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DESCRIPTION

Cross-Reference to Related Applications

[0001] This patent application claims priority to U.S. Patent Application Serial No. 13/294,889, filed November 11, 2011, entitled PIEZOELECTRIC DISPENSER WITH A LONGITUDINAL TRANSDUCER AND REPLACEABLE CAPILLARY TUBE, and U.S. Provisional Patent Application Serial No. 61/461,664, filed January 21, 2011, entitled PIEZOELECTRIC DISPENSER.

Background of the Invention

Field of the Invention

[0002] The invention relates in general to systems and methods for acquiring and dispensing predetermined volumes of liquids and, more particularly but not exclusively, to piezoelectric devices and methods for dispensing and transferring small volumes of fluid in the form of single droplets or drops, typically ranging in volume from picoliters to nanoliters.

[0003] Prior art document US 6387330 B1 discloses a method and device for storing and dispensing specified subsets from a collection of tens, hundreds or thousands of different reagents to specified locations within micro-titre trays or microarray substrates or the like. The reagents of interest are stored in racks of syringe-like dispensers. These dispensers and/or substrates and/or actuators are controllably moved by automated means to a dispensing position where a single action, vibration and weighing system transfers a controlled quantity to a specified location in a micro-titre tray or the like. Deficits of the prior art, such as evaporation, cross-contamination, oxidation, waste of reagents and lab-ware, and human operator non-reliability are overcome.

[0004] Prior art document DE 202006019795 discloses a micropipette for use in a sample dispensing unit comprises an upper section which holds the sample and a nozzle below this section. Full pipettes can be stored out of the dispenser without leaking. Independent claims are also included for the following: a dispensing unit using the pipettes; using the pipettes in which full pipettes are stored away from the dispensing unit; and use of the pipettes for storing samples separately from the dispensing unit.

Description of the Related Art

[0005] Conventional piezoelectric dispensing devices have a tube that is typically entirely surrounded by and bonded to a piezoelectric actuator to produce droplets. Activation of the piezoelectric actuator transmits acoustic pressure into and through the liquid in the tube. The acoustic pressure propagates through the liquid and to a dispensing opening of the tube. This results in ejection of a liquid drop from the device.

[0006] Such conventional devices have several disadvantages. One is that their operation is highly dependent on the characteristics and properties of the particular liquid to be dispensed. Thus, disadvantageously, dispensing parameters such as droplet size cannot be independently controlled and various compensative measures have to be taken which can increase cost and reduce efficiency.

[0007] Moreover, to transmit pressure to the liquid in the tube to dispense a droplet a relatively force (energy) needs to be imparted by the piezoelectric actuator. This can not only raise system and operational costs, but can undesirably lead to degradation, damage and denaturing of the liquid. Also, this further limits the actuator's operational frequency since higher frequencies may also cause liquid degradation, damage or denaturing. The transmission of a relatively high pressure to the liquid can lead to the formation of bubbles in the liquid which can undesirably cause dispensing inaccuracies, among other undesired operational complications.

[0008] Another disadvantage of such conventional devices is that the piezoelectric actuator is structurally bonded to the tube. Since many applications of dispensing using such devices involve the use of multiple liquids, such as, but not limited to, the fields of genomics and proteomics, among others, these devices fail to provide an efficient and cost-effective approach to a system involving handling of multiple liquids in small quantities, for example, biological and chemical reagents.

[0009] Typically, there are two options, neither one desirable, of addressing this situation. One is to simply discard the piezoelectric-tube device and use a new one for further processing of other liquids. The piezoelectric actuator is a relatively expensive component, and discarding it after a single use disadvantageously adds to the cost - given that some of the applications can involve the handling of hundreds or thousands, if not more, different liquids.

[0010] The second option is to rinse and clean the dispensing tube after each use to prevent contamination. Firstly, this undesirably adds additional steps to the liquid handling in terms of both efficiency and cost of the overall process. Secondly, in spite of any stringent rinsing or cleaning routines the risk of cross contamination always exists.

Summary of the Invention

[0011] It is one advantage of certain embodiments of the invention to provide systems, devices and methods comprising a piezoelectric dispenser or dispensing device that is configured so

that the dispensing tube and piezoelectric actuator are separable. This allows for the removal and replacement of the tube for subsequent use. Desirably, such embodiments with a separable tube, not only eliminate the need for cleaning and the risk of contamination from left over material transferred from prior use, but also advantageously increase system efficiency and are cost-effective.

[0012] Certain embodiments of the invention provide longitudinal transducers or transmission devices, and related methods of operation, for transmission or conversion of radial motion to axial or longitudinal motion. The longitudinal transducer generally comprises a piezoelectric actuator coupled to a tube or the like. Actuation of the piezoelectric actuator by a voltage pulse causes radially inwards motion of the tube and generates an acoustic pressure or stress wave through the wall of the tube which results in axial or longitudinal motion, or displacement of the tube wall at the distal tip of the tube. In other words, actuation of the actuator causes the distal tip to axially extend and then axially retract back to its original form on deactivation of the actuator and/or its pulse, that is, the distal tip oscillates. When multiple pulses are provided, the distal tip oscillates in response to each pulse cycle.

[0013] Certain embodiments of the invention provide systems, devices and methods comprising a liquid dispenser or dispensing device that includes and/or incorporates a longitudinal transducer with a piezoelectric actuator, as disclosed herein, for transmission or conversion of radial motion to axial or longitudinal motion to a dispensing tube thereby causing a droplet to be dispensed from an aperture or outlet orifice at the distal tip of the tube. Some of these embodiments are configured so that the dispensing tube and piezoelectric actuator are separable, as disclosed herein.

[0014] Some advantages of the dispensing embodiments utilizing a longitudinal transducer include, but are not limited to: since minimal or negligible force, pressure is imparted to the liquid in the dispensing tube several of the problems associated with conventional dispensing devices, as described above, are mitigated or substantially eliminated - such as greater dispensing flexibility and independence substantially regardless of the liquid properties or characteristics, general avoidance of problems associated with degradation, damage and denaturing of the liquid and undesirable bubble formation, and ability to operate at higher frequencies, among others.

[0015] One exemplary application of the dispensers or dispensing devices disclosed herein relates to the production of DNA arrays for genetic engineering uses, wherein a high clone density is achieved by means of a small droplet size, for which piezoelectric operated dispensers in accordance with embodiments of the invention are particularly suitable. Embodiments of the invention can be particularly advantageous for production of working copies for screening processes, for example, in the pharmaceutical industry in production of microarrays or for the production of multiply assays.

[0016] Some embodiments provide a piezoelectric micro-dispensing device, apparatus or system that enables automatic or manual transfer of small volumes of liquids typically ranging

in volume from picoliters to nanoliters. Advantageously, the device can allow for the disposal of the dispensing tube while permitting reuse of the piezoelectric actuator. Alternatively, or in addition, the device can desirably further comprise a longitudinal transducer for transmission or conversion of radial motion to axial or longitudinal motion to a dispensing tube thereby allowing for a liquid droplet to be dispensed from an aperture at the distal tip of the tube.

[0017] In some embodiments, the dispenser includes a main body portion or mounting bracket and comprises a tube which includes a dispensing nozzle at one end of the tube. The tube can comprise, for example, but not limited to, a glass capillary tube. The dispenser can further comprise a piezoelectric clamp for clamping to an outer circumferential or peripheral surface of the tube. The piezoelectric clamp can comprise two opposing jaws or clamping or supporting structures. The first jaw can include a piezoelectric actuator or transducer and the second jaw can include a preloading, clamping, retaining or biasing mechanism, device, assembly or structure to apply a predetermined reactive force to the tube.

[0018] In some embodiments, the preloading mechanism, device, assembly or structure includes a preloading screw. In other embodiments, the preloading mechanism, device, assembly or structure includes a preloading assembly of a spring, such as a leaf spring or the like, a mass providing ball or the like, and a knob or lever that is utilized to actuate or release the preloading.

[0019] In some embodiments, the clamp is operable to hold the tube in place and to transmit acoustic pressure to the clamped area of the tube on actuation of the piezoelectric actuator or transducer. Acoustic pressure or stress propagates longitudinally from the clamped area through the tube and toward the nozzle whereat axial displacement at the distal tip of the tube and/or transmission of acoustic pressure to the fluid in the area of the nozzle propels, ejects or dispenses a droplet of fluid having a predetermined volume or quantity, due at least in part to the solid-fluid interaction in the area of the nozzle. Thus, a wave passing longitudinally through the tube wall provides for transmission or conversion of tube radial motion to axial or longitudinal motion to the tube tip thereby allowing for a liquid droplet to be dispensed from an aperture at the tip of the tube. In some embodiments, this wave has a generally sinusoidal or cosine waveform, profile or configuration.

[0020] In some embodiments, following each use of dispensing a particular liquid the clamp may be released to replace the tube. As such, the tube may be disposed following each use with a particular liquid while the piezoelectric clamp is reused with another tube. Advantageously, this provides an economic utilization of the piezoelectric or piezoceramic actuator or transducer. In addition, and desirably, such an arrangement of a dispenser eliminates the need for cleaning the tube and the risk of cross contamination from left over material transferred from the prior use of the device.

[0021] Single droplets having a volume in the range from a few picoliters to a few nanoliters can be accurately and reliably dispensed, for example, in the range from about 50 picoliters to about 1,000 picoliters (1 nanoliter), including all values and sub-ranges therebetween.

[0022] In addition to dispensing droplets, fluid may also be acquired or aspirated into the tube. The fluid samples can be acquired, aspirated or drawn up into the tube by dipping its tip into a fluid source and applying vacuum, for example, using a pump or the like. The size of the tube can vary, as needed or desired, but is typically sufficiently small to draw fluid from a standard microtiter or micro-well plate, for example, one having a square or diametric dimension of about 5 mm or less.

[0023] The piezoelectric actuator, in some embodiments, comprises a monolithic co-fired ceramic stack which expands and contracts under the input of an alternating voltage. The stack can be a linear or longitudinal stack which expands and contracts generally linearly or longitudinally in the direction of the stack. The piezoelectric or piezoceramic stack is capable of applying a predetermined force in the radial direction against the tube. To prevent breakage of the tube, the tube may be provided with a sleeve, for example, a plastic or metal sleeve, which substantially evenly distributes the force around the clamping area of the tube.

[0024] Some embodiments are directed to systems, devices, methods, and techniques are provided, for acquiring and dispensing predetermined volumes of liquids and, in particular, to a unique piezoelectric dispensing device for acquiring and dispensing of volumes of liquids, specifically, but not exclusively, for use in dispensing and transferring of small volumes of fluid in, for example, automatic or manual production of DNA arrays and assays, wherein droplets are dispensed in a single drop format with volumes, for example, ranging from about a few picoliters to several nanoliters. The dispensing devices or dispensers can advantageously utilize a disposable capillary tube assembly while desirably retaining the piezoelectric actuator or transducer for subsequent further uses, thereby mitigating the possibility of cross contamination of fluids and providing an economical and cost effective approach with reuse of the piezoelectric actuator or transducer for further operation such as with a variety of liquids to be dispensed and transferred. The systems or devices can incorporate a unique longitudinal transducer that transmits or converts radial tube displacement or motion to controlled axial or longitudinal displacement motion of a distal tip of the tube.

[0025] In some embodiments of the piezoelectric dispenser disclosed herein, the piezoelectric device does not completely surround, encircle or circumscribe the outer periphery of the dispensing tube, but does so only partially. In other words, the piezoelectric device is on a first side of the tube while the preloading device, when included, is on a second substantially opposed second side of the tube. In other embodiments, such as those not incorporating a configuration in which the dispensing tube is separable from the piezoelectric device, the piezoelectric device can substantially completely surround, encircle or circumscribe the outer periphery of the dispensing tube, or it can do so only partially.

[0026] In accordance with some embodiments, a dispenser for transferring a predetermined quantity of a liquid is provided. The dispenser generally comprises a tube, a piezoelectric device and a preloading device. The tube contains a liquid to be dispensed into or onto one or more targets. The piezoelectric device is selectively communicable with a first side of the tube

and is responsive to an applied signal, and the preloading device is selectively communicable with a second side of the tube that is generally disposed in opposition to the first side, thereby allowing for separation of the tube and the piezoelectric device
In some embodiments, the piezoelectric device is configured such that when actuated the piezoelectric device transmits a generally radial first force to the tube. Actuation of the piezoelectric actuator by a voltage pulse causes radially inwards motion of the tube and generates an acoustic pressure or stress wave through the wall of the tube which results in axial or longitudinal motion or displacement of the tube wall at the distal tip of the tube thereby causing a droplet of predetermined volume to be ejected from the tube. The preloading device, when included, can be configured to provide a generally reactive and opposed second force to the tube.

[0027] In accordance with some embodiments, a method of transferring a predetermined quantity of a liquid is provided. The method generally comprises providing a tube with a liquid to be dispensed and a piezoelectric device in communication with the tube. The piezoelectric device is actuated such that a generally radial force is applied to the tube and which creates a longitudinal stress or pressure wave that propagates to and causes axial displacement of a distal tip of the tube so as to eject a predetermined volume of the liquid. Advantageously, in some embodiments, the dispensing tube can be replaced with another tube for dispensing of another liquid.

[0028] In some embodiments, the dispensing systems, devices and methods disclosed herein may be used for the delivery of surfactants to neonate/local anesthetic in laparoscopy. In some embodiments, the dispensing systems, devices and methods disclosed herein may be used for the delivery of aerosolized pharmaceuticals to human or animal subjects. In some embodiments, the dispensing systems, devices and methods disclosed herein may be used for dispensing of chemicals for microelectronic manufacturing. In some embodiments, the dispensing systems, devices and methods disclosed herein may be used for printing inert inks onto surfaces, papers or the like, among others.

[0029] In accordance with some embodiments, a longitudinal transducer for converting a radial displacement to an axial displacement is provided. The longitudinal transducer generally comprises a tube, a linear or longitudinal piezoelectric actuator and an energy source. The tube has a length, a wall with a predetermined thickness, a lumen with a predetermined size or diameter, and a tip at a distal end of the tube. The linear or longitudinal piezoelectric actuator is clamped to the tube at a location proximal of the tip. The energy source is configured to provide at least one voltage pulse to the piezoelectric actuator. Actuation of the piezoelectric actuator causes a pressure wave to propagate from the proximal location of the tube toward the tip of the tube such that radial motion at the proximal location of the tube is transmitted as distally extending axial motion of the tip of the tube.

[0030] In one embodiment, the voltage pulse and configuration of the tube are selected such that a peak of the pressure wave is located substantially at the tip of the tube.

[0031] In accordance with some embodiments, a method of converting a radial displacement into an axial displacement is provided. The method involves providing a transducer that comprises a piezoelectric actuator which is responsive to a voltage signal. The piezoelectric actuator is actuated to provide a generally radial force to a tube of the transducer at a region that is proximal to a distal end of the tube. Radial motion of the tube at the proximal region of the tube is converted to generally axial motion at the distal end of the tube.

[0032] In one embodiment, actuation of the piezoelectric actuator comprises providing at least one voltage pulse to the piezoelectric actuator.

[0033] In one embodiment, the piezoelectric actuator comprises a linear or longitudinal piezoelectric actuator that is clamped to the tube.

[0034] In one embodiment, the axial motion comprises distal axial motion, and on deactivation of a pulse of the voltage signal the distal end of the tube is subjected to a motion in a proximal axial direction, thereby providing an axial oscillation in response to at least one pulsed voltage cycle.

[0035] In accordance with some embodiments, a dispenser for transferring a predetermined quantity of a liquid is provided. The dispenser generally comprises a tube a piezoelectric actuator. The tube contains a liquid to be dispensed into or onto one or more targets. The piezoelectric actuator is operatively coupled to the tube and is responsive to an applied signal for dispensing one or more droplets of the liquid. The tube and the piezoelectric actuator are separable such that the tube may be replaced while allowing for the same piezoelectric actuator to be used with another tube for dispensing another liquid.

[0036] In one embodiment, the piezoelectric actuator is mounted on a first side of the tube. In one embodiment, a preloading device is mounted on a second side of the tube which is generally opposed to the first side. In one embodiment, the preloading device comprises a screw. In one embodiment, the preloading device comprises an actuable spring loaded device. In one embodiment, the preloading device is releasable to allow for removal and replacement of the tube.

[0037] In one embodiment, actuation of the piezoelectric actuator causes conversion of a radial motion of the tube into an axial motion at a tip of the tube to cause a droplet of predetermined volume to be ejected from the tip.

[0038] In one embodiment, the piezoelectric actuator is spaced from the tube by a sleeve attached to the tube.

[0039] In one embodiment, the tube is part of a replaceable assembly that comprises the tube and a sleeve that is bonded to the tube.

[0040] In one embodiment, the dispenser further comprises a first jaw and a second jaw

respectively engaged with the piezoelectric actuator and a preloading device. In one embodiment, the jaws comprise structures that engage a sleeve that is attached to the tube at a predetermined number of locations.

[0041] In one embodiment, a lumen of the tube has a generally annular configuration.

[0042] In one embodiment, the liquid to be dispensed within the tube is axially below the location of the piezoelectric actuator.

[0043] In one embodiment, the tube has an aperture plate with a generally curved funnel or conical configuration.

[0044] In one embodiment, the tube is part of a library of stored tubes with respective fluids pre-filled therein to allow for dispensing of multiple liquids while utilizing the same piezoelectric actuator.

[0045] In one embodiment, the dispenser is provided in combination with a fluid source that allows acquisition of liquid to be dispensed by the dispenser from the source.

[0046] In one embodiment, the dispenser is provided in combination with an imaging system to visualize and analyze dispensed droplets.

[0047] In one embodiment, the dispenser is provided in combination with a library of stored fluid samples that are selectively loadable within the tube.

[0048] In one embodiment, the piezoelectric actuator comprises a linear or longitudinal piezoelectric actuator that is clamped to the tube.

[0049] In accordance with some embodiments, a method of transferring a predetermined quantity of a liquid is provided. The method involves providing a tube from which a liquid is to be dispensed and a linear or longitudinal piezoelectric actuator clamped to the tube. The piezoelectric actuator is actuated to eject a droplet of liquid from a distal tip of the tube. The tube is separated from the piezoelectric actuator and replaced with another tube for dispensing of another liquid while utilizing the same piezoelectric actuator.

[0050] In one embodiment, the tube is selected from a library of stored tubes with respective liquids pre-filled therein.

[0051] In one embodiment, the liquid to be dispensed is aspirated from a fluid source.

[0052] In one embodiment, a library of stored fluid samples that are selectively loadable within the tube is provided.

[0053] In one embodiment, a lumen of the tube has a generally annular configuration.

[0054] In one embodiment, actuation of the piezoelectric actuator causes conversion of a radial motion of the tube into an axial motion at a tip of the tube to cause a droplet of predetermined volume to be ejected from the tip.

[0055] In accordance with some embodiments, a dispenser for transferring a predetermined quantity of a liquid is provided. The dispenser generally comprises a longitudinal transducer, an aperture and a liquid. The longitudinal transducer generally comprises a tube and a piezoelectric actuator. The tube has a length, a wall with a predetermined thickness, a lumen with a predetermined size or diameter, and a tip at a distal end of the tube. The piezoelectric actuator is operatively coupled to the tube at a location proximal of the tip. The aperture is at the tip of the tube. The liquid is to be dispensed into or onto one or more targets and is loaded within the tube. Actuation of the piezoelectric actuator causes a pressure wave to propagate from the proximal location of the tube toward the tip of the tube such that radial motion at the proximal location of the tube is transmitted as distally extending axial motion of the tip of the tube, thereby causing a droplet of a predetermined volume to be ejected from the aperture.

[0056] In one embodiment, the piezoelectric actuator comprises a linear or longitudinal piezoelectric actuator that is clamped to the tube.

[0057] In one embodiment, the dispenser further comprises an energy source that is configured to provide at least one voltage pulse to the piezoelectric actuator

[0058] In one embodiment, the tube and the piezoelectric actuator are separable.

[0059] In one embodiment, the tube is selected from a library of stored tubes with respective liquids pre-filled therein.

[0060] In one embodiment, a lumen of the tube has a generally annular configuration.

[0061] In one embodiment, the dispenser is provided in combination with a fluid source that allows acquisition of liquid to be dispensed by the dispenser from the source.

[0062] In one embodiment, the dispenser is provided in combination with a library of stored fluid samples that are selectively loadable within the tube.

[0063] In accordance with some embodiments, a method of transferring a predetermined quantity of a liquid is provided. The method involves providing a tube with a liquid to be dispensed. The tube comprises a distal end with a tip and an aperture thereat. A piezoelectric actuator is provided in communication with the tube at a location proximal to the tip of the tube. The piezoelectric actuator is actuated such that a pressure wave propagates from the proximal location of the tube toward the tip of the tube and radial motion at the proximal location of the tube is transmitted as axial motion of the tip of the tube, thereby causing a droplet of a predetermined volume to be ejected from the aperture.

[0064] In one embodiment, the piezoelectric actuator comprises a linear or longitudinal piezoelectric actuator that is clamped to the tube.

[0065] In one embodiment, the tube is replaced with another tube for dispensing of another liquid.

[0066] In one embodiment, the tube is selected from a library of stored tubes with respective liquids pre-filled therein.

[0067] In one embodiment, the liquid to be dispensed is acquired from a fluid source.

[0068] In one embodiment, a library of stored fluid samples that are selectively loadable within the tube is provided.

[0069] In one embodiment, a lumen of the tube has a generally annular configuration.

[0070] In one embodiment, the piezoelectric actuator is positioned axially above the liquid in the tube.

[0071] In accordance with some embodiments, a longitudinal transducer for converting a radial displacement to an axial displacement is provided. The longitudinal transducer generally comprises a tube, a linear or longitudinal piezoelectric actuator and an energy source. The tube comprises a generally rigid material and has a length, a wall with a predetermined thickness, a lumen with a predetermined size or diameter, and a tip at a distal end of the tube. The rigid material of the tube has a modulus of elasticity greater than about 10 GPa. The linear or longitudinal piezoelectric actuator is clamped to the tube at a location proximal of the tip of the tube. The energy source is configured to provide at least one voltage pulse to the piezoelectric actuator. Actuation of the piezoelectric actuator causes a pressure wave to propagate from the proximal location of the tube through the wall of the tube and toward the tip of the tube such that radial motion at the proximal location of the tube is transmitted as distally extending axial motion of the tip of the tube.

[0072] In one embodiment, the rigid material of the tube has a modulus of elasticity greater than about 50 GPa.

[0073] In one embodiment, an aperture is at the tip of the tube and a liquid to be dispensed into or onto one or more targets, by the actuation of the piezoelectric actuator, is contained in the tube. In one embodiment, the tube and the piezoelectric actuator are separable.

[0074] For purposes of summarizing the invention, certain aspects, advantages and novel features of the invention have been described herein above. Of course, it is to be understood that not necessarily all such advantages may be achieved in accordance with any particular embodiment of the invention. Thus, the invention may be embodied or carried out in a manner that achieves or optimizes one advantage or group of advantages as taught or suggested

herein without necessarily achieving other advantages as may be taught or suggested herein.

[0075] All of these embodiments are intended to be within the scope of the invention herein disclosed. These and other embodiments of the invention will become readily apparent to those skilled in the art from the following detailed description of the preferred embodiments having reference to the attached figures, the invention not being limited to any particular preferred embodiment(s) disclosed.

Brief Description of the Drawings

[0076] Having thus summarized the general nature of the invention and some of its features and advantages, certain preferred embodiments and modifications thereof will become apparent to those skilled in the art from the detailed description herein having reference to the figures that follow, of which:

FIG. 1A is a simplified schematic view of a piezoelectric fluid dispensing system illustrating features and advantages in accordance with certain embodiments of the invention.

FIG. 1B is a simplified schematic view of a longitudinal transducer for transmission or conversion of radial movement to axial movement illustrating features and advantages in accordance with certain embodiments of the invention.

FIG. 2 is a simplified schematic side view of a piezoelectric fluid dispenser in an unclamped position illustrating features and advantages in accordance with certain embodiments of the invention.

FIG. 3 is a simplified schematic side view of the piezoelectric fluid dispenser of **FIG. 2** in a clamped position illustrating features and advantages in accordance with certain embodiments of the invention.

FIG. 4 is a simplified schematic top view of the piezoelectric fluid dispenser of **FIG. 3** illustrating features and advantages in accordance with certain embodiments of the invention.

FIG. 5 is a simplified schematic side view of a piezoelectric fluid dispenser incorporating a tube with an annular gap illustrating features and advantages in accordance with certain embodiments of the invention.

FIG. 6 is a simplified schematic side view of a piezoelectric fluid dispenser incorporating a mounting bracket suitable for dispensing of fluid in the production of dot arrays or the like illustrating features and advantages in accordance with certain embodiments of the invention.

FIG. 7 is a simplified schematic side view of a capillary tube of a piezoelectric fluid dispenser illustrating features and advantages in accordance with certain embodiments of the invention.

FIG. 8 is a simplified schematic side view of a piezoelectric fluid dispenser incorporating one or more stored fluid samples within a capillary tube illustrating features and advantages in

accordance with certain embodiments of the invention.

FIG. 9 is a simplified schematic side view of a piezoelectric fluid dispenser with multiple clamping devices illustrating features and advantages in accordance with certain embodiments of the invention.

FIG. 10 is a simplified perspective view of a piezoelectric fluid dispenser incorporating a spring biased preloading mechanism illustrating features and advantages in accordance with certain embodiments of the invention.

FIG. 11 is a simplified exploded perspective view of the piezoelectric fluid dispenser of **FIG. 10** illustrating features and advantages in accordance with certain embodiments of the invention.

FIG. 12 is a simplified sectional perspective view of the piezoelectric fluid dispenser of **FIG. 10** illustrating features and advantages in accordance with certain embodiments of the invention.

FIG. 13 is a simplified sectional side view of the piezoelectric fluid dispenser of **FIG. 10** illustrating features and advantages in accordance with certain embodiments of the invention.

Detailed Description of the Preferred Embodiments

[0077] The preferred embodiments of the invention described herein relate generally to systems and methods for acquiring and non-contact dispensing of predetermined volumes of liquids and, in particular, to unique piezoelectric dispensing devices for acquiring and dispensing of volumes of liquids, specifically, but not exclusively, for use in dispensing and transferring small volumes of fluid in, for example, automatic production of DNA arrays or multiple assays, wherein droplets are dispensed in a single drop format with volumes, for example, ranging from about a few picoliters to several nanoliters. Embodiments of the dispensing devices advantageously utilize a disposable, removable or separable capillary tube assembly while desirably retaining the piezoelectric actuator or transducer for subsequent further uses, thereby mitigating the possibility of cross contamination of fluids and providing an economical and cost effective approach with reuse of the piezoelectric actuator or transducer for further operation such as with a variety of liquids to be dispensed and transferred.

[0078] While the description sets forth various embodiment specific details, it will be appreciated that the description is illustrative only and should not be construed in any way as limiting the invention. Furthermore, various applications of the invention, and modifications thereto, which may occur to those who are skilled in the art, are also encompassed by the general concepts described herein.

[0079] Turning now to the drawings, **FIG. 1A** illustrates a liquid dispensing (and aspirating or acquiring) system **10** for fluid handling and transfer in accordance with some embodiments. The system **10** generally comprises a piezoelectric dispensing device or dispenser **100** for

dispensing single liquid droplets or drops **12** onto or into one or more targets or substrates **14** from a fluid or liquid source **16,** such as a vessel or vial, among others, that holds or contains a liquid **18** to be dispensed

[0080] The source **16** is in fluid communication with the dispensing device or dispenser **100** via, for example, a flexible tube or the like. The relative Z-direction positioning between the source **16** and the dispenser **100** (and its capillary tube) is selected giving consideration to a balance between the hydrostatic pressure head on the capillary tube, capillary forces and surface tension of the liquid **18** so that no liquid is emitted from the dispenser **100** unless actuated to do so. This balance also depends at least on the tube dimensions such as the size of the droplet emitting outlet orifice.

[0081] In some embodiments, the dispenser **100** is also utilized to aspirate or acquire liquid directly from a source **20** (e.g., vial, microtiter or micro-well plate and the like) by dipping the tip of the capillary tube into the liquid to be aspirated and applying a vacuum or suction to draw fluid into the tube. This can be done by using a vacuum source, pump **22** such as a positive displacement pump or the like. The system **10** can be arranged to accommodate both modes of acquiring the liquid to be dispensed (i.e., from the source **16** or the source **20**), for example, by providing a two-way valve **24** or the like positioned as shown in **FIG. 1A.** Various other valves or the like may be provided in the system tubing to control fluid communication and flow, as needed or requires, with efficacy.

[0082] The liquids involved can include a wide variety wherein micro-volumes of fluid are to be handled, transferred and dispensed. These include, but not limited to, are liquids such as chemical and biological reagents, for example, DNA, cDNA, RNA, proteins, peptides, oligonucletides, chromosomal formulations, and other organic or inorganic compounds, among others, or the like as known in the art.

[0083] The target or substrate **14** can comprise, for example, but not limited to, a microtiter or micro-well plate, glass slide, receptive membrane, test strip, vial or other suitable target, among others, or the like as known in the art.

[0084] Relative motion between the various components of the system **10** can be provided to accurately place, position and move them relative to one another. An X-, X-Y or X-Y-Z motion system **26** can be used to move the one or more dispensers **100** relative to the one or more targets or substrates **14,** and/or the fluid or liquid sources **16** and **20** to provide the desired accuracy in dispensing and aspirating. For example, one or more suitable robot or robotic arms may be efficaciously used, as needed or desired, to provide the controlled relative motion

[0085] The one or more targets or substrates **14** can be mounted on a carrier platform, table or carriage **28** to provide X-, X-Y or X-Y-Z motion. Robot or robotic arms may be utilized with efficacy, as required or desired. Similarly, relative motion of the fluid or liquid sources **16** and **20** can be controlled in a coordinated manner to allow for efficient liquid transfer. Web, reel or conveyor belt transport mechanisms can be efficaciously utilized to move any of the fluid

targets or sources, as needed or desired.

[0086] In some embodiments, a droplet imaging system **30** is provided to analyze and visualize the dispensed droplet characteristics. These include, but are not limited to, the droplet volume, shape, sphericity, velocity, among others. This is not only useful during operation of the liquid handling system **10** but also initial system set-up for a particular application. For example, the imaging system **30** can be employed so that the various system operational parameters are fine tuned to the specific application. These parameters can then be adjusted to provide droplets having the required or desired properties.

[0087] The imaging system **30** can visualize and analyze droplets in flight. And, as such, cab adjust certain parameters, such as, but not limited to the, piezo-actuating voltage pulse profile, magnitude or frequency, and the like

[0088] In one embodiment, the imaging system **30** comprises a high speed video instrument model JetExpert manufactured by ImageXpert Inc., Nashua, New Hampshire, U.S.A. which is used to analyze and visualize droplet characteristics or properties such droplet size, droplet velocity, among others.

[0089] The liquid handling system further comprises a control system or controller **32** to monitor and control system operation. Suitable software **34** is utilized for users to control the various system parameters and operations. The controller **32** can include or be interfaced with various sub-controllers, such as, the piezoelectric dispenser **100,** control and electronics circuitry or module **36,** and those of the various motion, imaging and fluid flow and dynamic systems, among others, as needed or desired, with efficacy. The electronics module or energy source **36** provides a pulsed voltage signal **38** to actuate the piezoelectric dispenser **100.**

[0090] It is preferable to fine tune the pulsed voltage signal **138** such that it is not strictly in a square or rectangular format to avoid sudden impact with the dispensing tube, but rather such that it is adapted to desirably comprise smooth signal transitions. This can advantageously result in improved droplet structure, droplet volume control and the like. The electronics module or energy source **36** can be configured with an arrangement of resistors, capacitors and the like to ensure creation of such a preferred voltage signal **138.** The smooth transition can be more advantageous when relatively larger droplets are to be dispensed.

[0091] Though **FIG. 1A** shows only a single dispenser **100,** in other embodiments, it is contemplated that multiple dispensers in linear (1 x N) or two-dimensional (M x N) arrays are used. These may be provided and operated either in parallel or in another coordinated fashion, as desired. It should be understood that any discussion herein with specific reference to the single dispenser embodiment is substantially equally applicable, with possible modifications as apparent to the skilled artisan, to multiple dispensers actuated by one or more piezoelectric actuators or transducers. In addition, fluid may be provided to multiple dispensers using a manifold configuration, as needed or desired. Moreover, the system **10** can be configured to provide on-the-fly dispensing of liquid droplets **12** as deemed suitable. For example, as

disclosed in U.S. Patent No. 6,063,339, the entirety of which is hereby incorporated by reference herein.

[0092] FIG. 1B illustrates a longitudinal transducer or transmission **40** in accordance with some embodiments. The longitudinal transducer **40** generally comprises a piezoelectric actuator or device **126** operatively coupled to a tube **114.** The linear or longitudinal piezoelectric actuator **126** can be clamped to the tube **114,** as discussed further below and herein.

[0093] The longitudinal transducer **40** can further comprise a preloading, clamping, retaining or biasing screw, mechanism, device, assembly or structure **128, 176** that allows for the tube **114** and piezoelectric actuator **126** to be separated, as discussed further below and herein. Optionally, the piezoelectric actuator **126** can be fixedly attached (e.g., bonded) to the tube **114** and the preloading device may be replaced by a fixedly attached support structure or the like to provide a reactive force to the force generated by the piezoelectric actuator **126.** The piezoelectric actuator **126** can be on a portion or side of the tube **114** with the preloading device **128, 176** or support structure being on a generally opposed portion or side of the tube **114.** Optionally, the piezoelectric actuator **126** can substantially completely surround, encircle or circumscribe the outer periphery of the tube **114.** A sleeve, pad or the like may be provided intermediate the piezoelectric actuator **126** and the tube **114.** Similarly, a sleeve, pad or the like may be provided intermediate the preloading device **128, 176** (or support structure) and the tube **114.**

[0094] In operation, a voltage pulse (or alternating voltage) actuates the piezoelectric actuator **126** so that it expands and a generally radial force **52** is exerted or applied on the wall of the tube **114** at generally region **54** of the tube. The region **54** is spaced by a predetermined distance from a distal tip **42** of the tube **114.** This radial force **152** causes a small deformation **46** and radial motion, displacement or movement **48** of the tube **114.** Further, acoustic pressure or stress propagates or is transmitted axially or longitudinally from the region or area **54** of the tube **114,** through the wall of the tube **114** and toward the tube tip **42** which undergoes distal axial or longitudinal motion, displacement or movement **50** in a direction extending away from the piezoelectric actuator **126** (motion in a distal, or negative or -Z direction). Thus, a stress or pressure wave **44** passes longitudinally or axially through the tube wall and provides for transmission or conversion of tube radial motion **48** to axial or longitudinal motion **50** at the tube tip **42.** In some embodiments, the wave **44** has a generally sinusoidal or cosine waveform, profile or configuration.

[0095] On completion of one cycle, the tube **114** reverts back to its deactivated state with radially outward tube motion **48** and proximally retracting tube tip axial motion **50** in a direction extending toward the piezoelectric actuator **126** (motion in a proximal, or in a positive or +Z direction). When multiple pulses of an alternating voltage cause expansion and contraction of the piezoelectric actuator **126** the tube tip **42** undergoes multiple axial or longitudinal oscillations **50.**

[0096] It should be appreciated, that embodiments of the invention, contemplate and utilize the balance between the voltage pulse (or alternating voltage), the configurations, arrangements, sizes and/or dimensions of the piezoelectric actuator **126** and tube **114** to, in some embodiments, provide a stress or pressure profile and wave form that results in a controlled and/or predetermined axial displacement or oscillation at the distal tip **42** of the tube **114.**

[0097] The longitudinal transducer **40** may be utilized with any of the embodiments of the dispensers disclosed or suggested herein. These dispensers would generally comprise the longitudinal transducer **40** in combination with a liquid to be dispensed in the tube **114** and possibly a suitable nozzle or aperture plate to define an aperture or outlet orifice at the tube's distal tip **42.** Thus, in operation, the dispensers can provide for droplet dispensing (such as drop-on-demand dispensing) wherein the tube tip longitudinal or axial oscillation or motion creates a suitable solid-liquid dynamic interaction to facilitate ejection of single droplets of a predetermined size.

[0098] Embodiments of the longitudinal transducers and/or dispensers disclosed herein can be thought of as providing q unique ultrasonic horn wherein the transmission of longitudinal acoustic waves is utilized to transmit and/or convert radial tube motion to controlled and predetermined axial motion of the tube.

[0099] FIGS. 2 to **4** illustrate different views and/or arrangements of a piezoelectric dispensing device or dispenser **100** for fluid handling and transfer in accordance with some embodiments, with like reference numerals corresponding to like elements or structures. The dispenser **100** generally comprises, for illustrative purposes two assemblies, or sub-assemblies **110** and **112.**

[0100] The first structure, arrangement, assembly or sub-assembly **110** (bounded by dashed lines, merely for illustrative purposes, in **FIG. 2**) comprises a capillary tube **114** and a dispensing nozzle **116** generally including an aperture or outlet orifice structure or plate **118.** However, these are non-limiting descriptions such that the outlet **118** and nozzle **116** can be part of or incorporated into the tube **114** or assembly **110.**

[0101] The second structure, arrangement, assembly or sub-assembly **112** can be viewed as, for example, but not limited to, a piezoelectric C-Clamp sub-assembly or the like that comprises a mount, support structure or bracket **120.** The bracket **120** comprises a couple of opposed jaws or arms **122** and **124.** A piezoelectric actuator, transducer, element, stack or assembly **126** is mounted on the first arm **122** and a preloading, clamping, retaining or biasing screw, mechanism, device, assembly or structure **128** is mounted on the second arm **124.**

[0102] FIG. 3 illustrates the dispensing device or dispenser **100** in a preloaded or clamped position. The screw **128** is fastened and locks the capillary tube **114** in place by applying force in the radial direction of the tube **114** such that tube **114** is retained between the piezoelectric actuator, transducer or element **126** and the screw **128.** (Further structural details of the preloading clamping jaws are discussed below with particular reference to **FIG. 4,** and show that in accordance with some embodiments respective opposing portions of respective jaws

are positioned intermediate the piezoelectric element, the screw and the tube.)

[0103] The dispenser **100,** in some embodiments, includes or incorporates the longitudinal transducer **40.** This longitudinal transducer **140** can generally comprise the tube **114,** piezoelectric actuator **126** and the clamping or preloading device **128.** The piezoelectric actuator **126** can be a linear or longitudinal piezoelectric actuator **126** clamped to the tube **114.**

[0104] Upon actuation of the piezoelectric actuator, transducer or element **126,** such as by a voltage pulse or an alternating voltage, it expands and a pulse of force **52** is applied in a generally radial direction **130** toward the tube **114.** The force **52** produces stress in the tube wall at the clamped preloaded region **132** of the tube **114.** Stress or pressure in the region **132** produces an acoustic pressure or stress wave that propagates or is transmitted longitudinally through the wall of the tube **114** toward the nozzle aperture plate **118** and distal tip **42.** This involves transmission or conversion of the radial inward motion to be transmitted in a form that results in a distally extending axial or longitudinal motion or displacement **50.** This dynamic interaction between the solid wall of the tube **114** with the liquid at the aperture **136** causes an ejection of a droplet **12** of a predetermined size from the aperture **136.** Stated differently, or in other words, or explained differently, transmission of acoustic pressure to the fluid or liquid in the region of the aperture plate **118,** is at least partially responsible, for the propulsion or ejection of droplets **12** of fluid or liquid **134** through the aperture or outlet orifice **136.**

[0105] Thus, the pressure or stress wave passing longitudinally through the tube wall provides a unique axial displacement of the distal tube tip **42,** aperture plate **118** and/or aperture **136** for dispensing of single droplets **12.** In some embodiments, this wave has a generally sinusoidal or cosine waveform, profile or configuration. After application of each pulse, the piezoelectric actuator, transducer or element **126** radially expands and axially contracts back to its original size thereby involving an oscillation or oscillatory motion of the tube tip **42.**

[0106] The fluid or liquid **134** level **103** in the tube **114** may be at any point above or below the clamping area **132.** With respect to the liquid level **103** being below the clamping area **132** and/or the piezoelectric actuator, provides a major advantage over conventional piezoelectric dispensing technology, wherein the liquid level has to be at least at the level of the piezoelectric or higher. Again, this translates into the advantages of the unique features of at least the longitudinal transducer **140** wherein transmission or conversion of radial motion to axial motion provides a new dimension of control for accurately dispensing predetermined quantities of fluid in the form of single droplets from a distal tip of the dispenser.

[0107] Desirably, in accordance with some embodiments, prior to droplet ejection, the balance between the hydrostatic pressure head, surface tension and capillary forces maintains the liquid **134** within the lumen of the tube **114** and substantially no liquid is adhesively suspended from the aperture or outlet orifice **136.** The hydrostatic pressure head can be controlled, as needed or desired. (Optionally, the tube **114** can be open to the atmosphere or ambient conditions, as needed or desired.)

[0108] Accordingly, following each use the tube **114** may be removed and replaced by releasing preloading screw **128.** The tube **114** may be disposed following each use, such as with a particular liquid, therefore eliminating the need for cleaning and the risk of contamination from material left over from a prior use.

[0109] In some embodiments, the tube **114** comprises glass. In some embodiments, the tube **114** comprises another rigid material that has a predetermined or preselected modulus of elasticity. In one embodiment, the material forming the tube **114** has a modulus of elasticity greater than about 10 GPa. In one embodiment, the material forming the tube **114** has a module of elasticity greater than about 50 GPa. A higher module of elasticity produces higher stress in the tube wall since the stress is a product of the elasticity and the deformation. This higher stress desirably results in a higher amplitude of oscillation of the capillary tube **114.**

[0110] The capillary tube assembly **110** can comprise a sleeve **138** or the like that substantially surrounds or circumscribes the tube **114.** The sleeve **138** desirably distributes the force imposed by the piezoelectric actuator, transducer or element **126** and prevents stress concentration locally or in one spot which may cause breakage of the tube **114,** such as one made of glass, other rigid material or the like.

[0111] The sleeve **138** can comprise a variety of suitable materials. In one embodiment, the sleeve **138** is made of a metal or alloy such as stainless steel, brass or aluminum, or the like, among others. In another embodiment, the sleeve **138** is made of a plastic such as Delrin®, or the like, among others.

[0112] The sleeve **138** is bonded to the capillary tube **114** by a structural epoxy such as, but not limited to, LOCTITE® Hysol® type E-30CL. Thus, the capillary tube assembly **110** comprising the tube **114** and the sleeve **138** is separable from the dispenser **100** and disposable.

[0113] The aperture plate **118** can, in some embodiments, be bonded to the tube **114** and can be manufactured by electroforming. In one embodiment, the nozzle aperture plate **118** comprises or is made of electroformed nickel or electroformed palladium nickel. Optionally, the aperture plate **118** may be plated by inert material such as titanium nitride or the like with efficacy, as needed or desired. In one embodiment, the aperture plate **118** comprises synthetic sapphire, ruby or the like. The aperture plate **118** may be gold plated. In one embodiment, the thickness of the aperture plate **118** can be in the range of about 60 microns (μm), though higher or lower thicknesses may be efficaciously utilized, as required or desired.

[0114] As shown in the drawings, in some embodiments, the aperture plate **118** has a funnel-like, conical, frusto-conical structure or the like with a curvature that defines a first larger size or diameter at an upstream end and a second smaller size or diameter at a downstream end, that is, at the aperture or outlet orifice **136.** Advantageously, such a configuration can provide improved consistency in control of the droplet size and mitigation of "dead" fluid spots or regions. Moreover, this desirably results in improved overall system operation.

[0115] The piezoelectric or piezoceramic actuator, transducer or element **126** can comprise a co-fired monolithic linear or longitudinal stack which expands and contracts, generally linearly or longitudinally in the direction of the stack, under the input of an alternating voltage. In one embodiment, the piezoelectric or piezoceramic actuator, transducer or element **126** is manufactured by NEC part No. AE0203D04Fas sold by THORLAB. Inc, Newton, New Jersey, U.S.A.

[0116] The clamping or preloading force of the piezoelectric actuator **126** can be varied based on the input voltage signal as well as the configuration of the piezoelectric device itself. In one embodiment, the maximum clamping force of the actuator **126** is in the range of about 200 Newton, though clamping forces below about 2 Newton and above about 250 Newton may be efficaciously utilized, as required or desired.

[0117] The clamping or preloading force of the clamping screw **128** can be varied based on the device and screw configuration. In one embodiment, the clamping screw **128** provides a preloading or clamping force of in the range from about 30 Newton to about70 Newton, including all valued and sub-ranges therebetween, though higher or lower forces may be provided, as needed or desired. The screw **128** can be locked using a torque limiting screw driver which limits the linear force to a predetermined value, such as, but not limited to 70 Newton.

[0118] As discussed above with particular reference to **FIG. 1A,** the dispenser **100** may be used to acquire fluid or liquid samples as well as dispense fluid or liquid droplets. Acquiring samples is done by submerging the capillary tube **114** in a fluid sample and applying vacuum, suction or the like.

[0119] Capillary tube **114** has a generally tubular axis-symmetric shape with a generally thin wall having a thickness **T** as labeled in **FIG. 2.** In one embodiment, the thickness **T** is in the range from about 0.1 mm to about 0.5 mm, including all values and sub-ranges therebetween. In one embodiment, the length of the capillary tube **114** is about 25 mm and the distance of the tube aperture from the clamping point, location or region is desirably greater than about 13 mm such that the capillary tube can be conveniently submerged in a standard laboratory 10 mm deep well plate. Of course, these dimensions can be efficaciously modified to accommodate differently configured well plates, micro-titer plates and the like, among others, as required or desired.

[0120] In another embodiment, the thickness **T** is in the range from about 0.1 mm to about 0.3 mm, including all values and sub-ranges therebetween. Of course, higher or lower tube wall thicknesses may be provided with efficacy, as needed or desired. Advantageously, in accordance with certain embodiments, the generally thin wall structure of the capillary tube **114** allows for the piezo-induced stress to be substantially transmitted to the tube wall in a longitudinal manner as opposed to into the liquid therein, thereby providing additional control on the droplet ejection and the goal of achieving droplet sizes in the low picoliter range.

Moreover, the relatively thin tube wall allows for a low piezoelectric force to be applied thereat such that the low force creates a sufficiently high tube wall stress or pressure with a low radial tube bending and a controlled axial tube displacement or oscillation, while minimizing transmission of compression pressure/stress to the liquid in the tube at the region of application of the radial force.

[0121] Typically, the tube **114** and its lumen have a generally circular cross-section. However, the cross-section of the tube **114** and its lumen may have other shapes, such as, but not limited to square or hexagonal cross sectional shapes.

[0122] In one embodiment, the tube **114** may have two unequal outer diameters at each end labeled **D1** and **D2** in **FIG. 2** with **D2** being greater than **D1.** In another embodiment, the tube **114** may have an even diameter through its length. Diameter **D1** may be in the range from about 1 mm to about 5 mm and diameter **D2** is generally smaller than about 9 mm. Of course, larger or smaller diameters may be provided with efficacy, as needed or desired. In some embodiments, larger opening or diameter **D2** may be used for storage of fluid or liquid sample, such as DNA samples, as discussed further below.

[0123] In one embodiment, an alternating electrical signal at a frequency in the range from about 10 Kilohertz (KHz) to about 100 KHz is provided to the piezoelectric or piezoceramic actuator, transducer or element **126** to produce ejection of single droplets from the produces ejection of droplets **12** from the nozzle aperture plate **118.** In other embodiments, higher or lower frequencies may be utilized with efficacy, as needed or desired.

[0124] The time of actuation (or expansion) of the piezoelectric or piezoceramic actuator, transducer or element **126** depends on various factors, such as, but not limited to, the system or device configuration, dimensioning and droplet size. In some embodiments, this time is of the order of a microsecond (µsecond) up to about in the range of tens or hundreds of microseconds (µseconds), as required or desired. Of course, higher or lower actuation times may be utilized with efficacy.

[0125] Typically, a single oscillation cycle ejects a single droplet **12** which has a droplet diameter that is substantially equal to the diameter of the aperture or outlet orifice **136.** Thus for example, a 50 micron (µm) aperture size or diameter produces a droplet with a diameter of about 50 microns (µm) and having a volume of about 65 picoliters (pL). Similarly, an aperture of 70 µm produces a droplet with a volume of about 180 pL.

[0126] Fluids or liquids can be dispensed one droplet or drop at a time in a "drop-on-demand" mode at frequencies up to and in the range of about 1,000 drops per second. The dispensing device or dispenser **10**) may be used in the production of arrays, such as DNA microarrays and the like, and multiple assays. The placement of the droplets **12** on a target or substrate can be controlled, for example, by a programmable positioning table which may move along the three axis (X, Y and/or Z) of a Cartesian or equivalent coordinate system, as discussed above and with particular reference to **FIG. 1A.**

[0127] FIG. 4 illustrates a more detailed top view of the clamping area of the tube **114** and engaging structural portions **142** and **144** of respective jaws or arms **122, 124.** This drawing also shows the tube **114,** the piezoelectric device **126,** the clamping screw **128,** and the sleeve **138.** In one embodiment and as illustrated, the clamping jaw portions **142** and **144** have a generally V shape and which have four interface points **PI, P2, P3** and **P4** with the sleeve **138.** This configuration can advantageously contribute to and enhance a generally balanced and even distribution of the stress in the clamped region of the tube **114.**

[0128] The angle of the "V" shape may be efficaciously varied such that it can be greater or less than a right-angle (90 degrees) configuration. The number of interface points may also be varied, as needed or desired.

[0129] Clamping jaw portions **142** and **144** may optionally have a curved, arced or arcuate shape with a radius of curvature that is equal to or greater than the radius of (curvature) of the sleeve **138.** Of course, other configurations may be practiced in accordance with embodiments of the invention disclosed, taught or suggested herein. Arrows **146** and **148** schematically depict the clamping, preloading and/or piezo actuation forces.

[0130] FIG. 5 illustrates an arrangement of a piezoelectric dispensing device or dispenser **100a** for fluid handling and transfer in accordance with some embodiments, with like reference numerals corresponding to like elements or structures, which utilize a capillary tube **114** with a generally annular gap **152.** This annular gap **152** is provided between the tube **114** and a concentric core member **150** which would typically have, but not limited to, a cylindrical structure.

[0131] Many configurations and sizes of the gap **152** can be contemplated in accordance with embodiments of the dispenser **100a.** For example, if the internal diameter of the tube **114** is about 1 mm, then the outer diameter of the core member **150** can be about 0.9 mm, thereby providing a radial gap of about 0.05 mm between the tube **114** and the core member **150** which defines the size of the annular capillary gap. One advantage of such an annular gap **152** configuration is that it can assist in reducing the hydrostatic pressure head that acts against or on the nozzle aperture plate **118** and/or the aperture or orifice outlet **136** relative to the capillary forces and surface tension involved. Desirably, this can result in more consistency, accuracy and reliability in dispensing of a particular or predetermined droplet size.

[0132] Moreover, the piezoelectric dispenser **100a** further distinguishes over conventional devices which employ acoustic pressure wave propagation through the liquid for droplet dispensing. The droplet dispensing operation of the dispenser **100a** is substantially independent of how the liquid **134** is loaded within the tube **114.** At least one reason for this is that a longitudinal transducer **140** is utilized which converts radial tube motion to axial tube displacement at the distal tube tip **42** and/or the dynamic interaction between the solid wall of the tube **114** with the liquid at the aperture **136.**

[0133] FIG. 6 illustrates an arrangement of a piezoelectric dispensing device or dispenser **100b** for fluid handling and transfer in accordance with some embodiments, with like reference numerals corresponding to like elements or structures, which utilize a main body portion or bracket **154** and that can be particularly advantageous in dispensing of fluids or liquids suitable for in production of dot arrays or assays, among other applications as disclosed, taught or suggested herein.

[0134] The dispensing device or dispenser **100b** generally comprises a capillary tube assembly **110** that includes a tube **114** and a piezoelectric clamp assembly **112.** The tube **114** includes a dispensing nozzle **116** generally defined by an aperture plate **118.** The clamp assembly **112** can include a mounting bracket **120** that can be part of the main body portion **154** or incorporated therein. The bracket **120** has a first jaw or arm **122** that includes the piezoelectric or piezoceramic actuator, transducer or element **126** while a second jaw or arm **124** includes the preloading mechanism or screw **128.** The screw **128** preloads the tube **114** against the piezoelectric device **126** such that the tube is desirably locked or fixtured in place between the piezoelectric device **126** and the screw **128** in a manner as is described herein. The main body portion **154** can have various structural features that allow for the assembly of the dispensing system including, but not limited to, connection, attachment and coupling devices or the like, among others.

[0135] As taught herein, the piezoelectric device **126** expands and contracts in the direction **130** in response to an alternating electrical voltage which, in accordance with certain embodiments, can be in the range of about 50 volts (such as in the range from, but not limited to, about 59 or less to about 62 or more volts) at a frequency of about 30,000 Hertz (Hz). This displacement of the piezoelectric actuator, transducer or element **126** produces one or more pulses of force in the radial direction **130** toward the tube **114.** This force produces stress in the clamping region **132** of the capillary tube **114.** This stress generates a wave which propagates longitudinally through the tube wall toward the nozzle aperture plate **118** wherein transmission of acoustic pressure to the fluid or liquid **134** in the region of the aperture plate **118** (via solid-fluid/liquid interaction) propels a droplet **12** of fluid through the aperture or outlet orifice **136.** As also discussed above and herein, the stress/pressure wave passing longitudinally through the tube wall provides a unique oscillating distal tube tip **42,** aperture plate **118** and/or aperture **136.** In some embodiments, this wave has a generally sinusoidal or cosine waveform, profile or configuration.

[0136] FIG. 7 illustrates another embodiment of a capillary tube **114'** which may be used in conjunction of any of the dispensing systems and dispensers as disclosed, taught or suggested herein, as suitable, and as needed or desired. The tube **114'** of this embodiment comprises or is made of a high alumina ceramic material. The tube **114'** can have a shank diameter **D3** of about 1.588 mm ($1/16^{th}$ of an inch), a length **L** of about 25.4 mm (1 inch) and an orifice diameter of about 0.076 mm (0.003 inches).

[0137] FIG. 8 illustrates an arrangement of a piezoelectric dispensing device or dispenser **100c** for fluid handling and transfer in accordance with some embodiments, with like reference

numerals corresponding to like elements or structures, which can advantageously be used for storing and transporting pre-filled samples **164** of liquids, as disclosed or suggested herein, in generally sealed and sterile conditions and ambience within a container or tube assembly **160** that can be replaceable, removable and disposable. These embodiments provide a plurality of advantages wherein multiple liquids, such as chemical and biological reagents, may be utilized in an efficient and economical manner, given the unique nature of the replaceable features, in conjunction with a piezoelectric assembly **112** and device **126** that is reusable while the capillary tube assembly **110** is replaceable. Accordingly, a library of liquids and/or samples **164** can be stored in a multiple format of various containers or vessels **160** and retrieved and utilized efficaciously, as required or desired.

[0138] As such, in accordance with certain embodiments, the tube assembly **110** along with the vial containers **164** are readily replaceable. This provides a new dimension of handling and transferring liquids in a convenient, efficient and user-friendly environment. Also, and again, this advantageously not only mitigates the possibility of cross contamination of fluids but desirably and additionally provides an economical and cost effective approach with reuse of the piezoelectric actuator or transducer for further operation such as with a variety of liquids to be dispensed and transferred.

[0139] In accordance with certain embodiments, sample(s) **164** is stored inside a separate container (e.g., container **160**) which is placed, positioned or disposed inside the tube **114** such that its opening **162** is in close proximity to and/or in fluid communication with the aperture plate **118** and/or the aperture or outlet orifice **134.** This can involve that a liquid meniscus **163,** comprising a liquid to be dispensed from the container **160** is in close proximity to and/or in fluid communication with the aperture plate **118** and/or the aperture or outlet orifice **134.** It is important to note that the space or volume **165** does not contain the liquid to be dispensed and typically can comprise a free space such as containing air.

[0140] Actuation of the piezoelectric dispenser **100c** and/or the longitudinal transducer **40** causes transmission or conversion of radial tube motion into axial tube motion at the tip **42** and causes, at least partially due to the solid-liquid dynamic interaction, to eject droplets **12.** It should be noted that conventional piezoelectric technology wherein acoustic pressure is directly transmitted to the liquid to be dispensed, can simply not achieve the advantages provided by at least the dispensing operations employed by the embodiments of **FIG. 8.**

[0141] Container **160** is desirably provided with a cup **166** or the like for sealing its top opening and a second cup (not shown) for sealing its outlet opening **162.** Other methods of container closures such as Blow-Fill-Seal are common in aseptic packaging and may be used in conjunction with these embodiments of the invention, such as the dispenser **100c.**

[0142] In some embodiments, the vial with stored fluid or liquid can comprise the tube assembly **110** which is attached or connected to the dispenser **100c,** and used to dispense a particular liquid or reagent, and then simply removed and replaced by another tube assembly **110** with the a different or same fluid. Thus, these embodiments can provide storage vials or

tubes **114** with bonded sleeves **138** that are part of a library of the same for usage as needed or desired.

[0143] As such, in accordance with certain embodiments, advantageously a cost-effective, efficient and reliable (e.g., substantially eliminating the risk of cross contamination) is provided. The vials or tube assemblies **110** can have tracking numbers, barcodes or the like to identify the particular liquid stored therein and the specific volume of the liquid can be tailored to a specific application. Again, and desirably, such pre-filled vials, vessels or tube assemblies allow for a removable, separable and disposable arrangement while maintaining the integrity and reusability of the dispenser **100c** which employs relatively expensive componentry such as, but not limited to, the piezoelectric device **126.**

[0144] Accordingly, from a commercial standpoint, the pre-filled vials or tube assemblies **110** can be provided as needed or desired and can simply connect to the dispenser **100c** and then disposed and replaced. The pre-filled vials or tube assemblies **110** provide a storage means that allows for them to be used at a later date as needed. Advantageously, this storage can provide for long term accessibility and thus not cause delays when a particular reagent or liquid is required within a short period.

[0145] In one embodiment, the container comprises or is made of polypropylene. Advantageously, polypropylene can eliminate the need for a coating, in accordance with certain embodiments and applications, wherein such coatings are commonly used for protein immobilizing. Such coatings are described in U.S. Patent Nos. 6,852,851, 5,650,506 and 5,447,864.

[0146] FIG. 9 illustrates an arrangement of a piezoelectric dispensing device or dispenser **100d** for fluid handling and transfer in accordance with some embodiments, with like reference numerals corresponding to like elements or structures, which include a plurality or multiplicity of piezoelectric clamps or assemblies, such as **112'** and **112".** The dispenser or dispensing device **100d** and/or the respective assemblies **112'** and **112"** generally comprise two sets of piezoelectric clamps, elements, transducers or elements **126', 126"** which are operatively coupled to respective two preloading clamping screws **128', 128".** A bracket or main body portion **120'** comprises part of the device.

[0147] The piezoelectric dispensing device or dispenser **100d** includes the tube **114** which is closed at one end **168** and forms a shape of a vial (e.g., comprising glass) which can be used for storage of fluid or liquid samples.

[0148] In some embodiments, the screw **126'** can be provided with a resilient member such as a spring **170,** for example, a torsion spring or the like. The torsion spring **170** can be biased in a clockwise direction, or alternatively a counter-clockwise direction, to apply a substantially constant torque on the screw **112'** such that the radial (or axial if viewed relative to a X-Y-Z Cartesian coordinate system)/ force **172** applied by the screw **128'** remains substantially constant during operation of the dispensing device or dispenser **100d.**

[0149] Advantageously, the torsion spring **170** can prevent accidental damage which may be caused by manually over tightening of the screw **128".** In one embodiment, but not limited to, an M5-0.8 screw may be used in conjunction with the torsion spring **170** to apply a predetermined torque, for example, of about 0.03 Nm in a clockwise direction to produce a radial/linear force **172** of about 70 Newton.

[0150] FIGS. 10-13 illustrate different views and/or arrangements of a piezoelectric dispensing device or dispenser **100e** for fluid handling and transfer in accordance with some embodiments. The dispenser **100e** generally comprises a main body portion or bracket **174,** a capillary tube **114,** a piezoelectric actuator, transducer or element **126,** and a preloading, clamping, retaining or biasing mechanism, device, assembly or structure **176** that can clamp the linear or longitudinal piezoelectric actuator **126** to the tube **114.**

[0151] The dispenser **100e** further comprises a connector sleeve **178** that is coupled to or engaged with a pin **180** or the like which in turn is coupled to or engaged with one end of the piezoelectric actuator, transducer or element **126.** The other end of the piezoelectric actuator, transducer or element **126** is coupled to or engaged with a pad or sleeve **182** or the like which in turn is coupled to or engaged with the tube **114.** The pad or sleeve **182** can be bonded to the tube **114** and in combination advantageously provides for a replaceable, removable and disposable unit.

[0152] The main body portion or bracket **174** houses and/or supports the various dispenser components. Various clearance spaces and openings can be provided to allow for positioning of the components and passage of wires or cables and the like. The pad or sleeve **182** can be formed by various methods, such as, but not limited to, electrical discharge machining (EDM).

[0153] The preloading, clamping, retaining or biasing mechanism, device, assembly or structure **176** generally comprises a spring **184,** such as a leaf spring coupled to a mass ball **186** and an actuation arm or lever **188** to provide preloading or clamping on a portion of the tube **114** that is opposed to the piezoelectric actuator, transducer or element **126.** The radial forces are shown in **FIG. 13** as arrows **190** and **192.** The motion of the arm or lever **188** in directions **194** causes the leaf spring to apply and release a force on the mass ball **186** which in turn selectively applies a force on the clamped region **196** of the tube **114.** Desirably, the mass ball **186** provides a reactive opposing force in response to the actuation force of the piezoelectric actuator, transducer or element **126.** The mass ball 186 may comprise a magnet for coupling with, for example, the leaf spring **184,** such that in some embodiments it would provide clearance space for removal and replacement of the dispensing capillary tube **114.**

[0154] The preloading, clamping, retaining or biasing mechanism, device, assembly or structure **176** of the dispenser **100e** can be efficaciously employed with any of the dispensing systems and devices disclosed, taught or suggested herein. The operation of the piezoelectric actuator, transducer or element **126** of the dispenser **100e** is similar to as described above and herein.

[0155] It should be noted that, in accordance with embodiments of the piezoelectric dispenser disclosed herein, the piezoelectric device **126** does not completely surround, encircle or circumscribe the outer periphery of the dispensing tube **114,** but does so only partially. Stated otherwise, the piezoelectric device is on a first side of the tube while the preloading device is on a second substantially opposed second side of the tube. In any of the embodiments disclosed herein, the piezoelectric device can comprise a linear or longitudinal transducer **126** that is clamped to the capillary tube **114.**

[0156] The systems, devices, methods and techniques disclosed or suggested herein have various industrial applications. These may be used for dispensing and aspiration of any fluid, which has a viscosity, but not limited to, in the range of about 1 cps to about 30 cps, including all ranges and sub-ranges therebetween. The nozzle aperture plate may have one aperture or a plurality or multiplicity of apertures or outlet orifices.

[0157] The size or diameter of the aperture or outlet orifice may be in the range from about 5 microns (µm) or less to about 150 microns (µm) or more. In some embodiments, apertures or outlet orifices that have a size or diameter in the range from about 5 microns (µm) to about 10 microns (µm) can generally produces fine droplets which may be used in the production of a wide variety of aerosol and sprays of various chemical, biological or pharmaceutical materials and liquids.

[0158] In one embodiment, the dispensing device or dispenser as disclosed herein may be used as a hand held writing instrument such as an air brush instrument. In this embodiment, the tube may be filled with ink, coloring fluid(s), liquid(s) or the like. In another embodiment, the dispensing tube may comprise a hypodermic needle for delivery of local anesthetic into inflated abdominal space prior to or during a laparoscopy surgical procedure.

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- US29488911 **[0001]**
- US61461664 **[0001]**
- US6387330B1 **[0003]**
- DE202006019795 **[0004]**

- US6063339A **[0091]**
- US6852851B **[0145]**
- US5650506A **[0145]**
- US5447864A **[0145]**

Patentkrav

1. En langsgående eller lineær transducer til konvertering af en radial forskydning til en aksial forskydning, som omfatter:
et rør med en længde, en væg med en forudbestemt tykkelse, en lumen med en forudbestemt størrelse eller diameter og en spids i en distal ende af røret;
en piezoelektrisk aktuator, der er koblet funktionsmæssigt til røret på en placering proksimalt for spidsen, en generelt V-formet kæbekonfiguration, der bruges til at slutte den piezoelektriske aktuator til røret; og hvori aktivering af den piezoelektriske aktuator skaber en trykbølge, der spredes gennem rørvæggen fra nævnte placering af røret mod spidsen af røret, så radial bevægelse ved nævnte placering af røret transmitteres som distalt udstrækkende aksial bevægelse ved spidsen af røret.

2. Transduceren i krav 1, hvori transduceren desuden omfatter en energikilde, der er konfigureret til at levere mindst én spændingsimpuls til den piezoelektriske aktuator.

3. Transduceren i krav 2, hvori spændingsimpulsen og konfigurationen af røret er valgt, så en spidsværdi for trykbølgen forekommer ved spidsen af røret.

4. En dispenser til overførsel af en forudbestemt mængde af en væske, hvori dispenseren omfatter:
transduceren i ethvert af kravene 1 til 3; og en åbning ved spidsen af røret; hvori aktivering af den piezoelektriske aktuator og opbygning af trykbølgen og dens spredning fra nævnte placering af røret mod spidsen af røret med transmission af den radiale bevægelse til nævnte distalt udstrækkende aksiale bevægelse af spidsen af røret skaber en dråbe af en forudbestemt volumen af en væske, der er fyldt i røret, til udsprøjtning fra åbningen ind i eller på mindst ét mål.

5. Dispenseren i krav 4, hvori røret og den piezoelektriske aktuator kan adskilles, så røret kan udskiftes, mens det muliggør anvendelse af samme piezoelektriske aktuator med et andet rør til dispensering af en anden væske.

6. Dispenseren i krav 4 eller 5, hvori røret er valgt fra et bibliotek over gemte rør med respektive væsker påfyldt deri på forhånd.

7. Dispenseren i ethvert af kravene 4 til 6, hvori røret omfatter et generelt stift materiale, der har et elasticitetsmodul på over ca. 10 GPa eller et elasticitetsmodul på over ca. 50 GPa.

8. Dispenseren i ethvert af kravene 4 til 7 i kombination med en væskekilde, der muliggør opnåelse af en væske, der skal dispenseres med dispenseren fra kilden.

9. Dispenseren i ethvert af kravene 4 til 8 i kombination med et bibliotek over gemte væskeprøver, der selektivt kan fyldes i røret.

10. Dispenseren i ethvert af kravene 4 til 8, hvori den piezoelektriske aktuator er placeret over væsken i røret.

11. En fremgangsmåde til konvertering af en radial forskydning til en aksial forskydning, som omfatter:
tilvejebringelse af en langsgående eller lineær transducer, der omfatter en piezoelektrisk aktuator, der reagerer på et anvendt signal eller mindst ét spændingssignal eller en spændingsimpuls, en generelt V-formet kæbekonfiguration, der bruges til at slutte den piezoelektriske aktuator til røret; aktivering af den piezoelektriske aktuator for at tilvejebringe en generelt radial kraft på et rør på transduceren ved et område, der er proksimalt for en distal ende af røret; og konvertering af radial bevægelse af røret ved nævnte område af røret, som skal kontrolleres, og/eller generelt forudbestemt aksial bevægelse ved den distale ende af røret.

12. Fremgangsmåden i krav 11, hvori den aksiale bevægelse omfatter distal aksial bevægelse, og hvori ved deaktivering af det anvendte signal eller spændingsimpulsen eller -signalet den distale ende af røret udsættes for en bevægelse i en proksimal aksial retning, hvorved der skabes en aksial oscillation som reaktion på det anvendte signal eller mindst én cyklus af den pulserede spænding eller det pulserede signal.

13. Fremgangsmåden i krav 11 eller 12, hvori fremgangsmåden desuden omfatter valg af det anvendte signal eller mindst det ene spændingssignal eller den ene spændingsimpuls, så en spidsværdi for en transmitteret trykbølge forekommer ved omkring den distale ende af røret.

14. Fremgangsmåden i krav 11, hvori fremgangsmåden desuden omfatter:
forsyning af røret med en væske til dispensering, hvor røret omfatter en åbning ved den distale ende; og
aktivering af den piezoelektriske aktuator, så der spredes en trykbølge fra nævnte område af røret mod den distale ende af røret, og radial bevægelse ved nævnte område af røret transmitteres som aksial bevægelse ved den distale ende af røret, så der derved udsprøjtes en dråbe med en forudbestemt volumen fra åbningen.

15. Fremgangsmåden i krav 14, hvori:
fremgangsmåden yderligere omfatter placering af den piezoelektriske aktuator aksialt i forhold til eller over væsken inden i røret; eller
fremgangsmåden yderligere omfatter et bibliotek over gemte væskeprøver, der selektivt kan fyldes i røret.

DRAWINGS

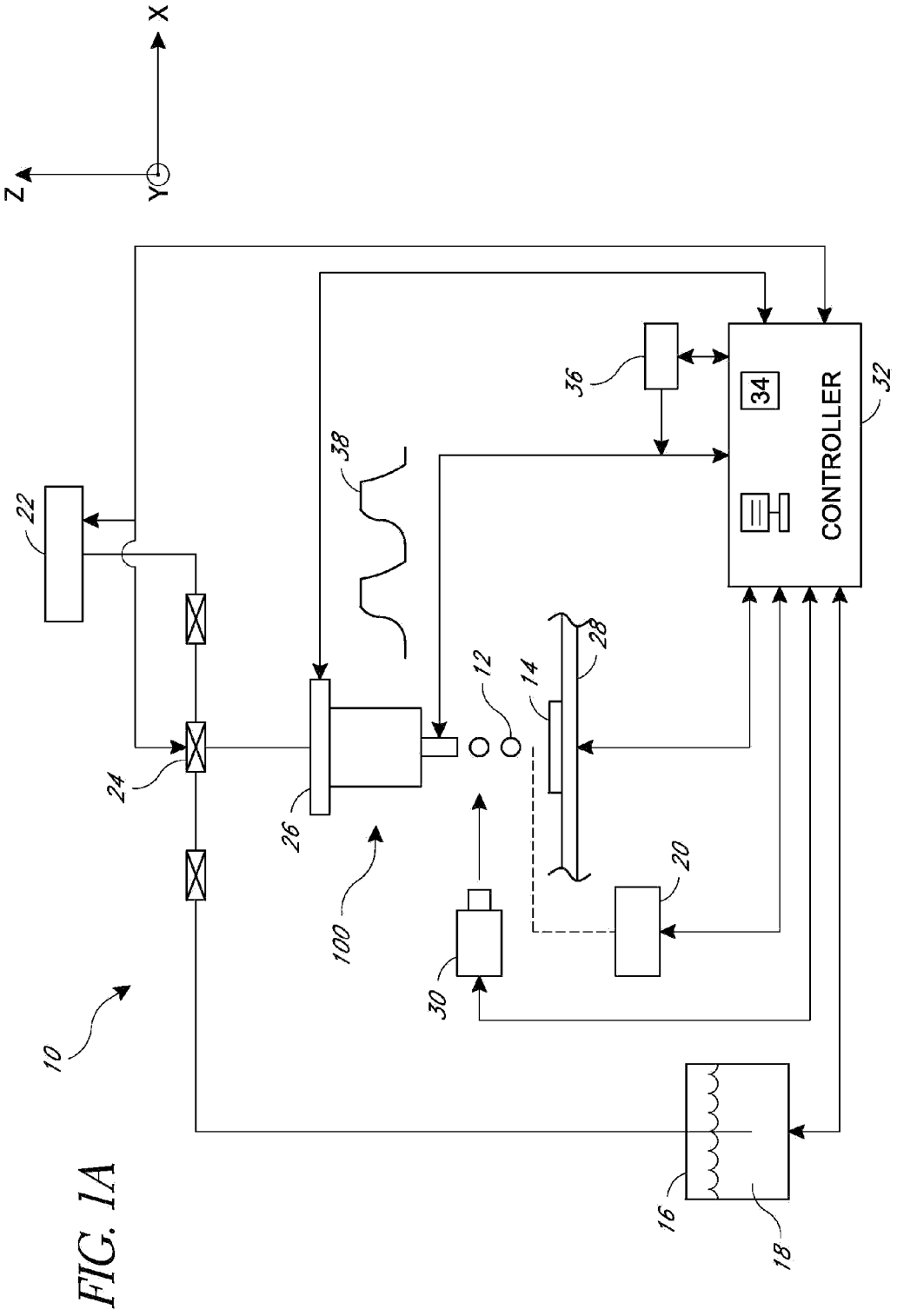


FIG. 1A

FIG. 1B

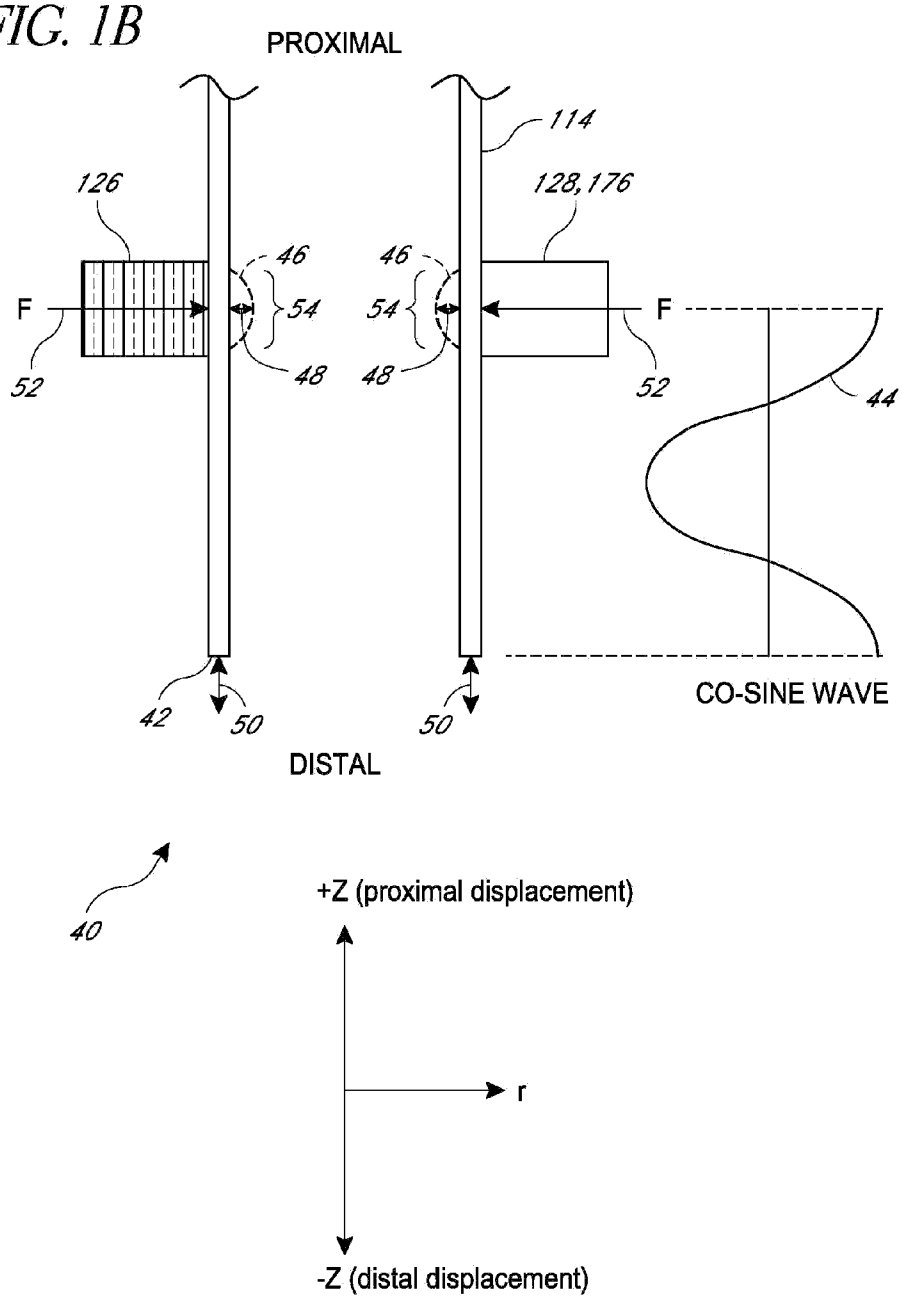

PROXIMAL
126
114
128,176
46
46
54
54
F
F
52
52
48
48
44
CO-SINE WAVE
42
50
50
DISTAL
40
+Z (proximal displacement)
r
-Z (distal displacement)

FIG. 2

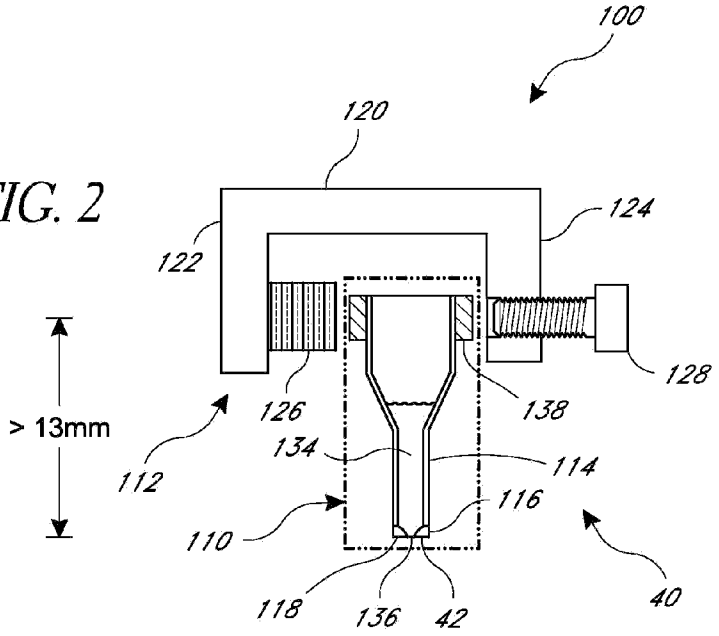

100
120
122
124
128
126
138
> 13mm
112
134
114
116
110
118
136
42
40

FIG. 3

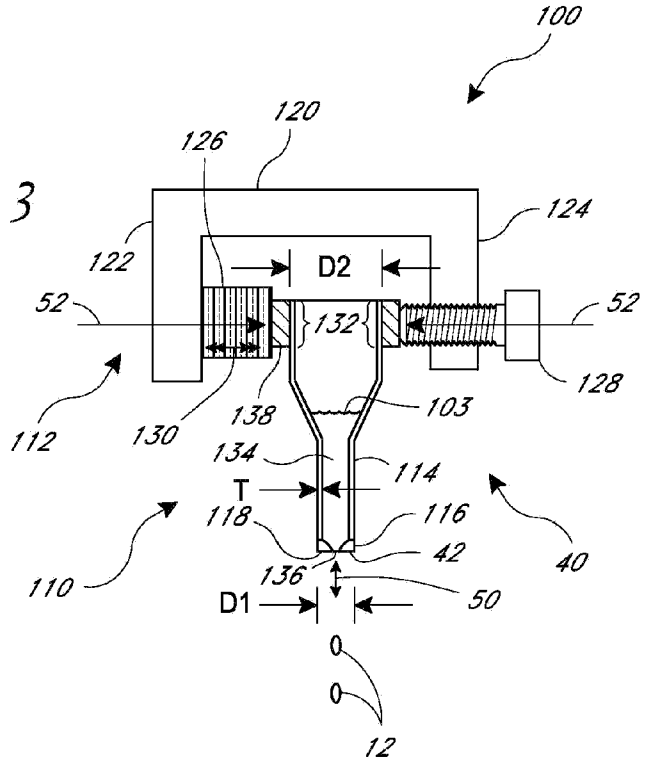

100
120
126
122
124
D2
52
52
132
128
112
130
138
103
134
114
T
118
116
42
110
136
40
D1
50
12

FIG. 4

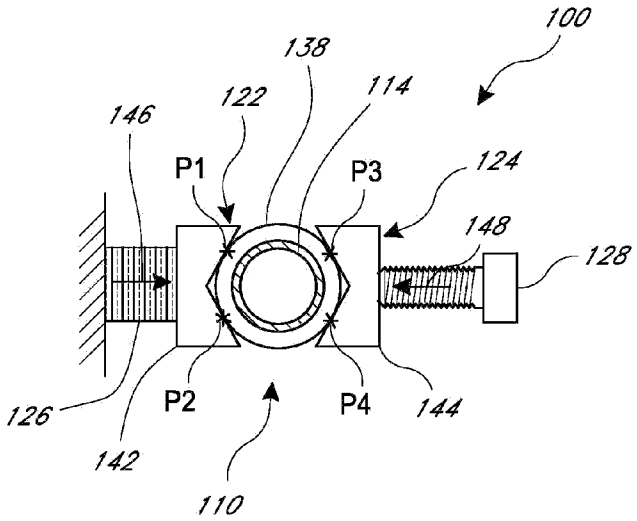

100
138
122
114
146
P1
P3
124
148
128
126
P2
P4
144
142
110

FIG. 5

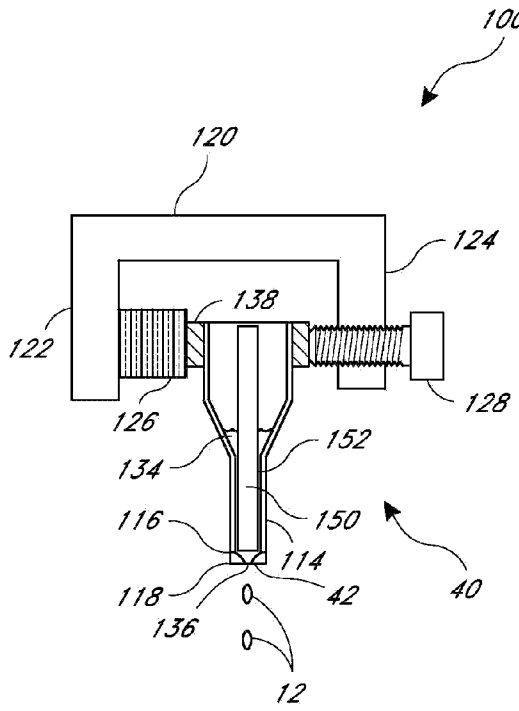
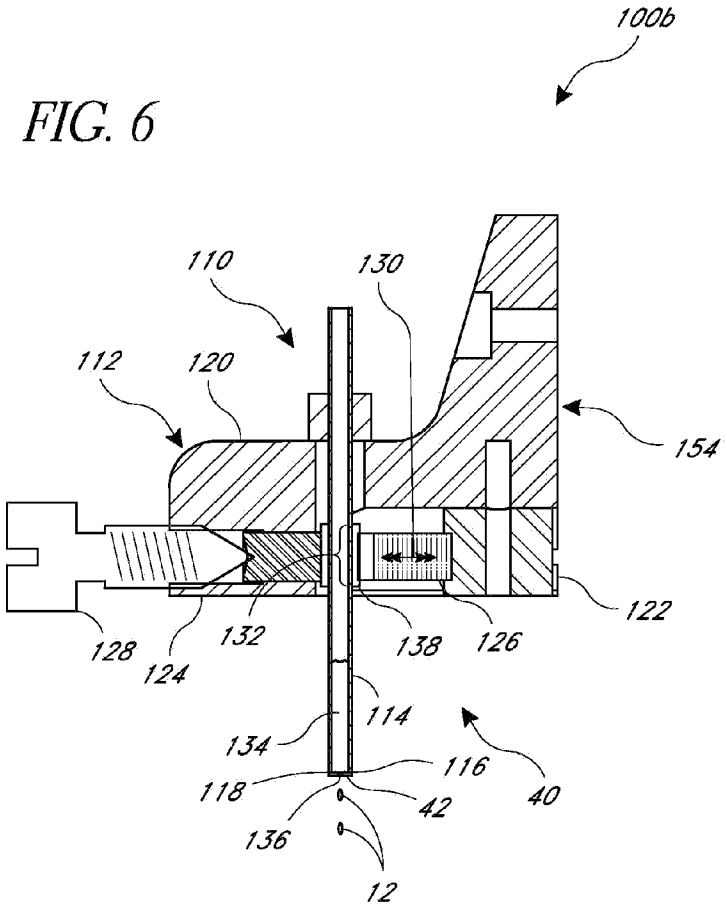

100a
120
124
138
122
126
128
152
134
150
116
114
40
118
42
136
12

FIG. 6


100b
110
130
112
120
154
122
128
124
132
138
126
114
134
116
118
42
40
136
12

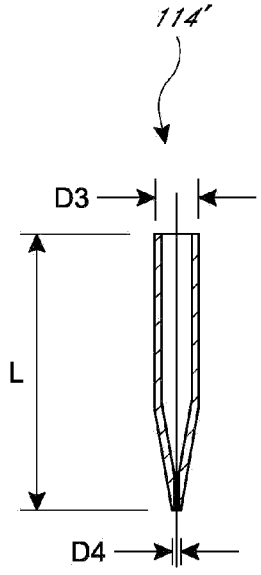

114'
D3
L
D4

FIG. 7

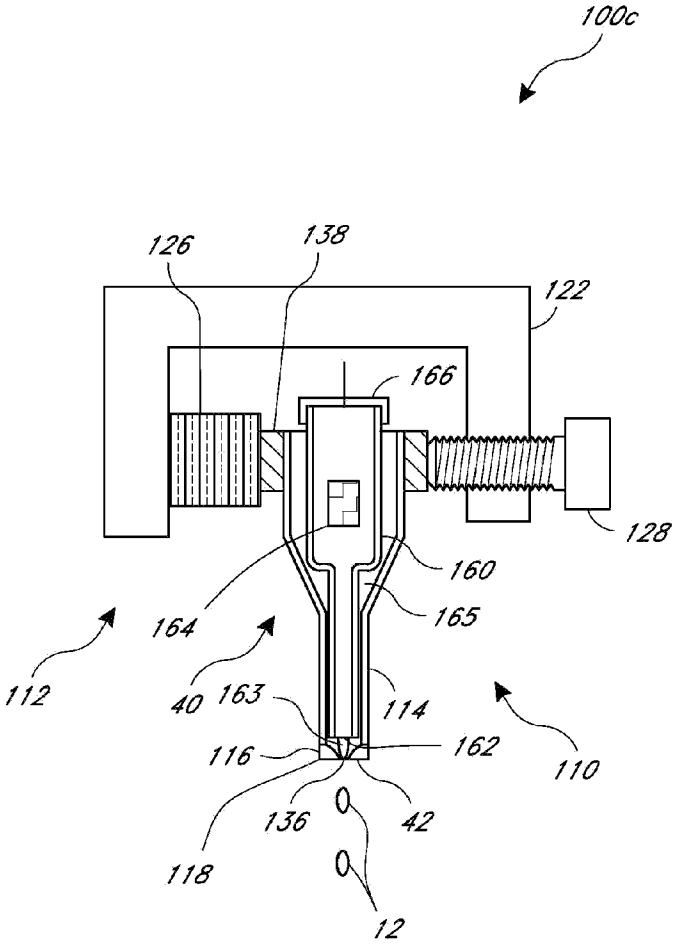

100c
126
138
122
166
128
160
165
164
112
40
163
114
116
162
110
136
42
118
12

FIG. 8

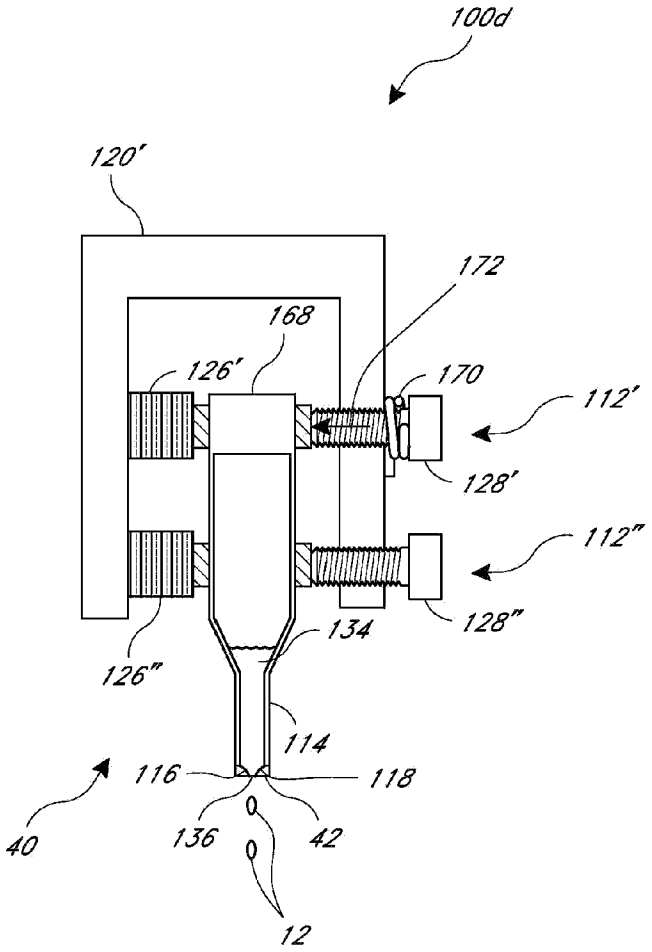

100d
120'
172
168
126'
170
112'
128'
112"
128"
134
126"
114
116
118
40
136
42
12

FIG. 9

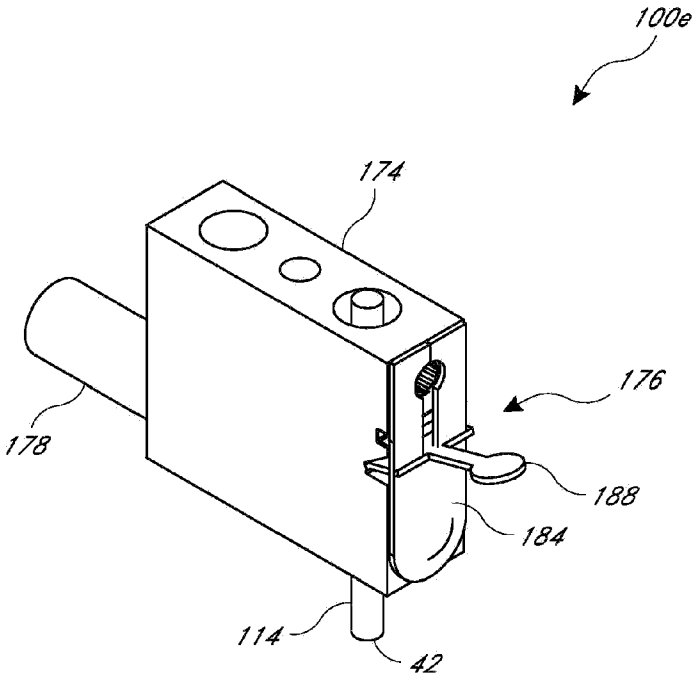


FIG. 10

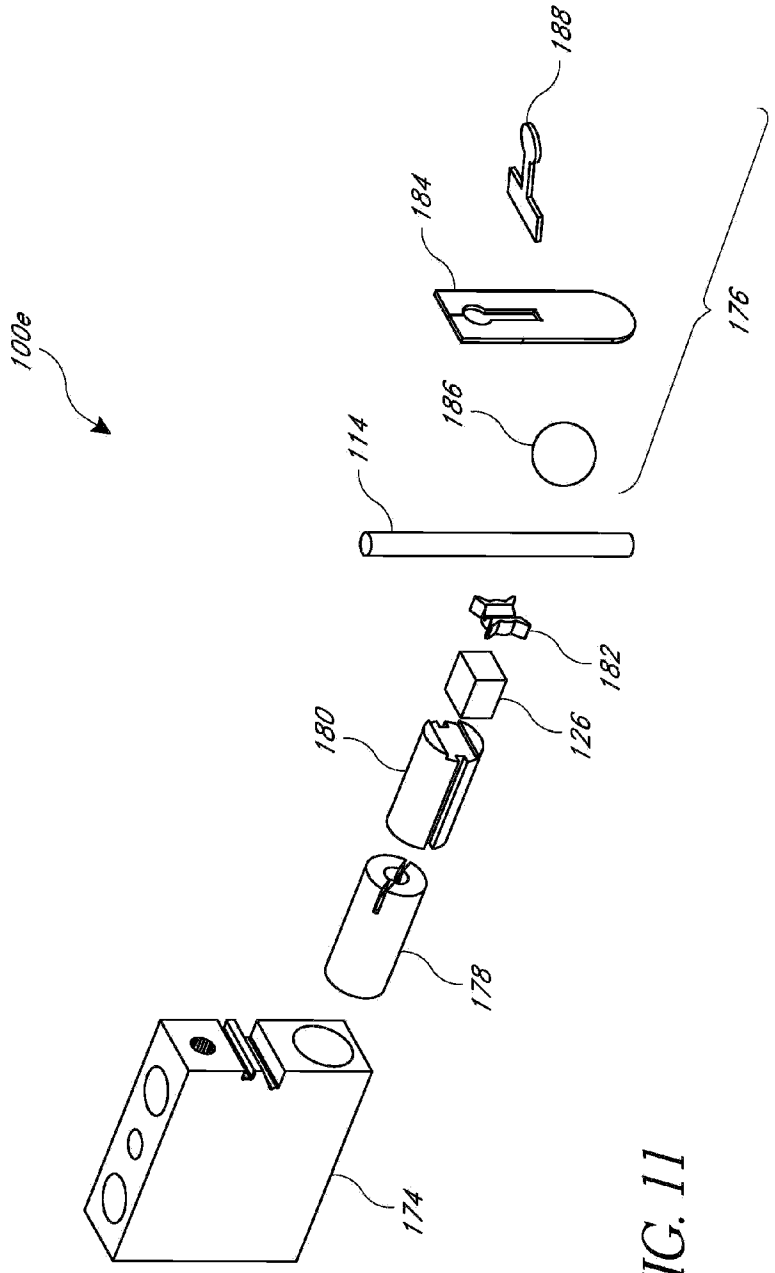


FIG. 11

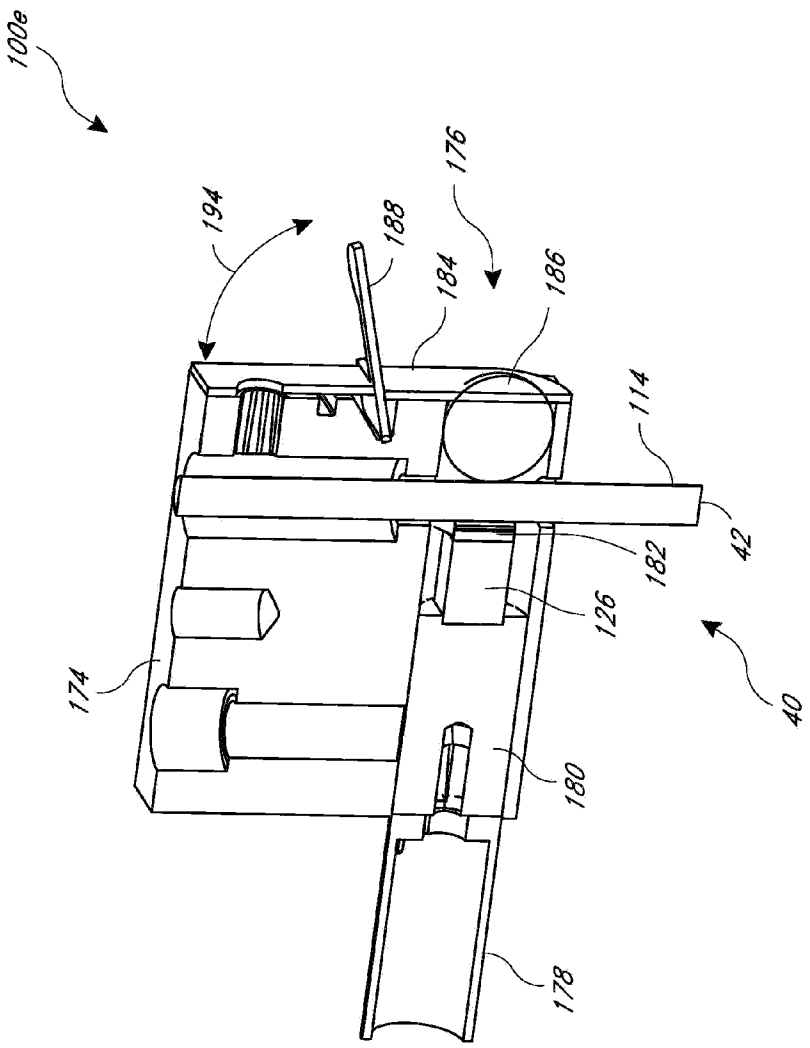


FIG. 12

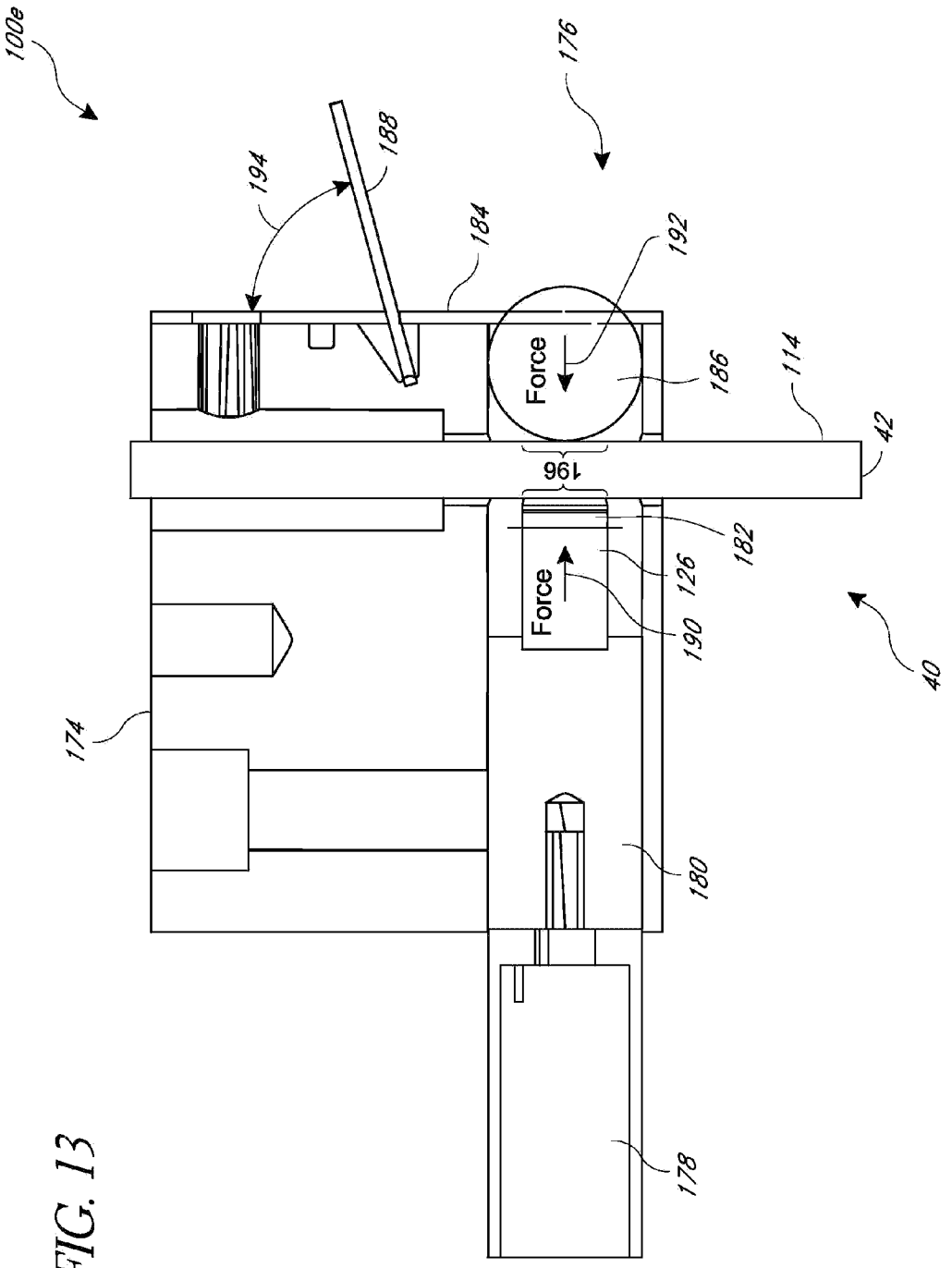

100e
176
188
194
184
192
Force
186
114
42
196
182
126
Force
190
40
174
180
178

FIG. 13