



(43) International Publication Date
7 November 2013 (07.11.2013)

- (51) **International Patent Classification:**
B01L 3/02 (2006.01)
- (21) **International Application Number:**
PCT/US2013/039142
- (22) **International Filing Date:**
1 May 2013 (01.05.2013)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
61/640,937 1 May 2012 (01.05.2012) US
- (71) **Applicant:** **LIFE TECHNOLOGIES CORPORATION**
[US/US]; IP Legal Department, 5791 Van Allen Way,
Carlsbad, California 92008 (US).
- (72) **Inventors:** **JACKSON, John**; 4939 Composition Court,
Oceanside, California 92057 (US). **BULLOCH, Kyle**; 850
Beech Street, Apartment 1403, Oceanside, California
92101 (US). **KAHATT, Espir**; 6430 La Vanco Street,
Carlsbad, California 92009 (US).
- (74) **Agent:** **SUBRAMONY, Priya**; Life Technologies Corpora-
tion, IP Legal Department, 5791 Van Allen Way, Carls-
bad, California 92008 (US).
- (81) **Designated States** (*unless otherwise indicated, for every
kind of national protection available*): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI,
NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU,
RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA,
ZM, ZW.

- (84) Designated States** (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- of inventorship (Rule 4.17(iv))

Published:

- *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

(54) Title: PIPPETTE DEVICES, SYSTEMS, AND METHODS OF USE THEREOF

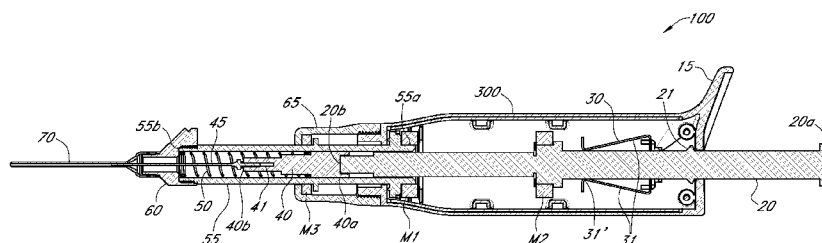


FIG. 1

(57) Abstract: In some embodiments the present disclosure describes novel pipette devices, pipetting systems and methods of use thereof which require a user to use less force for one or more functions such as to: load a pipette tip, aspirate sample, dispense sample and eject a pipette tip. A pipette device of the disclosure comprises: a pipette plunger; at least one pair of magnets; and at least one spring; wherein the pipette device is configured to reduce the force required by a user to aspirate, dispense, load and eject a pipette tip. In some embodiments, a pipette device of the disclosure further comprises a detent. In some embodiments a pipette according to the disclosure further comprises a trigger. Some embodiments describe electroporation systems comprising a pipette device of the disclosure as well as various configurations of electroporation systems and devices and methods of use thereof.

PIPETTE DEVICES, SYSTEMS AND METHODS OF USE THEREOF

by

Kyle Bulloch**Espir Kahatt****John Jackson****FIELD**

[0001] The present invention relates in some embodiments to pipette devices and to pipetting systems and methods of use thereof. In some embodiments, pipetting devices and systems may be used for electroporation. Accordingly, some embodiments describe electroporation systems comprising a pipette device of the disclosure as well as various configurations of electroporation systems and devices and methods of use thereof. In some embodiments the pipetting devices and systems may be used for pipetting fluids.

BACKGROUND

[0002] Pipettes are used extensively in biology and chemistry to pipette liquids. Several types of pipettes are used such as air-displacement pipettes and positive-displacement pipettes. Positive-displacement pipettes work like a syringe. For example, the pipette piston directly contacts the sample and there is no air cushion between the disposable piston and the sample. With no elastic air cushion to expand or contract, the aspiration force remains constant, unaffected by the physical properties of the sample allowing users to pipette very viscous or high density samples.

[0003] Pipette devices generally have a mechanism for a user to control the uptake of such liquids from a sample tube and to move liquids up and down. Typically a pipette user of a positive displacement pipette has to “aspirate,” “dispense load” and “eject a pipette tip.” Current pipette devices have a major disadvantage which requires a user to apply a lot of force to “aspirate” “dispense load” and “eject a pipette tip”. This results in user fatigue. Another disadvantage of current pipette systems is that users have to keep applying pressure on a pipette prior to loading a fresh pipette tip and to ensure that the plunger within the pipette tip (tip plunger) is fully extended to minimize air bubbles when drawing the sample up. To achieve this, a user has to use his or her fingers to maintain the pressure on the pipette which also leads to user fatigue and an inability to use their hands/fingers for other operations. Therefore, there is a need to develop a pipette device to address these disadvantages.

SUMMARY

[0004] The present disclosure in some embodiments provides pipettes for solving one or more of the above disadvantages. Various embodiments describe novel pipette devices (also referred to as pipette), pipetting systems and methods of use thereof. A pipette device of the disclosure, in some embodiments, is configured to reduce the force required by a user to aspirate, dispense, load and/or eject a pipette tip.

[0005] A pipette device of the disclosure comprises: a pipette plunger; at least one pair of magnets; and at least one spring. Some embodiments of a pipette device of the disclosure can comprise at least two pairs of magnets. Some embodiments of a pipette device of the disclosure can comprise three pairs of magnets. In some embodiments, a pipette device of the disclosure further comprises a detent. A detent can comprises a pair of cantilevers. In some embodiments the cantilevers may have a protrusion on each cantilever.

[0006] In some embodiments a pipette device according to the disclosure may further comprise a trigger.

[0007] A pipette device of the disclosure can be used with any tip that can be used with a positive displacement pipette and may include tips such as but not limited to, disposable plastic tips, reusable plastic tips, pipetteman tips, microman tips, Gilson pipetteman tips, Rainin microman tips, and pipette tips that are compatible with electroporation devices such as pipette tips compatible for use with the Neon® Transfection System or the Neon™ Transfection System of Life Technologies Corporation.

[0008] In some embodiments, pipette devices of the disclosure uses lesser force to load and/or eject a pipette tip as compared to other pipettes used in currently available pipette devices and systems. In some embodiments, a pipette device of the disclosure can lock in a fully depressed position, making loading a fresh pipette tip easier. In some embodiments, a pipette device of the disclosure can lock in a fully depressed position, making loading a sample and minimizing air bubbles in the tip easier.

[0009] In some embodiments, in comparison to currently available pipettes in the market which requires about ~15lb of force for some users for loading and/or ejecting a pipette tip a pipette device of this disclosure having a trigger the force by a user for loading and/or ejecting a pipette tip is reduced to ~4lb and for a pipette having a detent according to the present disclosure the force for loading and/or ejecting a tip is reduced to ~8lb.

[0010] In some embodiments, the present pipette devices use lesser force to aspirate up a sample and/or to dispense a sample as compared to other pipettes used in currently available pipette devices and systems.

[0011] In some embodiments, the pipette device described here is a positive displacement pipette.

[0012] In some embodiments, pipetting devices and pipetting systems may be used for electroporation. In some embodiments, the present disclosure describes a pipette device of an electroporation system comprising a plunger, at least one pair of magnets, at least one spring, and an electrode. Accordingly, some embodiments describe electroporation systems comprising a pipette device of the disclosure as well as various configurations of electroporation systems and devices and methods of use thereof. One or more of the configurations described herein provide ergonomic advantages to users. Some electroporation systems that are compatible with the pipette devices disclosed herein are the Neon® transfection system of Life Technologies™.

[0013] Some embodiments describe methods of using a pipette device of the disclosure and comprise: depressing a pipette plunger manually until it locks into a loading position; loading a new pipette tip by inserting the pipette into a pipette tip until it snaps on without the need to keep the pipette plunger depressed while inserting the pipette tip; aspirating a sample by pushing the pipette plunger up to an aspiration position (either by pushing on a trigger for a pipette having a trigger to push the plunger up to the aspirate position OR by loading a tip which generates force to move a pipette plunger to aspirate position in a pipette with a detent) and; depressing the pipette plunger to a dispense position to dispense aspirated sample; and ejecting a used pipette by pressing on the plunger. One or more of the following advantages may be realized by a user: a user needs much lesser force to load new pipette and/or a user needs much less force to eject a new pipette and/or a user needs no additional force and/or may have their hands/fingers free while loading a pipette by not having to keep the pipette plunger depressed into a locked position and/or maintain the tip in the fully dispensed position when loading a sample to ensure no air bubbles are introduced.

[0014] In some embodiments, methods for performing electroporation using an electroporation system comprising a pipette device are described. A method of the disclosure may comprise loading on to a pipette device of the disclosure an electroporation compatible pipette tip by depressing a pipette plunger manually until it locks into a loading position; loading the electroporation compatible pipette tip by inserting the pipette into a pipette tip until it snaps on without the need to keep the pipette plunger depressed while inserting the pipette tip; aspirating a sample containing cells and macromolecules to be electroporated into the cells by pushing the pipette plunger up to an aspiration

position (either by pushing on a trigger for a pipette having a trigger to push the plunger up to the aspirate position OR by loading a tip which generates force to move a pipette plunger to aspirate position in a pipette with a detent); providing an electrical pulse to the cells in the pipette tip to allow electroporation and; depressing the pipette plunger to a dispense position to dispense aspirated sample comprising electroporated cells; and ejecting a used pipette tip by pressing on the pipette plunger (or trigger).

[0015] The method may further comprise, removing the pipette from the pipette stand; dispensing the electrophoresed sample from the pipette tip into one or more container means for further sample processing; and depressing the pipette plunger until the used pipette tip ejects and the pipette returns to its locked position.

[0016] In some embodiments of a method of the disclosure, once a sample is drawn from a sample reservoir into a pipette tip, a sample reservoir is replaced with a reservoir containing an electrolytic solution. In some embodiments, applying an electric current to the sample located in a pipette tip of the electroporation system comprises applying electrical current to a plunger located within the body of the pipette tip and to an electrode contacting a sample in a sample reservoir or an electrolytic solution in an electrolytic solution reservoir such that any cell located in the sample drawn into the pipette tip may be electroporated by passing a current between the two electrodes and through any cells located between the two electrodes.

[0017] In some embodiments, pipette devices, systems comprising a pipette device and methods of use thereof may provide one or more advantages such as: facilitating pipetting by causing lesser user fatigue by causing a user to use lesser force to eject a tip as compared to other pipettes used in currently available pipettes; and/or making loading a fresh pipette tip easier as a pipette device can lock in the fully depressed position that needs lesser force for loading a new tip; and/or maintain the tip in the fully dispensed position when loading a sample to ensure no air bubbles are introduced; and/or facilitating electrophoresis by causing lesser user fatigue by causing a user to use lesser force to eject a tip as compared to other pipettes used in currently available electroporation systems; and/or by causing lesser user fatigue by locking into position to maintain pressure required to keep a sample in a pipette tip while applying current for electroporation which also allows a user to have their hands free to perform other tasks by for example setting the pipette with sample in a pipette stand while current is applied.

INCORPORATION BY REFERENCE

[0018] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] A better understanding of the features and advantages of the present disclosure 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:

[0020] **FIG. 1** is a cross-sectional view of a pipette device, according to one embodiment of the disclosure;

[0021] **FIG. 2A** is a cross-sectional view of a pipette device in a “loading position”, according to one embodiment of the disclosure;

[0022] **FIG. 2B & FIG. 2C** is a close up view of a gripper showing gripper fingers in pipette device, according to one embodiment of the disclosure;

[0023] **FIGS. 3A, 3B and 3C** depict the functioning of a pipette device of the disclosure wherein, **FIG 3A** is a cross-sectional view of a pipette device in an “aspirate position”, according to one embodiment of the disclosure; **FIG. 3B** is a cross-sectional view of a pipette device in a “dispense position”, according to one embodiment of the disclosure; and **FIG. 3C** is a cross-sectional view of a pipette device in an “eject/loading position”, according to one embodiment of the disclosure;

[0024] **FIG. 4** is a cross-sectional view of a pipette device, according to one embodiment of the disclosure;

[0025] **FIG 5A** is a cross-sectional view of a pipette device of FIG. 4 in a “loading position”, according to one embodiment of the disclosure;

[0026] **FIG. 5B & FIG. 5C** is a close up view of a gripper showing gripper fingers in pipette device of FIG. 4, according to one embodiment of the disclosure;

[0027] **FIGS. 6A, 6B and 6C** depict the functioning of a pipette device of the disclosure wherein, **FIG. 6A** is a cross-sectional view of a pipette device in an “aspirate position”, according to one embodiment of the disclosure; **FIG. 6B** is a cross-sectional view of a pipette device of FIG. 6 in a “dispense position”, according to one embodiment of the disclosure; and **FIG. 6C** is a cross-sectional view of a pipette device of FIG. 6 in an “eject/loading position”, according to one embodiment of the disclosure;

[0028] **FIG. 7A and FIG. 7B** are external views of components of a pipette device of the present disclosure, according to one embodiment of the disclosure;

[0029] **FIG. 7C** depicts views of components of a pipette device of the present disclosure, according to one embodiment of the disclosure;

[0030] **FIGS. 8A-8H** depict various components of a pipette device of the disclosure with regard to its location within the pipette device as well as the individual component, according to one embodiment of the disclosure, wherein: **FIG. 8A** depicts pipette body; **FIG. 8B(i)** depicts a pipette plunger located inside pipette body and **FIG. 8B(ii)** depicts a pipette plunger; **FIG. 8C(i)** depicts a pipette end located with regards to the pipette device and **FIG. 8C(ii)** depicts the pipette end alone; **FIG. 8D(i)** depicts a lock that secures pipette end and pipette body with respect to its location in a pipette device and **FIG. 8D(ii)** depicts the lock alone; **FIG. 8E(i)** depicts a detent located inside pipette body and **FIG. 8E(ii)** depicts the detent alone; **FIG. 8F** depicts two magnets inside pipette body; **FIG. 8G(i)** depicts an electrode tip with respect to its location in a pipette device and **FIG. 8G(ii)** depicts the electrode tip alone; and **FIG. 8H(i)** depicts a gripper with respect to its location in a pipette device and **FIG. 8H(ii)** depicts the gripper alone;

[0031] **FIG. 9** shows a system and device used for performing electroporation, according to one embodiment of the disclosure;

[0032] **FIG. 10** shows a configuration of a system having a pipette device of the disclosure, the system configured for performing electroporation, according to one embodiment of the disclosure;

[0033] **FIG. 11A** shows a configuration of a system having a pipette device of the disclosure, the system configured for performing electroporation, according to one embodiment of the disclosure;

[0034] **FIG. 11B** shows a configuration of a system having a pipette device of the disclosure, the system configured for performing electroporation, according to one embodiment of the disclosure;

[0035] **FIG. 11C** shows a configuration of a system having a pipette device of the disclosure, the system configured for performing electroporation, according to one embodiment of the disclosure;

[0036] **FIG. 11D** shows a configuration of a system having a pipette device of the disclosure, the system configured for performing electroporation, according to one embodiment of the disclosure; and

[0037] **FIG. 11E** shows a configuration of a system having a pipette device of the disclosure, the system configured for performing electroporation, according to one embodiment of the disclosure.

DETAILED DESCRIPTION

[0038] The present disclosure relates in some embodiments to pipette devices and to pipetting systems and methods of use thereof.

[0039] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of ordinary skill in the art to which this invention belongs.

[0040] As used herein, "a" or "an" means "at least one" or "one or more."

[0041] As used herein, "about" means that the numerical value is approximate and small variations would not significantly affect the practice of the disclosed embodiments. Where a numerical limitation is used, unless indicated otherwise by the context, "about" means the numerical value can vary by $\pm 10\%$ and remain within the scope of the disclosed embodiments.

[0042] Pipette devices of the present disclosure use magnets to reduce the force required by a user to aspirate, dispense, and load and/or eject a pipette tip. In some embodiments, the force required by a user to actuate a pipette device of the present disclosure, as compared to standard pipettes that are currently available, is greatly reduced. For example, loading a pipette tip and ejecting a pipette tip using available pipette devices (such as for example Gilson's pipetteman) requires about ~15lb of force while various embodiments of the pipette devices of the present disclosure can reduce the force required by a user to load and/or eject a pipette tip to less than about 15 lbs, less than about 14 lbs, less than about 13 lbs, less than about 12 lbs, less than about 11 lbs, less than about 10 lbs, less than about 9 lbs, less than about 8 lbs, less than about 7 lbs, less than about 6 lbs, less than about 5 lbs, less than about 4 lbs, less than about 3 lbs, less than about 2 lbs, less than about 1 lbs, and ranges between any two of these values. Furthermore some users of currently available pipette devices need to use both hands to eject a tip. The presently disclosed pipette devices do not require such large forces thereby offering one or more advantages such as: reduced user fatigue; and/or reduce the amount of force required by a user to use a pipette by about 50% less, to about 25% less; and/or ability of a user to use only one hand for pipetting; and/or allowing a user to free up both hands and fingers during an experiment using a pipette.

[0043] Pipettes of the disclosure may be used to pipette any liquids such as, but not limited to, chemicals, cells, cell suspensions, biological macromolecules such as proteins and/or nucleic acids and/or vitamins and/or pharmaceutical compounds, buffers, solutions and combinations of these. In some embodiments pipettes and pipetting systems as described here may be used for electroporation. Accordingly, some embodiments describe electroporation systems comprising a pipette device of the

disclosure as well as various configurations of electroporation systems and devices and methods of use thereof.

[0044] Several drawings have been used to illustrate and describe one or more embodiments. Part numbers used are the same across various drawings and parts may not be expressly labeled in each and every drawing. Similar parts may be referred to by part numbers shown in one drawing unless expressly labeled as different in another drawing. One or more figures may comprise optional parts and elements as described and are not always comprised in all embodiments. One of skill in the art will recognize that these figures are not limiting and are merely used for illustration of some embodiments that are described in this application.

[0045] One embodiment of an exemplary pipette device of the disclosure is shown in FIG. 1 which shows a cross-sectional view of the pipette for illustration of various components therein. FIG. 1 depicts a cross section of a pipette device 100 shown with a reversible attachable pipette tip 70 attached thereto, comprising a pipette body 300 which is a shell or a housing that further comprises several components. Pipette body 300 also has an external structure that provides an ergonomic grip to a pipette user. Pipette device 100 comprises a pipette plunger 20 having a first end 20a located external to the device and a second end 20b located inside the pipette body 300, a detent 30 enclosed inside pipette body 300. Detent 30 is operably in contact with pipette plunger 20, plunger 20 comprises a detent push-off surface 21 (depicted in a conical shape, but not limited to a conical shape). Plunger 20 can insert into and lock with the detent 30. Detent 30 can be made of metal or plastic. Pipette device 100 comprises a pair of magnets M1 and M2 that are in operable contact with plunger 20, wherein magnet M1 is affixed in position to other components inside pipette body 300 and magnet M2 is operable to move. Pipette device 100 comprises a gripper 40 having a first end 40a and a second end 40b. First end 40a of gripper 40 is configured to fit second end 20b of plunger 20 and second end 40b of gripper 40 has a slot 41 configured to fit a tip plunger 45. Gripper 40 comprises gripper spring 40'. Gripper spring 40' is shown in FIG. 4 and lies internal to gripper 40 in FIG. 1 and hence is not expressly visible in FIG. 1. Gripper 40 is operably attached to a pipette plunger spring 50. Pipette end 55 encloses gripper 40 and extends over first end 40a and second end 40b of gripper 40 and the over second end 20b of the plunger 20. Pipette end 55 has a first end 55a proximate magnet M1 and second end 55b in releasable contact with electrode 60. Pipette end 55 connects pipette body 300 to electrode tip 60 and provides a guide for gripper 40. In one embodiment, as depicted in FIG. 1, electrode 60 is screwed onto pipette end 55 by means of

threads/grooves on both electrode 60 and pipette end 55 that can be fit together by a threaded fit by rotating the two parts together along the threads.

[0046] Part 65 is an internally threaded cap (also referred to as a “lock”), which screws onto pipette body 300 on one side and pipette end 55 on another side to keep these components of pipette device 100 together. Lock 65 also keeps pipette end 55 centered and, in some embodiments, contains sensor magnet M3.

[0047] In some embodiments, magnets M1 and M2 are small magnets. Optionally, in some embodiments, handle 15 may be present attached to or as a continuation of pipette body 300 near the end 20a of the pipette plunger 20. Optionally, in some embodiments, an electrode 60 may be attached to or comprised in pipette device 100. Optionally, in some embodiments, a third magnet M3 may be present proximate gripper 40 in lock 65.

[0048] Magnet M3 can function to work with magnetic sensors that may be located in a pipette stand or pipette rack device to rest pipette device 100 (exemplary pipette stand or pipette rack devices are depicted in FIGS. 10 and 11A-11E as part 12). M3 works by triggering a hall effect sensor that is located in a pipette stand 12. As soon as a significant magnetic field comes close to a hall effect sensor, an instrument that is connected to it (such as an electroporation system 1000 in FIGS. 10 and 11A-11E) will know that a pipette is installed in the stand.

[0049] In some embodiments, a pipette device 100 as shown in FIG. 1 functions by magnetic attraction force of two magnets, *e.g.*, magnet M1 and magnet M2, to reduce spring forces (of the gripper spring 40' and the plunger spring 50) and a detent mechanism which locks a pipette 100 in a tip eject and/or a tip load position while loading a pipette tip. The attraction force between magnets M1 and M2 is inversely proportional to the distance between the magnets, hence, closer the magnets are the stronger the force between them.

[0050] A pipette of the disclosure as shown in the cross sections depicted in FIG. 1 functions as depicted in FIGS. 2A, 3A, 3B and 3C by moving one or more components therein into various positions for loading and/or ejecting a pipette tip; aspirating a sample; and dispensing a sample. Each of these positions are described here. At rest, a pipette 100, as shown in FIG. 1, is in a fully extended position kept extended by at least one spring. In the fully extended position the pair of magnets M1 and M2 are too far apart from each other to interact with each other. As a pipette plunger is depressed (pipette plunger 20 may be depressed by a user mechanically such as by pressing the plunger by hand or finger or by an automated means such as by a robotic device) the two magnets M1 and M2 come closer together, and their attraction force increases. First the pipette

is set to the load position (and/or eject position) as shown in FIG 2A, which is achieved by pressing pipette plunger 20 down (by a user or mechanical means) past a dispense stop position such that pipette plunger end 20a is closest to the pipette body 300. Magnets M1 and M2 are pushed close to one another by the locking of detent push off surface 21 into detent 30. Unlike a trigger pipette (shown and described below and in FIGS. 4-6C), in this position the force of magnet M1 and magnet M2 do not counteract the force of the pipette plunger spring and the gripper spring. The detent mechanism locks the pipette in this position.

[0051] The detent mechanism comprises a pair of protrusions 31' at the end of detent cantilevers 31. As pipette plunger 20 is pushed down (moves down), the detent push off surface 21 pushes the detent cantilevers 31 apart. As soon as pipette plunger 20 reaches the eject/load position (e.g., when a user or a mechanical means has compressed both the pipette plunger spring and the gripper spring), the detent cantilevers 31 fall off the detent push off surface 21 locking the pipette plunger 20 in the eject/load position. In some embodiments, a detent is made of sheet metal. In some embodiments a detent can be made of an injection molded plastic part. There may be some differences in geometry of the detent based on the material used to make the detent and the mode of manufacture. These minor differences are contemplated by the present disclosure.

[0052] FIGS. 2B and 2C depict a close-up of the electrode tip 60 through which gripper 40 extends in the load position of FIG. 2A and depicts gripper fingers 42 sticking out, thereby making the pipette 100 ready to receive pipette tip 70. Gripper 40 is a small collet that extends when plunger 20 is fully depressed. When plunger 20 is released, gripper 40 clamps down on a pipette tip 70 that is to be used for pipetting. Pipette tip 70 may be any consumable pipetting tip including electroporation tips.

[0053] The act of loading a pipette tip 70 generates enough force to separate the detents 31 and move the pipette plunger up unlocking the pipette plunger 20 out of the detent, the pipette plunger spring 50 then moves the plunger 20 to its most extended out position (with end 20a being farthest away from pipette body 300) also referred to as the aspirate position shown in FIG 3A (and FIG. 1).

[0054] A user (or mechanical means) can then press the pipette plunger to the dispense position shown in FIG 3B to dispense the aspirated sample. At the dispense position the pipette plunger end 20a is not as close as in the load/eject position to the pipette body 300. At the dispense position there is no lock, *i.e.*, the detent cantilevers 31 and detent protrusions 31' do not lock the detent push off surface 21, and a user will feel a "stop" since this position corresponds to pipette plunger spring 50 being fully compressed. The gripper spring 40' is much stronger than the pipette plunger spring

50, which enhances the “stop” feel at the dispense position. After a user has completed sample aspiration and sample dispensing, the user can proceed to the eject load position to eject a used tip 70 which is shown in FIG 3C (also FIG 2A). Pipette tips 70 that are used may be ejected by gripper fingers 42 shown in FIGS 2B and 2C pushing outward to push pipette tip 70 out.

[0055] In some embodiments, pipette devices as described herein eliminate the need for a user (or for any automated means) to continue to hold the plunger down. The installation force of installing a pipette tip to the end of the pipette body overcomes the detent mediated lock, which comprises the plunger’s conical part locked into the detent, causing the plunger to move all the way back to its fully extended position held so again by the spring force.

[0056] In another embodiment, a pipette device of the disclosure is a pipette device 200 as shown in FIG 4. FIG. 4 depicts a cross section of a pipette device 200 shown without a reversible attachable pipette tip 70. Parts not labeled are the same as those labeled in FIG. 1. Pipette 200 comprises a pipette body 300 which serves as a housing or shell for some pipette device components. Pipette device 200 also comprises a pipette plunger 20 having a first end 20a located external to the device and a second end 20b located inside the pipette body 300. Pipette plunger 20 comprises a trigger push-off surface 71 (depicted in a conical shape, but not limited to a conical shape) that is operably linked to trigger 70. Pipette device 200 also comprises a pair of magnets 1 and 2 that are in operable contact with pipette plunger 20, wherein magnet M1 is affixed in position to other components located in pipette body 300 as depicted and magnet M2 is operable to move,; and a gripper 40 having a first end 40a and a second end 40b, the first end 40a of gripper 40 configured to fit second end 20b of plunger 20 and the second end 40b of gripper 40 having a slot 41 configured to fit a tip plunger 45 (not expressly shown), gripper 40 comprising a gripper spring 40’, gripper 40 further operably attached to a pipette plunger spring 50, a pipette end 55 enclosing gripper 40 and the second end 20b of the plunger 20. In some embodiments, magnets M1 and M2 are small magnets.

[0057] Pipette end 55 encloses gripper 40 and extends over first end 40a and second end 40b of gripper 40 and the over second end 20b of the plunger 20. Pipette end 55 has a first end 55a proximate magnet M1 and second end 55b in releasable contact with electrode 60. Pipette end 55 connects pipette body 300 to electrode tip 60 and provides a guide for gripper 40. In one embodiment, as depicted in FIG. 4, electrode 60 is screwed onto pipette end 55 by means of threads/grooves on both electrode 60 and pipette end 55 that can be fit together by a threaded fit by rotating the two parts together along the threads.

[0058] Part 65 is an internally threaded cap (also referred to as a “lock”), which screws onto pipette body 300 on one side and pipette end 55 on another side to keep these components of pipette device 200 together. Lock 65 also keeps pipette end 55 centered and, in some embodiments, contains sensor magnet M3.

[0059] Optionally, in some embodiments, handle 15 may be present attached to or as a continuation of pipette body 300 near the end 20a of the pipette plunger 20. Optionally, in some embodiments, handle 15 may be attached to or as a continuation of trigger 70. Optionally, in some embodiments, an electrode 60 may be attached to, detachably attached to or comprised in pipette 200.

[0060] Pipette 200 functions by magnetic attraction force of two magnets, e.g., magnet M1 and magnet M2, to counteract spring forces (of the gripper spring 40' and the plunger spring 50) and locks the pipette 200 in different positions. This magnetic force also counteracts the spring force reducing the amount of force required by a user in depressing pipette plunger 20. The attraction force between the magnets is inversely proportional to the distance between the magnets, the closer the magnets are the stronger the force between them.

[0061] A pipette of the disclosure as shown in the cross sections depicted in FIG. 4 functions as depicted in FIGS. 5A-C, and FIGS. 6A-C by moving one or more components therein into various positions for loading and/or ejecting a pipette tip 70; aspirating a sample; and dispensing a sample. Each of these positions are described here. At rest, a pipette 200 is in a fully extended position kept extended by at least one spring as shown in FIG. 4. In the fully extended position the pair of magnets are too far apart from each other to interact with each other. As a pipette plunger 20 is depressed (pipette plunger 20 may be depressed by a user mechanically such as by pressing the plunger by hand or finger or by an automated means) the two magnets M1 and M2 come closer together, and their attraction force increases. First the pipette is set to the load position as shown in FIG 2A, which is achieved by pressing pipette plunger 20 down (by a user or mechanical means) past a dispense stop position such that pipette plunger end 20a is closest to the pipette body 300. At this position, the force of magnet M1 and magnet M2 counteract the force of the pipette plunger spring 50 and the gripper spring 40' and lock the pipette 200 in this position.

[0062] FIGS 5B and 5C depict a close-up of electrode tip 60 showing part of gripper 40 protruding down in the load position shown in FIG. 5A, and depict how gripper fingers 42 stick out, thereby making the pipette 200 ready to receive a pipette tip 70.

[0063] A pipette tip 70 is loaded by pressing pipette 200 into a tip 70 which can be located in a tip box (like a standard air displacement pipette). The force of loading tip 70 moves pipette 200 to its next lock position described as the dispense position shown in FIG 6A.

[0064] In the dispense position the attraction force of the magnets is strong enough to counteract the pipette plunger spring 50 but not the gripper spring 40', so the pipette 200 is locked in this dispense position. In the dispense position the tip plunger 45 is at the bottom of its stroke. In the dispense position a user would be ready to aspirate a sample or would have just finished dispensing a sample. When a user wants to aspirate a sample they would press trigger 70, this would cause the trigger mechanism to contact trigger push off surface 71 and apply extra force against the magnet attraction forces of magnets M1 and M2, separating the two magnets enough for pipette plunger spring 50 to become the dominant force and push pipette plunger up 20 to its aspirate position shown in FIG 6B.

[0065] This can be repeated as many times as required by a user or an application. When a user has completed working with a pipette tip 70 and needs to replace it he/she can push plunger 20 past the dispense position to the eject/load position as shown in FIG 6C. As the magnets M1 and M2 get closer and closer together the attraction force will increase to the point where it overpowers both springs 40' and 55 and locks pipette 200 in the eject position. One advantage of a pipette having a trigger is that a user can control the rate of drawing a liquid sample (including but not limited to an electroporation sample) up and also minimizing air bubbles in pipette tip 70.

[0066] FIGS 7A and 7B depict external views of one embodiment of a pipette device of the present disclosure and show portions of pipette body 300, lock 65, pipette end 55, electrode tip 60 and pipette plunger 20 with end 20a and handle 15. FIG. 7C depicts exemplary components that can be present in a pipette device of the present disclosure, according to some embodiments. Parts shown in FIG. 7C include detent 30, pipette plunger 20, magnet 1 and magnet 2, pipette body or housing 300 opened to show the external side 300a and internal side 300b, gripper 40, pipette spring 50, pipette end 55, magnet M3, lock 65 and electrode tip 65, according to one example embodiment.

[0067] FIGS. 8A-8H depict various components of a pipette device of the disclosure with regard to their location in the pipette device, according to one embodiment of the disclosure. FIG. 8A depicts pipette body 300 as part of the remainder pipette device which comprises a housing or shell inside which are comprised several pipette components. Pipette body 300 has an aperture on the top through which extends a plunger 20 located inside pipette body 300. Pipette body 300 may be made of plastic materials, although metals may also be used in the construction. FIG. 8B(i) depicts a pipette plunger 20 located inside pipette body 300 and FIG. 8B(ii) depicts a pipette plunger 20

according to one example embodiment. FIG. 8C(i) depicts a pipette end 55 located in a pipette device and FIG. 8C(ii) depicts an example pipette end 55 alone, according to one example embodiment. FIG. 8D(i) depicts an example lock 65 as located in a pipette device. Lock 65 secures pipette end 55 and pipette body 300. FIG. 8D(ii) depicts an example lock 65 alone. FIG. 8E(i) depicts an example detent 30 located inside pipette body 300 and FIG. 8E(ii) depicts detent 30 alone. FIG. 8F depicts two magnets M1 and M2 located inside pipette body 300. FIG. 8G(i) depicts an electrode tip 60 with respect to its location in a pipette device of the disclosure and FIG. 8G(ii) depicts an example electrode tip 65 alone. FIG. 8H(i) depicts a gripper 40 with respect to its location in a pipette device and FIG. 8H(ii) depicts the gripper alone according to one example embodiment.

[0068] One of skill in the art will note that these figures are exemplary embodiments and do not restrict the pipette devices of this disclosure to the illustrated embodiments in FIGS. 1-8H as shown herein and the present teachings encompass other devices as described.

[0069] In some embodiments, the present disclosure describes, a pipette device comprising: a pipette plunger; at least one pair of magnets; and at least one spring; wherein the pipette device is configured to reduce the force required by a user to aspirate, dispense, load and eject a pipette tip. In some embodiments, a pipette device of the disclosure can comprise two springs. In some embodiments, a pipette device of the disclosure may comprise three magnets.

[0070] In some embodiments a pipette according to the disclosure may further comprise a trigger. In some embodiments a pipette according to the disclosure may not comprise a trigger.

[0071] In some embodiments, a pipette device of the disclosure further comprises a detent. A detent may comprise a pair of cantilevers. In some embodiments the cantilevers may have a protrusion on each cantilever. In some embodiments, a pipette device of the disclosure may not comprise a detent.

[0072] A pipette device of the disclosure may further comprise one or more components including: a pipette plunger, an electrode tip, a gripper, a pipette end, a lock, at least one pipette body or at least one housing or a shell or a housing means. One or more of these components may be detachably attached to each other to form a pipette device. Detachable attachment can comprise complementary threaded means on each component that can be detachably attached and/or other male and female components that can interlock with each other.

[0073] In some embodiments, the present pipette devices uses lesser force to load and/or eject a pipette tip as compared to other pipettes used in currently available pipette devices and systems. In

some embodiments, a pipette device of the disclosure can lock in the fully depressed position, making loading a new (fresh) pipette tip easier.

[0074] In some embodiments, the pipette device described here is a positive displacement pipette. In some embodiments, the pipette device described here is a positive displacement pipette or a pipette with a disposable microsyringe tip where the plunger directly displaces the liquid.

[0075] A pipette of the disclosure may be used with any tip that can be used with an positive displacement pipette and may include tips such as but not limited to, disposable plastic tips, reusable plastic tips, pipetteman tips, microman tips, Gilson pipetteman tips, Rainin microman tips, and pipette tips that are compatible with electroporation devices such as pipette tips compatible for use with a Neon® Transfection System or a Neon™ Transfection System of Life Technologies Corporation.

[0076] Some embodiments describe a pipette device comprising: a pipette plunger; at least one pair of magnets comprising a first and a second magnet; and at least one spring; the pipette device configured to reduce the force required by a user to aspirate, dispense, load and eject a pipette tip to between about 1 lb and 5 lbs. In some embodiments, a pipette device as described above can further comprise a detent. In some embodiments, a pipette device as described above can further comprise a trigger. In some embodiments, a pipette device as described above further comprises a third magnet.

[0077] Some embodiments describe methods of using a pipette device of the disclosure and comprise: depressing a pipette plunger manually until it locks into a loading position; loading a new pipette tip by inserting the pipette into a pipette tip until it snaps on without the need to keep the pipette plunger depressed while inserting the pipette tip; aspirating a sample by pushing the pipette plunger up to an aspiration position (either by pushing on a trigger for a pipette having a trigger to push the plunger up to the aspirate position OR by loading a tip which generates force to move a pipette plunger to aspirate position in a pipette with a detent) and; depressing the pipette plunger to a dispense position to dispense aspirated sample; and ejecting a used pipette by pressing on the plunger. One or more of the following advantages may be realized by a user: a user needs much lesser force to load new pipette and/or a user needs much less force to eject a new pipette and/or a user needs no additional force and/or may have their hands/fingers free while loading a pipette by not having to keep the pipette plunger depressed into a locked position.

[0078] In some embodiments, in comparison to currently available pipettes in the market which requires about ~15lb of force for some users for loading and/or ejecting a pipette tip a pipette device of this disclosure having a trigger the force by a user for loading and/or ejecting a pipette tip is

reduced to ~4lb and for a pipette having a detent according to the present disclosure the force for loading and/or ejecting a tip is reduced to ~8lb.

[0079] In some embodiments, the present pipette devices uses lesser force to aspirate up a sample and/or to dispense a sample as compared to other pipettes used in currently available pipette devices and systems.

[0080] In some embodiments, a method of using a pipette of the disclosure can comprise: depressing a pipette plunger manually until it locks into a loading position; loading a new pipette tip by inserting the pipette into a pipette tip until it snaps on without the need to keep the pipette plunger depressed while inserting the pipette tip; aspirating a sample by pushing the pipette plunger up to an aspiration position; depressing the pipette plunger to a dispense position to dispense aspirated sample; and ejecting the pipette tip a used pipette by pressing on the plunger. In some embodiments of this method, the pipette device according to the present disclosure reduces the force required by a user to aspirate, dispense, load and eject a pipette tip as compared to currently available pipette devices. In some embodiments of this method, the pipette device of the disclosure, reduces the force required by the user for loading and ejecting a pipette tip from about ~15lb of force to about ~5lb of force. In some embodiments of this method, the pipette device of the disclosure, reduces the force required by the user for loading and ejecting a pipette tip from about ~15lb of force to about ~8lb of force.

[0081] FIG. 9 describes an exemplary embodiment of an electroporation system 1000 of the disclosure comprising: a pulse generator 10; a pipette device 100 or 200 or other such as described in the embodiments above comprising at least one pipette plunger, at least one pair of magnets, at least one spring; an electrode; and a pipette tip removably attachable to the pipette device in electrical communication with at least one electrode. A pipette device of the disclosure, in some embodiments, may further comprise a detent as described above. A pipette device of the disclosure, in some embodiments, may further comprise a trigger. An electroporation system 1000 may also comprise a sample reservoir and an electrolytic solution reservoir (both depicted as 400) and another electrode 500 all in electrical communication with each other. An electroporation system 1000 may also comprise a pipette stand or pipette rack 12 (not expressly depicted here but see FIGS. 10 and 11A-E) to rest a pipette device 100/200/other. Electroporation systems 1000 of the disclosure may also comprise a computer system comprising a computer readable medium for setting parameters relating to electroporation and may include a graphical user interface (GUI) for a user to navigate steps of electroporation protocols (not expressly shown). In some embodiments all these

components of an electroporation system may be contained in a single unit. In some embodiments all these components of an electroporation system may be contained in two or more units.

[0082] In some embodiments, pipette devices as disclosed herein may be used with electroporation devices and systems where the pipette tip itself can serve as an electrode and thereby apply and electric current to the sample without the need of a separate structure serving as the electrode.

[0083] A pipette device of the disclosure is compatible and may be used with electroporation devices, systems and apparatus described in U.S. Patent Application Serial No. 13/060,682 (Atty. Docket No. LT00013), filed July 13, 2011, claiming priority to Korean Patent Application KR 10-2008-0034744 filed Apr. 15, 2008, entitled "Pipette Tip for Electroporation Device", which applications are incorporated herein by reference in its entirety and to U.S. Patent Application Serial No. 10/560,301, filed May 30, 2007, (Atty. Docket No. LT00012), claiming priority to Korean patent Application's KR 10-2004-0043312 filed Jun 12, 2004 and KR10-2004-0088245, filed Nov 2, 2004, the entire contents of which are incorporated herein by reference. In some embodiments, electroporation devices that may be used with a pipette device may be a Neon® transfection system of Life Technologies™.

[0084] FIG. 10 describes one example configuration of an electroporation system 1000 of the disclosure comprising a pipette device such as but not limited to 100 or 200 as described in the embodiments above, and a pipette stand or pipette rack 12, into which a pipette device 100 or 200 may be removably placed. Pipette stand 12 can be in electrical contact via cable 1 with an electroporation device 600 comprising at least a pulse generator 10, and optionally a computer system comprising a display screen 13 (such as but not limited to an LCD) or a monitor 13 and a computer readable medium for setting parameters relating to electroporation and may include a graphical user interface (GUI) for a user to navigate steps of electroporation protocols (not expressly shown). Electroporation device 600 or alternatively the system 1000 can further comprise a sample reservoir and an electrolytic solution reservoir and one or more additional electrodes all in electrical communication with each other. In some embodiments, pipette stand or pipette rack 12 may comprise a magnetic detector component that can recognize a magnetic component such as magnet M3 in a pipette device 100 or 200 (not expressly depicted here) that is operable to sense the presence of the pipette in or out of the rack and communicate this to electroporation device 600. The electroporation device 600 will not apply an electric current to the pipette stand 12 while the magnetic detector component does not sense the presence of a pipette device 100 or 200. For safety the pipette stand will not be powered until the pipette is first detected in the pipette stand.

[0085] In some embodiments, a system as depicted in FIG. 10 advantageously allows a pipette device 100/200 in pipette rack 12, as well as samples, sample reservoir and electrolyte reservoir components to be placed in a sterile chamber (such as a laminar flow hood) needed for safe electroporation and preventing contamination while placing the bulkier electroporation device 600 outside the sterile chamber providing convenience to a user.

[0086] FIGS. 11A-11E depict various configurations of electroporation systems 1000 comprising a pipette device 100/200 (shown as body 300 and optional handle 15) as described in the embodiments above. The configurations depicted herein are illustrative examples of how a pipette device of the disclosure may be placed at various positions into an electroporation system. One of skill in the art, in light of this disclosure, will realize that other configurations may be possible and that the teachings are not limited to these configurations shown.

[0087] One of skill in the art will also recognize that the embodiments shown in FIGS 10, 11A-11E are not limited to electroporation systems and may include any system wherein a pipette of the disclosure may be used. These system configurations may comprise any device/system with a pipette stand for resting a pipette of the disclosure and may optionally include a GUI screen, a computer screen, an LCD display screen, or even an instrument for performing any experiment attached to the pipette rack.

[0088] One or more of these configurations provide different ergonomic advantages to users such as but not limited to: having a pipette rack/stand 12 to rest a pipette during an experiment; ability to use free up hands while resting a pipette; ease of picking a pipette device using a handle; having a GUI screen at an eye level; and/or having the ability to keep a pipette in a sterile chamber (e.g., the embodiment shown in FIG. 10).

[0089] FIG. 11A depicts four views of one embodiment of an electroporation system 1000 wherein a pipette device 100 or 200 (shown as pipette body 300) as described herein is disposed on a pipette stand 12 located on one side of electroporation system 1000. FIG. 11A (i) is a front perspective view is seen where a pipette body 300 is shown inserted into a pipette stand 12 and a screen 10 adjacent to the pipette stand depicts a display screen (e.g. an LCD screen) that may have a GUI on it. 15 depicts a handle on the pipette body 300 that may be used by a user to lift the pipette out. FIG. 11A (ii) is a side perspective view of the device of FIG 11A (i); FIG. 11A (iii) is a top perspective view of the device of FIG 11A (i); and FIG. 11A (iv) is a top, front and side perspective view of the device of FIG 11A (i).

[0090] FIG. 11B depicts four views of one embodiment of an electroporation system 1000 wherein a pipette body 300 as described herein is disposed on a pipette stand 12 located on one side of electroporation system 1000. FIG. 11B (i) is a front perspective view is seen where a pipette body 300 is shown inserted into a pipette stand 12 and a screen 10 adjacent to the pipette stand depicts an LCD screen that may have a GUI on it. FIG. 11B (ii) is a side perspective view of the device of FIG 11B(i) and 15 depicts a handle on the pipette body 300 that may be used by a user to lift the pipette out; FIG. 11B (iii) is a top perspective view of the device of FIG 11B (i); and FIG. 11B (iv) is a top, front and side perspective view of the device of FIG 11B(i).

[0091] FIG. 11C depicts four views of one embodiment of an electroporation system 1000 wherein a pipette body 300 as described herein is disposed on a pipette stand 12 located on one side of electroporation system 1000. FIG. 11C (i) is a front perspective view is seen where a pipette body 300 is shown inserted into a pipette stand 12 and a screen 10 adjacent to the pipette stand depicts an LCD screen that may have a GUI on it. FIG. 11C (ii) is a side perspective view of the device of FIG 11C(i); FIG. 11C (iii) is a top perspective view of the device of FIG 11C (i); and FIG. 11C (iv) is a top, front and side perspective view of the device of FIG 11C(i) showing handle 15 that may be used by a user to lift the pipette out.

[0092] FIG. 11D depicts four views of one embodiment of an electroporation system 1000 wherein a pipette body 300 as described herein is disposed on a pipette stand 12 located embedded into one side of electroporation system 1000. FIG. 11D (i) is a front perspective view is seen where a pipette body 300 is shown inserted into a pipette stand 12 and a screen 10 adjacent to the pipette stand depicts an LCD screen that may have a GUI on it. FIG. 11D (ii) is a side perspective view of the device of FIG 11D(i) and 15 depicts a handle on the pipette body 300 that may be used by a user to lift the pipette out; FIG. 11D (iii) is a top perspective view of the device of FIG 11D (i); and FIG. 11D (iv) is a top, front and side perspective view of the device of FIG 11D(i).

[0093] FIG. 11E depicts four views of one embodiment of an electroporation system 1000 wherein a pipette body 300 as described herein is disposed on a pipette stand 12 located on one side of electroporation system 1000. FIG. 11E (i) is a front perspective view is seen where a pipette body 300 is shown inserted into a pipette stand 12 and a screen 10 adjacent to the pipette stand depicts an LCD screen that may have a GUI on it. FIG. 11E (ii) is a side perspective view of the device of FIG 11E(i) and 15 depicts a handle on the pipette body 300 that may be used by a user to lift the pipette out; FIG. 11E (iii) is a top perspective view of the device of FIG 11E (i); and FIG. 11E (iv) is a top, front and side perspective view of the device of FIG 11E(i).

[0094] In some embodiments, the present disclosure describes an electroporation system comprising: a pulse generator; a sample reservoir; an electrolyte reservoir; and a pipette device comprising: a pipette plunger; at least a first and a second magnet; and at least one spring. In some embodiments, an electroporation system may further comprise a pipette device further comprising a detent. In some embodiments, an electroporation system may further comprise a pipette device further comprising a trigger. In some embodiments, an electroporation system may further comprise a pipette device further comprising a third magnet. In some embodiments, an electroporation system may further comprise a pipette rack and a cable means to electrically connect the pipette rack to the other components.

[0095] Some embodiments describe methods of using a pipette device of the disclosure and comprise: methods for performing electroporation using an electroporation system comprising a pipette device are described. A method of the disclosure may comprise loading on to a pipette device of the disclosure an electroporation compatible pipette tip by depressing a pipette plunger manually until it locks into a loading position; loading the electroporation compatible pipette tip by inserting the pipette into a pipette tip until it snaps on without the need to keep the pipette plunger depressed while inserting the pipette tip; aspirating a sample containing cells and macromolecules to be electroporated into the cells by pushing the pipette plunger up to an aspiration position (either by pushing on a trigger for a pipette having a trigger to push the plunger up to the aspirate position OR by loading a tip which generates force to move a pipette plunger to aspirate position in a pipette with a detent); applying/providing an electrical pulse to the cells in the pipette tip to allow electroporation and; depressing the pipette plunger to a dispense position to dispense aspirated sample comprising electroporated cells; and ejecting a used pipette tip by pressing on the pipette plunger (or trigger).

[0096] In some embodiments a method may also comprise: inserting the pipette into a pipette stand prior to providing/applying an electrical pulse; begin electroporation by applying an electrical current (this may be done mechanically by a user or automatically by pressing for example a switch on an electroporation system such a “Run” button on a GUI); removing the pipette from the pipette stand; dispensing the electrophoresed sample from the pipette tip into one or more container means for further sample processing; and depressing the pipette plunger until the used pipette tip ejects and the pipette returns to its locked position. Electroporation of cells located in a sample within a pipette tip of an electroporation system of the disclosure causes cell membranes to become more permeable thereby facilitates the introduction of macromolecules, molecular probes, drugs, DNA, RNA,

bacteria, genes, protein material, cells, or any other suitable substance which normally cannot penetrate a cell membrane, into a cell.

[0097] A method may further comprise, removing the pipette from the pipette stand; dispensing the electrophoresed sample from the pipette tip into one or more container means for further sample processing; and depressing the pipette plunger until the used pipette tip ejects and the pipette returns to its locked position.

[0098] In some embodiments of a method of the disclosure, once a sample is drawn from a sample reservoir into a pipette tip, a sample reservoir is replaced with a reservoir containing an electrolytic solution. In some embodiments, applying an electric current to the sample located in a pipette tip of the electroporation system comprises applying electrical current to a plunger located within the body of the pipette tip and to an electrode contacting a sample in a sample reservoir or an electrolytic solution in an electrolytic solution reservoir such that any cell located in the sample drawn into the pipette tip may be electroporated by passing a current between the two electrodes and through any cells located between the two electrodes.

[0099] 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. 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. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

CLAIMS

WHAT IS CLAIMED IS:

1. A pipette device comprising:
a pipette plunger;
at least one pair of magnets comprising a first and a second magnet; and
at least one spring;
the pipette device configured to reduce the force required by a user to aspirate, dispense, load and eject a pipette tip to between about 1 lb and 5 lbs.
2. The pipette device of claim 1 further comprising a detent.
3. The pipette device of claim 1 further comprising a trigger.
4. The pipette device of claim 1, further comprising a third magnet.
5. A method of using a pipette of claim 1 comprising:
depressing a pipette plunger manually until it locks into a loading position;
loading a new pipette tip by inserting the pipette into a pipette tip until it snaps on without the need to keep the pipette plunger depressed while inserting the pipette tip;
aspirating a sample by pushing the pipette plunger up to an aspiration position;
depressing the pipette plunger to a dispense position to dispense aspirated sample; and
ejecting the pipette tip a used pipette by pressing on the plunger.
6. The method of claim 5, wherein the pipette device reduces the force required by a user to aspirate, dispense, load and eject a pipette tip as compared to currently available pipette devices.
7. The method of claim 6, wherein the pipette device reduces the force required by the user for loading and ejecting a pipette tip from about ~15lb of force to about ~5lb of force.
8. The method of claim 6, wherein the pipette device reduces the force required by the user for loading and ejecting a pipette tip from about ~15lb of force to about ~8lb of force.

9. A electroporation system comprising:
 - a pulse generator;
 - a sample reservoir;
 - an electrolyte reservoir; and
 - a pipette device comprising:
 - a pipette plunger;
 - at least a first and a second magnet; and
 - at least one spring.
10. The electroporation system of claim 9, wherein the pipette device further comprises a detent.
11. The electroporation system of claim 9, wherein the pipette device further comprises a trigger.
12. The electroporation system of claim 9, wherein the pipette device further comprises a third magnet.
13. The electroporation system of claim 9, further comprising a pipette rack and a cable means to electrically connect the pipette rack to the other components.

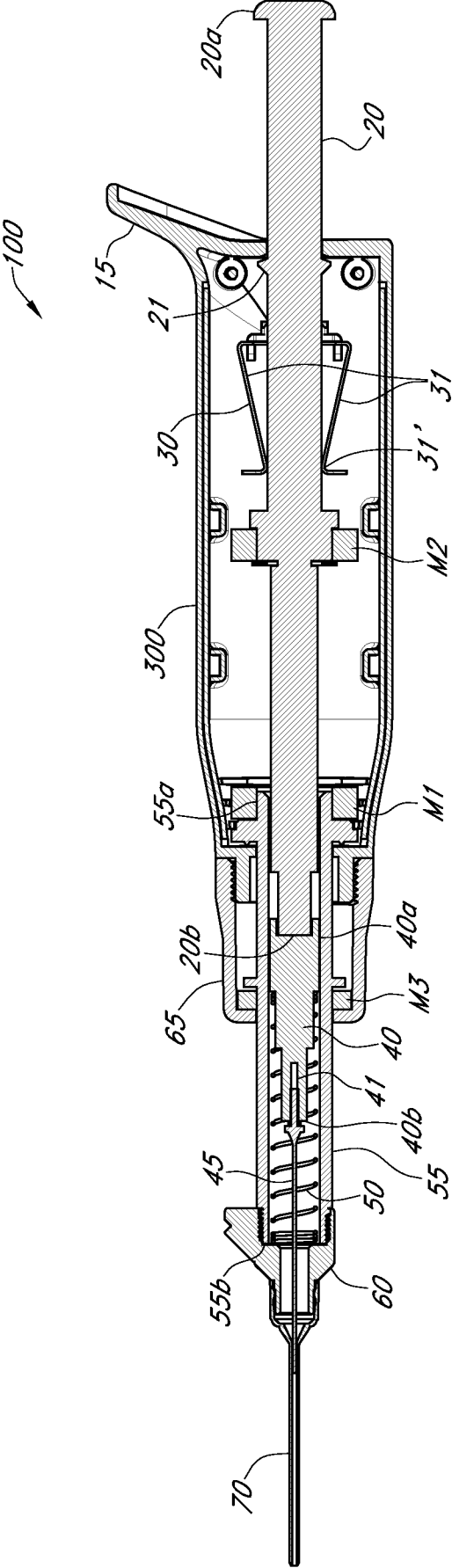


FIG. 1

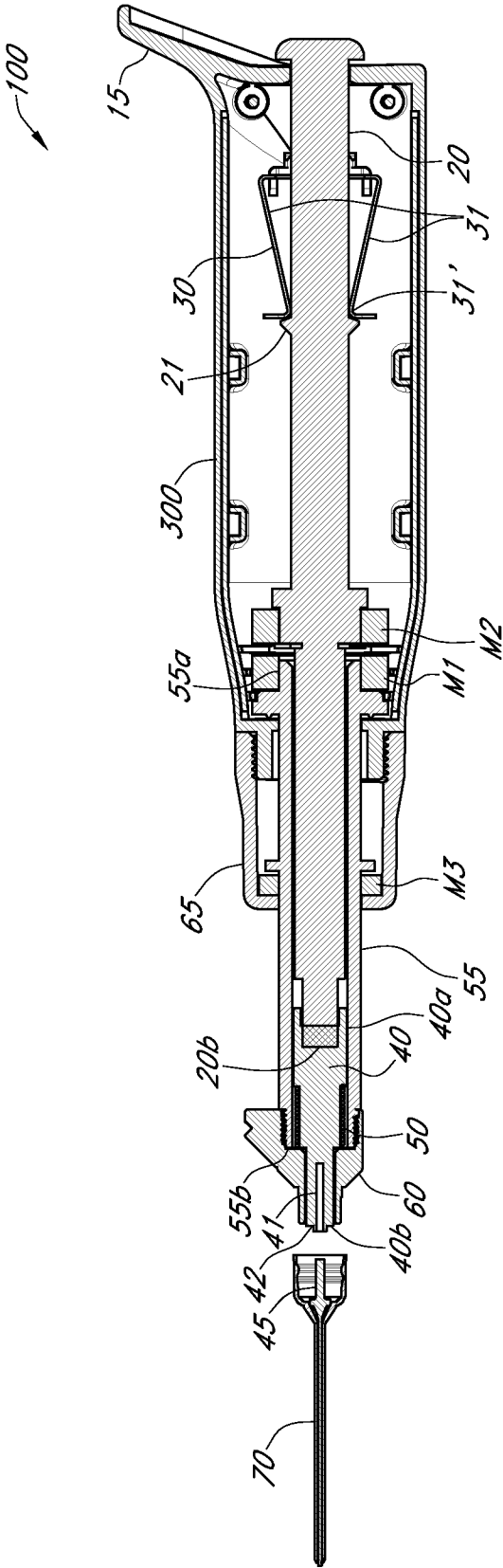


FIG. 2A

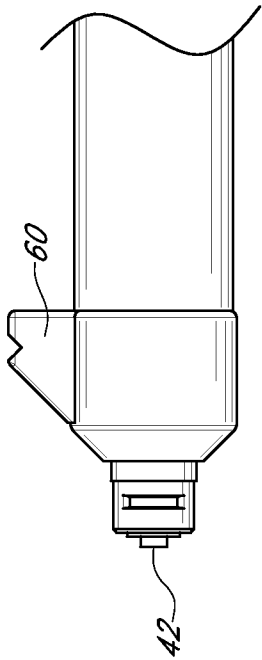


FIG. 2B

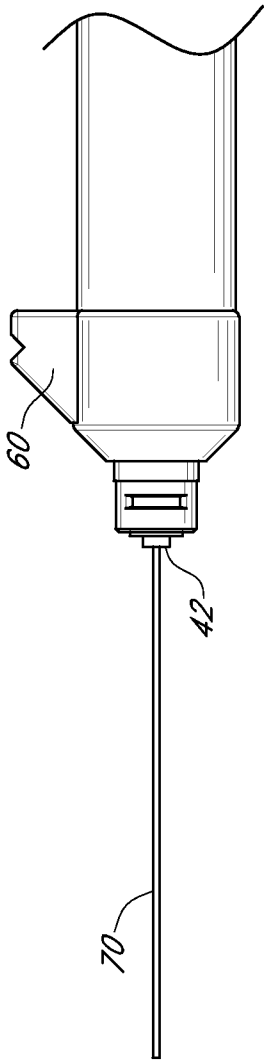


FIG. 2C

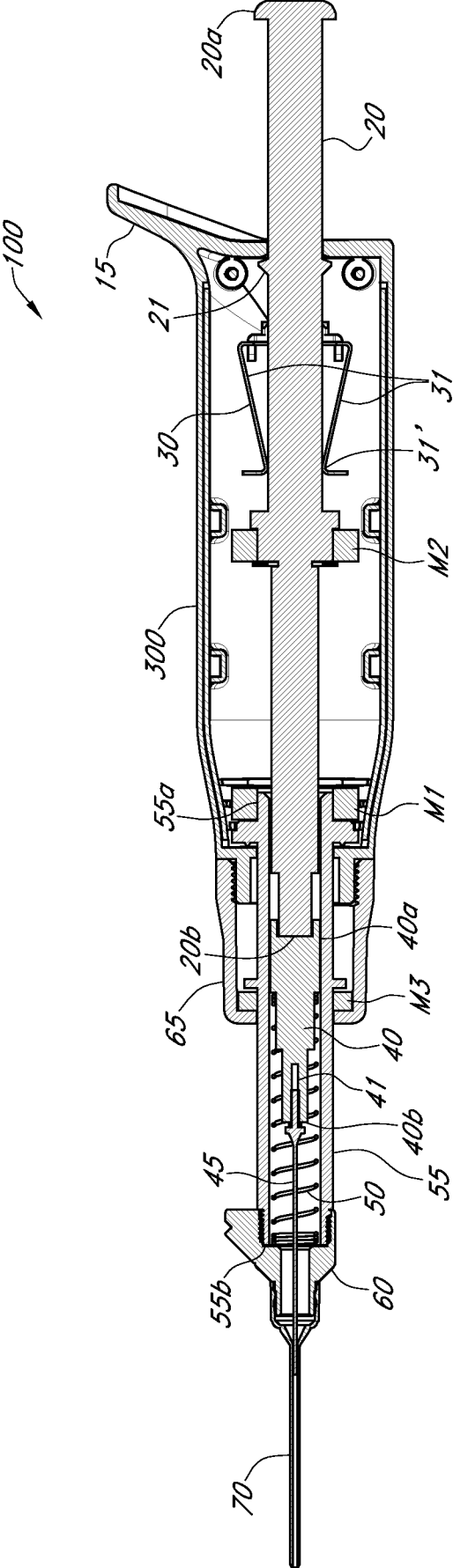


FIG. 3A

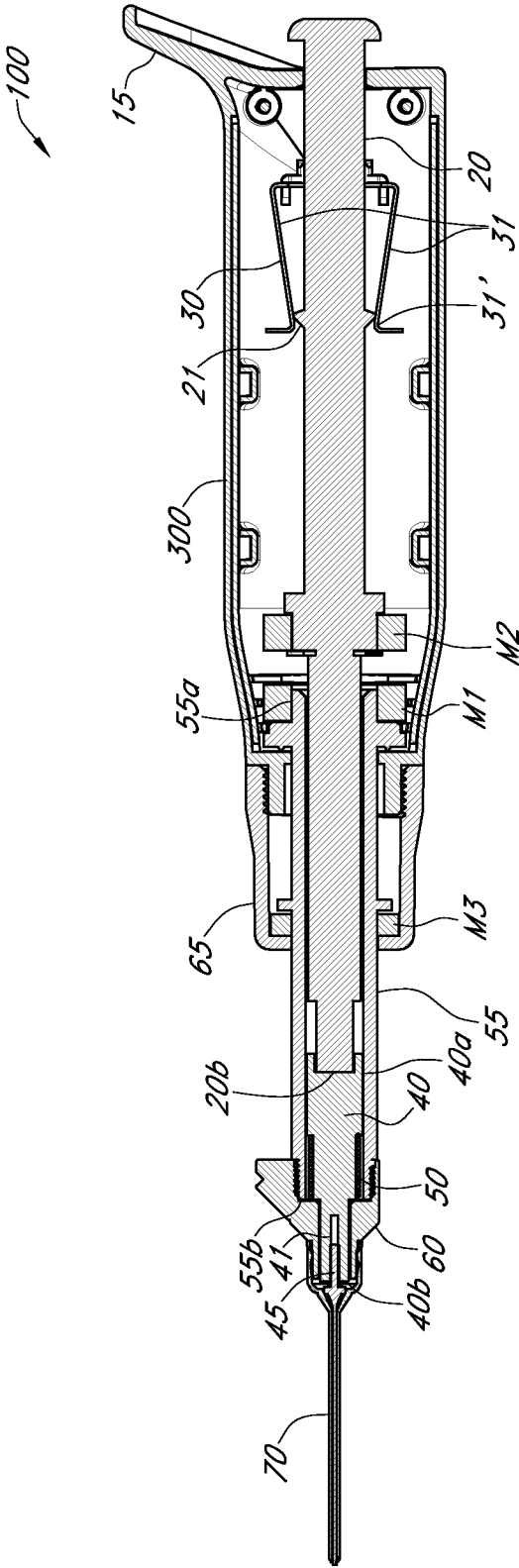


FIG. 3B

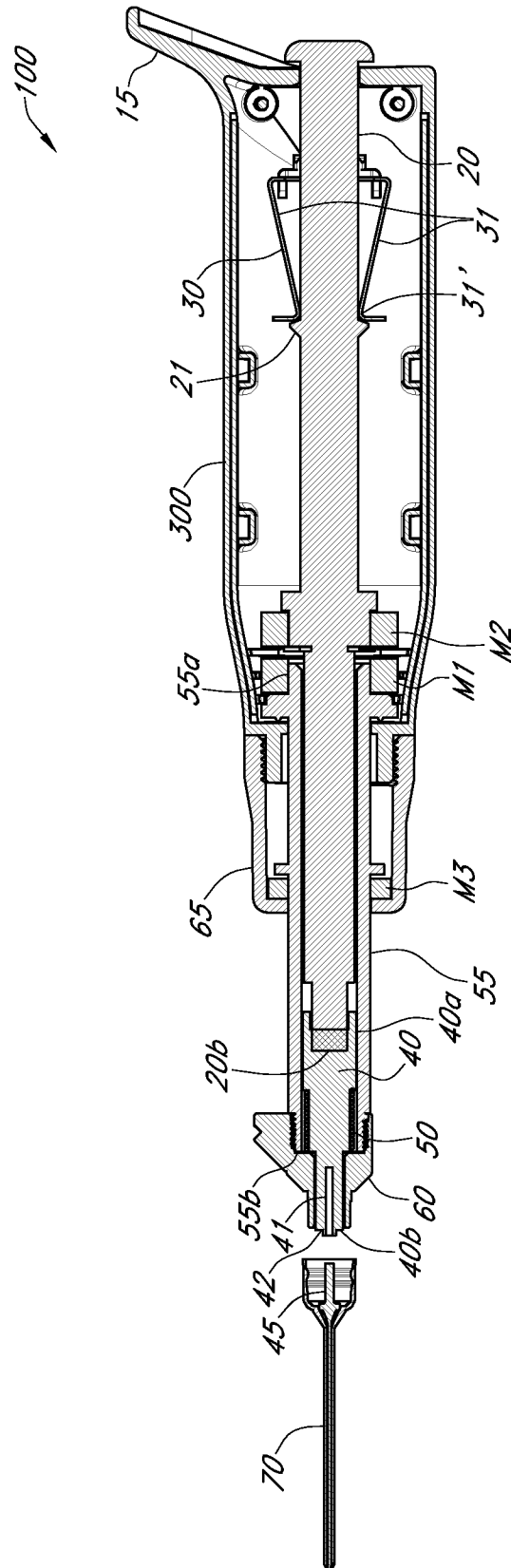


FIG. 3C

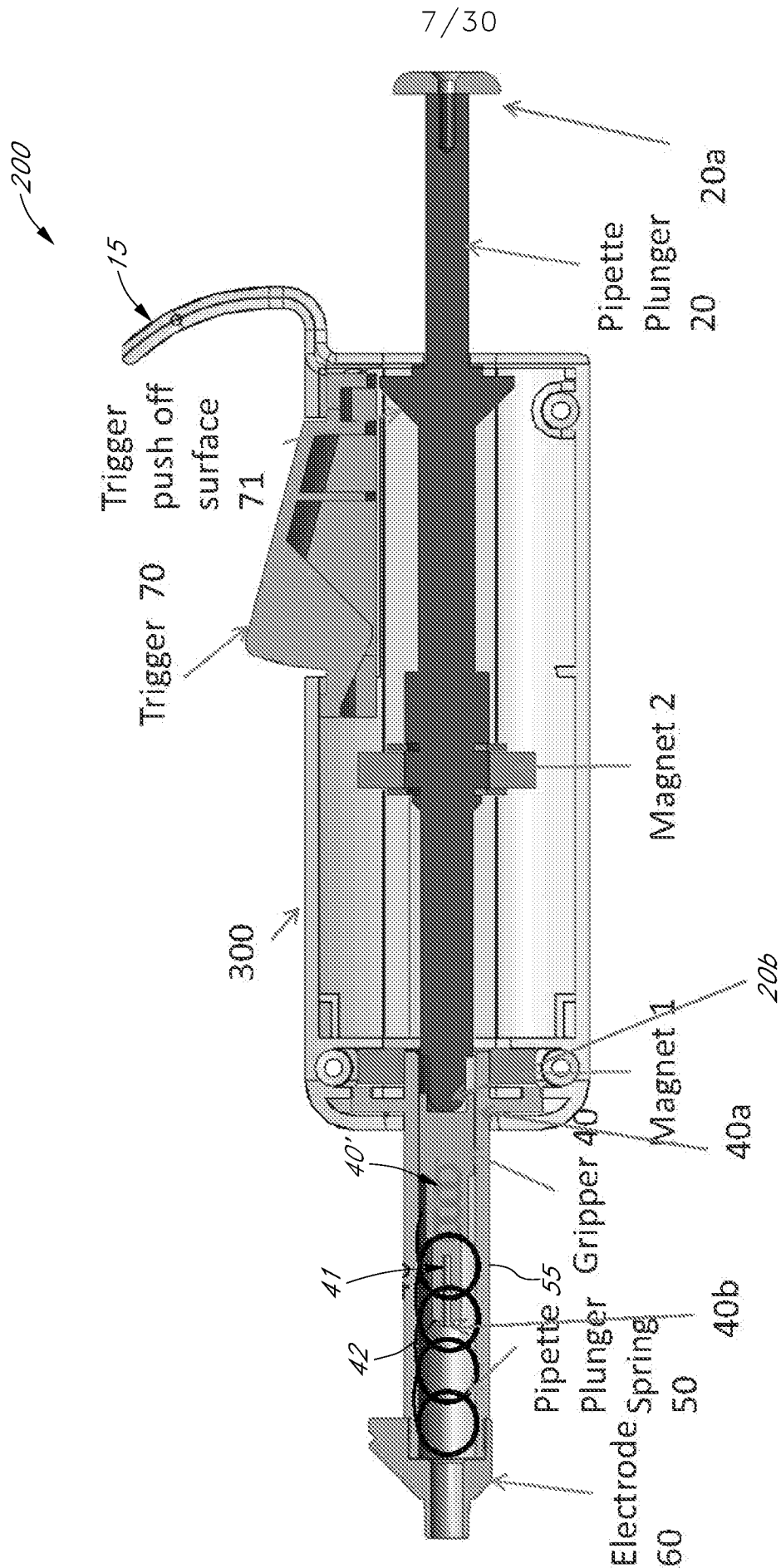


FIG. 4

8/30

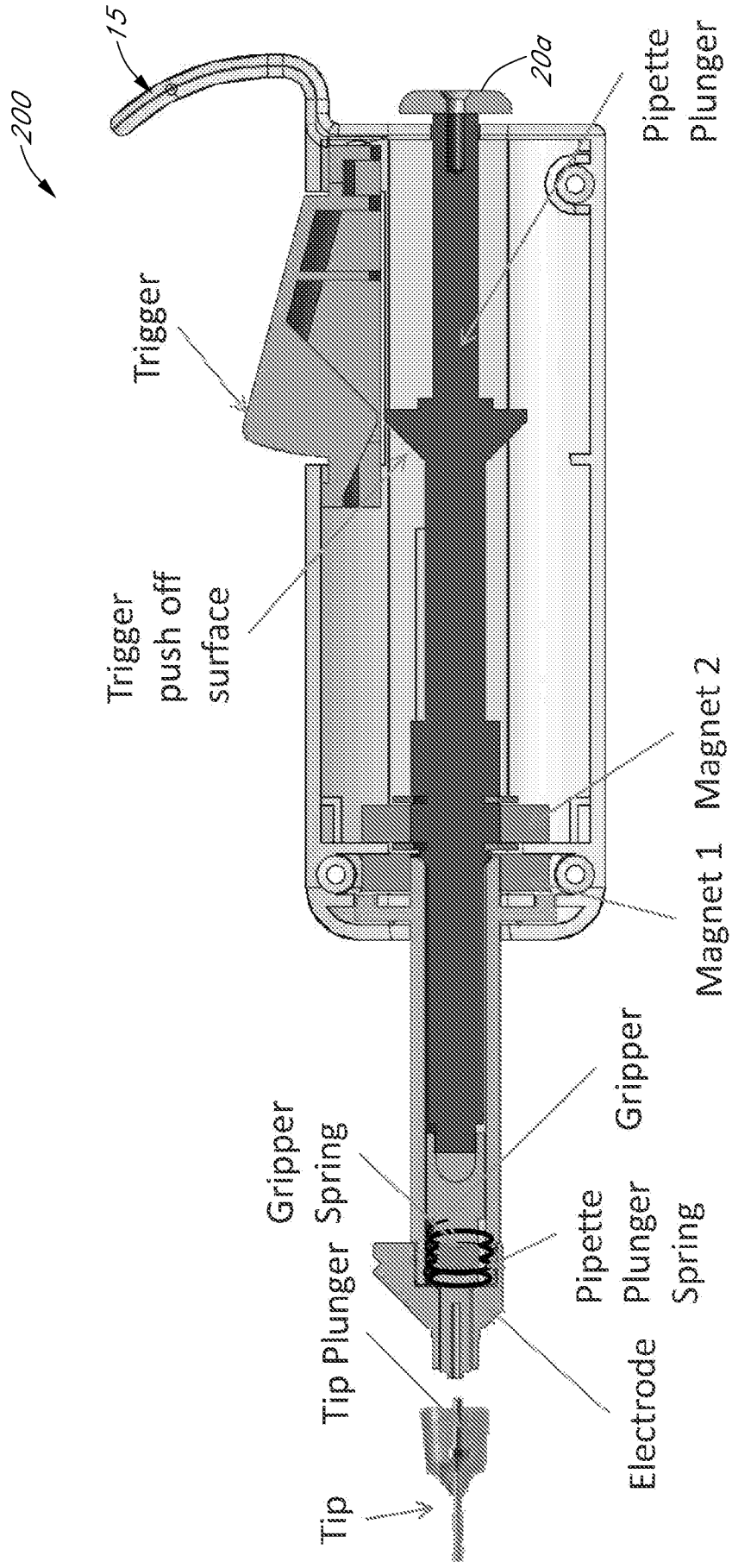


FIG. 5A

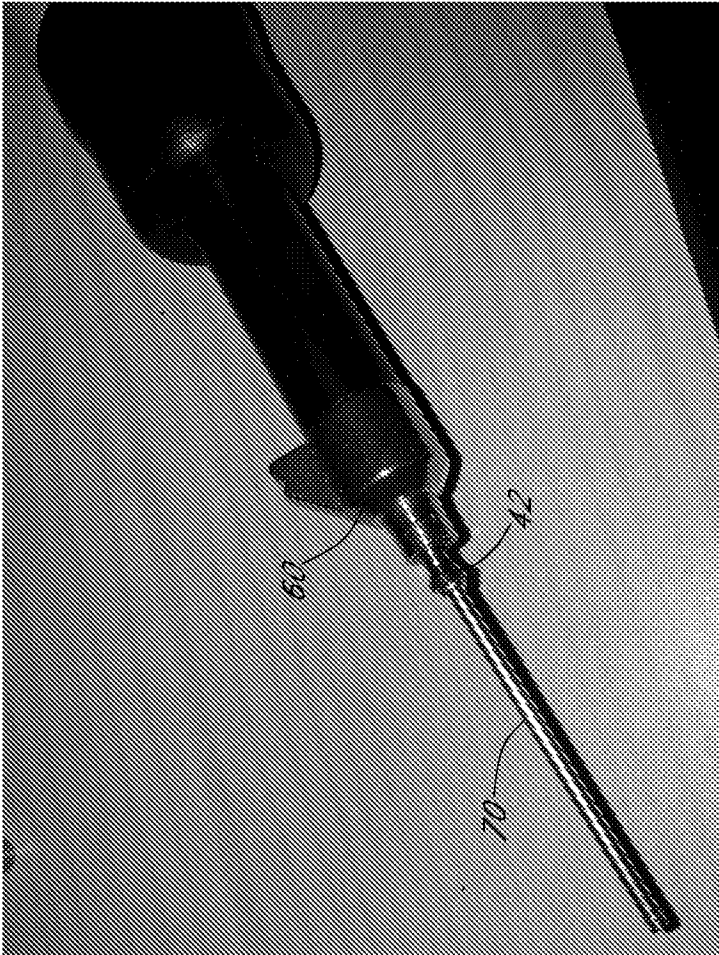


FIG. 5C



FIG. 5B

42

10/30

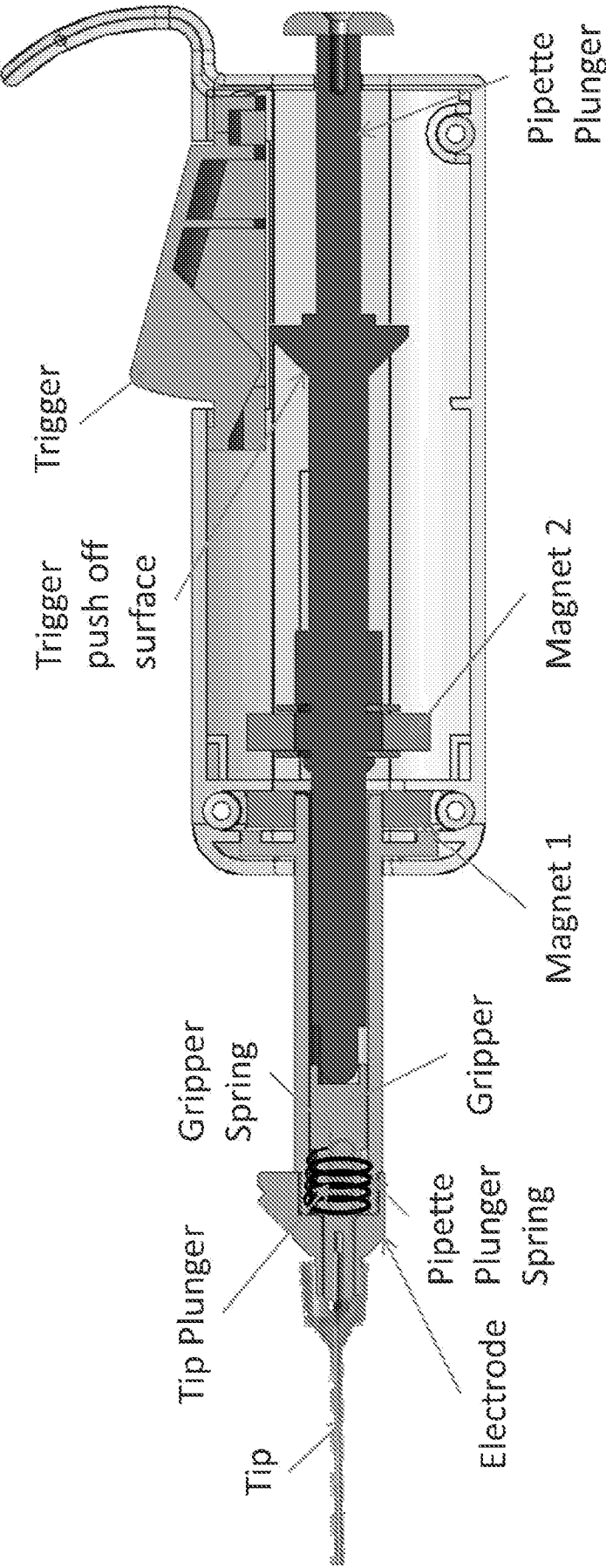


FIG. 6A

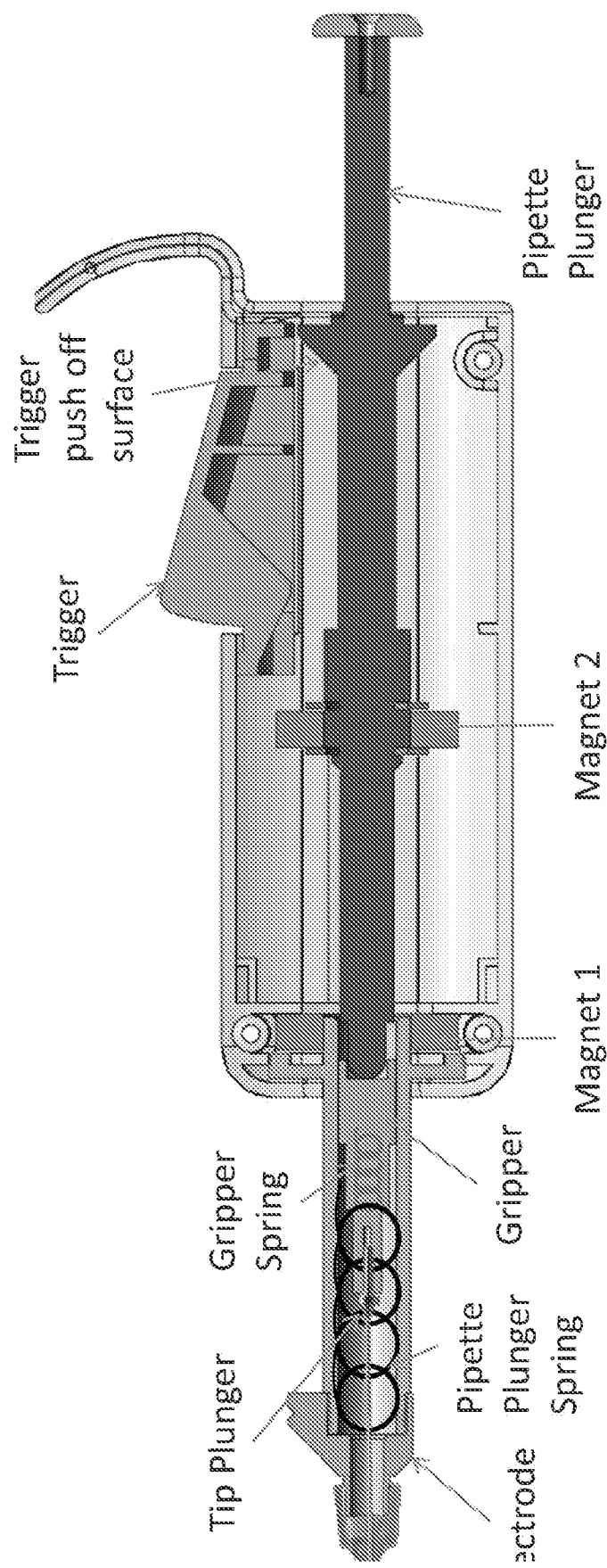


FIG. 6B

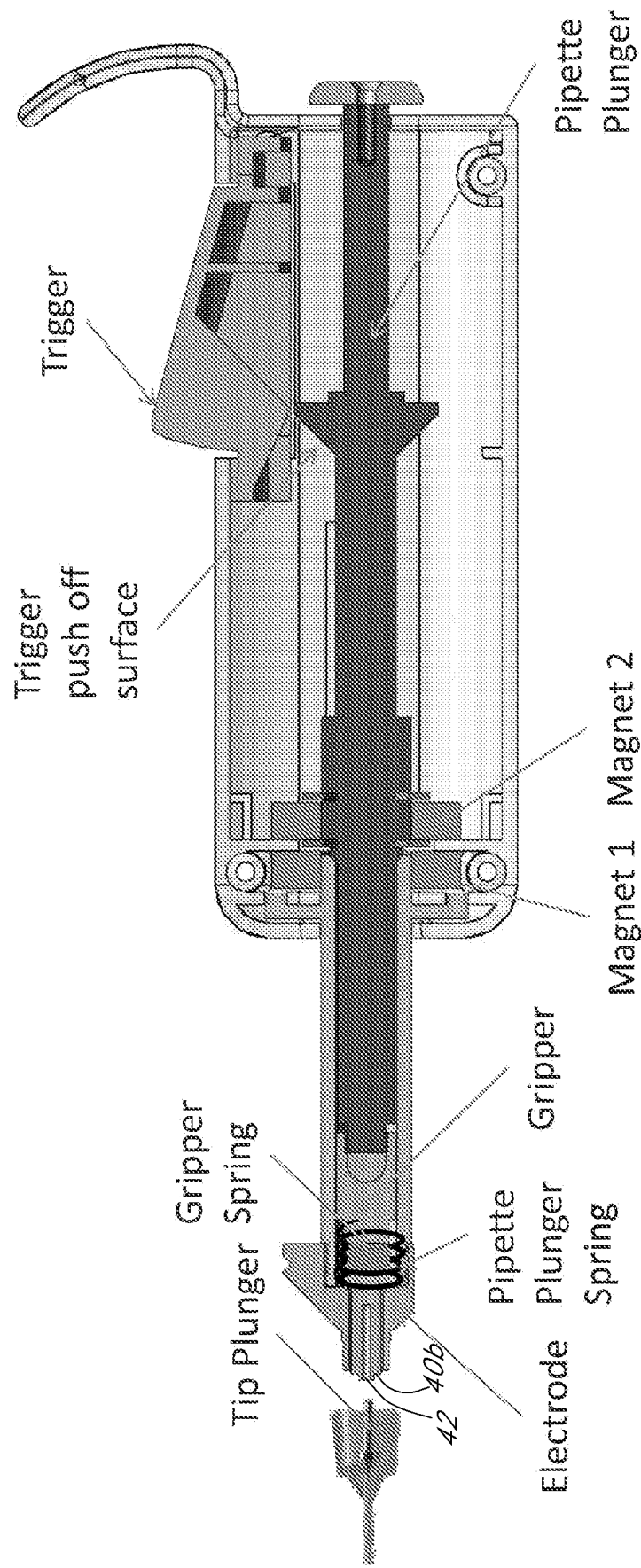


FIG. 6C

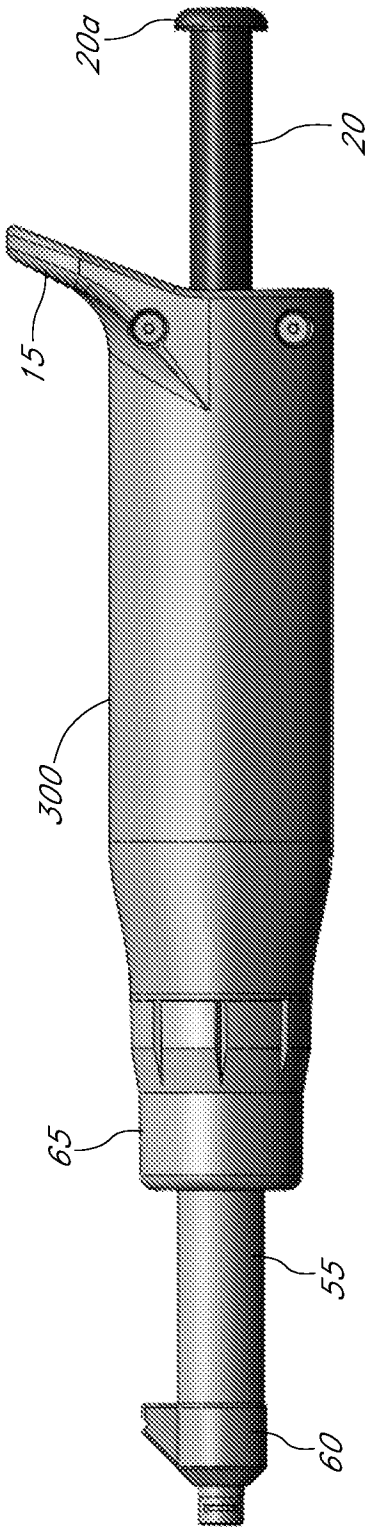


FIG. 7A

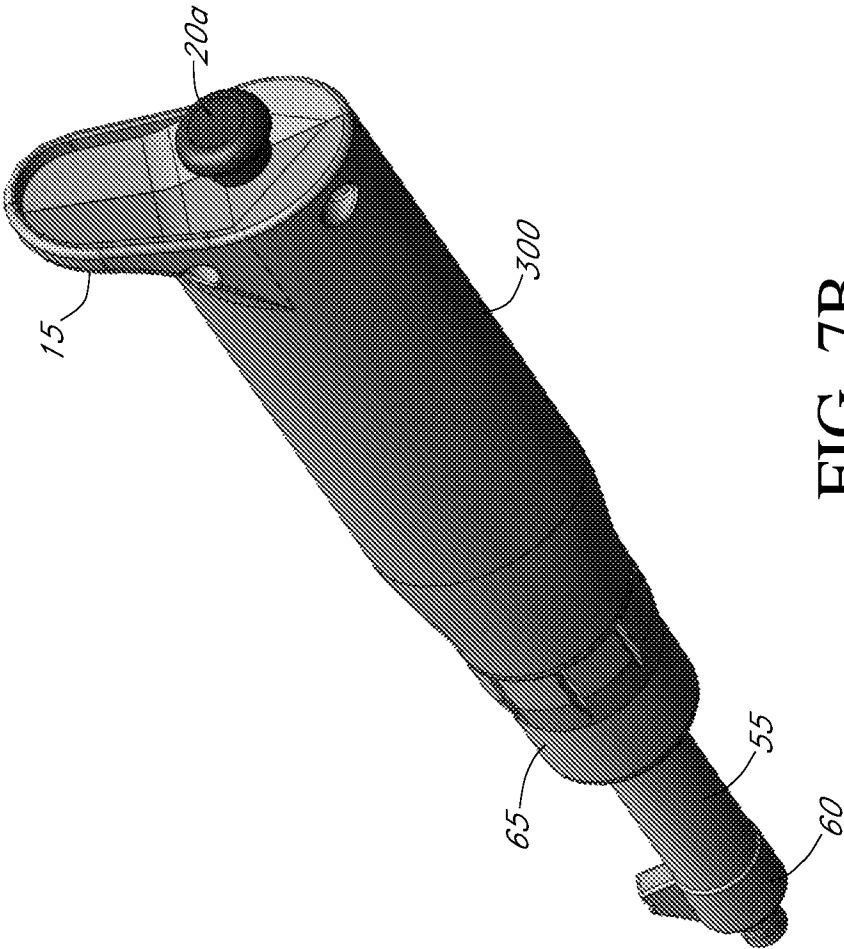


FIG. 7B

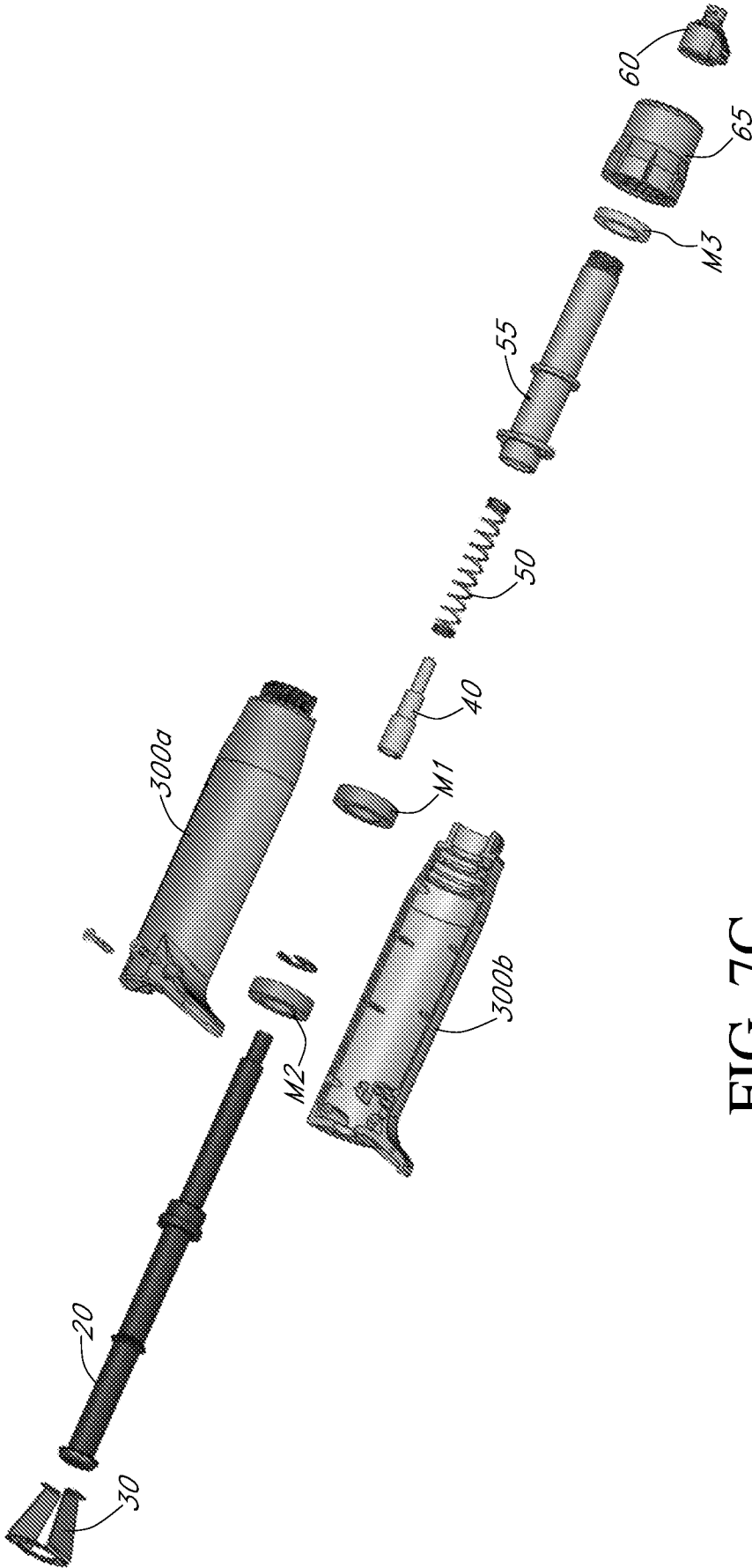


FIG. 7C

16/30

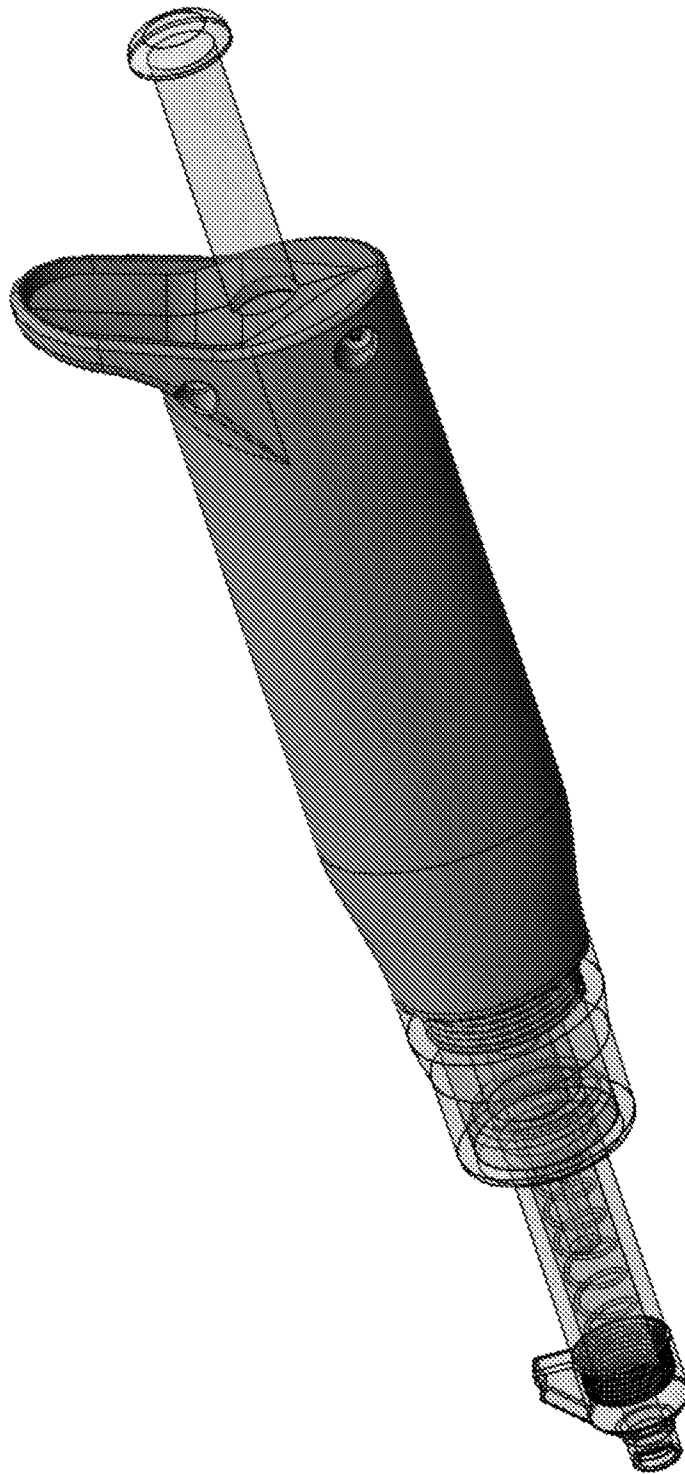


FIG. 8A

17/30

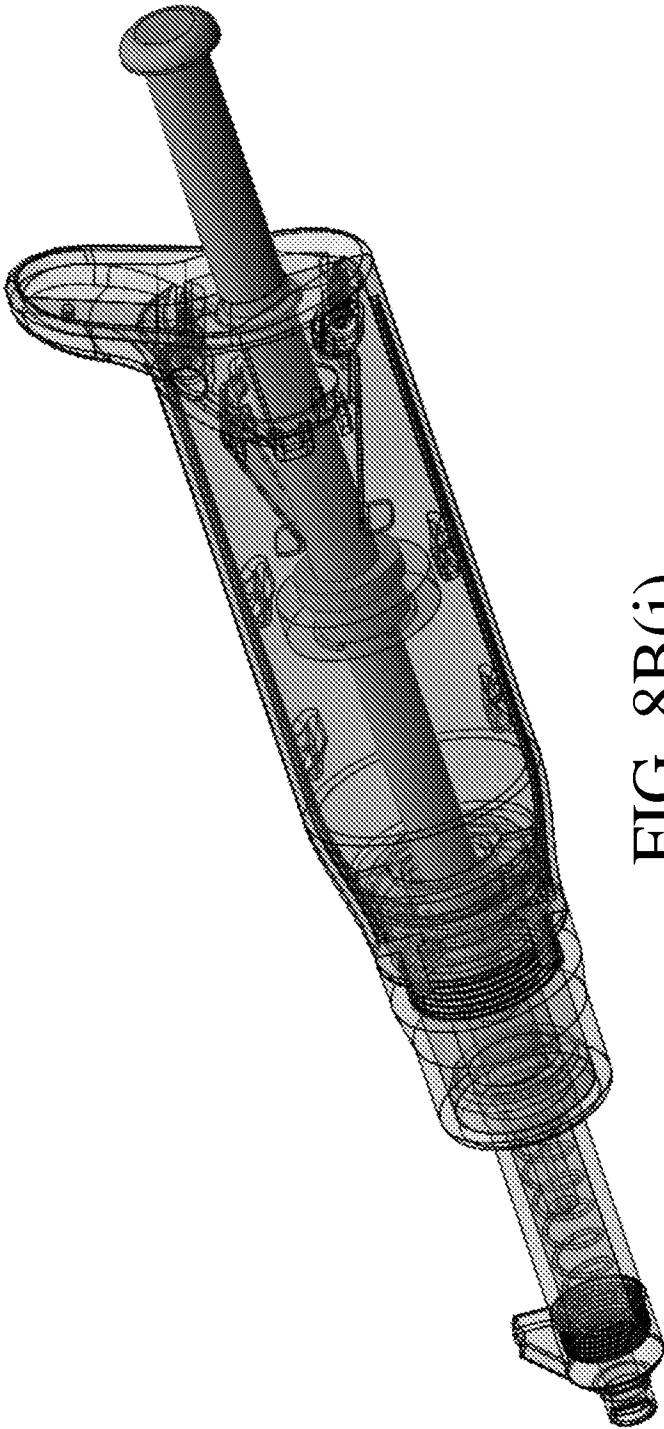


FIG. 8B(i)

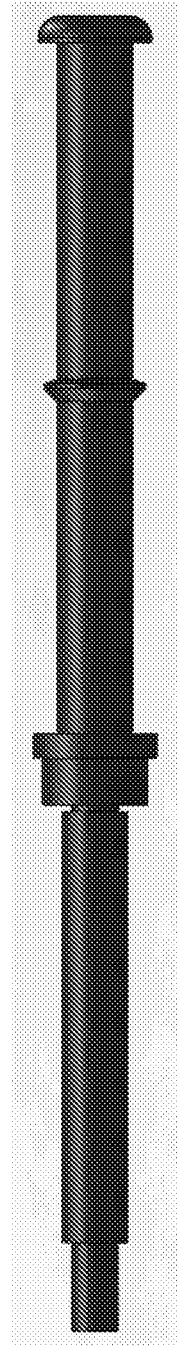


FIG. 8B(ii)

18/30

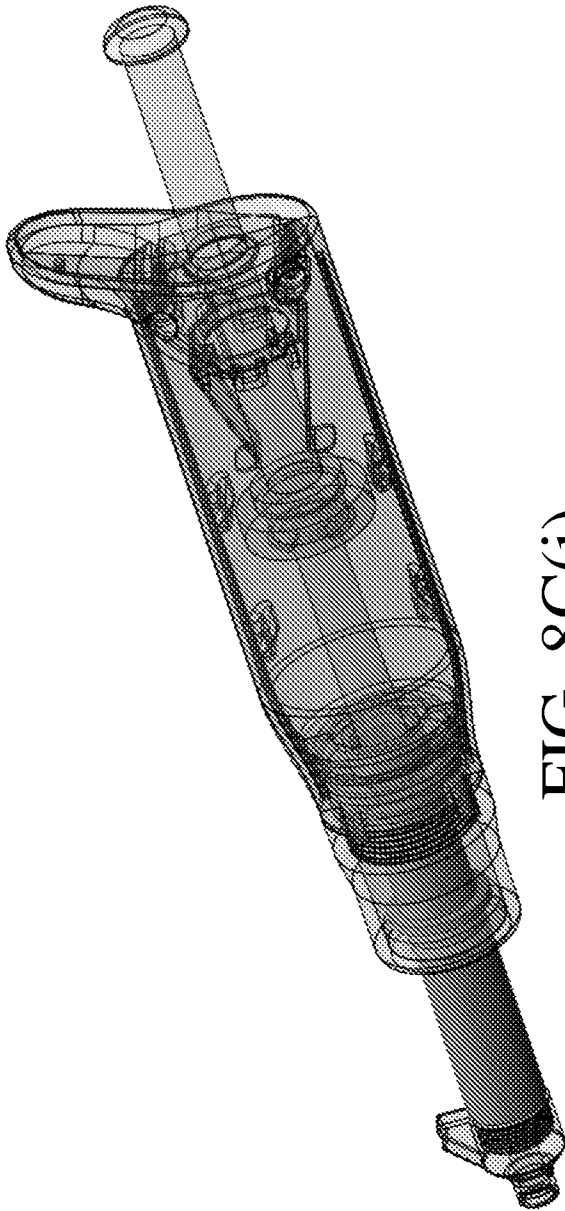


FIG. 8C(i)

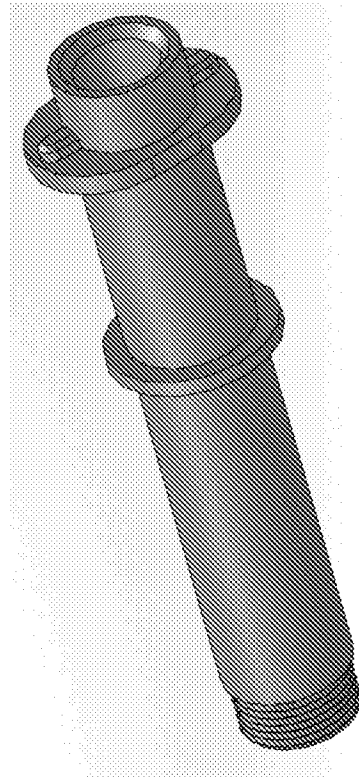


FIG. 8C(ii)

19/30

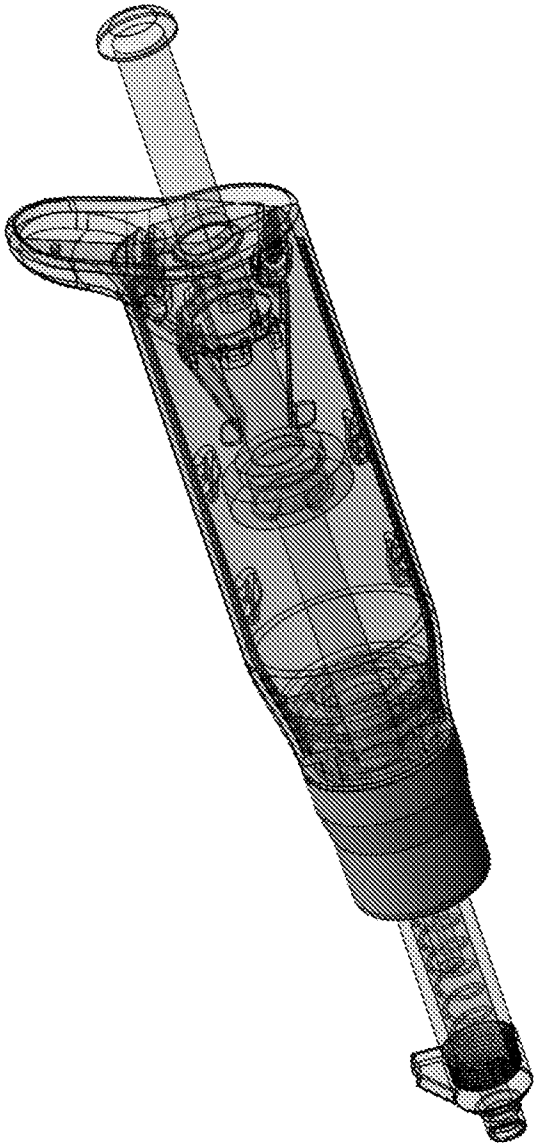


FIG. 8D(i)

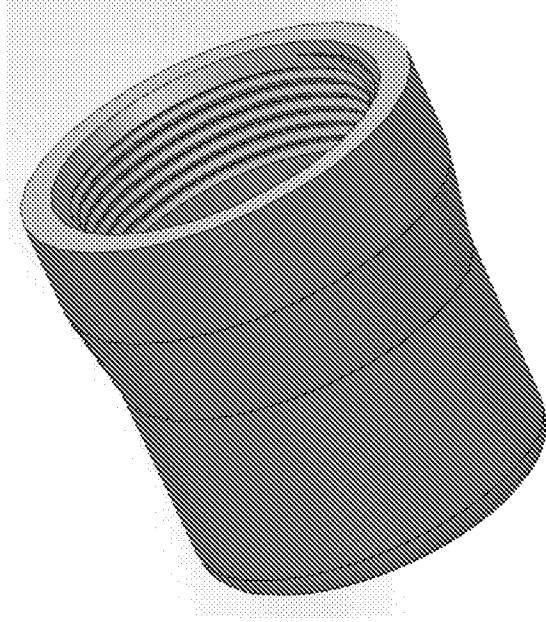


FIG. 8D(ii)

20/30

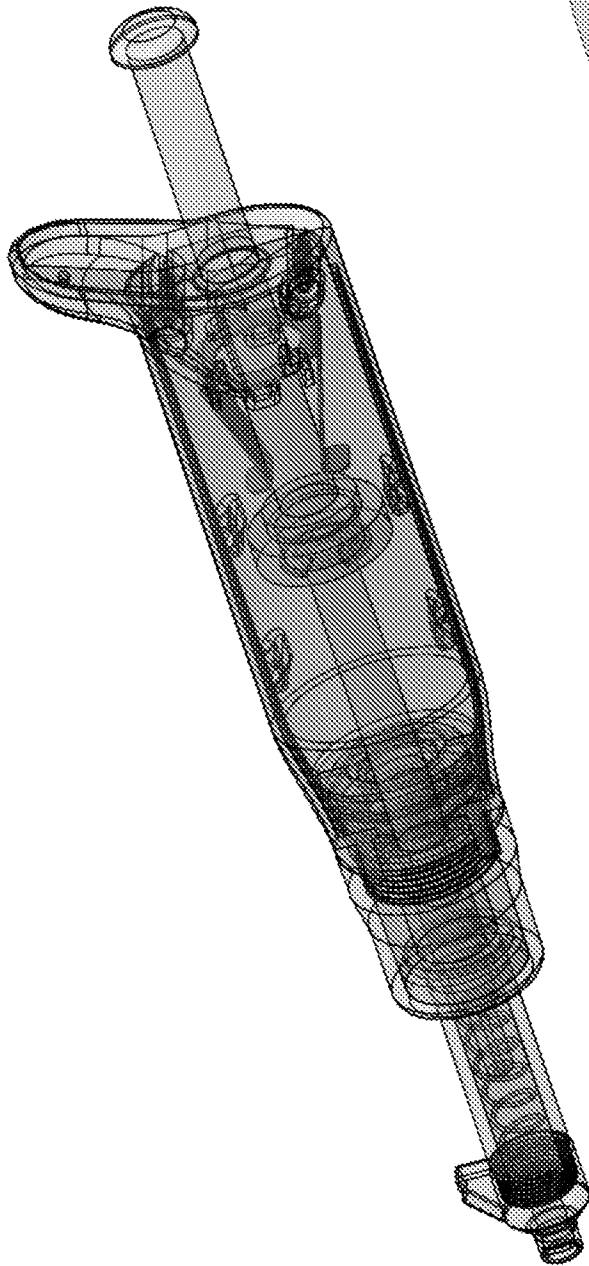


FIG. 8E(i)

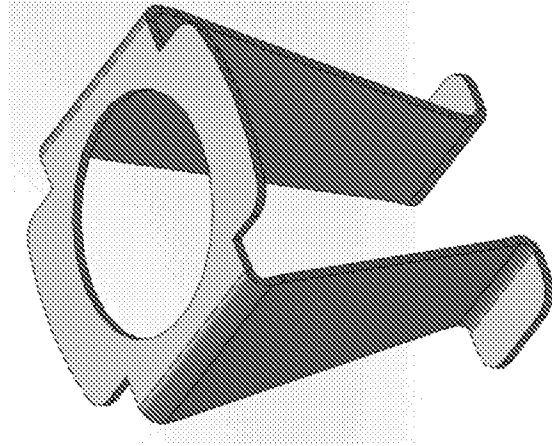


FIG. 8E(ii)

21/30

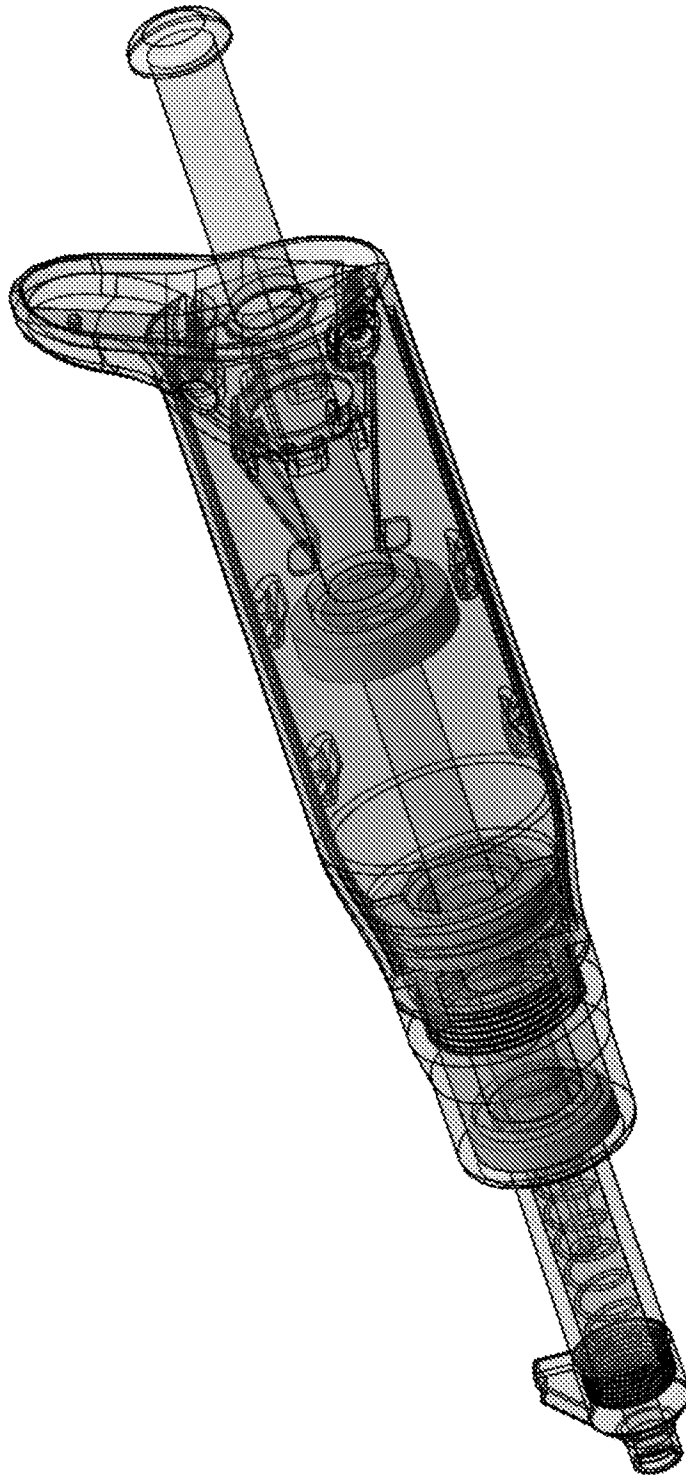


FIG. 8F

22/30

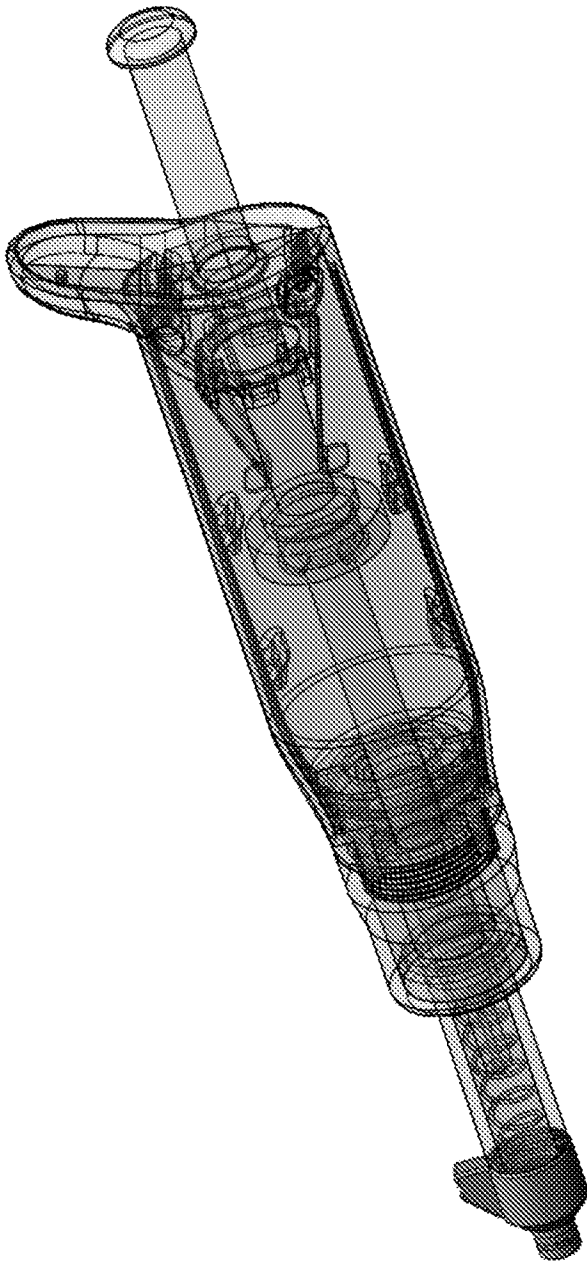


FIG. 8G(i)

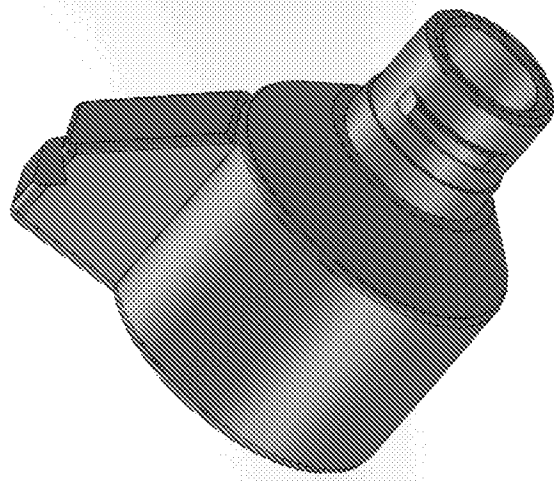


FIG. 8G(ii)

23/30

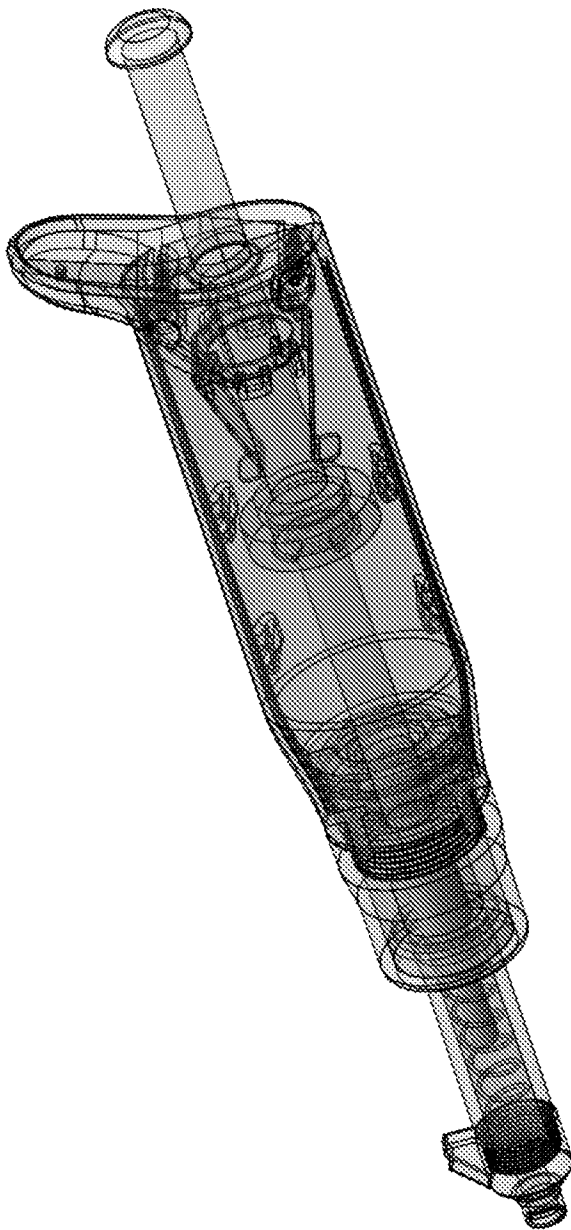


FIG. 8H(i)

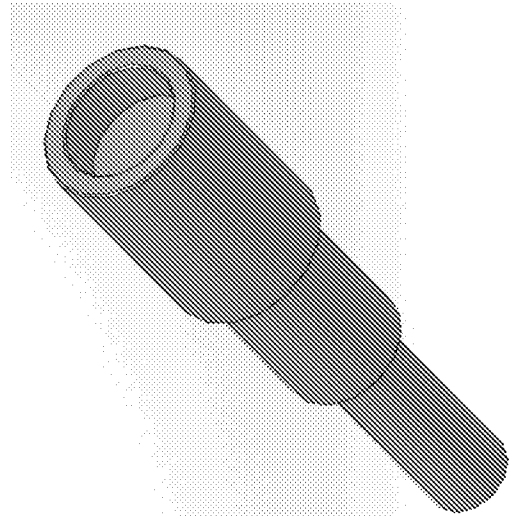


FIG. 8H(ii)

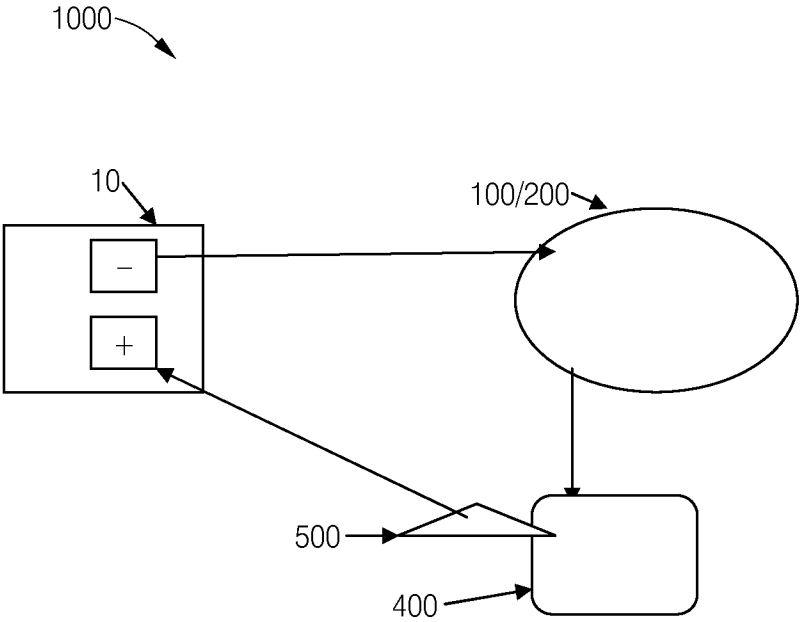


FIG. 9

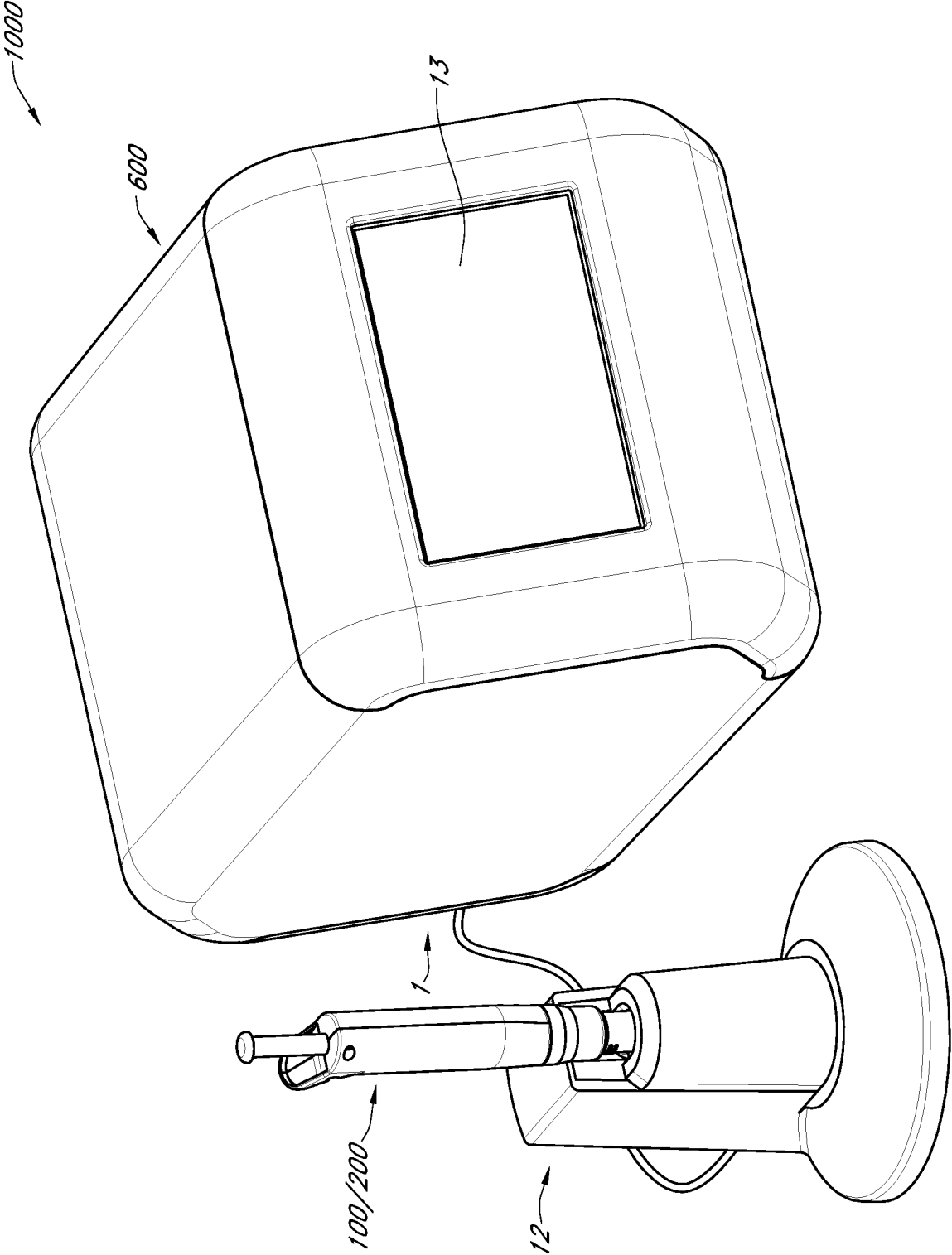


FIG. 10

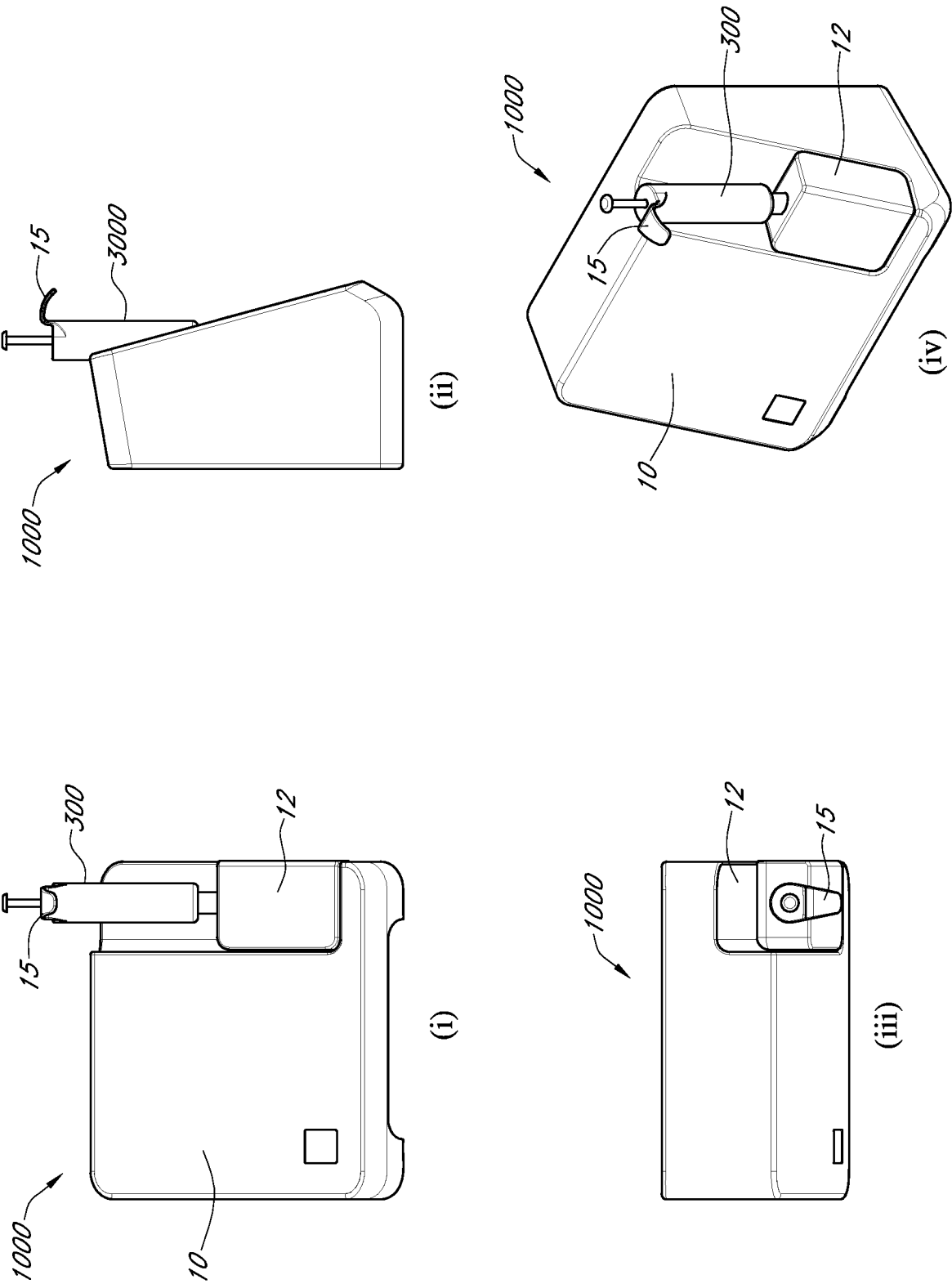


FIG. 11A

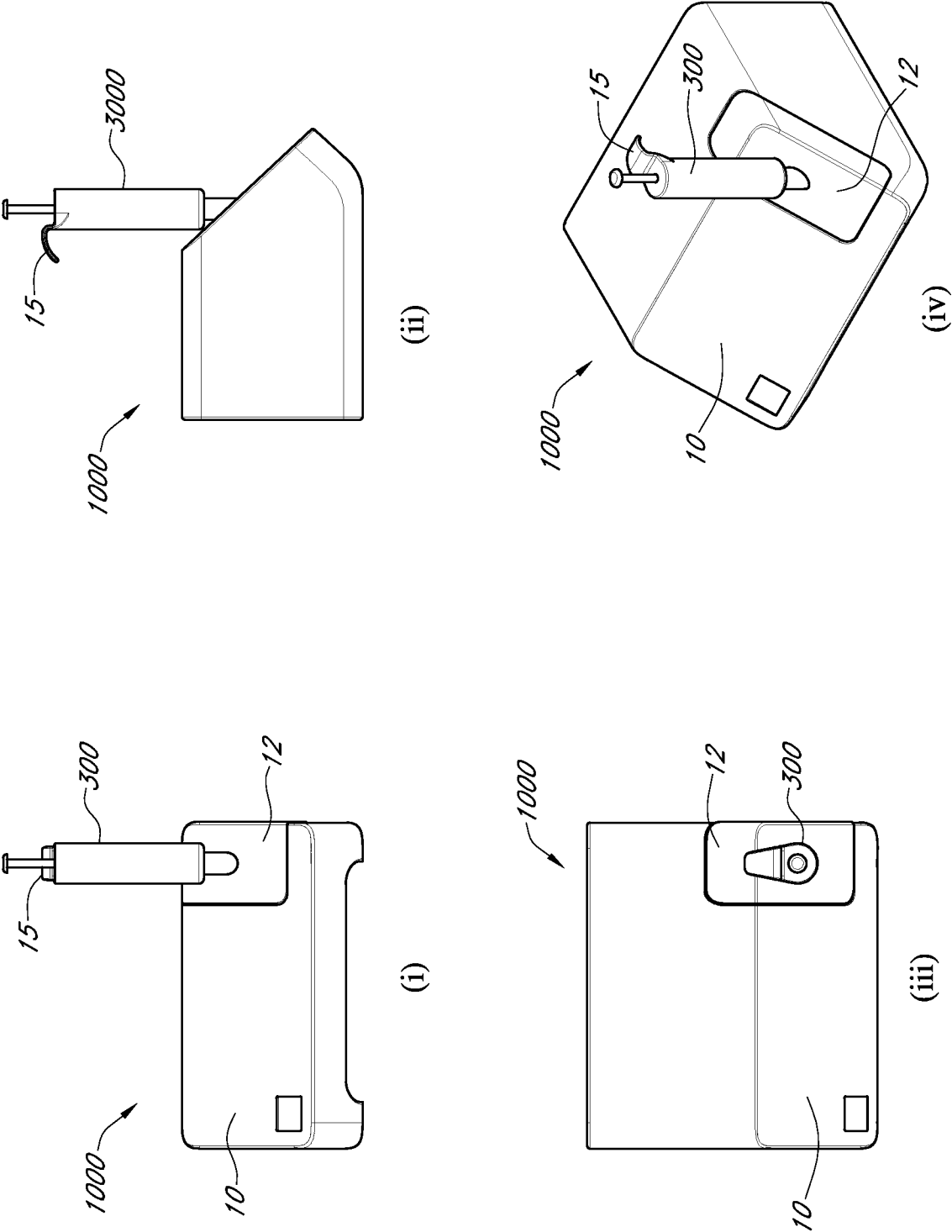


FIG. 11B

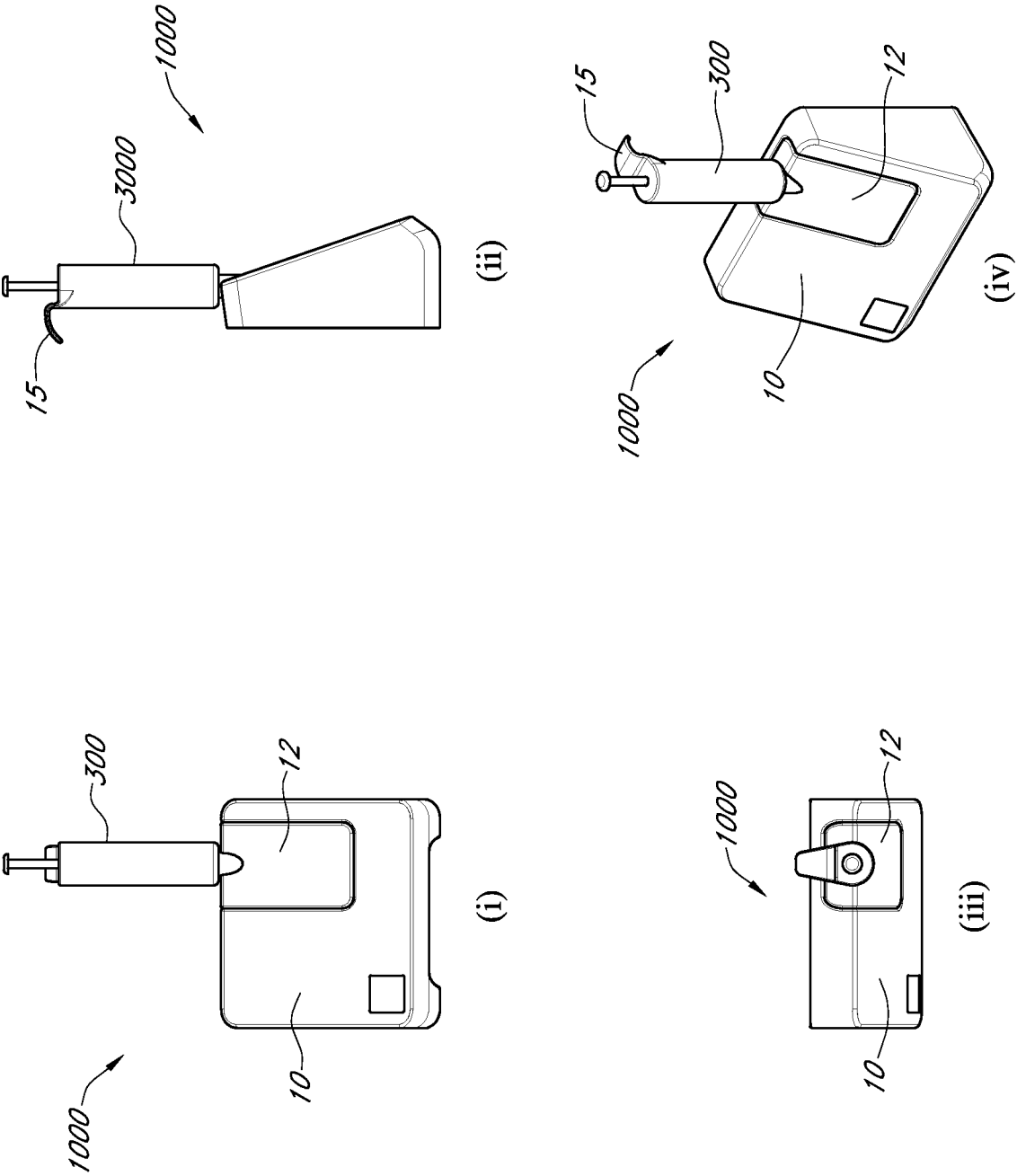


FIG. 11C

29/30

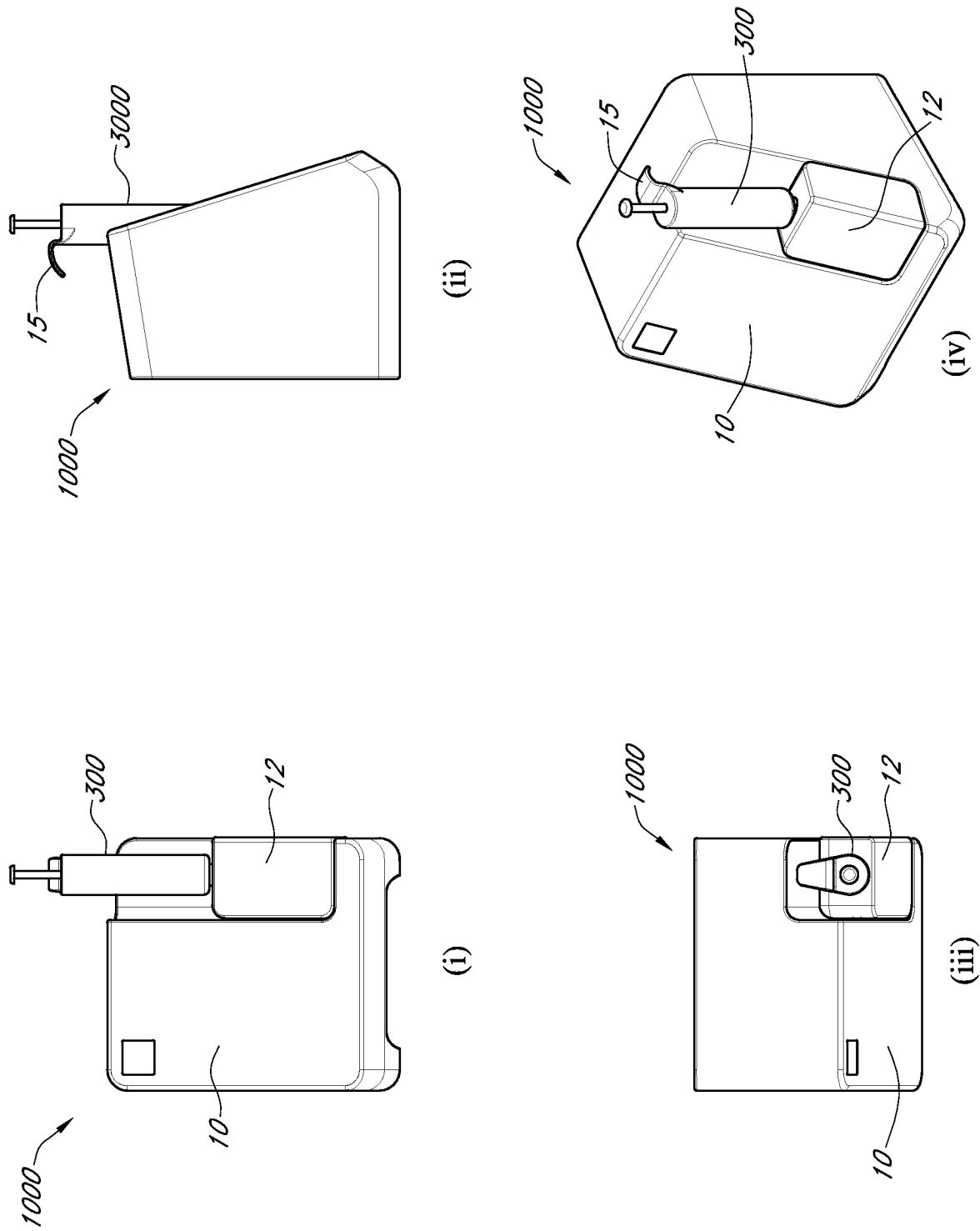


FIG. 11D

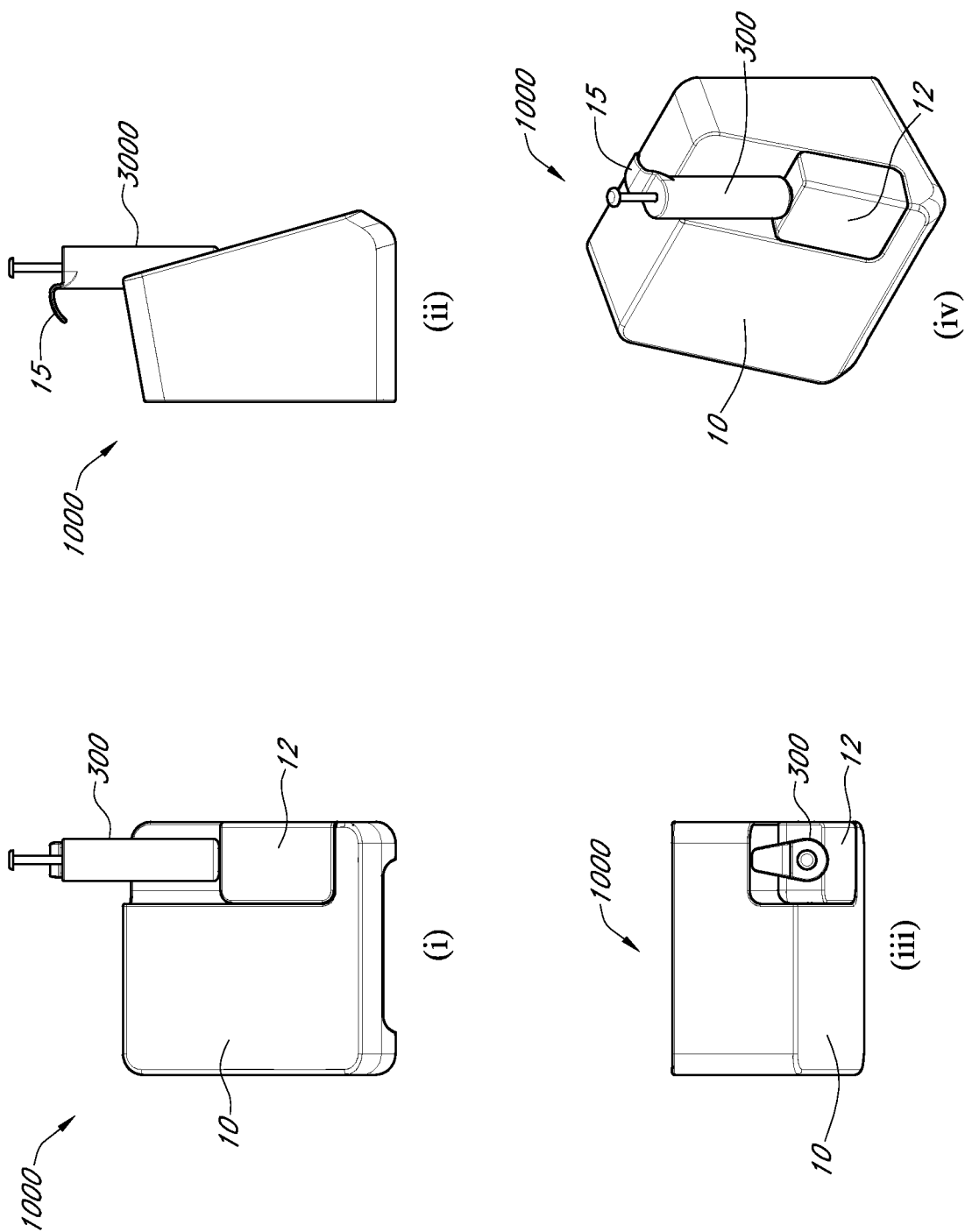


FIG. 11E