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DESCRIPTION

FIELD OF THE INVENTION

[0001] The present invention relates to a pipette tip for electroporation.

BACKGROUND OF THE INVENTION

[0002] Electroporation is a technique for introducing macromolecules, which cannot penetrate the cell membrane, into cells using electric pulses. Electroporation is a widely used, and strongly recommended, method for cellular experiments and gene therapy. When a high electric field is applied, the cell membrane becomes temporarily porous and permeable to foreign materials, such as macromolecules. The electroporabilization of the membrane depends on various parameters of the electric field, such as pulse width, pulse duration, the number of pulses, as well as other experimental conditions. Studies have been performed regarding the above-mentioned parameters in order to understand the mechanism of the electroporation which promotes the effect of transfection. For example, the magnitude of the electric field is reported to be an important parameter for increasing the permeability of the membrane and for controlling the portion of the cell membrane across which transmission occurs.

[0003] There are various devices for performing electroporation. **FIG. 1** is a perspective view of a prior art cuvette that can be used for performing electroporation. **FIG. 2** shows an electroporation device and system described in related U.S. Patent Application Publication No. 2007/0275454 A1. **FIG. 3** is a side view of the electroporation device shown in **FIG. 2**. **FIG. 4** is a side view illustrating the components of a pipette tip used with the device shown in **FIGS. 2 & 3**.

[0004] An electric field can be applied to a cell suspension and/or gene mixture using the cuvette illustrated in **FIG. 1**. In such a system, the cuvette may be equipped with two parallel electrode plates **1**. When a high electric field is applied between the two electrode plates, the cell membrane becomes permeable, making it is possible to introduce a gene or other foreign matter into the cell. Aluminum electrodes are cheap and may be used with a disposable cuvette. However, using Al creates Al^{3+} ions dissolved from the aluminum electrodes, which ions have been found to negatively influence the cells. Furthermore, when aluminum electrodes are used, the magnitude of the electric field may vary due to a drop in electric voltage caused by the build up of oxide layers on the electrodes. Therefore, to generate a more constant electric field, it may be preferable to use platinum or gold electrodes. However, electrodes made from these materials are costly and therefore it is impractical to use electrodes made from these materials for consumable goods.

[0005] Thus, current electroporation devices have the following disadvantages. First, using the cuvette for electroporation may be expensive depending on the electrode material used since there are two electrodes mounted on two opposite side of the cuvette, and since each electrode has a wide surface area. Additionally, it is recommended that the cuvettes be single use. However, many users conduct experiments several times using the same cuvette, thus creating a high possibility of occurrence of experimental error. Second, because the electrode material (Al) is reactive in solution, and the overpotential relative to hydrogen generation is low, performing electroporation using current electroporation devices creates air bubbles due to decomposition of water on the surfaces of the electrodes. Third, the generated ion (Al^{3+}) byproduct has been found to have a negative effect on cells. Fourth, surface resistance on the electrode is markedly increased due to the generation of an oxide layer (Al_2O_3) on the electrode surface. Fifth, the electric field between electrodes may not remain constant. This may be due to large quantities of current flowing through corners of the electrodes, thereby distorting the electric field. Finally, the sample volume needed may be large, which may make it difficult to analyze a small quantity of cells in the sample. Therefore, there is a need to develop a new electroporation device to address these disadvantages.

[0006] FIGS. 2-4 illustrate prior art versions of an electroporation device, pipette tip, and detailed components thereof for solving the above disadvantages. Referring to FIGS. 2-4, current electroporation devices may include a pulse generator **10** for generating an electric pulse; a sample reservoir **20**; a pipette **30** with one side in electrical communication with the pulse generator; and a pipette tip **40**, one end of which may be inserted onto the end portion of the pipette **30** and the other end of which may be inserted into the sample reservoir **20** and may be in fluid communication with the sample. Additionally, the distal end of the pipette **30**, or the pipette tip **40**, may be in fluid communication with the sample and the pipette **30** may be capable of drawing a sample into the pipette tip **40**. Additionally, an electrode **50** may be inserted into the sample reservoir **20** and may be in fluid communication with the sample. The outer circumferential surface of the pipette **30** comprises a contact body **31** formed with conductive materials, wherein the contact body **31** may be electrically connected with a plunger **42** located inside the pipette tip **40** as shown in FIG. 3. The pipette tip **40** comprises a tubular body **41** which has openings at both ends, wherein the opening at one end may be a ring-shaped section having a relatively large diameter so as to be inserted into the end portion of the pipette **30**, and the other end may be a ring-shaped section having a relatively small diameter. The pipette tip **30** is then inserted into the sample reservoir **20**, and the plunger **42** located through body 41 of the pipette tip **40**.

[0007] In performing electroporation using the system and electroporation device shown in FIGS.2-4, the pipette draws the sample into the interior of the pipette tip **40** while maintaining pressure and thereby keeping the sample within the pipette tip **40**. The sample reservoir **20** can then be replaced with a reservoir containing an electrolytic solution. By applying an electric current to the plungers **42** located within the body **41** of the pipette tip **40** and to the electrode **50** contacting the sample in the sample reservoir **40** or the electrolytic solution in the electrolytic solution reservoir, a cell located in the sample drawn into the pipette tip **40** may be electroporated, by passing a current between the two electrodes and through any cells located

between the two electrodes. The electroporation of the cells located in the sample within the pipette tip **40** causes the cell membranes to become more permeable, and therefore facilitates the introduction of macromolecules, molecular probes, drugs, DNA, RNA, bacteria, genes, protein material, cells, or any other suitable substance which normally cannot penetrate the cell membrane, into the cell.

[0008] In the prior art electroporation system and device as shown in **FIGS. 2-4**, the outer circumferential surface of the pipette **30** comprises a separate contact body **31**, and a separate plunger **42** which may be in electrical communication with the contact body **31** in the body **41** of the pipette tip **40**. Since the outer circumferential surface of the pipette **30** includes a separate contact body **31** and a separate plunger **42** in electrical communication connecting with the contact body **31**, the structure of the device may be complex which may make manufacturing the device both costly and time consuming. Since the contact body **31** and the plunger **42** formed on the outer circumferential surface of the pipette **30** are connected together in the interior of the device, it may be difficult for a user to determine the state of the connection between the plunger and the contact body.

[0009] Therefore, it would be useful to develop an electroporation device where the pipette tip itself can serve as an electrode and thereby apply an electric current to the sample without the need of a separate structure (such as plunger **42**) serving as the electrode.

[0010] WO 03/057819 relates to devices used for the electroporation of selected items that are particularly adapted to allow use by automated or semi-automated systems.

SUMMARY OF THE INVENTION

[0011] Provided herein is a pipette tip for use with an electroporation device including an outer surface, a void located within the outer surface, and a conductor located at one side of the outer surface. The conductor is capable of applying an electric field to the void of the pipette tip and thereby applying an electric field to the sample located within the pipette tip and any cells therein. The cell membranes of the cells are then electroporated by the pipette tip, and any material located within the sample can then be transferred into the cells.

[0012] Further provided herein is a pipette tip for use with an electroporation device wherein the pipette tip itself serves as an electrode for performing electroporation wherein the pipette tip/electrode contacts the sample without the need of a separate electrode structure. Additionally, this may have the added effect of easily performing electroporation by reducing the error rate and reducing the number of trial and error with the simplified design. For example, although meant for single use, cuvettes currently used for electroporation can in fact be used multiple times. With the release of ions into solution from the electrodes located in the cuvettes and the negative effect these ions have on the cells, the error rate between runs can increase. Additionally, because the void of the pipette tip does not contain an additional structure serving as the electrode, such as a plunger which serves as the electrode, the void of

the pipette tip of the present invention can easily suction in and expel the sample from the pipette tip by simply using air pressure.

[0013] In a first aspect, the present invention provides a pipette tip for use in carrying out electroporation comprising: a combining part having a body, a proximal end, a distal end, and a combining part void; a connecting part having a proximal end, a distal end and a connecting part void, and located at least partially on or within the distal end of the body; an elongated part having an elongated part void and located at the distal end of the connecting part, wherein the void of the combining part, the void of the connecting part, and the void of the elongated part are in fluid communication with each other, the pipette tip having an outer surface and a void located within the outer surface comprising the combining part void, the connecting part void and the elongated part void; and further comprising a conductor located at least partially on or within the outer surface, wherein the conductor is in electrical communication with at least a portion of the outer surface and the void, the conductor having an inner surface capable of applying an electric current to the connecting part void, whereby the conductor can provide a single electrode of the electrode pair required for performing electroporation and the pipette tip contains no other electrode structure, and a sample drawn into both the connecting part void and the elongated part void can be subjected to an electric field when the pipette tip is combined with another electrode in an electroporation system. Having the conductor located at least partially on or within the outer surface of the pipette tip eliminates the need for an electrical conducting structure or an electrode within the void. Thus the void is only filled with the sample. The conductor is in fluid communication with the void. In some embodiments, the conductor may be ring-shaped. Additionally, the conductor may include a body and a surface, where the body includes a conductive material selected from at least one of copper, brass, nickel, gold, silver, aluminum, any combination thereof, or any other suitable conductive material. In some embodiments, the body of the conductor may be an injection molded conductor, wherein the injection molded conductor includes at least one of plastic or conductive polymer. In some embodiments, the surface of the conductor may include at least one of brass, copper, aluminum, nickel, gold, silver, any combination thereof, or any other suitable conductive material. In some embodiments, the pipette tip may further comprise at least one connecting post. The connecting post may or may not be funnel shaped. In some embodiments, the pipette tip may include at least one, at least two, or at least three connecting posts. In some embodiments, the three connecting posts may be located at 120 degrees in respect to each other and in respect to the outer surface.

[0014] Further provided herein is a pipette tip for use with an electroporation device comprising: a body having a proximal end, a distal end, and a void; a connector having a proximal end, a distal end, and a void and further located at the distal end of the body, the connector comprising: at least one connecting post; a connecting part in mechanical communication with the at least one connector; a conductor located at least partially on or within the body and surrounding at least a portion of the at least one connecting post; and an elongated part having a void and located at the distal end of the connector, wherein the void of the body, the connector, and the elongated part are in fluid communication. Having the conductor located at least partially on or within the outer surface of the pipette tip eliminates

the need for an electrical conducting structure or an electrode within the void. Thus the void is only filled with the sample. The conductor may or may not be capable of surrounding the at least one connecting post. The conductor may further include an inner surface capable of applying an electric current to the void of the connector part. The conductor may be a conductive material selected from at least one of nickel, gold, silver, copper, brass, or aluminum. The inner surface of the conductor may be plated with a conductive material selected from at least one of brass, aluminum, copper, nickel, gold, silver, any combination thereof, or any other suitable conductive material. The conductor may be injection molded with plastic or a conductive polymer. Additionally, the pipette tip may include a combining part diameter and a conductor diameter, wherein the conductor diameter may or may not be less than the combining part diameter. The elongated part may be tapered along its length. The connecting part may include a connecting hole in communication with the void of the combining part. The connecting hole may further include a groove extending radially from the connecting hole. The connecting part may further include at least one connecting projection and a fixing projection, wherein the at least one connecting projection and the fixing projection are capable of interlocking together.

[0015] In a second aspect, the present invention provides an electroporation system comprising a pulse generator; a pipette having a pipette tip of the first aspect in electrical communication with the pulse generator; and an electrode in communication with the pulse generator. The pipette tip may be in electrical communication with the electrode.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

FIG. 1 is a perspective view of a cuvette currently used for performing electroporation;

FIG. 2 shows an example of a system and device used for performing electroporation in the prior art;

FIG. 3 is a side view of the device shown in **FIG. 2**;

FIG. 4 is a side view of the components of a pipette tip used with the device shown in **FIG. 2**;

FIG. 5 is a perspective view illustrating a pipette tip that is an embodiment of the invention;

FIG. 6 is a perspective view illustrating the pipette tip shown in **FIG. 5** with the conductor removed;

FIG. 7 is a cross sectional view of the pipette tip shown in **FIG. 5**;

FIG. 8 is a perspective view of a pipette tip that is an embodiment of the invention;

FIG. 9 is a cross sectional view of the pipette tip shown in **FIG. 8**.

FIG. 10 is a perspective view of a pipette tip that is an embodiment of the invention;

FIG. 11 is a cross sectional view of the pipette tip shown in **FIG. 10**; and

FIG. 12 shows an electroporation device and system.

DETAILED DESCRIPTION OF THE INVENTION

[0017] Provided herein is a pipette tip for use with an electroporation device. The pipette tip facilitates electroporation since the pipette tip itself can be used to provide an electrode and/or electric current to the sample without the need of having a separate electrode, such as the plunger electrode shown in **FIGS. 3 & 4**. Thus, the pipette tip described herein may reduce the unit cost of manufacture of an electroporation device and may thus facilitate performing electroporation on a sample and its contents.

[0018] In some embodiments, provided herein is a pipette tip for use with an electroporation device including an outer surface, a void located within the outer surface, and a conductor located at one side of the outer surface. The conductor is capable of applying an electric field to the void of the pipette tip and to any sample and/or cells located within the pipette tip. Application of an electric field to the cell membrane of a cell by the pipette tip electroporates the cells, and material located within the sample may then be transferred into the cells. Examples of material that can be introduced into cells include macromolecules, molecular probes, drugs, therapeutics, DNA, RNA, bacteria, genes, protein material, cells, or any other suitable material.

[0019] Referring now to **FIGS. 5-7**, **FIGS. 5-7** show various views of an embodiment of a pipette tip wherein the pipette tip **400** includes: a combining part **410** with a void **411** which may be connected to an end of a pipette **300** (as shown in **FIG. 12**). The pipette **300** is in fluid communication with the void **411**. The pipette tip further includes an elongated part **430** extending from the combining part **410**. In some embodiments, the elongated part **430** has a smaller diameter when compared to the combining part **410**. A void **431** is also located within the elongated part **430** and is formed so as to contact the sample to be drawn into the pipette tip. The pipette tip further includes a connecting part **420** located between the combining part **410** and the elongated part **430**. The connecting part **420** further includes a void **421** which is in communication with the void **411** of the combining part **410** and the void **431** of the elongated part **430**. The connection between the voids **411**, **421**, **431** of the combining part **410**, connecting part **420**, and elongated part **430**, respectively, facilitates the application of an electric field by the connecting part to the sample. In some embodiments, suction can be

applied by the pipette **300**. When the plunger on the pipette is depressed, suction created by the pipette **300** is transferred through the voids **411**, **421**, **431** of the combining part **410**, connecting part **420**, and elongated part **430**, respectively, to draw a sample into void **431** of the elongated part **430** and into void **421** the connecting part **420**. In some embodiments, the pipette tip **400** is calibrated to draw a sufficient amount of sample, such that the sample only fills the voids **431**, **421** of the elongated part **430** and the connecting part **420**, respectively. In some embodiments, the sample may be drawn into the voids **411**, **421**, **431** of the combining part **410**, connecting part **420**, and elongated part **430**, respectively.

[0020] The combining part **410** has two ends a distal end, or end furthest from the user/pipette, and a proximal end, or end closest to the user/pipette. Both ends of the combining part **410** have openings, and a void **411** surrounded by an outer surface into which the sample may be drawn. Additionally, an upper outer circumferential surface of the combining part **410** has a predetermined length so as to easily connect or disconnect the pipette tip **400** from the end of the pipette **300**, and may further include projections **412** which extend radially from the combining part **410**.

[0021] Referring to **FIG. 6**, in some embodiments, the pipette tip includes a connecting part **420** comprising at least one, at least two, at least three, or more than three cylinder-shaped connecting posts **423** fixed on one end of the combining part **410**, a funnel-shaped connecting part **424** fixed on the ends of the one or plurality of connecting posts **423**; and a conductor **422** surrounding the connecting posts **423**. In some embodiments, the conductor is located at least partially on or within the surface of the combining part **410**. Having the conductor located at least partially on or within the combining part eliminates the need for an electrical conducting structure, or an electrode, within the void. Thus the void is only filled with the sample. In some embodiments, there may be three connecting posts **423**. The conductor **422** may surround the connecting posts **423** at least partially or entirely. In some embodiments, the conductor **422** is a ring-shaped conductor. The connecting posts **423** may be disposed at any position around the combining part **420**. In some embodiments, the connecting posts **423** may be disposed at an angle of 120° respective to the other connecting posts and relative to the lower surface of the combining part **410**, and a void **421** is formed through the center of the connecting part **424**. The inner circumferential surface of the conductor **422** may be exposed through gaps between the connecting posts **423** to facilitate the application of electric field to a sample drawn into the pipette tip. In some embodiments, the conductor consists of a conductive material such as, for example purposes only, nickel, gold, silver, copper, brass, aluminum, any combination thereof, or any other suitable conductive material, and/or the surface of the conductor may be plated with a conductive material such as, for example purposes only, nickel, gold, silver, copper, brass, aluminum, any combination thereof, or any other suitable conductive material. In some embodiments, the conductor may be injection molded with a plastic. The surface of the conductor may then be plated with a conductive material such as copper, brass, aluminum, nickel, gold, silver, any combination thereof, or any other suitable conductive material. In some embodiments, the conductor may be injection molded with a conductive polymer.

[0022] The elongated part **430** may have any suitable predetermined length in a longitudinal

direction of the connecting part **424** by being fixed to the lower surface of the connecting part **424**, and a void **431** communicating with the void **421** of the connecting part **424** may be formed through its center. In some embodiments, the elongated part **430** may taper in diameter along its length so as to reduce the quantity of the sample remaining in the end of the elongated part **430** when the pipette tip **400** is removed from the sample reservoir.

[0023] Referring now to FIGS. 8 & 9, FIG. 8 is a perspective view of an embodiment of a pipette tip provided herein, the exterior of which is similar to the pipette tip shown in FIG. 5; FIG. 9 is a cross-sectional view of the pipette tip shown in FIG. 8. The pipette tip **600** for the electroporation device according to another embodiment of the present invention includes: a combining part **610** with a void **611** into which an end of a pipette **300** (as shown in FIG. 12) may be inserted so as to communicate with the void **611**; an elongated part **630** having a void **631** into which the sample can be drawn; and a connecting part **620** provided between said combining part **610** and said elongated part **630**, having a void **621** inside so that the void **631** of said combining part **630** can communicate with the void **611** of said elongated part **610**. The connector part may have a smaller diameter than the combining part **610**. The connecting part **620** includes a conductor **622** for applying an electric field to the sample in the void of the pipette tip **600**.

[0024] The combining part **610** has two ends with openings located at each end and a void **611** in the center. The void **611** is located in the center of the combining part **610**. The void **411** is in fluid communication with the voids **421**, **431** of the connecting part **420**, and the elongated part **430**, respectively, into which the sample may be drawn. In some embodiments, the sample may also be drawn into the void **611** of the connecting part **610**. The upper outer circumferential surface of the combining part **610** has a predetermined length so as to easily connect or disconnect the pipette tip **600** from the end of the pipette **300**, and may further include projections **612** extending radially from the combining part **610**.

[0025] Referring to FIG. 9, in some embodiments, the pipette tip **600** has a connecting hole **613** communicating with the void **611** formed on a lower surface of the combining part **610**, and a ring-shaped groove **614** extending radially from the connecting hole **613** and recessed at the side of the connecting hole **613** so as to fit an upper end of the connecting part **620**. A connecting projection **623** having the corresponding shape to the connecting hole **613** of the combining part **610** to be fitted is formed on the upper end, and a fixing projection **624** having the corresponding shape to the connecting groove **614** is formed on the side of the connecting projection **623** to be inserted into the connecting groove **614**, thereby connecting the combining part **610** and the connecting part **620**. Further, a connecting projection **623'** having the corresponding shape to the connecting hole **613'** of the elongated part **630** to be fitted thereto is formed on the lower end, and a fixing projection **624'** having the corresponding shape to the connecting groove **614'** is formed on the side of the connecting projection **623'** to be inserted into the connecting groove **614'**, thereby connecting the combining part **610** and the elongated part **630**.

[0026] A void **621** into which a sample may be drawn may be formed through the center of the

connecting part **620**. The connecting part **620** includes a conductor **622** which may be made from a material selected from a conductive material such as, for example purposes only, nickel, gold, silver, copper, brass, aluminum, any combination thereof, or any other conductive material. The conductor **622** may be located at least partially on or within the surface of the connecting part **620**. Having the conductor **622** located at least partially on or within the surface of the connecting part **620** eliminates the need for an electrical conducting structure or an electrode within the void. Thus the void is only filled with the sample. The conductor **622** may thus apply an electric field to the sample located within either the void **621** of the connecting part **620** or the void **631** of the elongated part **630**, or both voids **621** and **631**. The surface of the conductor may be plated with a conductive material such as, for example purposes only, nickel, gold, silver, copper, brass, aluminum, any combination thereof, or any other suitable conductive material. In some embodiments, the conductor **622** may be injection molded with plastic, the surface of which may then be coated or plated with a conductive material such as, for example, brass, aluminum, copper, nickel, gold, silver, any combination thereof, or any other suitable conductive material. In some embodiments, the conductor **622** may be injection molded with a conductive polymer.

[0027] As previously described, the shape of the upper surface of the elongated part **630** may correspond to the shape of the surface of the combining part **610** to facilitate the connection of the combining part **610**, the connecting part **620**, and the elongated part **630**. A void **631** communicating with the combining part **621** of the connecting part **620** is formed through its center and extends in a longitudinal direction. In some embodiments, the elongated part **630** may taper along its length. In some embodiments, the end of the elongated part **630** tapers in diameter from the top or proximal end to the distal end so as to reduce the quantity of the sample in the end of the elongated part **630** when the elongated part **630** is removed from the sample reservoir.

[0028] By the above structures, in case of extracting the specimen by using the pipette tip for electroporation according to one embodiment of the present invention, the construction of the electroporation device may be made simpler by making electroporation possible by using the pipette tip itself to apply the electricity to the specimen without having an additional plunger, thereby the present invention can reduce the unit cost of manufacture. Additionally, the present invention can easily perform electroporation by reducing the error rate and reducing the number of trials and errors with a simple structure of applying the electrode to the sample. Also, since current pipette tips for use in an electroporation device may have a separate structure serving as the electrode, such as the plunger described in the prior art, the separate structure may interfere with using air pressure to draw up or eject the sample from the pipette tip. Since the pipette tip for electroporation according to an embodiment of the present invention does not have a separate electrode, the pipette tip may easily draw in or eject a sample using air pressure to create a vacuum or to expulse the sample.

[0029] FIG. 10 is a perspective view illustrating an embodiment of a pipette tip provided herein, and FIG. 11 is a cross sectional figure of FIG. 10. Referring now to FIGS. 10-11, the pipette tip **700** for electroporation includes: a combining part **710** with a void **711** into which an end of a

pipette **300** is inserted so as to communicate with the void **711**; and an elongated part **730** having a void **731** communicating with the void **711** of the combining part **710** into which the sample is drawn into, and a conductor **732** having a relatively smaller diameter than the combining part **710**, being fixed to the end of the combining part **710**, and consisting of a conductive material on its side. In some embodiments, the conductive material may be on the internal side of the conductor.

[0030] The combining part has a proximal end and a distal end, and both proximal and distal ends of the combining part **710** have openings. The combining part also has a void **711** formed through its center into which the sample can be drawn. Additionally, an upper outer circumferential surface of the combining part **710** has a predetermined length so as to easily connect or disconnect the pipette tip **700** from the end of the pipette **300**. In some embodiments, the upper outer circumference of the combining part **710** may further include projections **712** formed extending radially from the combining part **710**.

[0031] A connecting projection **713** having a predetermined height is located on the distal end of the combining part **710**. The connecting projection **713** may be inserted into a fixing projection **714** located on the proximal end of the elongated part **730**. When joined together, the connecting projection **713** and the fixing projection **714** fix the combining part **710** and the elongated part **730** on the side of the connecting projection **730**. A connecting groove **732** having a shape corresponding to the connecting projection **713** may be formed on the proximal end of the elongated part **730** into which the connecting projection **713** to be inserted. In some embodiments, a fixing groove **733**, wherein the fixing projection **714** is inserted and combined is formed on inner side of the connecting groove **732**. In some embodiments, the end of the elongated part **730** tapers along its length. In some embodiments, the elongated part **730** tapers in diameter from the top or proximal end to the distal end so as to reduce the amount of sample remaining on the end of the elongated part **730** after the elongated part **730** has been removed from the sample reservoir. The conductor **734** may be located at least partially on or within the connecting projection **713**. Having the conductor located at least partially on or within the outer surface of the pipette tip eliminates the need for an electrical conducting structure or an electrode within the void. Thus the void is only filled with the sample. The connector is located at least partially on or within the combining part **710**. In some embodiments, the conductor **734** may consist of conductive materials such as copper, brass, aluminum, nickel, gold, silver, any combination thereof or any other suitable conductive material, and the surface thereof can be plated with any conductive materials such as, for example, copper, brass, aluminum, nickel, gold, silver, any combination thereof, or any other suitable conductive material. In some embodiments, the conductor can be injection molded with plastic, or with a conductive polymer.

[0032] Referring now to FIG. 12, FIG. 12 shows an electroporation system including an electroporation device comprising a pipette on which a pipette tip for electroporation may be mounted. Additionally, provided herein is a method of use of the device and system. The electroporation system includes a pulse generator **100** for generating an electric pulse; a sample reservoir **200**; a pipette **300** capable of drawing the sample from the sample reservoir

and which is capable of maintaining the drawn up sample; a pipette tip **400** electrically connected with the pulse generator **100** of which one end is connected to the end portion of the pipette **300**, and of which the other end is inserted into the sample reservoir **200** and into which the sample is drawn into by the pipette **300**; and an additional electrode **500** electrically connected with the pulse generator **100** and dipped in the reservoir **200**. After the sample is drawn into the pipette tip **400** using the pipette **300** as a pressure maintaining means, a cell or cells, if present, in the sample drawn up into the pipette tip **400** may then be electroporated by applying an electric pulse to the conductors **422** of the electrode **500** and the pipette tip **400** using the pulse generator **100**. In some embodiments, the sample reservoir **200** may contain an electrolyte for conducting current, in addition to the sample. In some embodiments, the sample reservoir **200** may be replaced with an electrolyte reservoir containing an electrolyte for conducting current after the sample has been drawn into the pipette tip **400**. The pipette tip **400** and the additional electrode **500** may then be placed in the electrolyte reservoir. Pulses of current then can be applied to the cell membrane using the electrode and the pipette tip by passing current between the electrode and the conductor located on the pipette tip. The pulses of current may then change the configuration of the lipid bi-layer of the cell membrane to allow materials located in the sample that are typically unable to pass through the cell membrane to pass through the cell membrane. The pulses applied are of sufficient strength and duration to create temporary pass-throughs for the impermeable materials, which may then reseal without damaging or destroying the cell. Examples of materials that can then be passed through the cell membrane include, but are not limited to, macromolecules, molecular probes, drugs, therapeutics, DNA, RNA, bacteria, genes, protein material, cells, or any other suitable material. The pipette can use vacuum and expulsion to draw in and eject a sample by moving the plunger on the distal end of the pipette as indicated by the arrows in **FIG. 12**.

[0033] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. The extent of protection is determined by the claims. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention.

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- US20070275454A1 [0003]
- WO03057819A [0010]

PATENTKRAV

1. Pipettespids (400, 600, 700) til anvendelse ved udførelse af elektroporese, hvilken pipettespids omfatter:

en kombinationsdel, der har et legeme (410, 610, 710), en proksimal ende, en distal

ende og et hulrum (411, 611, 711) i kombinationsdelen;

en forbindelsesdel (420, 620), der har en proksimal ende, en distal ende og et hulrum (421, 621) i forbindelsesdelen og er placeret mindst delvist på eller inde i den distale ende af legemet;

en aflang del (430, 630, 730), der har et hulrum (431, 631, 731) i den aflange del og er placeret ved den distale ende af forbindelsesdelen, hvor kombinationsdelens hulrum, forbindelsesdelens hulrum og hulrummet i den aflange del står i fluidforbindelse med hinanden,

hvor pipettespiden har en ydre overflade og et hulrum, der er placeret inde i den ydre overflade, og som omfatter kombinationsdelens hulrum, forbindelsesdelens hulrum og hulrummet i den aflange del; og

som endvidere omfatter en leder (422, 622, 734), der er placeret mindst delvist på eller inde i den ydre overflade, hvor lederen er elektrisk forbundet med mindst en del af den ydre overflade og hulrummet, hvilken leder har en indre overflade, der er i stand til at tilføre en elektrisk strøm til forbindelsesdelens hulrum,

hvorved lederen kan tilvejebringe en enkelt elektrode af det elektrodepar, der er krævet for udførelse af elektroporese, og pipettespiden ikke indeholder nogen anden elektrodestruktur, og

en prøve, der er trukket ind i både forbindelsesdelens hulrum og hulrummet i den aflange del kan udsættes for et elektrisk felt, når pipettespiden kombineres med en anden elektrode i et elektroporesesystem.

2. Pipettespids ifølge krav 1, hvor lederen (422, 734) endvidere delvist eller helt omgiver mindst én forbindelsesstang (423, 713), hvilken mindst én forbindelsesstang er placeret i forbindelsesdelen.

3. Pipettespids ifølge krav 1 eller krav 2, hvor lederen er ringformet.

4. Pipettespids ifølge krav 1 eller krav 2, hvor lederen har et sprøjtestøbt legeme, der indbefatter mindst én plastpolymer og eller ledende polymer, hvor, hvis lederens legeme er af

plast, overfladen er pletteret med et ledende metal.

5. Pipettespids ifølge krav 1 eller krav 2, hvor lederen indbefatter et legeme og en overflade og overfladen er pletteret med mindst én af messing, kobber, aluminium, nikkel, guld eller sølv.

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6. Pipettespids ifølge krav 1 eller krav 2, hvor lederen indbefatter et legeme og en overflade og legemet indbefatter et ledende metal, fortrinsvis mindst én af kobber, messing, nikkel, guld, sølv eller aluminium.

10 **7.** Pipettespids ifølge krav 1 eller krav 2, hvor den indre overflade af lederen, der er i stand til at tilføre en elektrisk strøm til forbindelsesdelens hulrum, er pletteret med et ledende metal, der er udvalgt fra mindst én af messing, aluminium, kobber, nikkel, guld eller sølv.

15 **8.** Pipettespids ifølge krav 2, der omfatter tre forbindelsesstænger, der fortrinsvis er placeret i 120 grader i forhold til hinanden og i forhold til den ydre overflade.

9. Pipettespids ifølge krav 2, hvor forbindelsesdelen (420) omfatter en flerhed af forbindelsesstænger (423), der er fastgjort på én ende af kombinationsdelen (410), en tragtformet konnektor (424), der er fastgjort på ender af forbindelsesstængerne og lederen
20 (422), hvor lederen delvist eller helt omgiver forbindelsesstængerne.

10. Pipettespids ifølge krav 1, hvor forbindelsesdelen indbefatter (i) lederen (622), (ii) et forbindelsesfremspring (623) ved den øvre ende, der passer ind i et forbindelseshul (613) i den nedre overflade af forbindelsesdelen, hvilket forbindelsesfremspring har et
25 fastgørelsesfremspring (624), der indføres i en ringformet rille (614), der strækker sig radialt fra forbindelseshullet, og (iii) et forbindelsesfremspring (623') ved den nedre ende, der passer ind i et forbindelseshul (613') i den aflange del, hvilket forbindelsesfremspring har et fastgørelsesfremspring (624'), der indføres i en forbindelsesrille (614'), hvorved kombinationsdelen forbindes med både forbindelsesdelen og den aflange del.

30

11. Pipettespids ifølge et hvilket som helst af de foregående krav, hvor den aflange del er konisk i dens længde.

12. Elektroporesesystem, der omfatter

- a. en impulsgenerator (100);
- b. en pipette (300), der har en pipettespids ifølge krav 1, og som er elektrisk forbundet med impulsgeneratoren og
- c. en elektrode (500), der er forbundet med impulsgeneratoren.

5

13. Elektroporesesystem ifølge krav 12, hvor pipettespidsen er elektrisk forbundet med elektroden.

DRAWINGS

[*Prior Art*]

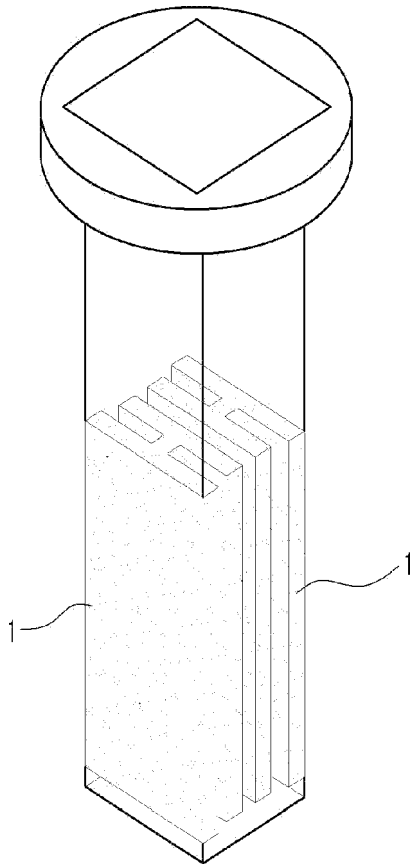


FIG. 1

[*Prior Art*]

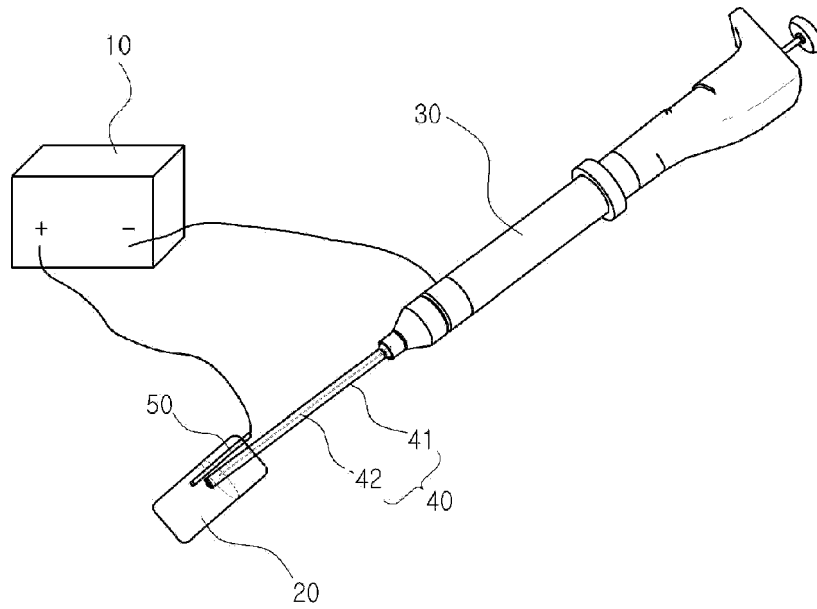


FIG. 2

[*Prior Art*]

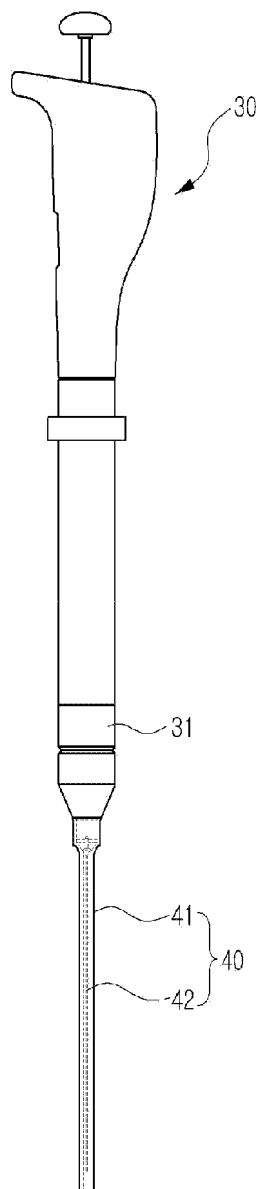


FIG. 3

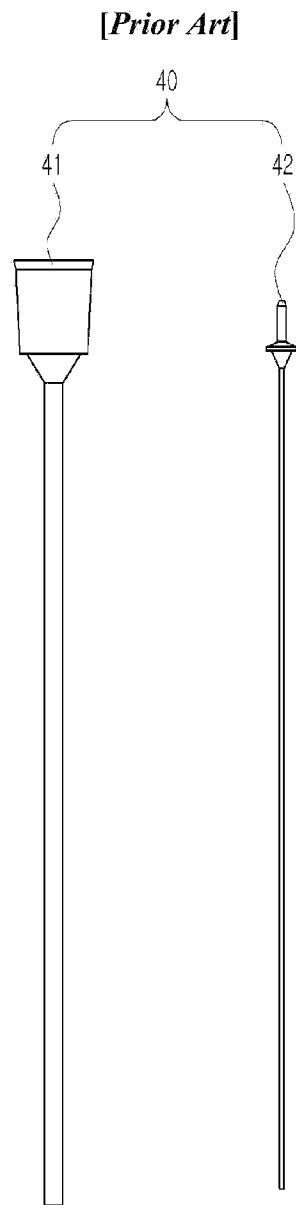


FIG. 4

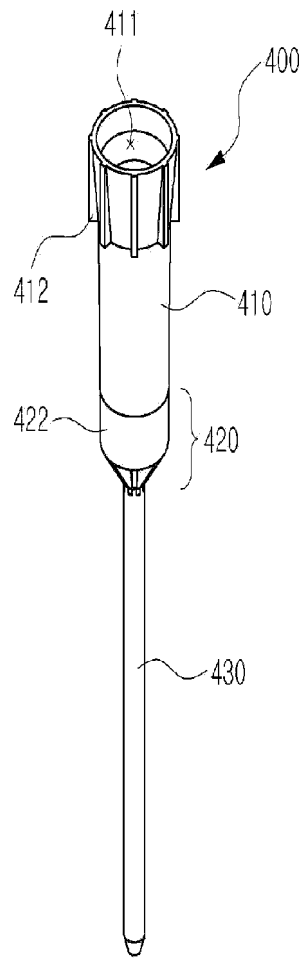


FIG. 5

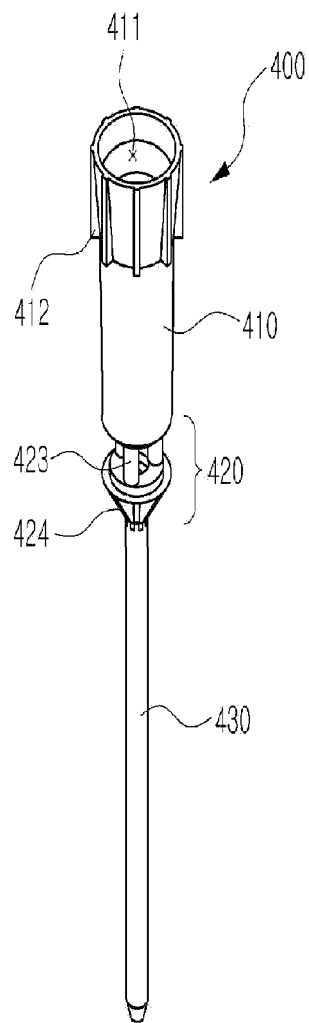


FIG. 6

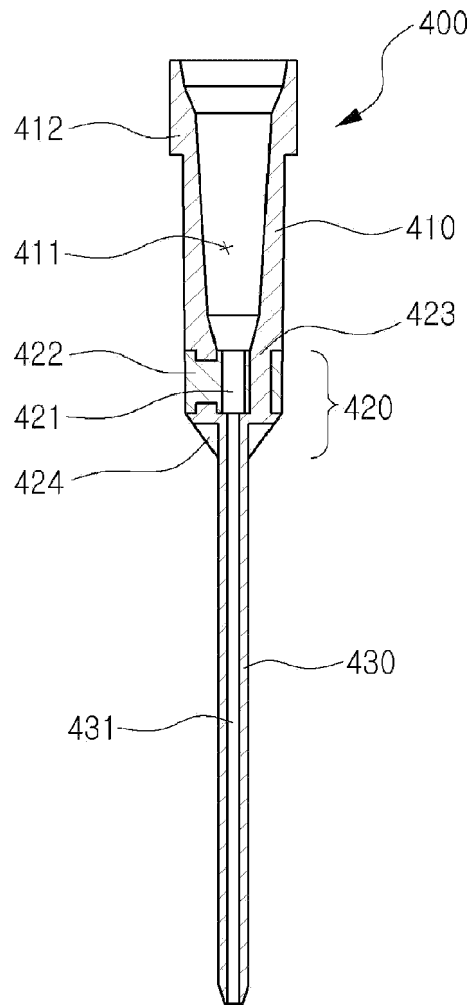


FIG. 7

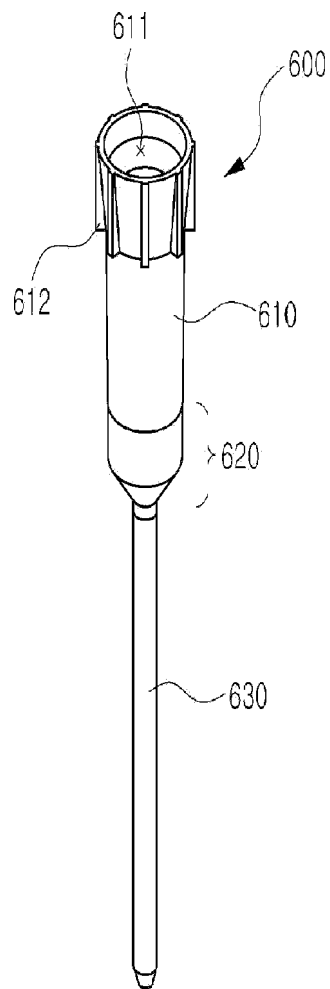


FIG. 8

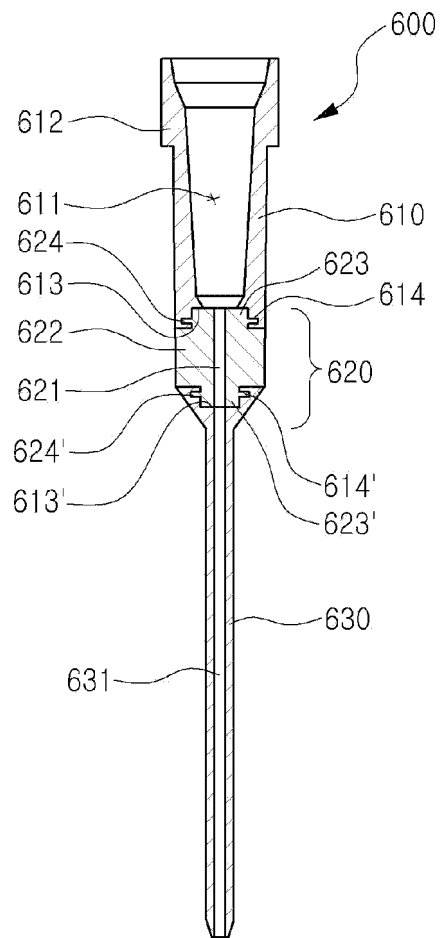


FIG. 9

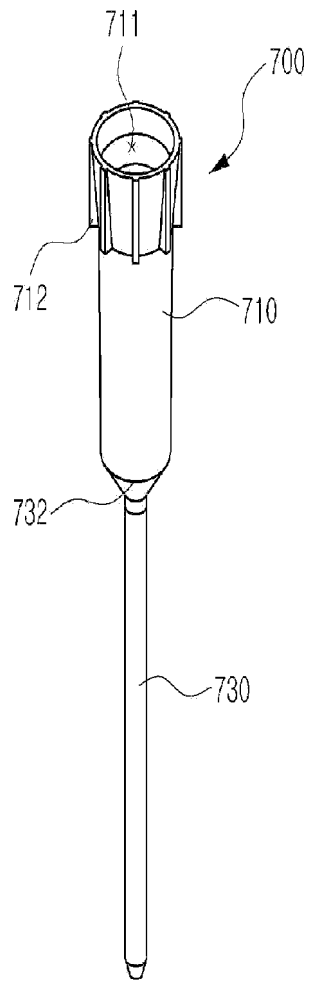


FIG. 10

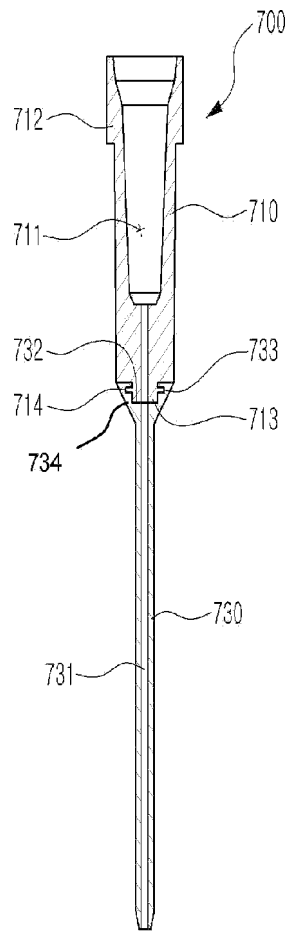


FIG. 11

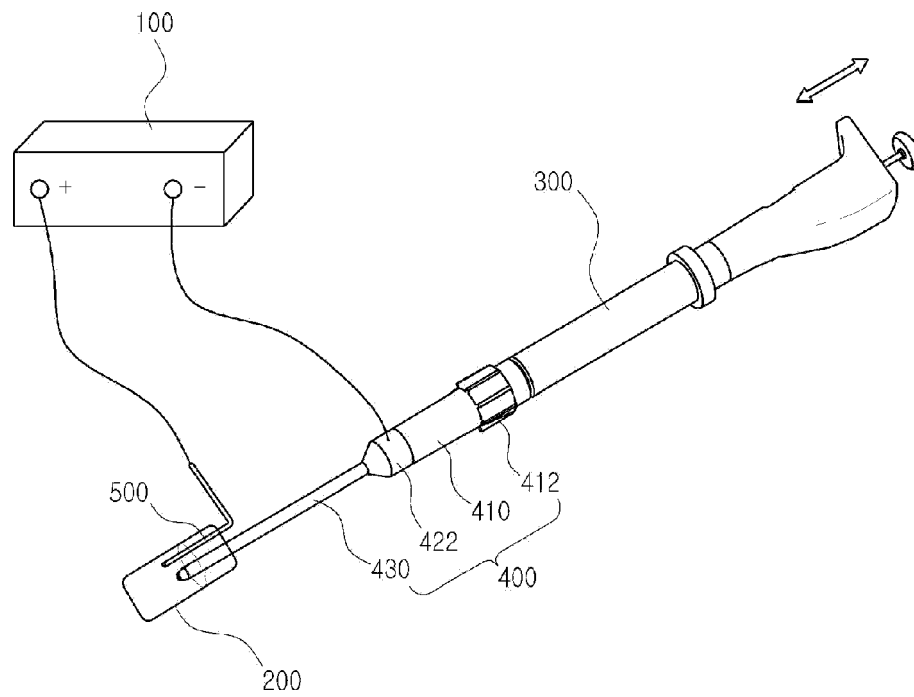


FIG. 12