a flat, uniform surface and/or is orthogonal to a longitudinal axis of the electroporation chamber.

8. The electroporation cartridge of any one of claims 1-7, further comprising a volume reducing sleeve configured in size and shape to fit within the electroporation chamber.

9. 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 the electroporation cartridge of any one of claims 1-8, the 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.

10. The electroporation system of claim 9, further comprising one or more of:

a bag compartment configured for receiving and supporting an input bag and/or output bag;

a cooling module in thermal contact with the electroporation chamber and configured to regulate the temperature of the electroporation chamber;

a sample input assembly;

a sample input sensor assembly;

a chamber sealing assembly;

a pre-cooling assembly;

at least one flow sensor;

one or more flow indicators;

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;

an electroporation cartridge attachment feature coupled to the electroporation cartridge, the attachment feature optionally including a flexible biasing element that biases the electroporation cartridge toward a cooling module integrated within the casing.

11. The electroporation system of claim 9 or claim 10, 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, wherein the electroporation cartridge optionally 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.

12. The electroporation system of any one of claims 9-11, 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,

13. The electroporation system of claim 12, 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.

14. The electroporation system of claim 12 or claim 13, 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.

15. The electroporation system of claim 14, 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.

16. The electroporation system of any one of claims 12-15, 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.

17. The electroporation system of any one of claims 12-16, 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.

18. The electroporation system of any one of claims 12-17, 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.

19. The electroporation system of any one of claims 12-18, 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).

20. The system of claim 19, 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.