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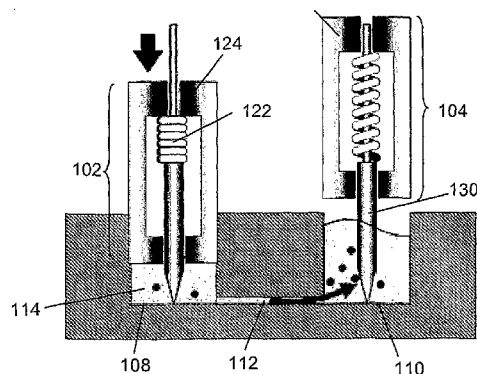
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(54) Title: AN ELECTRO-FLUIDIC INTERFACE TO A MULTI-WELL PLATE

Figure 1C



(57) Abstract: In an embodiment, an electro-fluidic interface to a multi-well plate may be provided. The multi-well plate may include at least one first well and at least one second well, the at least one first well may be connected to the at least one second well via at least one channel. The electro-fluidic interface may include a sealing portion configured to be inserted into the at least one first well and to thereby seal the at least one first well; at least one electrode configured to be inserted through the sealing portion; and at least one biasing structure; wherein the at least one biasing structure may be positioned relative to the sealing portion and the at least one electrode so as to allow movement of the sealing portion relative to the at least one electrode so as to induce a change in pressure in the at least one first well, thereby allowing fluid to be transported away or into the at least one first well.

AN ELECTRO-FLUIDIC INTERFACE TO A MULTI-WELL PLATE

Technical Field

[0001] Embodiments relate to an electro-fluidic interface to a multi-well plate, the multi-well plate including at least one first well and at least one second well, the at least one first well may be connected to the at least one second well via at least one channel.

Background

[0002] A microtiter multi-well plate or microplate has become a routine tool in analytical research, drug discovery, and clinical diagnostic laboratories. Basically, it is an injection molded flat plastic with an array of identical wells where each isolated well acts as a small test tube. The format of the wells including the plate overall dimension has been set by the international standards. For instance, a standard plate typically may contain 96, 384, 1536 or 3456 wells in a rectangular matrix with liquid holding capacity of an individual well varying from several milliliters down to tens of nanoliters. Dispensing liquids into these wells may be automated and performed by precision robots known as liquid handling stations. Such robots may be available from various suppliers at a costly capital investment.

[0003] As the microplates became the industry standard, research in microfluidics has intensified over the past decade signaling the trend that the microfluidic devices may replace the microplates in the years to come. Unlike the microplates which are composed of merely simple wells, these microfluidic devices may contain a network of microfluidic channels interconnecting the wells. The wells, however, may not comply with the

standards in terms of their dimensions and positions which may be arbitrarily set according to the preference of the designer. Besides, since many of the microfluidic devices function under pressure-driven flow, leak-proof connections need to be established between these wells and tubings. These tubings may be typically linked to a syringe pump, pressurized gas or a vacuum source.

[0004] Given the sizable capital investment in the robotic liquid-handling stations, it may be unlikely that the community may move away from the microplates anytime soon. Instead, the community may adopt microfluidics by integrating it into the existing microplate platform. In fact, one example may include a microplate with integrated micro-capillary structures. However, this approach may also bring new challenges and needs, particularly on the front of electrical and fluidic interfacing to a hybrid plate with large number of wells.

[0005] Therefore, there is a need for an electro-fluidic interfacing to a microfluidic based plate or multi-well plate which may provide electrical access and be able to drive fluid through the multi-well plate.

Summary

[0006] In various embodiments, an electro-fluidic interface to a multi-well plate may be provided. The multi-well plate may include at least one first well and at least one second well, the at least one first well may be connected to the at least one second well via at least one channel. The electro-fluidic interface may include a sealing portion configured to be inserted into the at least one first well and to thereby seal the at least one first well; at least one electrode configured to be inserted through the sealing portion; and at least

one biasing structure; wherein the at least one biasing structure may be positioned relative to the sealing portion and the at least one electrode so as to allow movement of the sealing portion relative to the at least one electrode so as to induce a change in pressure in the at least one first well, thereby allowing fluid to be transported away or into the at least one first well.

[0007] In various embodiments, an electro-fluidic interface to a multi-well plate may be provided. The multi-well plate may include at least one first well and at least one second well, the at least one first well may be connected to the at least one second well via at least one channel. The electro-fluidic interface may include a sealing portion configured to be inserted into the at least one first well and to thereby seal the at least one first well; and at least one electrode coupled to the sealing portion; wherein the at least one electrode may be configured to allow movement of the sealing portion relative to the at least one electrode so as to induce a change in pressure in the at least one first well, thereby allowing fluid to be transported away or into the at least one first well.

Brief Description of the Drawings

[0008] In the drawings, like reference characters generally refer to the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead generally being placed upon illustrating the principles of various embodiments. In the following description, various embodiments of the invention are described with reference to the following drawings, in which:

FIGs. 1A to 1C show respective cross-sectional views of two electro-fluidic interfaces in use, one of the two electro-fluidic interfaces used for transporting fluid away from a first well according to an embodiment;

FIGs. 2A to 2C show respective cross-sectional views of two electro-fluidic interfaces in use, one of the two electro-fluidic interfaces used for transporting fluid into a first well according to an embodiment;

FIG. 3A shows a bottom view of an electro-fluidic interface including a plurality of second electrode portions arranged in a 4X4 matrix grid according to an embodiment;

FIGs. 3B to 3D show respective side views of the electro-fluidic interface as shown in FIG. 3A when in use according to an embodiment;

FIG. 4A shows a photomicrograph of a planar view of a microchip corresponding to a single unit of a multi-well plate with 1536 wells prior to placement of a capping layer according to an embodiment; FIG. 4B shows a close-up view of a centre of the microchip as shown in FIG. 4A according to an embodiment; FIG. 4C shows a scanning electron microscope (SEM) image of a section of a microchannel sidewall in a centre of the single unit of the multi-well plate as shown in FIG. 4A according to an embodiment;

FIG. 5 shows an image of a capping layer being aligned and bonded to the microchip as shown in FIGs. 4A to 4C to form a multi-well plate according to an embodiment;

FIG. 6A shows a proof-of-concept demonstration of a cell capture via unplugging of a sealing portion from a respective well according to an embodiment; FIG.

6B shows an insertion of the sealing portion into a respective well according to an embodiment; FIG. 6C shows a removal of the sealing portion from a respective well according to an embodiment; FIG. 6D shows a microscope image taken under visible light of a cell being captured at a microcapillary opening linked to a respective well which may have been unplugged according to an embodiment; FIG. 6E shows a microscope image taken under fluorescent microscope of a cell being captured at a microcapillary opening linked to a respective well which may have been unplugged according to an embodiment;

FIG. 7 shows a cross-sectional view of an electro-fluidic interface, the electro-fluidic interface including a sealing portion sized to seal the first well when in contact according to an embodiment

FIGs. 8A and 8A' show respective cross-sectional views of an electro-fluidic interface in use, the electro-fluidic interface including the sealing portion as shown in FIG. 7 and a further sealing portion surrounding the sealing portion positioned around the sealing portion according to an embodiment;

FIGs. 8B and 8B' shows a cross-sectional view of an electro-fluidic interface in use, the electro-fluidic interface including a sealing portion and a further sealing portion positioned within the sealing portion according to an embodiment;

FIGs. 8C and 8C' show respective cross-sectional views of an electro-fluidic interface in use, the electro-fluidic interface including a sealing portion and a further sealing portion positioned within the sealing portion according to an embodiment;

FIGs. 9A and 9B show respective cross-sectional views of an electro-fluidic interface in use according to an embodiment;

FIGs. 10A and 10B show respective cross-sectional views of an electro-fluidic interface in use according to an embodiment;

FIGs. 11A to 11C show respective cross-sectional views of an electro-fluidic interface in use, the electro-fluidic interface including a deformable electrode configured in a first manner and a sealing portion with a first shape according to an embodiment;

FIG. 12 show a cross-sectional view of an electro-fluidic interface in use, the electro-fluidic interface including a deformable electrode configured in a first manner and a sealing portion with a second shape according to an embodiment;

FIG. 13 show a cross-sectional view of an electro-fluidic interface in use, the electro-fluidic interface including a deformable electrode configured in a second manner and a sealing portion with a first shape according to an embodiment; and

FIGs. 14A to 14E show respective cross-sectional views of the electro-fluidic interface as shown in FIG. 13 in use in a patch clamp application according to an embodiment.

Description

[0009] The following detailed description refers to the accompanying drawings that show, by way of illustration, specific details and embodiments in which the invention may be practiced. These embodiments are described in sufficient detail to enable those skilled in the art to practice the invention. Other embodiments may be utilized and structural, logical, and electrical changes may be made without departing from the scope of the invention. The various embodiments are not necessarily mutually exclusive, as some embodiments can be combined with one or more other embodiments to form new embodiments.

[0010] The word "exemplary" is used herein to mean "serving as an example, instance, or illustration". Any embodiment or design described herein as "exemplary" is not necessarily to be construed as preferred or advantageous over other embodiments or designs.

[0011] An embodiment may provide an electro-fluidic interface to a multi-well plate, the multi-well plate may include at least one first well and at least one second well, the at least one first well may be connected to the at least one second well via at least one channel. The electro-fluidic interface may include a sealing portion configured to be inserted into the at least one first well and to thereby seal the at least one first well; at least one electrode configured to be inserted through the sealing portion; and at least one biasing structure; wherein the at least one biasing structure may be positioned relative to the sealing portion and the at least one electrode so as to allow movement of the sealing portion relative to the at least one electrode so as to induce a change in pressure in the at least one first well, thereby allowing fluid to be transported away or into the at least one first well.

[0012] The number of wells or channels may vary depending on design and user requirements.

[0013] In an embodiment, the sealing portion may be decoupled from the at least one electrode via the at least one biasing structure.

[0014] In an embodiment, the at least one electrode may be configured to provide a constant electrical access to the at least one first well.

[0015] In an embodiment, the at least one electrode may be configured to be connected to an external device. The external device may be a power supply or a measuring device for

measuring an electrical characteristics of a fluid or an electrolyte housed in the respective at least one first well or at least one second well.

[0016] In an embodiment, the at least one biasing structure may be configured to be in an uncompressed state or a compressed state. The default position of the at least one biasing structure may be in the uncompressed state or in the compressed state depending on whether to transport the fluid away or into the respective first well or second well. The at least one biasing structure may also be positioned at any suitable distance away from the multi-well plate or respective first well or second well so as to prevent contact with the fluid to be housed within the respective first well or second well.

[0017] In an embodiment, a change in state of the at least one biasing structure from the uncompressed state to the compressed state upon pushing the sealing portion into the at least one first well may enable the sealing portion to move relative to the at least one electrode in a direction towards the at least one first well so as to transport fluid away from the at least one first well.

[0018] In an embodiment, a change in state of the at least one biasing structure from the compressed state to the uncompressed state upon pulling the sealing portion out from the at least one first well may enable the sealing portion to move relative to the at least one electrode in a direction away from the at least one first well so as to transport fluid into the at least one first well. When the at least one biasing structure may be in a compressed state, the sealing portion may be in sealing contact with the at least one first well. As the at least one biasing structure changes from the compressed state to the uncompressed state, the sealing portion may move in a direction away from the at least one first well.

[0019] In an embodiment, the at least one electrode may include a single elongated portion or separate portions. The separate portions may be bonded together by any suitable process. The at least one electrode may be of any suitable shape or length depending on user and design requirements.

[0020] In an embodiment, the at least one electrode may include at least one first electrode portion and at least one second electrode portion.

[0021] In an embodiment, the at least one first electrode portion may include a cross-sectional dimension same or different from that of the at least one second electrode portion. The at least one first electrode portion may include a cross-sectional shape same or different from that of the at least one second electrode portion. The cross-sectional shape may include a circle, a triangle, a square, a rectangle, for example.

[0022] In an embodiment, the at least one first electrode portion may include a smaller cross-sectional dimension than the at least one second electrode portion so as to support the at least one biasing structure at an interface between the at least one first electrode portion and the at least one second electrode portion when in use. The difference in cross-sectional dimension between the at least one first electrode portion and the at least one second electrode portion may prevent the at least one biasing structure from slipping through the at least one electrode in a default position.

[0023] In an embodiment, the at least one first electrode portion may include a cross-sectional dimension in a range from about 0.1 mm to about 5 mm.

[0024] In an embodiment, the at least one second electrode portion may include a cross-sectional dimension in a range from about 0.1 mm to about 5 mm, for example about 0.5 mm.

[0025] In an embodiment, the at least one first electrode portion may be of a same or a different material from the at least one second electrode portion.

[0026] In an embodiment, the at least one first electrode portion may include a material selected from a group consisting of silver (Ag), silver chloride (AgCl), gold, platinum, titanium, and all common materials available in a clean room which may be suitable for a patch clamp application. For example, the at least one first electrode portion may also include any suitable combinations of materials. The at least one first electrode portion may include a silver wire coated with a layer of silver chloride.

[0027] In an embodiment, the at least one second electrode portion may include a material selected from a group consisting of silver, silver chloride, platinum, titanium, and all common materials available in a clean room which may be suitable for a patch clamp application. For example, the at least one second electrode portion may also include any suitable combinations of materials. The at least one second electrode portion may include a silver wire coated with a layer of silver chloride.

[0028] In an embodiment, number of the at least one first electrode portion may be same or different from number of the at least one second electrode portion. The number of the at least one first electrode portion or the at least one second electrode portion may be equivalent to or more than the number of the respective first and second wells in the multi-well plate. The number of the respective at least one first electrode portion or the at least one second electrode portion may range from 1 to 3456, for example.

[0029] In an embodiment, the at least one biasing structure may include at least one spring or an elastomer layer. The at least one biasing structure may include any other suitable component or material which can introduce a spring effect. The at least one

biasing structure may include any suitable number of springs depending on user and design requirements.

[0030] In an embodiment, the sealing portion may include a flexible insulating material configured to seal the at least one first well when in contact. The insulating nature of the sealing portion may also prevent adjacent electrodes from establishing an electrical contact when placed near to each other.

[0031] In an embodiment, the sealing portion may include a material selected from a group consisting of plastic, polydimethylsiloxane (PDMS), acrylic or polycarbonate. As an example, if the respective at least one first well or the at least one second well may include a relatively soft material, then the sealing portion may be of a relatively rigid material and vice versa.

[0032] In an embodiment, the at least one electrode may be of a rigid electrically conducting material so as to establish an electrical connection to the fluid housed within the respective first well or second well.

[0033] In an embodiment, the at least one electrode may further include at least one intermediate portion, the at least one intermediate portion positioned between the at least one first electrode portion and at the least one second electrode portion, the at least one intermediate portion may be configured to support the at least one biasing structure when in use. The addition of the at least one intermediate portion may provide an alternative configuration to the difference in cross-sectional dimension of the at least one first electrode portion and the at least one second electrode portion.

[0034] In an embodiment, the at least one intermediate portion may include a same or a different material from the at least one first electrode portion or the at least one second

electrode portion. The at least one first electrode portion, the at least one second electrode portion and the at least one intermediate portion may be fabricated in a single process or by separate processes.

[0035] In an embodiment, the at least one intermediate portion may be arranged at a direction substantially perpendicular to the at least one first electrode portion and the at least one second electrode portion. The at least intermediate portion may be arranged at any suitable position or may be of any suitable shape or dimension so as to support the at least one biasing structure on the at least one intermediate portion when in use.

[0036] In an embodiment, the at least one first electrode portion may include two substantially parallel first electrode portions, the two substantially parallel first electrode portions may be spaced apart by a first electrode predetermined distance.

[0037] In an embodiment, the first electrode predetermined distance may be in a range of about 1 mm to about 50 mm.

[0038] In an embodiment, the at least one second electrode portion may include a plurality of substantially parallel second electrode portions, each of the plurality of substantially parallel second electrode portions may be spaced apart by a second electrode predetermined distance.

[0039] In an embodiment, the second electrode predetermined distance may be in a range of about 1 mm to about 10 mm.

[0040] In an embodiment, the first electrode predetermined distance may be same or different from the second electrode predetermined distance. For example, the first electrode predetermined distance may be larger or smaller than the second electrode predetermined distance depending on design and user requirements.

[0041] In an embodiment, the at least one first well may include a plurality of first wells, each of the plurality of first wells spaced apart by a well predetermined distance, the second electrode predetermined distance may correspond to the well predetermined distance. The well determined distance may be determined by a user when fabricating the multi-well plate. For example, for a multi-well plate with 1536 wells, the second electrode predetermined distance may be about 2.25 mm center-to-center of the adjacent second electrode portions. For a multi-well plate with 384 wells, the second electrode predetermined distance may be about 4.5 mm center-to-center of the adjacent second electrode portions. For a multi-well plate with 96 wells, the second electrode predetermined distance may be about 9 mm center-to-center of the adjacent second electrode portions.

[0042] In an embodiment, the sealing portion may further include at least one arm portion. The sealing portion may include two arm portions so as to facilitate an ease of activating or moving the sealing portion onto the at least one first well. The sealing portion may also include any suitable number of arm portions depending on user and design requirements. Each of the at least one arm portion may extend in a substantially perpendicular direction away from the at least one first electrode portion.

[0043] In an embodiment, the electro-fluidic interface may further include a viewing window so as to allow a user to align the electro-fluidic interface to the multi-well plate.

[0044] In an embodiment, the viewing window may further include a dimension in a range from about 0.5 mm to about 2 mm, typically about 1 mm.

[0045] In an embodiment, the viewing window may be formed from a part of the sealing portion and from a part of the at least one intermediate portion. An opening may be

formed in the part of the sealing portion and the part of the at least one intermediate portion. Further, a transparent material may be optionally positioned over the formed opening. The viewing window may be positioned at any suitable position along the length of the sealing portion or the at least one intermediate portion as long as the position along the length of the sealing portion corresponds to the position along the length of the at least one intermediate portion to allow the user to view the multi-well plate or the sample housed within the at least one first well.

[0046] In an embodiment, the electro-fluidic interface may further include a further sealing portion configured to surround the at least one electrode.

[0047] In an embodiment, the further sealing portion may be positioned within sealing portion or be configured to surround the sealing portion.

[0048] In an embodiment, the sealing portion may be of a same or a different material as the further sealing portion.

[0049] In an embodiment, the further sealing portion may include a plug formed of a gasket material or an O-ring.

[0050] In an embodiment, the at least one electrode may be configured to be in an unstretched state or a stretched state.

[0051] In an embodiment, a change in state of the at least one electrode from the unstretched state to the stretched state upon pushing the sealing portion into the at least one first well may enable the sealing portion to move in a direction towards the at least one first well so as to transport fluid away from the at least one first well.

[0052] In an embodiment, a change in state of the at least one electrode from the stretched state to the unstretched state upon pulling the sealing portion out from the at

least one first well may enable the sealing portion to move in a direction away from the at least one first well so as to transport fluid into the at least one first well.

[0053] An embodiment may provide an electro-fluidic interface to a multi-well plate. The multi-well plate may include at least one first well and at least one second well, the at least one first well may be connected to the at least one second well via at least one channel. The electro-fluidic interface may include a sealing portion configured to be inserted into the at least one first well and to thereby seal the at least one first well; and at least one electrode coupled to the sealing portion; wherein the at least one electrode may be configured to allow movement of the sealing portion relative to the at least one electrode so as to induce a change in pressure in the at least one first well, thereby allowing fluid to be transported away or into the at least one first well.

[0054] In an embodiment, the at least one electrode may be of a deformable electrically conducting material configured to deform upon an application of a pressure.

[0055] In an embodiment, the at least one electrode may include a material selected from a group consisting silver-doped poly(dimethylsiloxane), poly(acetylene)s, poly(pyrrole)s, poly(thiophene)s, polyanilines, polythiophenes, poly(p-phenylene sulfide), poly(p-phenylene vinylene)s (PPV), poly(3-alkylthiophenes) polyindole, polypyrene, polycarbazole, polyazulene, polyazepine, poly(fluorene)s, polynaphthalene.

[0056] In an embodiment, wherein the sealing portion may include an insulating material configured to seal the at least one first well when in contact.

[0057] In an embodiment, the sealing portion may include a material selected from a group consisting of plastic, polydimethylsiloxane, acrylic, polycarbonate.

[0058] In an embodiment, the at least one electrode may be of a different material from the sealing portion.

[0059] In an embodiment, the at least one electrode may be configured to provide a constant electrical access to the at least one first well.

[0060] In an embodiment, the at least one electrode may be configured to be connected to an external device.

[0061] In an embodiment, the at least one electrode may be configured to be inserted at least partially through the sealing portion.

[0062] In an embodiment, the at least one electrode may be configured to be in an uncompressed state or a compressed state.

[0063] In an embodiment, a change in state of the at least one electrode from the uncompressed state to the compressed state upon pushing the sealing portion into the at least one first well may enable the sealing portion to move in a direction towards the at least one first well so as to transport fluid away from the at least one first well.

[0064] In an embodiment, a change in state of the at least one electrode from the compressed state to the uncompressed state upon pulling the sealing portion out from the at least one first well may enable the sealing portion to move in a direction away from the at least one first well so as to transport fluid into the at least one first well.

[0065] In an embodiment, the electro-fluidic interface may further include a further sealing portion configured to surround the at least one electrode.

[0066] In an embodiment, the further sealing portion may be positioned within sealing portion or be configured to surround the sealing portion.

[0067] In an embodiment, the sealing portion may be of a same or a different material as the further sealing portion.

[0068] In an embodiment, the further sealing portion may include a plug formed of a gasket material or an O-ring.

[0069] In an embodiment, an electro-fluidic interface (or a pogo-pin plug) as an electrical and fluidic interface to a multi-well plate or microplate may be disclosed.

[0070] In an embodiment, an insertion or a removal of the pogo-pin plug which may induce a desired effect of pressure or suction into a well may be disclosed. An electrode or a contact pin within the pogo-pin plug may provide an electrical access route to an electrolyte dispensed in the well. The electrical access may remain uninterrupted during the insertion or removal of the pogo-pin plug due to compression and uncompression of a spring element which may decouple movement of the insulating portion or plug from the electrode or contact pin.

[0071] In an embodiment, a relatively simple and effective means to introduce pressure or vacuum into wells as and when desired while maintaining a constant electrical access to each well may be disclosed.

[0072] In an embodiment, a plurality of pogo-pin plugs (which may or may be arranged according to a standard microplate format) may be pushed into or pulled from the respective wells so as to create the effect of pressure or vacuum while maintaining an uninterrupted electrical access to the respective wells. The uninterrupted electrical access during the action of plugging or unplugging of the wells may be possible due to a functionality of a pogo pin. A pogo-pin is a spring-loaded electrical contact often used in electronics for establishing temporary electrical connections between circuit components.

Structurally, a pogo-pin contains a straight contact bolt with a shank or stem slidably mounted in a sleeve and projects exteriorly from the sleeve due to loading under a compressed coil spring inside the sleeve.

[0073] One advantage of this approach may be that it may be immuned to air bubbles that may already be present in the wells or introduced with the plugging of the wells. The pogo-pins push the bubbles aside and bypassing the bubbles to remain in contact with the electrolyte in the wells. The coil springs in the pogo-pins serve to decouple the mechanical movement of the insulating portion or plugs from the electrodes or pins. Thus, the electrodes or pins may remain in position and in contact with the electrolyte while unplugging the wells to create the effect of suction.

[0074] In an embodiment, the invention may include use of a plunger-like plug or a sealing portion to exert an effect of pressure or vacuum in the wells without the requirement of an external pneumatic supply and use of a mechanical spring or springs (for example a pogo-pin type configuration) to decouple the movement of sealing portions or plugs from the electrical pins or electrodes to establish a temporary but uninterrupted electrical access with the electrolyte in the wells.

[0075] In an embodiment, the pogo-pin plug may allow an user to measure the real-time electrical resistance as the user may carry out the push and pull action of the sealing portions or plugs.

[0076] In an embodiment, the at least one biasing structure or spring may not be a coil spring and may be substituted with any suitable part that may create the effect of a spring (for example an elastomer membrane) to decouple the movement of the sealing portion or plug from the electrode or contact pin.

[0077] In an embodiment, a single spring element may be utilized to decouple a plurality of plungers from a plurality of contact pins. In this configuration, all the plungers or all the contact pins may move in unison and each plunger may not be controlled independently as opposed to the case with the configuration of a single spring element dedicated to a pair of sealing portion or plunger and electrode or contact pin.

[0078] In an embodiment, the electro-fluidic interface may be used for drug discovery, for example secondary and toxicity screening. The electro-fluidic interface may also be used for automated electrophysiology, for example high throughput patch-clamping on living cells.

[0079] In an embodiment, the electro-fluidic interface may be used for integration in a fully automated high-throughput patch-clamping system based on a lateral approach. The electro-fluidic interface may also be adapted to a chip-based patch-clamping for research as well.

[0080] In an embodiment, the electro-fluidic interface may be immune to air bubbles as the electrodes or contact pins may bypass the air bubbles by pushing the air bubbles aside to remain in contact with the electrolyte in the well. With the electro-fluidic interface, there may not be a requirement of an external pressure or a vacuum source. In addition, the electro-fluidic interface may be compatible with liquid dispensing robots for filling the wells and up or down precise plunger movement of the robot arm.

[0081] In an embodiment, a pressure-driven transport of fluid through channels may be disclosed.

[0082] In an embodiment, the electro-fluidic interface may include a piston-driven plunger or sealing portion which may translate sealingly through a well on a multi-well

plate or microplate. The electro-fluidic interface may include an electrical contact pin or electrode which may protrude from the plunger but able to slide in once contact may be made with the bottom of the well. The electro-fluidic interface may include a spring load to decouple the plunger movement from the contact pin as soon as the contact pin may be in contact with the bottom of the well. The electro-fluidic interface may include a plurality of pogo-pins, each being individually controlled.

[0083] FIGs. 1A to 1C show respective cross-sectional views of two electro-fluidic interfaces 102, 104 in use, one of the two electro-fluidic interfaces 102, 104 used for transporting fluid 114 away from a first well 108 according to an embodiment.

[0084] FIG. 1A shows a multi-well plate 106 which may include a first well 108 and a second well 110, the first well 108 may be connected to the second well 110 via a channel 112. The multi-well plate 106 may include more than two wells depending on user and design requirements. The multi-well plate 106 may be formed as a single integrated plate or may be formed by bonding two separate portions together as may be described later in FIGs. 4A to 4C and FIG. 5 for example. The multi-well plate 106 may be formed of any suitable material or combinations of material depending on user and design requirements. In FIG. 1A, a fluid 114 (including cells 170 or particles) or any sample of interest may be dispensed into the first well 108 by any suitable means, for example a pipette 136 or a liquid-handling station for example.

[0085] FIG. 1B shows two electro-fluidic interfaces 102, 104 to the multi-well plate 106. An electro-fluidic interface 102 may be positioned over the first well 108 housing the fluid 114 and a further electro-fluidic interface 104 may be positioned over the second

well 110 with no fluid. However, the second well 110 may also be configured to house a fluid depending on user and design requirements.

[0086] The electro-fluidic interface 102 may include a sealing portion 124 configured to be inserted into the first well 108 and to thereby seal the first well 108; an electrode 116 configured to be inserted through the sealing portion 124; and a biasing structure 122; wherein the biasing structure 122 may be positioned relative to the sealing portion 124 and the electrode 116 so as to allow movement of the sealing portion 124 relative to the electrode 116 so as to induce a change in pressure in the first well 108, thereby allowing fluid to be transported away or into the first well 108.

[0087] The sealing portion 124 may be decoupled from the electrode 116 via the biasing structure 122. The electrode 116 may be configured to provide a constant electrical access to the first well 108. The electrode 116 may be configured to be connected to an external device (not shown).

[0088] The biasing structure 122 may be configured to be in an uncompressed state or a compressed state. A change in state of the biasing structure 122 from the uncompressed state to the compressed state upon pushing the sealing portion 124 into the first well 108 may enable the sealing portion 124 to move relative to the electrode 116 in a direction towards the first well 108 so as to transport fluid away from the first well 108. A change in state of the biasing structure 122 from the compressed state to the uncompressed state upon pulling the sealing portion 124 out from the first well 108 may enable the sealing portion 124 to move relative to the electrode 116 in a direction away from the first well 108 so as to transport fluid into the first well 108.

[0089] Similarly, the further electro-fluidic interface 104 may include a further sealing portion 134 configured to be inserted into the second well 110 and to thereby seal the second well 110; a further electrode 126 configured to be inserted through the further sealing portion 134; and a further biasing structure 132; wherein the further biasing structure 132 may be positioned relative to the further sealing portion 134 and the further electrode 126 so as to allow movement of the further sealing portion 134 relative to the further electrode 126 so as to induce a change in pressure in the second well 110, thereby allowing fluid to be transported away or into the second well 110.

[0090] The further sealing portion 134 may be decoupled from the further electrode 126 via the further biasing structure 132. The further electrode 126 may be configured to provide a constant electrical access to the second well 110. The further electrode 126 may be configured to be connected to an external device (not shown).

[0091] The further biasing structure 132 may be configured to be in an uncompressed state or a compressed state. A change in state of the further biasing structure 132 from the uncompressed state to the compressed state upon pushing the further sealing portion 134 into the second well 110 may enable the further sealing portion 134 to move relative to the further electrode 126 in a direction towards the second well 110 so as to transport fluid away from the second well 110. A change in state of the further biasing structure 132 from the compressed state to the uncompressed state upon pulling the further sealing portion 134 out from the second well 110 may enable the further sealing portion 134 to move relative to the further electrode 126 in a direction away from the second well 110 so as to transport fluid into the second well 110.

[0092] The electro-fluidic interface 102 may be the same or different from the further electro-fluidic interface 104. Each of the electro-fluidic interface 102 or the further electro-fluidic interface 104 may be controlled independently or may be controlled simultaneously. Each of the biasing structure 122 or the further biasing structure 132 may be configured to be in a default uncompressed state or a compressed state.

[0093] In an embodiment, the electrode 116 of the electro-fluidic interface 102 may include a single elongated portion or separate portions. Similarly, the further electrode 126 of the further electro-fluidic interface 104 may include a single elongated portion or separate portions. In FIG. 1B, the electrode 116 may include a first electrode portion 118 and a second electrode portion 120. The further electrode 126 may include a further first electrode portion 128 and a further second electrode portion 130.

[0094] In an embodiment, the first electrode portion 118 may include a smaller cross-sectional dimension than the second electrode portion 120 so as to support the biasing structure 122 at an electrode interface 138 between the first electrode portion 118 and the second electrode portion 120 when in use. The first electrode portion 118 may include a cross-sectional dimension in a range from about 0.1 mm to about 5 mm and the second electrode portion 120 may include a cross-sectional dimension in a range from about 0.1 mm to about 5 mm. Similarly, the further first electrode portion 128 may include a smaller cross-sectional dimension than the further second electrode portion 130 so as to support the further biasing structure 132 at a further electrode interface 140 between the further first electrode portion 128 and the further second electrode portion 130 when in use. The further first electrode portion 128 may include a cross-sectional dimension in a

range from about 0.1 mm to about 5 mm and the further second electrode portion 130 may include a cross-sectional dimension in a range from about 0.1 mm to about 5 mm.

[0095] In an embodiment, the first electrode portion 118 may be of a same or a different material from the second electrode portion 120. The first electrode portion 118 may include a material selected from a group consisting of silver, silver chloride, gold, platinum, titanium and the second electrode portion 120 may include a material selected from a group consisting of silver, silver chloride, gold, platinum, titanium. Similarly, the further first electrode portion 128 may be of a same or a different material from the further second electrode portion 130. The further first electrode portion 128 may include a material selected from a group consisting of silver, silver chloride, gold, platinum, titanium and the further second electrode portion 130 may include a material selected from a group consisting of silver, silver chloride, gold, platinum, titanium.

[0096] In FIGs. 1B and 1C, the number of the first electrode portion 118 may be the same as the number of the second electrode portion 120. However, the number of the first electrode portion 118 may also differ from the number of second electrode portion 120 depending on design and user requirements. Similarly, the number of the further first electrode portion 128 may be the same as the number of the further second electrode portion 130. However, the number of the further first electrode portion 128 may also differ from the number of further second electrode portion 130 depending on design and user requirements.

[0097] In an embodiment, the biasing structure 122 may include a spring. Similarly, the further biasing structure 132 may include a spring.

[0098] In an embodiment, the sealing portion 124 may include a flexible or stiff insulating material configured to seal the first well 108 when in contact. The sealing portion 124 may include a material selected from a group consisting of plastic, PDMS, acrylic, polycarbonate. Similarly, the further sealing portion 134 may include a flexible or stiff insulating material configured to seal the second well 110 when in contact. The further sealing portion 134 may include a material selected from a group consisting of plastic, PDMS, acrylic, polycarbonate.

[0099] In FIGs. 1A to 1C, one of the electro-fluidic interface 102 and the further electro-fluidic interface 104 may be used for recording or measurement and the other may be used for reference depending on user and design requirements.

[00100] The respective electro-fluidic interface 102 and the further electro-fluidic interface 104 when in use may be described below. First in FIG. 1A, the fluid 114 or any sample of interest may be dispensed into the first well 108. The fluid 114 may include a cell suspension or any other desired fluid 114 depending on user requirements. Upon dispensing of the fluid 114 into the first well 108, the channel 112 may be filled under capillary forces. The second well 110 may be relatively empty or may also be filled with a same or different fluid from that housed in the first well 108 depending on user requirements.

[00101] Then in FIG. 1B, the respective electro-fluidic interface 102 and the further electro-fluidic interface 104 may be brought over the respective first well 108 or the second well 110. At least one portion of the second electrode portion 120 of the electro-fluidic interface 102 may be positioned within the first well 108 and in contact with the fluid 114 housed within the first well 108 so as to provide a constant electrical access to

the first well 108. The at least one portion of the second electrode portion 120 may or may not be in contact with the bottom of the first well 108. At least one portion of the further second electrode portion 130 of the further electro-fluidic interface 104 may be positioned within the second well 110 so as to provide a constant electrical access to the second well 110. The at least one portion of the further second electrode portion 130 may or may not be in contact with the bottom of the second well 110. The respective biasing structure 122 and further biasing structure 132 may be in a default uncompressed state and the sealing portion 124 and the further sealing portion 134 may not be in contact with the respective first well 108 and the second well 110.

[00102] Further in FIG. 1C, a downward pressure (as indicated by the arrow) may be exerted on the sealing portion 124 of the electro-fluidic interface 102. When the downward pressure may be exerted on the sealing portion 124, the biasing structure 122 of the electro-fluidic interface 102 may change from the uncompressed state to a compressed state. The downward pressure may first drive the sealing portion 124 of the electro-fluidic interface 102 to be in sealing contact with the first well 108 and then further drive the fluid 114 housed within the first well 108 to be transported along the channel 112 into the second well 110. The fluid 114 may then be in contact with the further second electrode portion 130 of the further electro-fluidic interface 104. The further sealing portion 134 of the further electro-fluidic interface 104 may or may not be activated at the same time depending on user requirements. The downward pressure may be by an user, by mechanical means or by any other suitable means.

[00103] FIGs. 2A to 2C show respective cross-sectional views of two electro-fluidic interfaces 102, 104 in use, one of the two electro-fluidic interfaces 102, 104 used for transporting fluid 114 into a first well 108 according to an embodiment.

[00104] The two electro-fluidic interfaces 102, 104 as shown in FIGs. 2B and 2C may be similar to that as shown in FIGs. 1B and 1C.

[00105] FIGs. 2A to 2C may differ from FIGs. 1A to 1C in that FIGs. 2A to 2C shows the transporting of fluid 114 from the second well 110 into the first well 108 while FIGs. 1A to 1C shows the transporting of fluid 114 away from the first well 108 into the second well 110.

[00106] The respective electro-fluidic interface 102 and the further electro-fluidic interface 104 when in use may be described below. First in FIG. 2A, a fluid 114 or any sample of interest may be dispensed into the second well 110 by any suitable means such as a pipette 136 or a liquid-handling station for example. The fluid 114 may include a cell suspension or any other desired fluid 114 depending on user requirements. Upon dispensing of the fluid 114 into the second well 110, the channel 112 may be filled under capillary forces. The first well 108 may be relatively empty or may also be filled with fluid 114 depending on user requirements.

[00107] Then in FIG. 2B, the respective electro-fluidic interface 102 and further electro-fluidic interface 104 may be brought over the respective first well 108 and second well 110. At least one portion of the second electrode portion 120 of the electro-fluidic interface 102 may be positioned within the first well 108 so as to provide a constant electrical access to the first well 108 and at least one portion of the further second electrode portion 130 of the further electro-fluidic interface 104 may be positioned within

the second well 110 in contact with the fluid 114 housed within the second well 110 so as to provide a constant electrical access to the second well 110. The sealing portion 124 may be in sealing contact with the first well 108 and the biasing structure 122 may in a compressed state while the further sealing portion 134 may not be in contact with the second well 110 and the further biasing structure 132 may be in a default uncompressed state.

[00108] Further in FIG. 2C, an upward pressure (as indicated by the arrow) may be exerted on the sealing portion 124 of the electro-fluidic interface 102. When the upward pressure may be exerted on the sealing portion 124, the biasing structure 122 of the electro-fluidic interface 102 may change from the compressed state to an uncompressed state. The upward pressure may create a suction force and drive the sealing portion 124 of the electro-fluidic interface 102 away from the first well 108 and also drive the fluid 114 housed within the second well 110 to be transported along the channel 112 into the first well 108. The fluid 114 may then be in contact with the second electrode portion 120 of the electro-fluidic interface 102. Then the fluid 114 may or may not be in contact with the further second electrode portion 130 of the further electro-fluidic interface 104, depending on user and design requirements. The further sealing portion 134 of the further electro-fluidic interface 104 may or may not be activated at the same time depending on user requirements.

[00109] FIG. 3 shows a bottom view of an electro-fluidic interface 102 including a plurality of second electrode portions 120 arranged in a 4X4 matrix grid according to an embodiment.

[00110] From the bottom view as shown in FIG. 3A, it may be seen that the electro-fluidic interface 102 may include a viewing window 148, a plurality of second electrode portions 120, respective portions of the sealing portion 124 surrounding each of the plurality of second electrode portions 120 and respective portions of the sealing portion 124 which may not surround any second electrode portion 120, thereby seen as a plurality of openings 152 from the bottom view.

[00111] FIGs. 3B to 3D show respective side views of the electro-fluidic interface 102 as shown in FIG. 3A when in use according to an embodiment. The electro-fluidic interface 102 may be used for transporting fluid (not shown) away or into a plurality of first wells depending on the state of two biasing structures 122 at an initial stage.

[00112] Each of FIGs. 3B to 3D shows a electro-fluidic interface 102 to a multi-well plate 106, the multi-well plate 106 including a plurality of first wells (not shown) and a plurality of second wells (not shown), each of the plurality of first wells may be connected to the plurality of second wells via at least one channel (not shown).

[00113] The electro-fluidic interface 102 may include a sealing portion 124 configured to be inserted into each of the plurality of first wells and to thereby seal each of the plurality of first wells; an electrode 116 configured to be inserted through or housed within the sealing portion 124; and two biasing structures 122; wherein the two biasing structures 122 may be positioned relative to the sealing portion 124 and the electrode 116 so as to allow movement of the sealing portion 124 relative to the electrode 116 so as to induce a change in pressure in each of the plurality of first wells, thereby allowing fluid to be transported away or into each of the plurality of first wells.

[00114] The sealing portion 124 may be decoupled from the electrode 116 via the two biasing structures 122. The electrode 116 may be configured to provide a constant electrical access to the first well 108. The electrode 116 may be configured to be connected to an external device (not shown).

[00115] The two biasing structures 122 may be configured to be in an uncompressed state or a compressed state. A change in state of the two biasing structures 122 from the uncompressed state to the compressed state upon pushing the sealing portion 124 into each of the plurality of first wells may enable the sealing portion 124 to move relative to the electrode 116 in a direction towards each of the plurality of first wells so as to transport fluid away from each of the plurality of first wells. A change in state of the two biasing structures 122 from the compressed state to the uncompressed state upon pulling the sealing portion 124 out from each of the plurality of first wells may enable the sealing portion 124 to move relative to the electrode 116 in a direction away from each of the plurality of first wells so as to transport fluid into each of the plurality of first wells 108.

[00116] In an embodiment, the electrode 116 of the electro-fluidic interface 102 may include a single elongated portion or separate portions. From FIG. 3A, it may be seen that the electro-fluidic interface 102 may include more than four second electrode portions 120. However, only four second electrode portions 120 may be seen in each of FIGs. 3B to 3D in view of the alignment of the other second electrode portions 120 there-behind. Similarly, the electro-fluidic interface 102 may include any suitable number of first electrode portions although this may not be seen in FIG. 3A. Therefore, from the side view, the electrode 116 in each of FIGs. 3B to 3D may be seen to include two first electrode portions 118 and four second electrode portions 120.

[00117] In an embodiment, each of the two first electrode portions 118 may include a cross-sectional dimension same or different from each of the four second electrode portions 120.

[00118] In an embodiment, each of the two first electrode portions 118 may include a cross-sectional dimension in a range from about 0.1 mm to about 5 mm. Each of the two first electrode portions 118 may include a cross-sectional dimension the same or different from each other.

[00119] In an embodiment, each of the four second electrode portions 120 may include a cross-sectional dimension in a range from about 0.1 mm to about 5 mm. Each of the four second electrode portions 120 may include a cross-sectional dimension the same or different from each other.

[00120] In an embodiment, each of the two first electrode portions 118 may be of a same or a different material from each of the four second electrode portions 120.

[00121] In an embodiment, each of the two first electrode portions 118 may include a material selected from a group consisting of silver, silver chloride, gold, platinum, titanium. Each of the two first electrode portions 118 may also include any suitable combinations of materials.

[00122] In an embodiment, each of the four second electrode portions 120 may include a material selected from a group consisting of silver, silver chloride, gold, platinum, titanium. Each of the four second electrode portions 120 may also include any suitable combinations of materials.

[00123] In an embodiment, number of the first electrode portion 118 may be the same or different from number of the second electrode portion 120.

[00124] In an embodiment, each of the two biasing structures 122 may include at least one spring or an elastomer layer.

[00125] In an embodiment, the sealing portion 124 may include a flexible or stiff insulating material configured to seal each of the plurality of first wells when in contact.

[00126] In an embodiment, the sealing portion 124 may include a material selected from a group consisting of plastic, PDMS, acrylic polycarbonate.

[00127] In an embodiment, the electrode 116 may further include an intermediate portion 144, the intermediate portion 144 may be positioned between the two first electrode portions 118 and the four second electrode portions 120, the intermediate portion 144 may be configured to support the two biasing structures 122 when in use.

[00128] In an embodiment, the intermediate portion 144 may include a substrate with a plurality of electrical traces (not shown) disposed thereon. The substrate may include any suitable material for example insulating plastic. The intermediate portion 144 may include a printed circuit board (PCB). Each of the first electrode portions 118 may include a plurality of independently insulated electrical cables, such that each of the insulated electrical cables of the first electrode portion 118 may be coupled to each second electrode portion 120 via one of the electrical traces on the intermediate portion 144.

[00129] In an embodiment, the intermediate portion 144 may be arranged at a direction substantially perpendicular to the respective two first electrode portions 118 and the four second electrode portions 120.

[00130] In an embodiment, each of the two first electrode portions 118 may be positioned at a first electrode predetermined distance away from each other. The first electrode predetermined distance may be in a range of about 1 mm to about 50 mm.

[00131] In an embodiment, each of the four second electrode portions 120 may be positioned at a second electrode predetermined distance away from each other. The second electrode predetermined distance may be in a range of about 1 mm to about 50 mm, for example about 2.25 mm.

[00132] In an embodiment, the first electrode predetermined distance may be the same or different from the second electrode predetermined distance.

[00133] In an embodiment, the multi-well plate may include a plurality of first wells, each of the plurality of first wells may be spaced apart by a well predetermined distance, the second electrode predetermined distance may correspond approximately to the well predetermined distance.

[00134] In an embodiment, the electro-fluidic interface 102 may include a plurality of arm portions 146. For example, the electro-fluidic interface 102 may include four arm portions 146 for a 4X4 matrix grid. From the side view of the electro-fluidic interface, it may be seen that the sealing portion 124 may further include two arm portions 146, each of the two arm portions 146 positioned on each side of the two biasing structures 122.

[00135] In an embodiment, the electro-fluidic interface 102 may further include a viewing window 148 so as to allow a user to align the electro-fluidic interface 102 to the multi-well plate 106.

[00136] In an embodiment, the viewing window 148 may include a dimension in a range from about 0.5 mm to about 2 mm, for example about 1 mm.

[00137] In an embodiment, the viewing window 148 may be formed from a part of the sealing portion 124 and from a part of the intermediate portion 144.

[00138] In an embodiment, a microscope lens 150 may be positioned above the electro-fluidic interface 102 such that the microscope lens 150 may be aligned with the viewing window 148. One purpose for the microscope lens 150 may be to achieve a magnifying effect.

[00139] In an embodiment, the sealing portion 124 may be configured to include respective openings 152 to accommodate each of the four second electrode portions 120. Each of the openings 152 may be sized so as to allow respective gaps between the sealing portion 124 and each of the four second electrode portions 120 to facilitate ease of movement of the sealing portion 124 relative to the electrode 116.

[00140] In this embodiment, the sealing portion 124 may be in contact with four of the corresponding first wells at the same time as compared to that in FIGs. 1B and 1C or FIGs. 2B and 2C where the respective sealing portion 124 corresponding to each first well may be independently controlled.

[00141] The electro-fluidic interface 102 when in use may be described below. First, FIG. 3A shows the electro-fluidic interface 102 being positioned over the multi-well plate 106. In FIG. 3B, each of the four second electrode portions 120 may be brought to be in contact with the multi-well plate 106. In FIG. 3C, a downward pressure (as indicated by the respective arrows) may be exerted onto the respective two arm portions 146. The downward pressure may drive the sealing portion 124 to be in sealing contact with each of the plurality of first wells of the multi-well plate 106 so as to induce a change in

pressure in each of the plurality of first wells, thereby allowing fluid to be transported away or into each of the plurality of first wells.

[00142] FIG. 4A shows a photomicrograph of a planar view of a microchip 154 corresponding to a single unit of a multi-well plate 106 with 1536 wells 174 including a plurality of first wells and second wells prior to placement of a capping layer according to an embodiment.

[00143] The single unit of the multi-well plate 106 with 1536 wells may contain 16 wells 174 in a 4-by-4 rectangular matrix. The layout of the multi-well plate 106 may be designed such that all the 16 wells 174 may be in fluidic communication via the respective channels 112 with a main microchannel 158 in a centre of the unit. Six wells 174 may be positioned at each side of the main microchannel 158 and a pair of wells 174 may be located at each end of the main microchannel 158 to deliver cell suspension and extracellular buffer. The orthogonal separation between the adjacent wells 174 may be about 2.25 mm centre to centre.

[00144] In an embodiment, the multi-well plate 106 may be used for patch clamping.

[00145] FIG. 4B shows a close-up view of a centre of the microchip 154 as shown in FIG. 4A according to an embodiment. From the close-up view of the centre of the microchip 154, six channels 112 may be shown on each side of the main microchannel 158. Each channel 112 may be connected to each well (not shown).

[00146] FIG. 4C shows a scanning electron microscope (SEM) image of a section of a microchannel 158 sidewall in a centre of the single unit of the multi-well plate 106 as shown in FIG. 4A according to an embodiment. As may be seen from FIG. 4C, five of the six side channels 112 may be visible with their accompanying buried glass capillaries.

The inset may show a close-up view of one patch aperture or opening 172 to the microchannel 158.

[00147] FIG. 5 shows an image of a capping layer 166 being aligned and bonded to the microchip 154 as shown in FIG. 4A to 4C to form a multi-well plate 106 according to an embodiment.

[00148] The capping layer 166 may be fabricated in PDMS according to the multi-well plate 106 with 1536 wells 174 through a dual-step molding method for example. Using a commercial multi-well plate 106 with 1536 wells as a first mold, one may create a second mold in PDMS which may be an array of pillars. A thin film of Teflon coating may then be deposited on the second mold. The second mold may be placed on a silicon wafer with a thin film of SU8 resist, with the array of pillars in direct contact with the SU8 resist. Without the SU8 resist coating on the silicon wafer, any subsequent layer replicated may contain an array of PDMS membranes which may be partially broken rather than relatively well-defined. After oxygen plasma treatment, the PDMS array of pillars may be aligned and bonded to the microchip 154 forming the multi-well plate 106.

[00149] Experiments may have been conducted to demonstrate the current invention. FIG. 6A shows a proof-of-concept demonstration of a cell capture via unplugging of a sealing portion 124 from a respective well 174 according to an embodiment. FIG. 6B shows an insertion of the sealing portion 124 into a respective well 174 according to an embodiment. FIG. 6C shows a removal of the sealing portion 124 from a respective well 174 according to an embodiment.

[00150] The sealing portion 124 has been formed by a customized metallic pin which may be bent in a L shape for example as shown in FIG. 6A. The sealing portion 124 or

pin, despite the slightly larger outer diameter with respect to the wells 174 may be inserted into the wells 174 by a manual push as shown in FIG. 6B. Similarly, the sealing portion 124 may be removed manually from the respective wells 174 by a pull action as shown in FIG. 6C. The pushing and pulling of the sealing portion 124 with respect to the wells 174 may be used to demonstrate a change in pressure in the wells 174, thereby allowing fluid to be transported away or into the wells 174.

[00151] FIG. 6D shows a microscope image taken under visible light of a cell 170 being captured at a microcapillary opening or channel opening 172 linked to a respective well (not shown) which may have been unplugged according to an embodiment. FIG. 6E shows a microscope image taken under fluorescent microscope of a cell 170 being captured at a microcapillary opening or channel opening 172 linked to a respective well (not shown) which may have been unplugged according to an embodiment. In both FIG. 6D and FIG. 6E, the cells 170 may be stained with a fluorescent dye before injecting into the microchip.

[00152] FIG. 6D and FIG. 6E show respective bright-field and fluorescent photomicrographs of a cell 170 (for example rat basophilic leukemia) being captured at the microcapillary opening or channel opening 172 by unplugging the respective well (not shown) by a manual pull action of the sealing portion (not shown) or pin. The electrical resistance across the microcapillary opening or channel opening 172 may subsequently increased from about 7 M Ω to about 20 M Ω with the capture of the cell 170. The resistance values for the remaining microcapillaries or channels may also be measured one at a time before and after capturing a cell 170 by applying the same method. The resistance values after capturing a cell 170 may exceed 200 M Ω and may

appeared to be no different than those achievable with a pneumatic suction applied through a tubing connection. This may allow an ability to measure real-time electrical resistance as a user may carry out the push and pull action of the sealing portion.

[00153] FIG. 7 shows a cross-sectional view of an electro-fluidic interface 102, the electro-fluidic interface 102 including a sealing portion 124 sized to seal the first well 108 when in contact according to an embodiment.

[00154] The electro-fluidic interface 102 as shown in FIG. 7 may be similar to the electro-fluidic interface 102 as shown in FIGS. 1B and 1C except the sealing portion 124 as shown in FIG. 7 may be sized or dimensioned so as to seal the first well 108 when in contact. This may mean that the cross-sectional diameter of the sealing portion 124 may be similar or comparable to the diameter of the first well 108, thereby sealing the first well 108 when in contact.

[00155] FIGs. 8A and 8A' show respective cross-sectional views of an electro-fluidic interface 102 in use, the electro-fluidic interface 102 including the sealing portion 124 as shown in FIG. 7 and a further sealing portion 176 positioned around the sealing portion 124 according to an embodiment.

[00156] Each of FIGs. 8A and 8A' shows a multi-well plate 106 which may include a first well 108 and a second well 110, the first well 108 may be connected to the second well 110 via a channel 112. The multi-well plate 106 may include more than two wells depending on user and design requirements. The multi-well plate 106 may be formed as a single integrated plate or may be formed by bonding two separate portions together. The multi-well plate 106 may be formed of any suitable material or combinations of material depending on user and design requirements.

[00157] Further, each of FIGs. 8A and 8A' shows the electro-fluidic interface 102 to the multi-well plate 106. The electro-fluidic interface 102 may be positioned over the first well 108 housing the fluid 114. The second well 110 may also be configured to house a fluid 114, the volume of the fluid 114 depending on user and design requirements. The fluid 114 in the respective first well 108 and the second well 110 may be the same or different depending on user and design requirements.

[00158] The electro-fluidic interface 102 may include a sealing portion 124 configured to be inserted into the first well 108; an electrode 116 configured to be inserted through the sealing portion 124; and a biasing structure 122; wherein the biasing structure 122 may be positioned relative to the sealing portion 124 and the electrode 116 so as to allow movement of the sealing portion 124 relative to the electrode 116 so as to induce a change in pressure in the first well 108, thereby allowing fluid 114 to be transported away or into the first well 108. If cross-sectional dimension of the sealing portion 124 may not be comparable with the cross-sectional dimension of the first well 108, then the electro-fluidic interface 102 may further include the further sealing portion 176 configured to surround the sealing portion 124 and the electrode 116 so as to seal the first well 108 upon contact (i.e. compensate for the difference in cross-sectional dimension between the sealing portion and the first well). The position of the further sealing portion 176 along the length of the sealing portion 124 may vary depending on the length of the electrode 116 and the depth of the first well 108.

[00159] In FIGs. 8A and 8A', either or both the sealing portion 124 and the further sealing portion 176 may include an insulating material. However, either or both the sealing portion 124 and the further sealing portion 176 may also be conductive and the

electro-fluidic interface 102 may still work. One likely issue with having a conductive sealing portion 124 and further sealing portion 176 may be the risk of an electrical shorting between adjacent sets of the combination of the sealing portion 124 and the further sealing portion 176 (in array configuration) when positioned relatively closely (due to liquid spill over for example). In an embodiment, the sealing portion 124 and the further sealing portion 176 may be formed as separate structures or may also be formed as a single integrated structure.

[00160] The electro-fluidic interface 102 when in use may be described below. First in FIG. 8A, the fluid 114 or any sample of interest may be dispensed into the first well 108 by any suitable means, for example a pipette or a liquid-handling station for example. The fluid 114 may include a cell suspension or any other desired fluid depending on user requirements. Upon dispensing of the fluid 114 into the first well 108, the channel 112 may be filled under capillary forces. The second well 110 may be relatively empty or may also be filled with fluid 114 depending on user requirements.

[00161] Then the electro-fluidic interface 102 may be brought over the first well 108. One end of the electrode 116 of the electro-fluidic interface 102 may be positioned within the first well 108 and in contact with the fluid 114 housed within the first well 108 so as to provide a constant electrical access to the first well 108. The other end of the electrode 116 may be coupled to the biasing structure 122. The biasing structure 122 may be in a default uncompressed state and both the sealing portion 124 and the further sealing portion 176 may not be in contact with the respective first well 108.

[00162] In FIG. 8A', both the sealing portion 124 and the further sealing portion 176 may be brought into contact with the first well 108 such that the one end of the electrode

116 positioned within the first well 108 may be in contact with a bottom of the first well 108. Then a downward and/or sideward force or pressure may be exerted on the further sealing portion 176 such that the further sealing portion 176 may be fitted within the first well 108 and thereby seal the first well 108. Then a further downward pressure (as indicated by the arrow) may be exerted on the sealing portion 124 of the electro-fluidic interface 102. When the further downward pressure may be exerted on the sealing portion 124, the biasing structure 122 of the electro-fluidic interface 102 may change from the uncompressed state to a compressed state. The further downward pressure may also drive the fluid 114 housed within the first well 108 to be transported along the channel 112 into the second well 110.

[00163] FIGs. 8B and 8B' shows a cross-sectional view of an electro-fluidic interface 102 in use, the electro-fluidic interface 102 including a sealing portion 124 and a further sealing portion 176 positioned within the sealing portion 124 according to an embodiment.

[00164] The electro-fluidic interface 102 as shown in FIG. 8B' may be similar to the electro-fluidic interface 102 as shown in FIGs. 8A and 8A' except that the sealing portion 124 may include a wider opening at one end (i.e the end to be brought towards the first well 108), surrounding the electrode 116. To prevent fluid 114 from entering the sealing portion 124 and to also allow the sealing portion 124 to seal the first well 108 when in contact, the electro-fluidic interface 102 as shown in FIGs. 8B and 8B' may include a further sealing portion 176 positioned within the sealing portion 124 rather than surrounding the sealing portion 124 as shown in FIGs. 8A and 8A'. The further sealing portion 176 as shown in FIGs. 8B and 8B' may be in the form a plug which may be made

of a gasket material for example. The further sealing portion 176 may fill the space between the sealing portion and the electrode 116 to prevent any entry of the fluid 114. The further sealing portion 176 may include any other suitable materials or components as long as the material does not prevent relative movement of the electrode 116 with respect to the sealing portion 124.

[00165] In FIG. 8B, the electro-fluidic interface 102 may be brought over the first well 108. One end of the electrode 116 of the electro-fluidic interface 102 may be positioned within the first well 108 and in contact with the fluid 114 housed within the first well 108 so as to provide a constant electrical access to the first well 108. The other end of the electrode 116 may be coupled to the biasing structure 122. The biasing structure 122 may be in a default uncompressed state and both the sealing portion 124 and the further sealing portion 124 may not be in contact with the respective first well 108.

[00166] In FIG. 8B', both the sealing portion 124 and the further sealing portion 176 may be brought into contact with the first well 108 such that the one end of the electrode 116 positioned within the first well 108 may be in contact with a bottom of the first well 108. Then a downward and/or sideward force or pressure may be exerted on the respective sides of the sealing portion 124 such that the sealing portion 124 together with the further sealing portion 176 seals the first well 108. Then a further downward pressure (as indicated by the arrow) may be exerted on the sealing portion 124 of the electro-fluidic interface 102. When the further downward pressure may be exerted on the sealing portion 124, the biasing structure 122 of the electro-fluidic interface 102 may change from the uncompressed state to a compressed state. The further downward pressure may

also drive the fluid 114 housed within the first well 108 to be transported along the channel 112 into the second well 110.

[00167] FIGs. 8C and 8C' show respective cross-sectional views of an electro-fluidic interface 102 in use, the electro-fluidic interface 102 including a sealing portion 124 and a further sealing portion 176 positioned within the sealing portion 124 according to an embodiment.

[00168] Like in FIGs. 8B and 8B', the further sealing portion 176 as shown in FIGs. 8C and 8C' may be positioned within the sealing portion 124. However, unlike the sealing portion 124 in FIGs. 8B and 8B', the sealing portion 124 as shown in FIGs. 8C and 8C' may include an O-ring instead of the plug which may be made of a gasket material. Any other suitable sealing portion 124 and further sealing portion 176 may be used. As an example, both the sealing portion 124 and the further sealing portion 176 may be formed from the O-ring. As a further example, the sealing portion 124 may be formed of a relatively stiff material while the further sealing portion 176 may be formed of a relatively flexible material (thereby allowing it to be compressed upon an application of a pressure).

[00169] In FIG. 8C, the electro-fluidic interface 102 may be brought over the first well 108. One end of the electrode 116 of the electro-fluidic interface 102 may be positioned within the first well 108 and in contact with the fluid 114 housed within the first well 108 so as to provide a constant electrical access to the first well 108. The other end of the electrode 116 may be coupled to the biasing structure 122. The biasing structure 122 may be in a default uncompressed state and both the sealing portion 124 and the further sealing portion 176 may not be in contact with the respective first well 108.

[00170] In FIG. 8C', both the sealing portion 124 and the further sealing portion 176 may be brought into contact with the first well 108 such that the one end of the electrode 116 positioned within the first well 108 may be in contact with a bottom of the first well 108. Then a downward and/or sideward force or pressure may be exerted on the respective sides of the sealing portion 124 such that the sealing portion 124 together with the further sealing portion 176 seals the first well 108. Then a further downward pressure (as indicated by the arrow) may be exerted on the sealing portion 124 of the electro-fluidic interface 102. When the further downward pressure may be exerted on the sealing portion 124, the biasing structure 122 of the electro-fluidic interface 102 may change from the uncompressed state to a compressed state. The further downward pressure may also drive the fluid 114 housed within the first well 108 to be transported along the channel 112 into the second well 110.

[00171] FIGs. 9A and 9B show respective cross-sectional views of an electro-fluidic interface 102 in use according to an embodiment.

[00172] The electro-fluidic interface 102 as shown in FIGs. 9A and 9B may be similar to the electro-fluidic interface 102 as shown in FIGs. 1A to 1C except that the biasing structures 122 as shown in FIGs. 9A and 9B may be arranged in a different configuration compared to that in FIGs. 1A to 1C. The biasing structures 122 in FIGs. 9A and 9B may be directly coupled to both the electrode 116 and the sealing portion 124 while the biasing structure 122 as shown in FIGs. 1A to 1C may just be positioned between the electrode 116 and the sealing portion 124.

[00173] In FIG. 9A, the electro-fluidic interface 102 may just be positioned over the first well 108 housing a fluid 114. In FIG. 9B, a downward pressure (as indicated by the

arrow) may be exerted on the sealing portion 124 of the electro-fluidic interface 102. When the downward pressure may be exerted on the sealing portion 124, the biasing structure 122 of the electro-fluidic interface 102 may change from an unstretched state to a stretched state or vice versa depending on the initial stage of the biasing structure 122. The downward pressure may also drive the sealing portion 124 of the electro-fluidic interface 102 to be in sealing contact with the first well 108 and drive fluid 114 housed within the first well 108 out of the first well 108 (direction as shown by arrow)

[00174] FIGs. 10A and 10B show respective cross-sectional views of an electro-fluidic interface 102 in use according to an embodiment.

[00175] The electro-fluidic interface 102 as shown in FIGs. 10A and 10B may be similar to the electro-fluidic interface 102 as shown in FIGs. 9A to 9C except for the positioning of the sealing portion 124 relative to the biasing structures 122. The sealing portion 124 may be attached to a lower end of the biasing structures 122 in FIG. 10A and 10B as compared to that as shown in FIGs. 9A and 9B.

[00176] FIGs. 11A to 11C show respective cross-sectional views of an electro-fluidic interface 102 in use, the electro-fluidic interface 102 including a deformable electrode 116 configured in a first manner and a sealing portion 124 with a first shape according to an embodiment.

[00177] FIG. 11A shows an electro-fluidic interface to a multi-well plate 106, the multi-well plate 106 including at least one first well 108 and at least one second well (not shown), the at least one first well 108 is connected to the at least one second well via at least one channel (not shown).

[00178] The electro-fluidic interface 102 may include a sealing portion 124 configured to be inserted into the at least one first well 108 and to thereby seal the at least one first well 108 and an electrode 116 coupled to the sealing portion 124; wherein the at least one electrode 116 may be configured to allow movement of the sealing portion 124 relative to the electrode 116 so as to induce a change in pressure in the at least one first well 108, thereby allowing fluid 114 to be transported away or into the at least one first well 108.

[00179] The electrode 116 may be of a deformable electrically conducting material configured to deform upon an application of a pressure. The electrode 116 may include conductive polymers with different elasticity such as silver-doped poly(dimethylsiloxane), poly(acetylene)s, poly(pyrrole)s, poly(thiophene)s, polyanilines, polythiophenes, poly(p-phenylene sulfide), poly(p-phenylene vinylene)s (PPV), poly(3-alkylthiophenes) polyindole, polypyrene, polycarbazole, polyazulene, polyazepine, poly(fluorene)s, polynaphthalene.

[00180] The sealing portion 124 may include an insulating material configured to seal the at least one first well 108 when in contact. The sealing portion may include a material selected from a group consisting of plastic, polydimethylsiloxane (PDMS), acrylic, polycarbonate. The sealing portion 124 may be either flexible like PDMS or stiff like acrylic depending on user and design requirements. The sealing portion 124 may include a first shape, for example a rectangular shape. The sealing portion 124 may also include any other suitable shapes or combination of shapes depending on user and design requirements.

[00181] The electrode 116 may be of a different material from the sealing portion 124. The electrode 116 may be configured to provide a constant electrical access to the at least

one first well 108. One end of the electrode 116 may be in contact with the fluid 114 housed within the at least one first well 108 and the other end of the electrode 116 may be configured to be connected to an external device.

[00182] The electrode 116 may include an elongated structure and the electrode 116 may be configured to be inserted at least through the sealing portion 124. The electrode 116 may be configured to be in an uncompressed state or a compressed state. A change in state of the electrode 116 from the uncompressed state to the compressed state upon pushing the sealing portion 124 into the at least one first well 108 may enable the sealing portion 124 to move in a direction towards the at least one first well 108 so as to transport fluid 114 away from the at least one first well 108. A change in state of the electrode 116 from the compressed state to the uncompressed state upon pulling the sealing portion 124 out from the at least one first well 108 may enable the sealing portion 124 to move in a direction away from the at least one first well 108 so as to transport fluid into the at least one first well 108.

[00183] The electro-fluidic interface 102 when in use may be described below. First in FIG. 11A, the electro-fluidic interface 102 may be brought over the at least one first well 108. One end of the electrode 116 may be positioned within the at least one first well 108 and in contact with the fluid 114 housed within the at least one first well 108 so as to provide a constant electrical access to the at least one first well 108. The electrode 116 may be in a default uncompressed state and the sealing portion 124 may not be in contact with the at least one first well 108.

[00184] Further in FIG. 11B, the electro-fluidic interface 102 may be lowered into the at least one first well 108 such that the one end of the electrode 116 may be in contact

with a bottom of the at least one first well 108. The sealing portion 124 may or may not be in contact with the at least one first well 108.

[00185] Further in FIG. 11C, a downward pressure (as indicated by the arrow) may be exerted on the sealing portion 124 of the electro-fluidic interface 102. The downward pressure may first drive the sealing portion 124 of the electro-fluidic interface 102 to be in sealing contact with the at least one first well 108 and then further downward pressure may drive the fluid 114 housed within the at least one first well 108 to be transported out of the at least one first well 108. The one end of the electrode 116 in contact with the fluid 114 and in contact with the bottom of the at least one first well 108 may be compressed or deformed. The extent of compression and deformation of the electrode 116 depends on the amount of downward pressure exerted onto the sealing portion 124 and also the extent that the sealing portion 124 may be fitted within the at least one first well 108. Further, the extent of compression and deformation of the electrode 116 may also depend on the elasticity of the material of the electrode 116.

[00186] FIG. 12 shows a cross-sectional view of an electro-fluidic interface 102 in use, the electro-fluidic interface 102 including a deformable electrode 116 configured in a first manner and a sealing portion 124 with a second shape according to an embodiment.

[00187] The electro-fluidic interface 102 as shown in FIG. 12 may be similar to the electro-fluidic interface 102 as shown in FIGs. 11A to 11C with the difference such that the sealing portion 124 in FIG. 12 may include a different shape from the sealing portion 124 as shown in FIGs. 11A to 11C. The sealing portion 124 in FIG. 12 may include L-shape. However, the sealing portion 124 in FIG. 12 may include any suitable shape or combination of shapes depending on user and design requirements.

[00188] FIG. 13 show a cross-sectional view of an electro-fluidic interface 102 in use, the electro-fluidic interface 102 including a deformable electrode 116 configured in a second manner and a sealing portion 124 with a first shape according to an embodiment.

[00189] The electro-fluidic interface 102 as shown in FIG. 13 may be similar to the electro-fluidic interface 102 as shown in FIGs. 11A to 11C with the difference such that the electrode 116 in FIG. 13 may be configured in a different manner from the electrode 116 as shown in FIGs. 11A to 11C. The electrode 116 in FIG. 13 may include a first electrode portion 118 housed within the sealing portion 124 and a second electrode portion 120 configured to be in contact with fluid (not shown). The first electrode portion 118 may be an elongated portion and the second electrode portion 120 may be a helix or a coil or spring-like portion. The first electrode portion 118 may subsequently be electrically coupled to an insulated rigid electrical cable 182 for connection to an external device. However, the electrode 116 as shown in FIGs. 11A to 11C may include a single elongated portion which may extend all the way through the sealing portion 124. Having said that, the electrode 116 as shown in FIG. 13 may be configured in any suitable configuration depending on user and design requirements.

[00190] The change in the deformation of the second electrode portion 120 may be as shown in FIG. 13. The change in the deformation of the second electrode portion 120 may correspond to the direction in which pressure may be exerted or released from the sealing portion 124.

[00191] FIGs. 14A to 14E show respective cross-sectional views of the electro-fluidic interface 102 as shown in FIG. 13 in use in a patch clamp application according to an embodiment.

[00192] Patch clamp requires two electrical connections or two electrodes, one recording electrode for recording purpose and the other reference electrode for reference purpose. The recording electrode may be built in a sealing portion or so-called pogo-pin plug and the reference electrode may or may not be built in the sealing portion. This may be because the reference electrode may need to be immersed into a well that is in fluidic communication with a bath solution including cell suspension.

[00193] FIG. 14A shows a multi-well plate 106 which may include a first well 108 and a second well 110, the first well 108 may be connected to the second well 110 via a channel 112. The multi-well plate 106 may include more than two wells depending on user and design requirements. The multi-well plate 106 may be formed as a single integrated plate or may be formed by bonding two separate portions together. The multi-well plate 106 may be formed of any suitable material or combinations of material depending on user and design requirements. In FIG. 14A, a fluid 114 may be housed within the first well 108 and a further fluid 180 may be housed within the second well 110. The fluid 114 and the further fluid 180 may be the same or different saline solutions.

[00194] As an example, the fluid 114 may be an intracellular buffer solution whereas the further fluid 180 may be an extracellular buffer solution or vice versa. The intracellular solution may contain about 120 mM potassium gluconate (K-gluconate), about 10 mM ethylene glycol tetraacetic acid (EGTA), about 10 mM 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) and about 10 mM sodium chloride (NaCl). The extracellular solution may contain about 123 mM NaCl, about 40 mM potassium chloride (KCl), about 1 mM magnesium chloride (MgCl_2), about 1 mM calcium chloride (CaCl_2)

and about 10 mM HEPES. As an example, all chemicals may be obtained from Sigma Aldrich except for MgCl_2 , which may be obtained from Merck & Co., Inc.

[00195] The pH value of the respective intracellular buffer solution and the extracellular solution may be adjusted to about 7.4 by adding sufficient volumes of about 1 M sodium hydroxide (NaOH) (Sigma). Conductivity may be measured with a conductivity meter (Accumet Research AR50, Thermo Fisher Scientific Inc.) when about 10.7 mS/cm for the intracellular buffer solution and about 15.1 mS/cm for the extracellular solutions may be used. The respective intracellular buffer solution and the extracellular solution may be filtered through a 10.22 μm syringe-driven filter unit to remove particulate impurities before use.

[00196] The electro-fluidic interface 102 may be positioned over the first well 108, with one end of the electrode 116 (or so called recording electrode) in contact with the fluid 114 housed within the first well 108. A reference electrode 178 may also be positioned over the second well 110, with one end of the reference electrode 178 in contact with the further fluid 180 housed within the second well 110. The other end of the electrode 116 and the other end of the reference electrode 178 may be in respective contact with an external device 184, for example an electronic instrument via respective electrical cables 182. The electronic instrument may be a patch clamp amplifier.

[00197] When in use, starting from FIG. 14A, both the electrode 116 and the reference electrode 178 may be lowered into the respective first well 108 and the second well 110 to measure an electrical resistance across the channel 112 (or so called integrated micro- or nano-capillary).

[00198] Next in FIG. 14B, the first well 108 (or chamber) may be pressurized by lowering the sealing portion 124 with the electrode 116 being in contact with a bottom of the first well 108.

[00199] Then in FIG. 14C, cells 170 may be injected into the second well 110.

[00200] Further in FIG. 14D, the sealing portion 124 may be pulled upwards and in a direction away from the first well 108 in order to generate a vacuum effect which may attract nearby cells 170 housed within the second well 110 towards the channel 112.

[00201] Finally, in FIG. 14E, when the sealing portion 124 may be further pulled upwards, the cells 170 may be trapped and may then block the opening to the channel 112.

[00202] While the invention has been particularly shown and described with reference to specific embodiments, it should be understood by those skilled in the art that various changes in form and detail may be made therein without departing from the spirit and scope of the invention as defined by the appended claims. The scope of the invention is thus indicated by the appended claims and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced.

Claims

What is claimed is:

1. An electro-fluidic interface to a multi-well plate, the multi-well plate including at least one first well and at least one second well, the at least one first well is connected to the at least one second well via at least one channel; the electro-fluidic interface comprising:

a sealing portion configured to be inserted into the at least one first well and to thereby seal the at least one first well;

at least one electrode configured to be inserted through the sealing portion; and

at least one biasing structure;

wherein the at least one biasing structure is positioned relative to the sealing portion and the at least one electrode so as to allow movement of the sealing portion relative to the at least one electrode so as to induce a change in pressure in the at least one first well, thereby allowing fluid to be transported away or into the at least one first well.

2. The electro-fluidic interface of claim 1,

wherein the sealing portion is decoupled from the at least one electrode via the at least one biasing structure.

3. The electro-fluidic interface of claim 1 or 2,

wherein the at least one electrode is configured to provide a constant electrical access to the at least one first well.

4. The electro-fluidic interface of any one of claims 1 to 3,

wherein the at least one electrode is configured to be connected to an external device.

5. The electro-fluidic interface of any one of claims 1 to 4,

wherein the at least one biasing structure is configured to be in an uncompressed state or a compressed state.

6. The electro-fluidic interface of claim 5,

wherein a change in state of the at least one biasing structure from the uncompressed state to the compressed state upon pushing the sealing portion into the at least one first well enables the sealing portion to move relative to the at least one electrode in a direction towards the at least one first well so as to transport fluid away from the at least one first well.

7. The electro-fluidic interface of claim 5,

wherein a change in state of the at least one biasing structure from the compressed state to the uncompressed state upon pulling the sealing portion out from the at least one first well enables the sealing portion to move relative to the at least one electrode in a direction away from the at least one first well so as to transport fluid into the at least one first well.

8. The electro-fluidic interface of any one of claims 1 to 7,

wherein the at least one electrode comprises a single elongated portion or separate portions.

9. The electro-fluidic interface of any one of claims 1 to 8,

wherein the at least one electrode comprises at least one first electrode portion and at least one second electrode portion.

10. The electro-fluidic interface of claim 9,

wherein the at least one first electrode portion comprises a cross-sectional dimension same or different from the at least one second electrode portion.

11. The electro-fluidic interface of claim 10,

wherein the at least one first electrode portion comprises a smaller cross-sectional dimension than the at least one second electrode portion so as to support the at least one biasing structure at an interface between the at least one first electrode portion and the at least one second electrode portion when in use.

12. The electro-fluidic interface of any one of claims 9 to 11,

wherein the at least one first electrode portion comprises a cross-sectional dimension in a range from 0.1 mm to 5 mm.

13. The electro-fluidic interface of any one of claims 9 to 12,

wherein the at least one second electrode portion comprises a cross-sectional dimension in a range from 0.1 to 5 mm.

14. The electro-fluidic interface of any one of claims 9 to 13,

wherein the at least one first electrode portion is of a same or a different material from the at least one second electrode portion.

15. The electro-fluidic interface of any one of claims 9 to 14,

wherein the at least one first electrode portion comprises a material selected from a group consisting of silver, silver chloride, gold, platinum, titanium.

16. The electro-fluidic interface of any one of claims 9 to 15,

wherein the at least one second electrode portion comprises a material selected from a group consisting of silver, silver chloride, gold, platinum, titanium.

17. The electro-fluidic interface of any one of claims 9 to 16,

wherein number of the at least one first electrode portion is same or different from number of the at least one second electrode portion.

18. The electro-fluidic interface of any one of claims 1 to 17,

wherein the at least one biasing structure comprises at least one spring, an elastomer layer.

19. The electro-fluidic interface of any one of claims 1 to 18,

wherein the sealing portion comprises a flexible insulating material or a stiff insulating material configured to seal the at least one first well when in contact.

20. The electro-fluidic interface of any one of claims 1 to 19,

wherein the sealing portion comprises a material selected from a group consisting of plastic, polydimethylsiloxane, acrylic, polycarbonate.

21. The electro-fluidic interface of any one of claims 1 to 20,

wherein the at least one electrode is of a rigid electrically conducting material.

22. The electro-fluidic interface of any one of claims 9 to 21,

wherein the at least one electrode further comprises at least one intermediate portion, the at least one intermediate portion positioned between the at least one first electrode portion and at the least one second electrode portion, the at least one intermediate portion is configured to support the at least one biasing structure when in use.

23. The electro-fluidic interface of claim 22,

wherein the at least one intermediate portion is arranged at a direction substantially perpendicular to the at least one first electrode portion and the at least one second electrode portion.

24. The electro-fluidic interface of any one of claims 9 to 23,

wherein the at least one first electrode portion comprises two substantially parallel first electrode portions, the two substantially parallel first electrode portions spaced apart by a first electrode predetermined distance.

25. The electro-fluidic interface of claim 24,
wherein the first electrode predetermined distance is in a range of 1 mm to 50 mm.

26. The electro-fluidic interface of any one of claims 9 to 25,
wherein the at least one second electrode portion comprises a plurality of substantially parallel second electrode portions, each of the plurality of substantially parallel second electrode portions spaced apart by a second electrode predetermined distance.

27. The electro-fluidic interface of claim 26,
wherein the second electrode predetermined distance is in a range of 1 mm to 10 mm.

28. The electro-fluidic interface of claim 26 or 27,
wherein the first electrode predetermined distance is same or different from the second electrode predetermined distance.

29. The electro-fluidic interface of any one of claims 26 to 28,
wherein the at least one first well comprises a plurality of first wells, each of the plurality of first wells spaced apart by a well predetermined distance, the second electrode predetermined distance corresponds to the well predetermined distance.

30. The electro-fluidic interface of any one of claims 1 to 29,
wherein the sealing portion further comprises at least one arm portion.

31. The electro-fluidic interface of any one of claims 22 to 30,
wherein the electro-fluidic interface further comprises a viewing window so as to allow a user to align the electro-fluidic interface to the multi-well plate.

32. The electro-fluidic interface of claim 31,
wherein the viewing window comprises a dimension in a range from 0.5 mm to 2 mm.

33. The electro-fluidic interface of claim 31 or 32,
wherein the viewing window is formed from a part of the sealing portion and from a part of the at least one intermediate portion.

34. The electro-fluidic interface of any one of claims 1 to 33,

further comprising a further sealing portion configured to surround the at least one electrode.

35. The electro-fluidic interface of claim 34,

wherein the further sealing portion is positioned within the sealing portion or configured to surround the sealing portion.

36. The electro-fluidic interface of claim 35,

wherein the sealing portion is of a same or a different material as the further sealing portion.

37. The electro-fluidic interface of claim 36,

wherein the further sealing portion includes a plug formed of a gasket material or an O-ring.

38. The electro-fluidic interface of any one of claims 1 to 4,

wherein the at least one biasing structure is configured to be in an unstretched state or a stretched state.

39. The electro-fluidic interface of claim 38,

wherein a change in state of the at least one biasing structure from the unstretched state to the stretched state upon pushing the sealing portion into the at least one first well enables the sealing portion to move relative to the at least one electrode in a direction towards the at least one first well so as to transport fluid away from the at least one first well.

40. The electro-fluidic interface of claim 38,

wherein a change in state of the at least one biasing structure from the stretched state to the unstretched state upon pulling the sealing portion out from the at least one first well enables the sealing portion to move relative to the at least one electrode in a direction away from the at least one first well so as to transport fluid into the at least one first well.

41. An electro-fluidic interface to a multi-well plate, the multi-well plate including at least one first well and at least one second well, the at least one first well is connected to the at least one second well via at least one channel; the electro-fluidic interface comprising:

a sealing portion configured to be inserted into the at least one first well and to thereby seal the at least one first well; and

at least one electrode coupled to the sealing portion;

wherein the at least one electrode is configured to allow movement of the sealing portion relative to the at least one electrode so as to induce a change in pressure in the at least one first well, thereby allowing fluid to be transported away or into the at least one first well.

42. The electro-fluidic interface of claim 41,

wherein the at least one electrode is of a deformable electrically conducting material configured to deform upon an application of a pressure.

43. The electro-fluidic interface of claim 41 or 42,

wherein the at least one electrode comprises a material selected from a group consisting silver-doped poly(dimethylsiloxane), poly(acetylene)s, poly(pyrrole)s, poly(thiophene)s, polyanilines, polythiophenes, poly(p-phenylene sulfide), poly(p-phenylene vinylene)s (PPV), poly(3-alkylthiophenes) polyindole, polypyrene, polycarbazole, polyazulene, polyazepine, poly(fluorene)s, polynaphthalene.

44. The electro-fluidic interface of any one of claims 41 to 43,

wherein the sealing portion comprises an insulating material configured to seal the at least one first well when in contact.

45. The electro-fluidic interface of any one of claims 41 to 44,

wherein the sealing portion comprises a material selected from a group consisting of plastic, polydimethylsiloxane, acrylic, polycarbonate.

46. The electro-fluidic interface of any one of claims 41 to 45,

wherein the at least one electrode is of a different material from the sealing portion.

47. The electro-fluidic interface of any one of claims 41 to 46,

wherein the at least one electrode is configured to provide a constant electrical access to the at least one first well.

48. The electro-fluidic interface of any one of claims 41 to 47,

wherein the at least one electrode is configured to be connected to an external device.

49. The electro-fluidic interface of any one of claims 41 to 48,

wherein the at least one electrode is configured to be inserted at least partially through the sealing portion.

50. The electro-fluidic interface of any one of claims 41 to 49,

wherein the at least one electrode is configured to be in an uncompressed state or a compressed state.

51. The electro-fluidic interface of claim 50,

wherein a change in state of the at least one electrode from the uncompressed state to the compressed state upon pushing the sealing portion into the at least one first well enables the sealing portion to move in a direction towards the at least one first well so as to transport fluid away from the at least one first well.

52. The electro-fluidic interface of claim 50,

wherein a change in state of the at least one electrode from the compressed state to the uncompressed state upon pulling the sealing portion out from the at least one first well enables the sealing portion to move in a direction away from the at least one first well so as to transport fluid into the at least one first well.

53. The electro-fluidic interface of any one of claims 41 to 52,

further comprising a further sealing portion configured to surround the at least one electrode.

54. The electro-fluidic interface of claim 53,

wherein the further sealing portion is positioned within the sealing portion or configured to surround the sealing portion.

55. The electro-fluidic interface of claim 54,

wherein the sealing portion is of a same or a different material as the further sealing portion.

56. The electro-fluidic interface of claim 55,

wherein the further sealing portion includes a plug formed of a gasket material or an O-ring.

57. The electro-fluidic interface of any one of claims 41 to 49,

wherein the at least one electrode is configured to be in an unstretched state or a stretched state.

58. The electro-fluidic interface of claim 57,

wherein a change in state of the at least one electrode from the unstretched state to the stretched state upon pushing the sealing portion into the at least one first well enables the sealing portion to move in a direction towards the at least one first well so as to transport fluid away from the at least one first well.

59. The electro-fluidic interface of claim 57,

wherein a change in state of the at least one electrode from the stretched state to the unstretched state upon pulling the sealing portion out from the at least one first well enables the sealing portion to move in a direction away from the at least one first well so as to transport fluid into the at least one first well.

Figure 1A

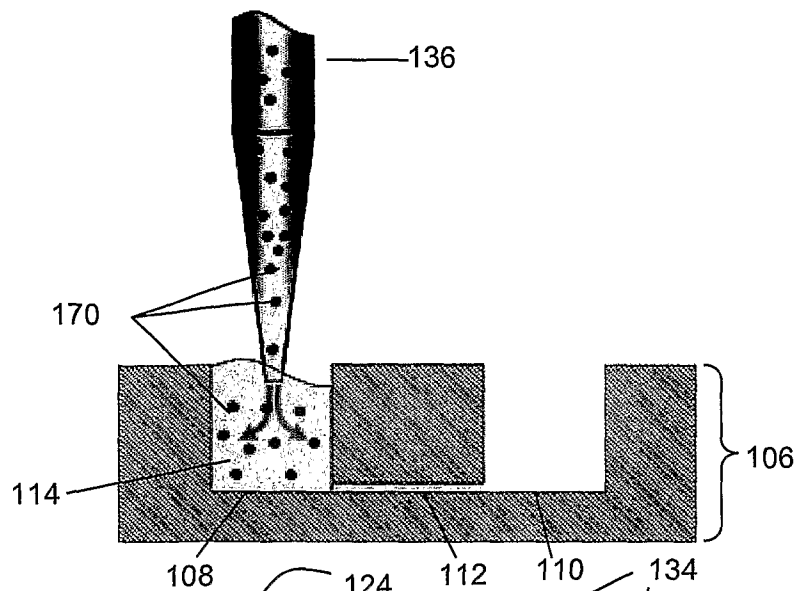


Figure 1B

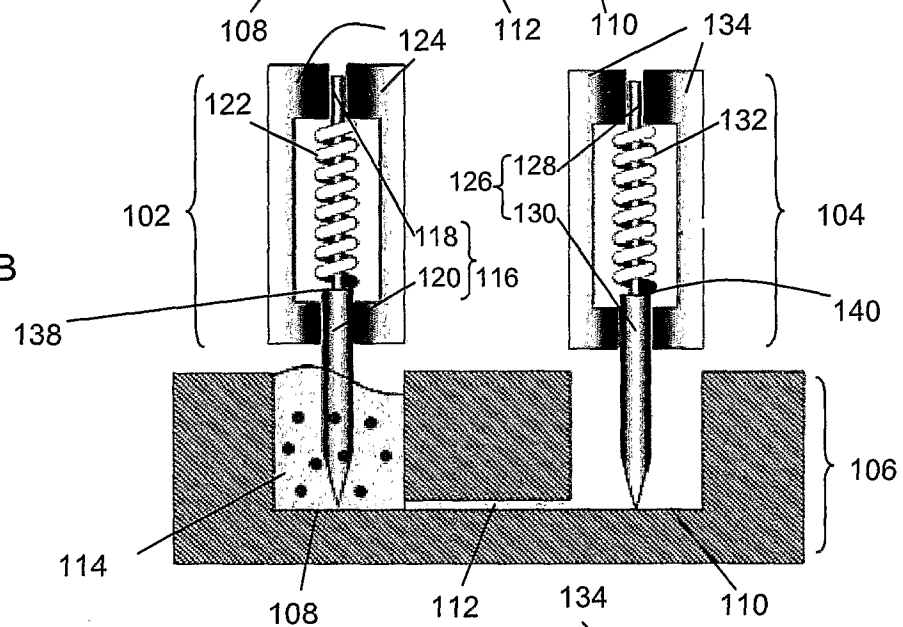


Figure 1C

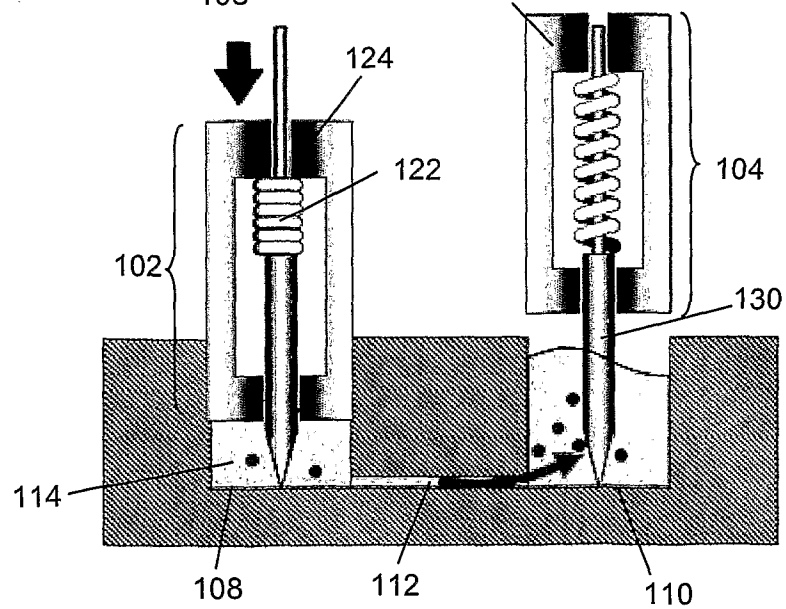


Figure 2A

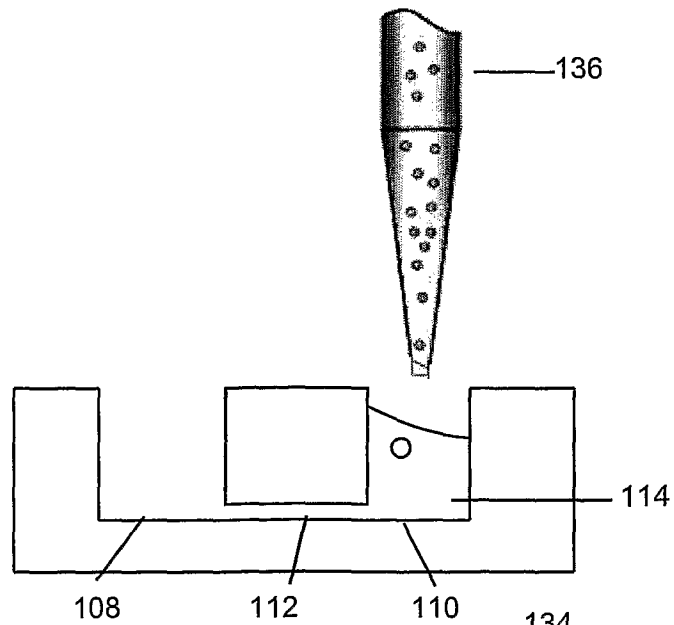


Figure 2B

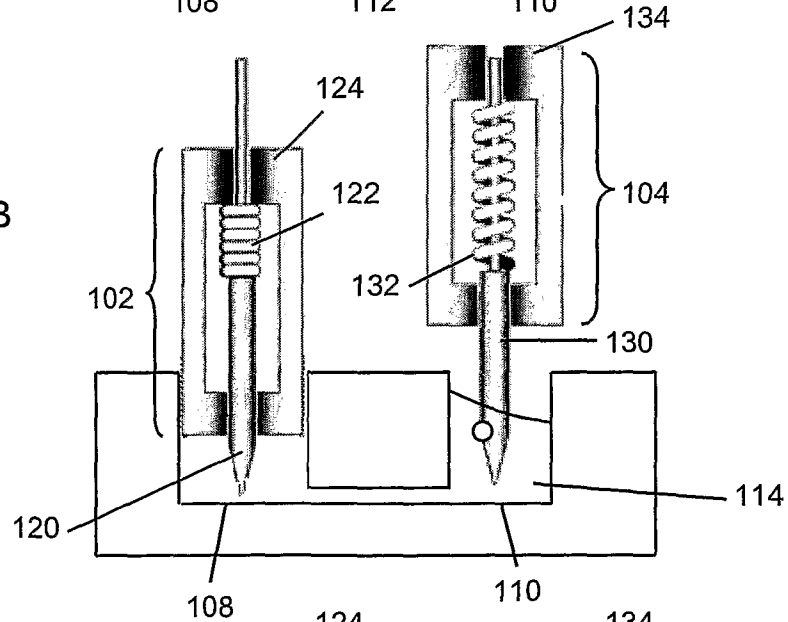
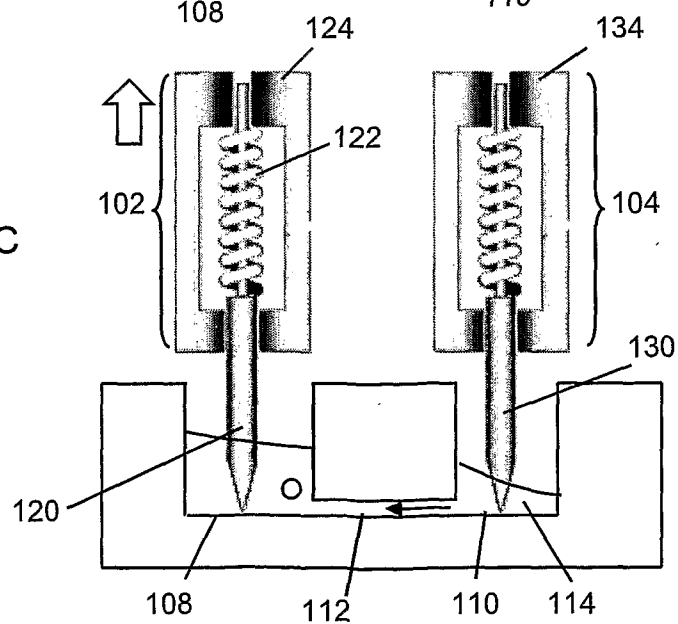


Figure 2C



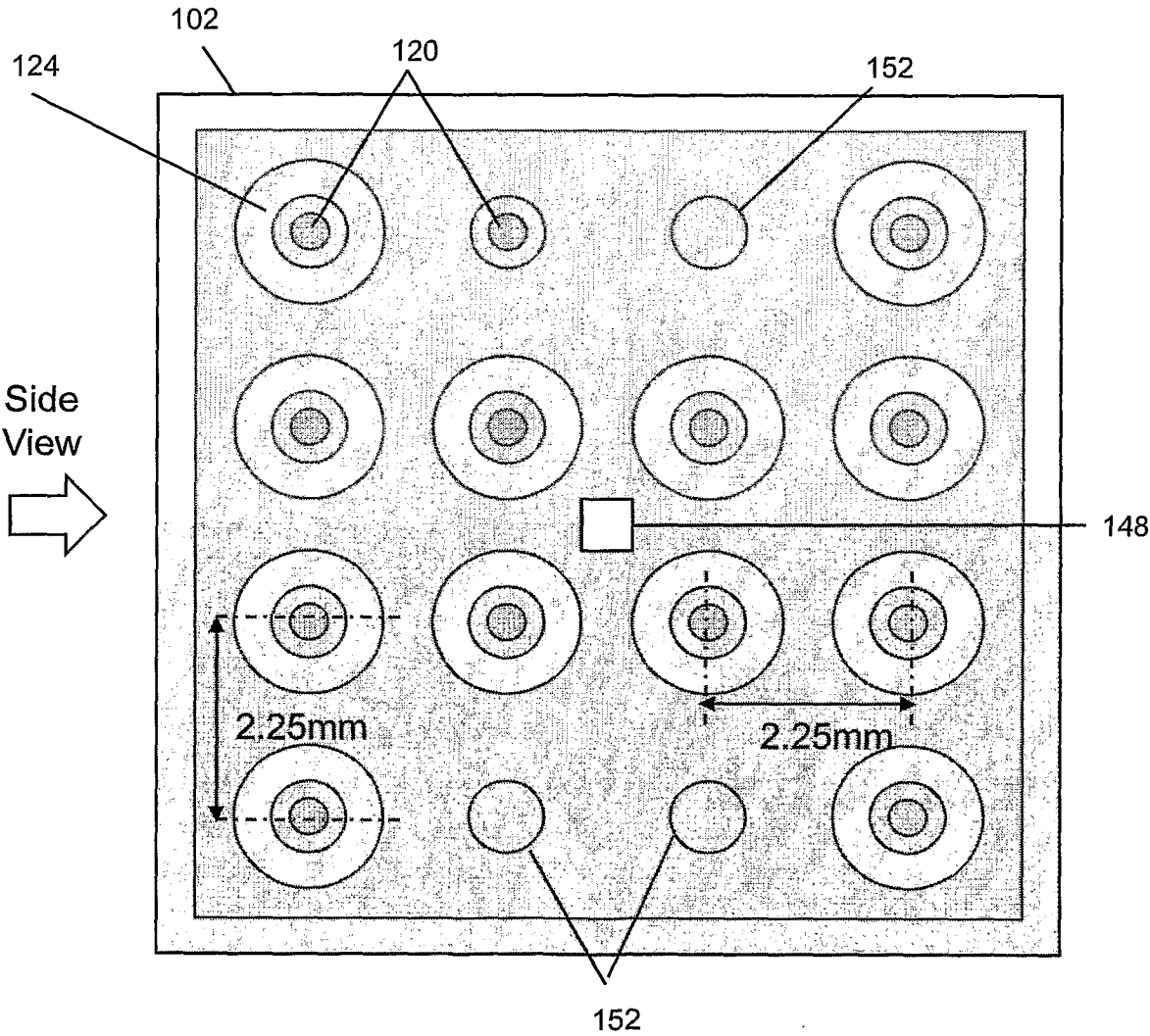


Figure 3A

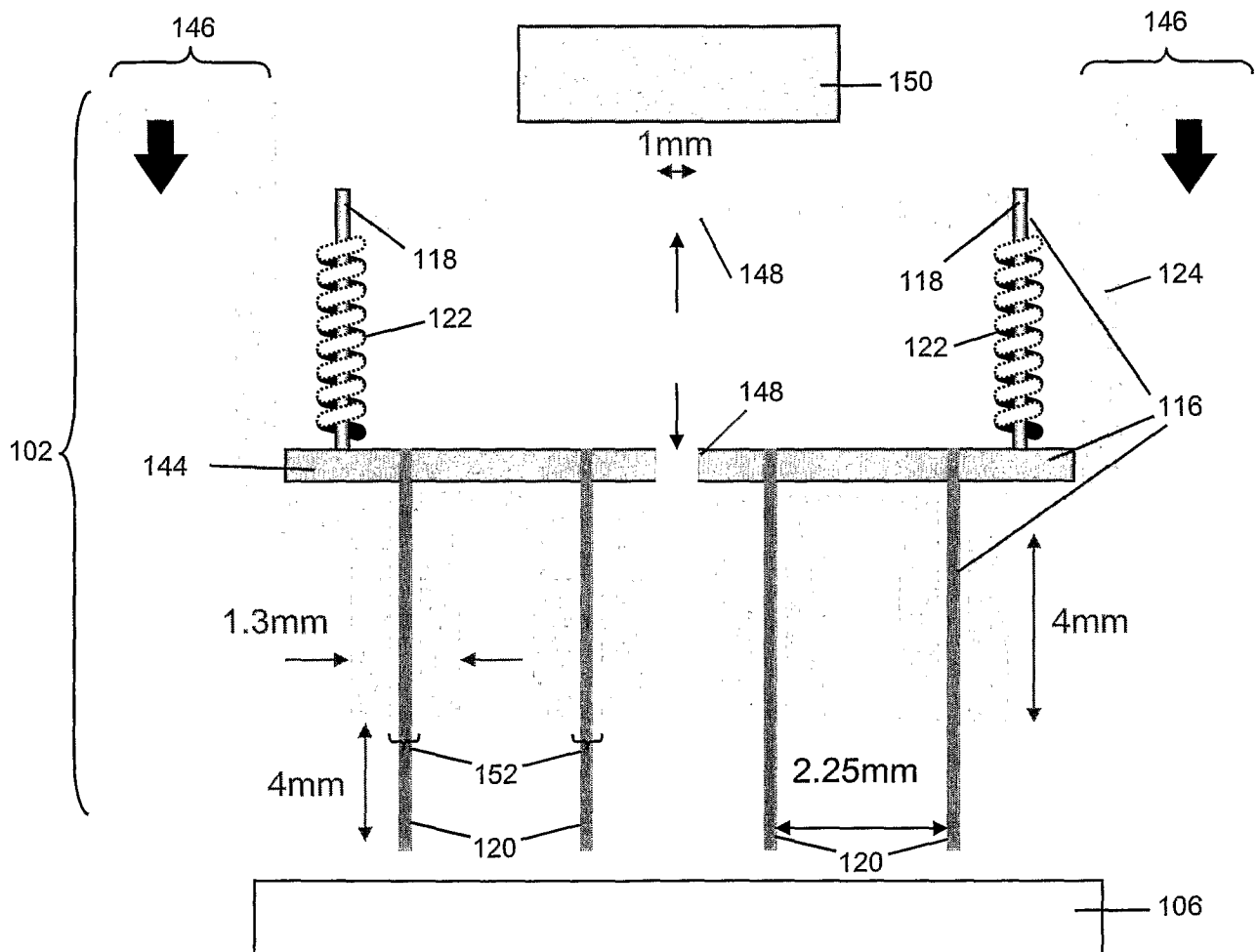


Figure 3B

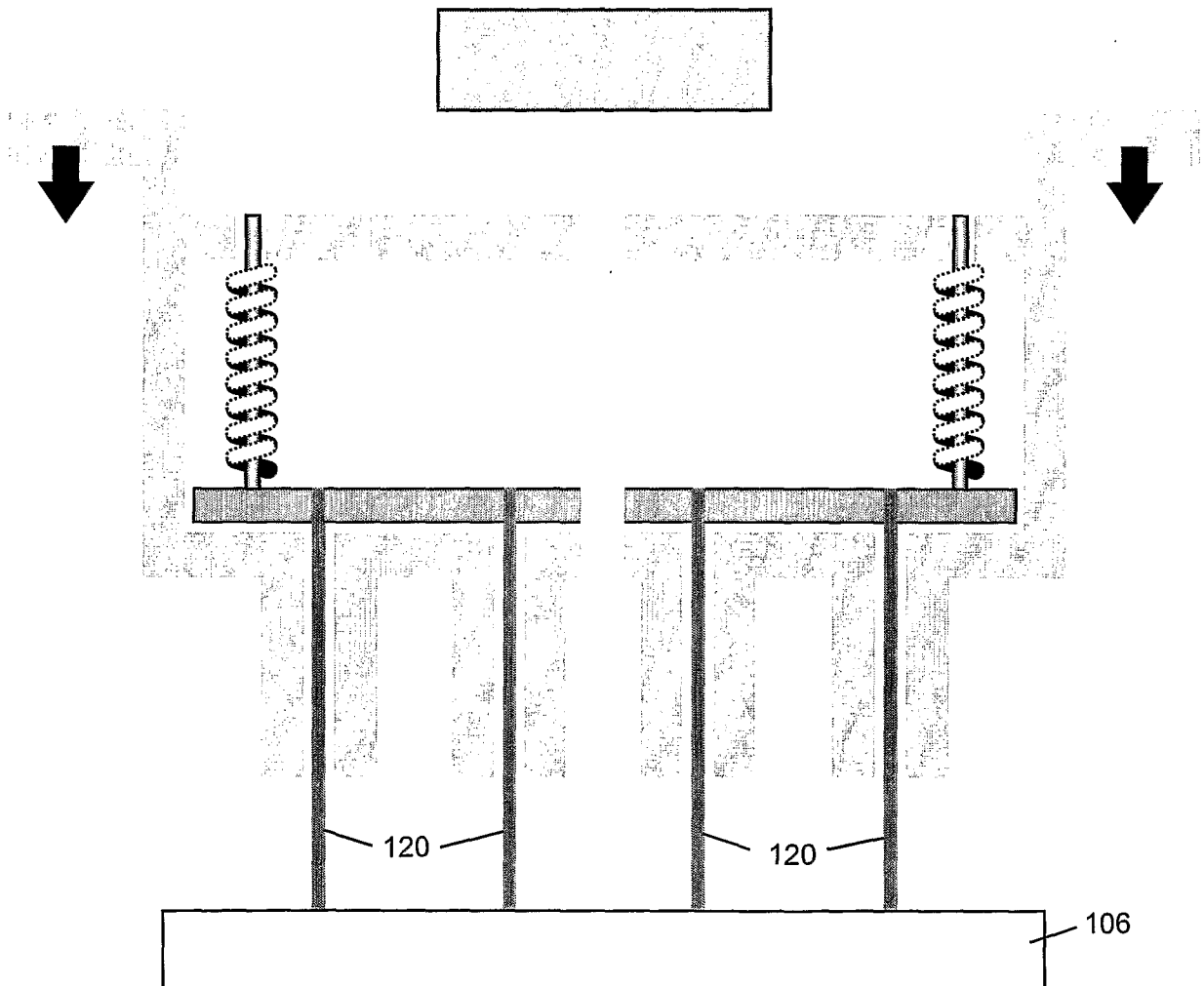


Figure 3C

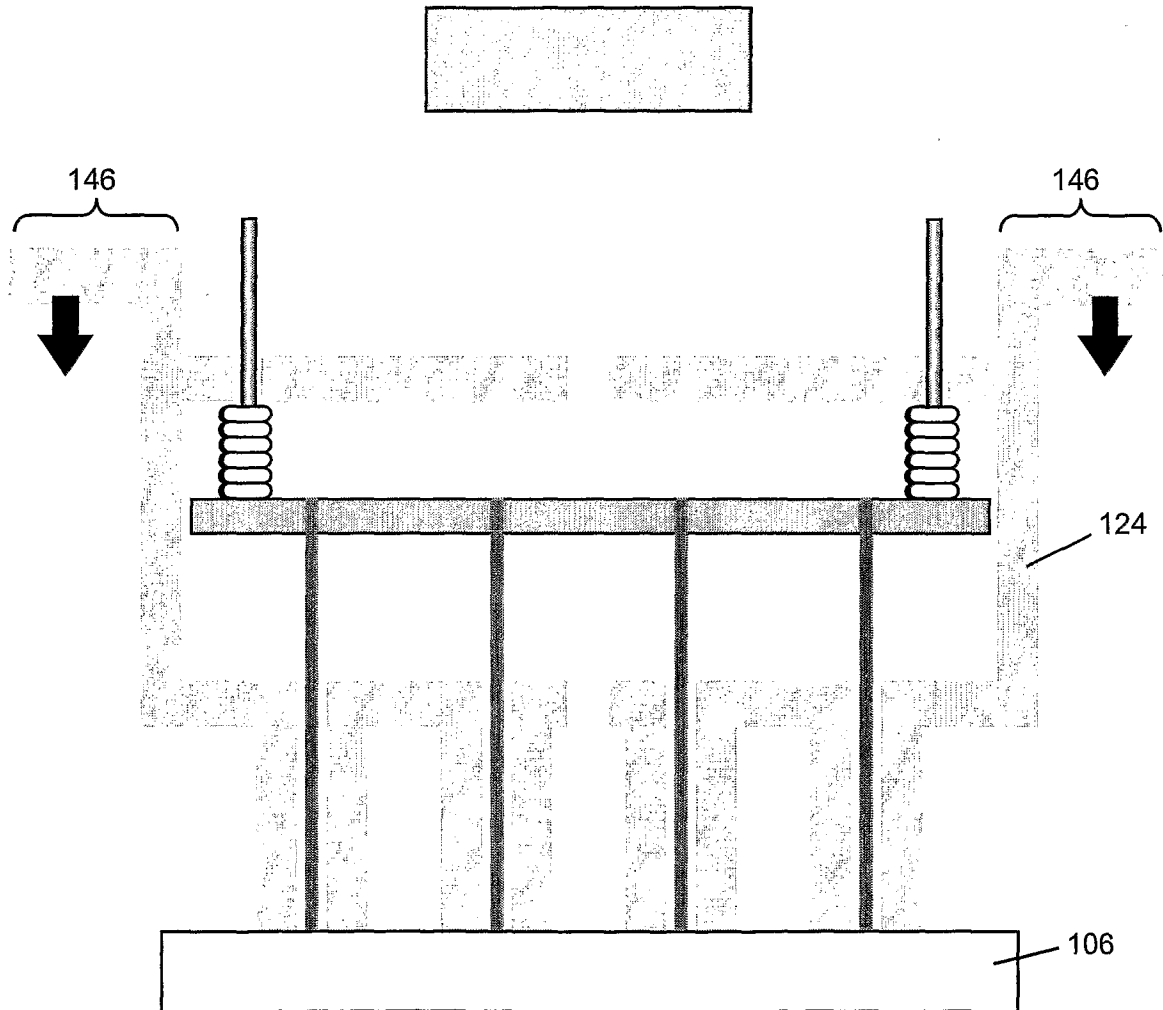


Figure 3D

Figure 4A

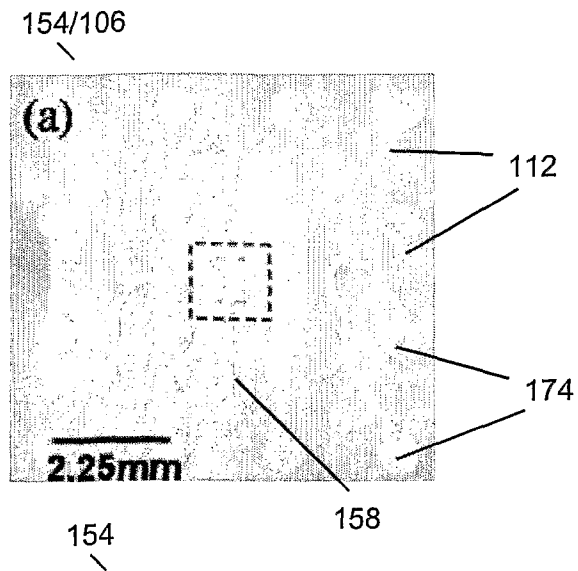


Figure 4B

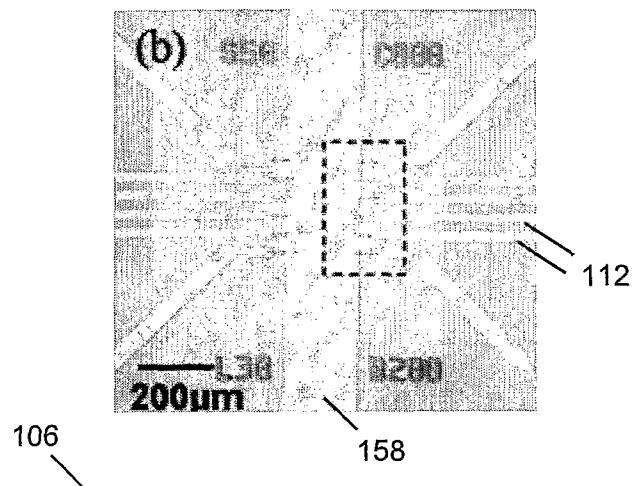
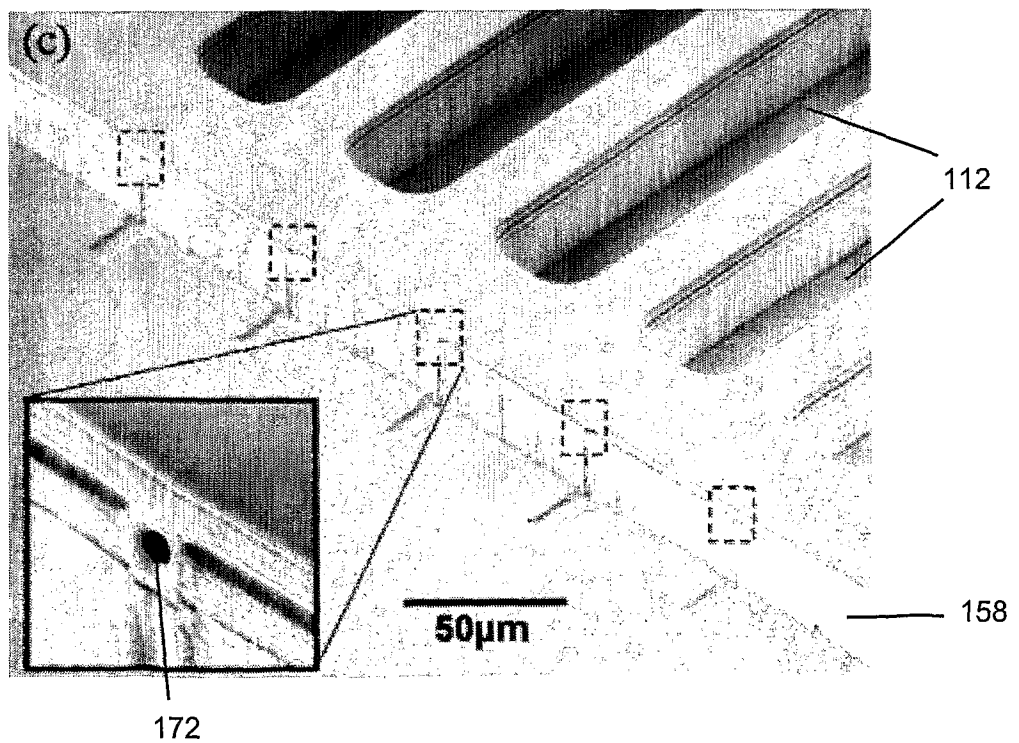


Figure 4C



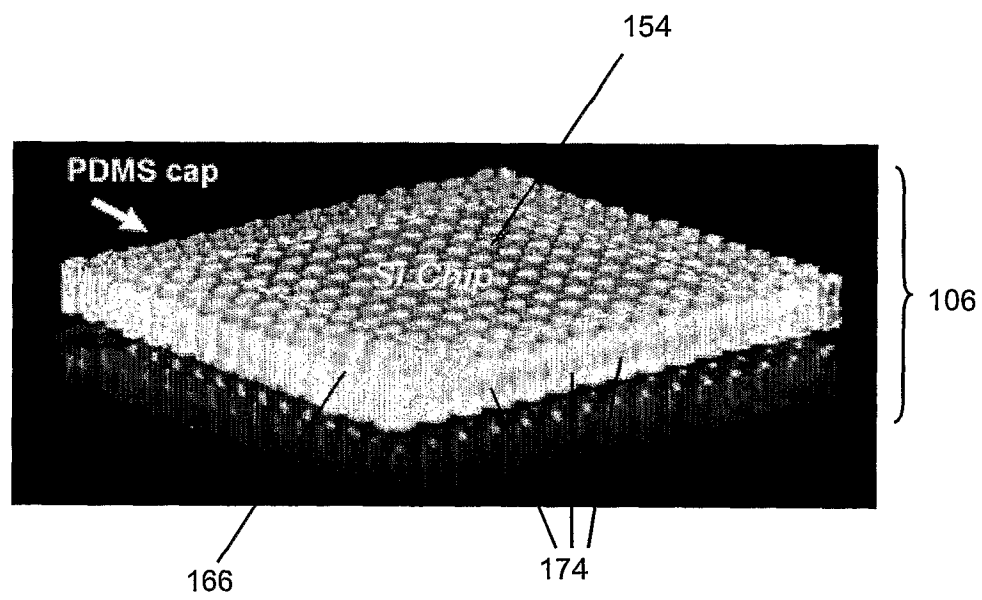


Figure 5

Figure 6A

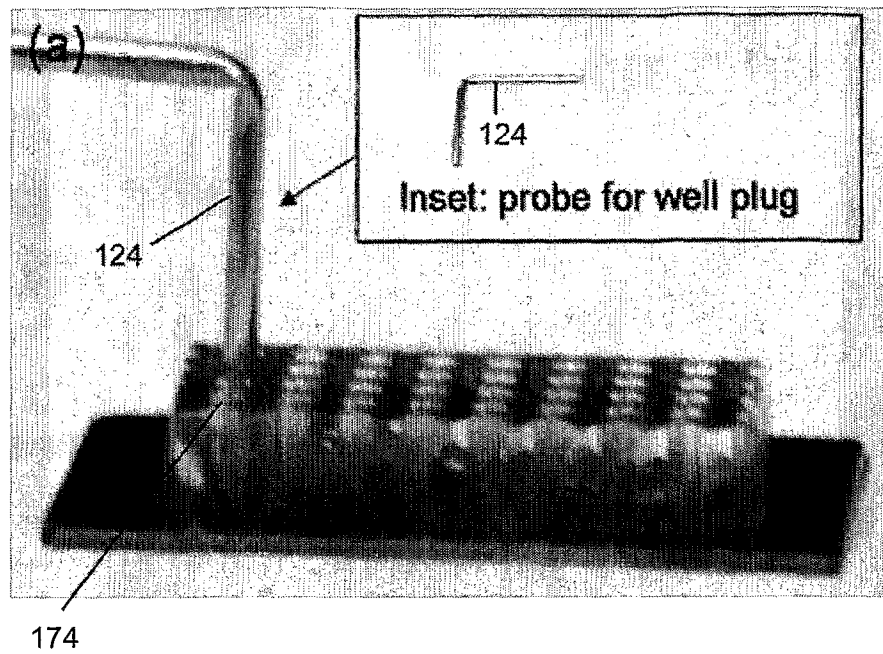


Figure 6B

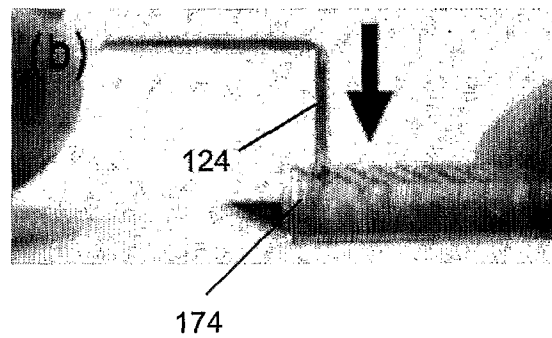
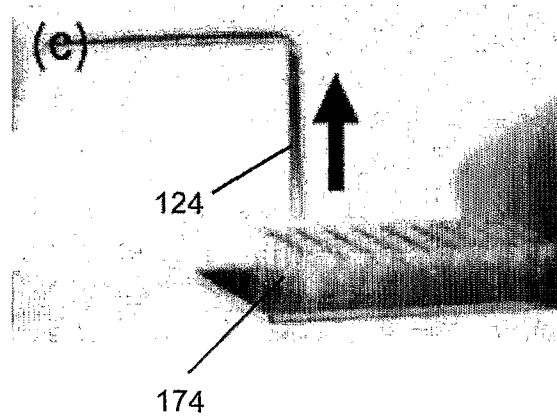


Figure 6C



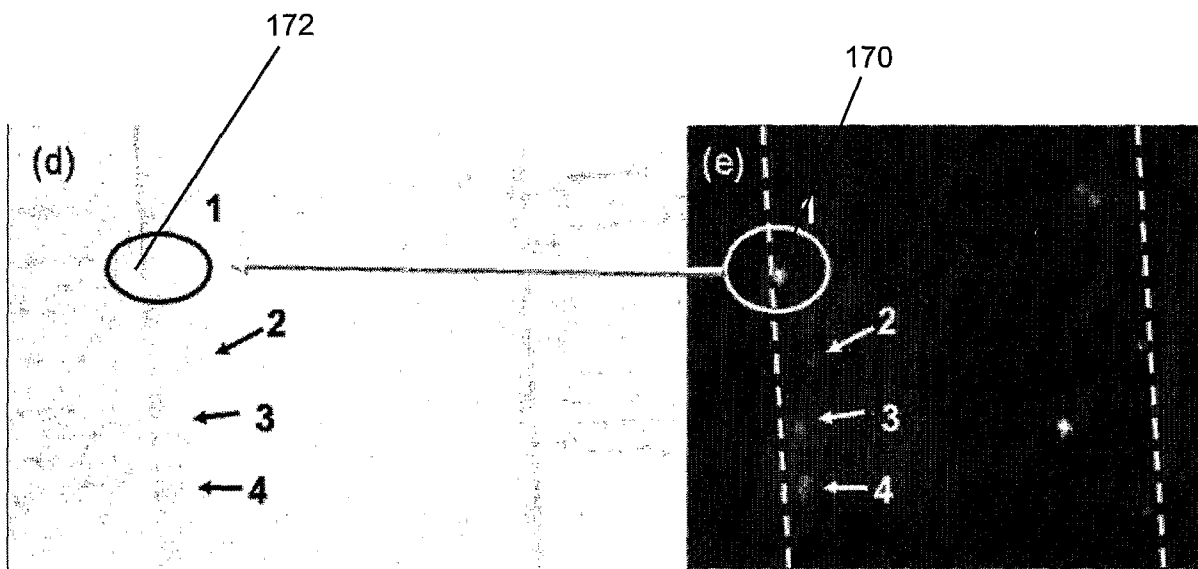


Figure 6D

Figure 6E

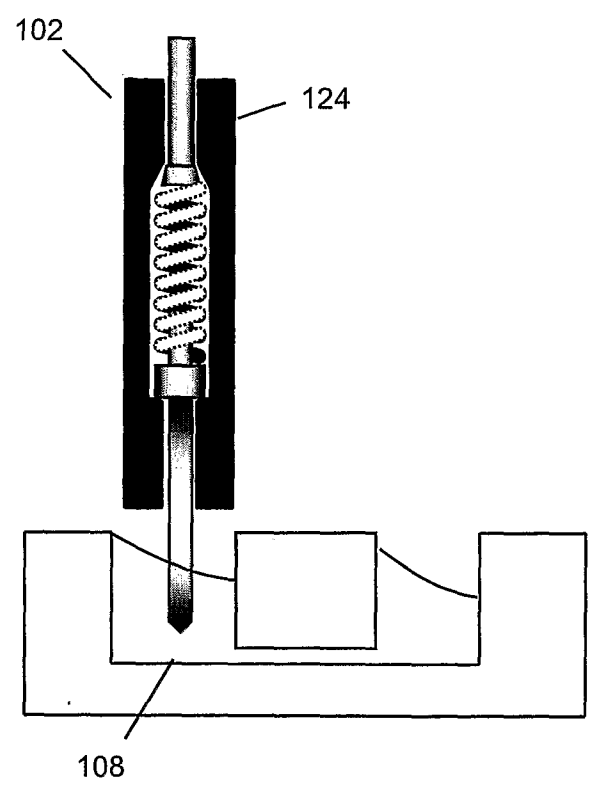


Figure 7

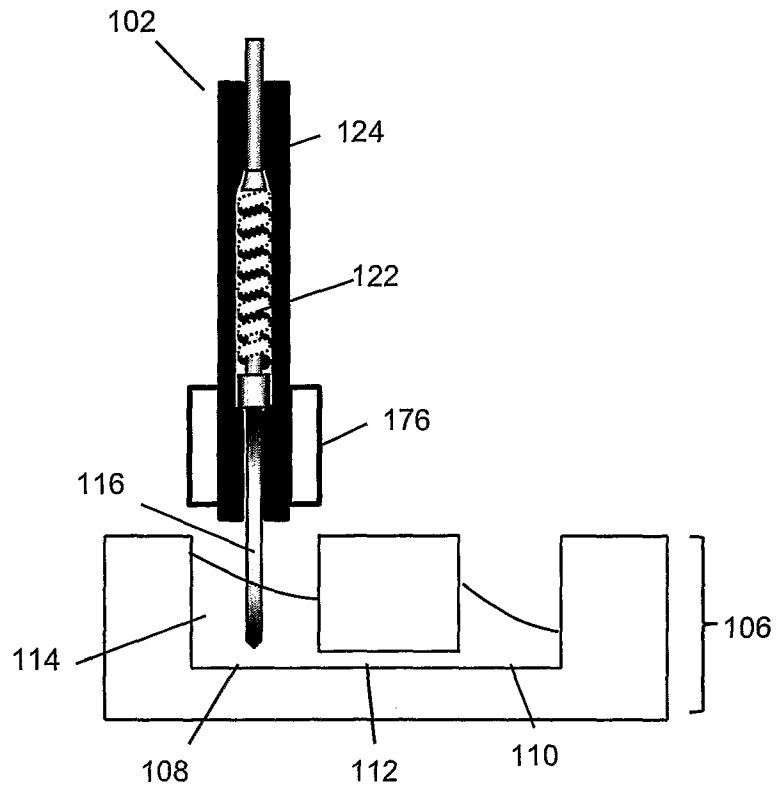


Figure 8A

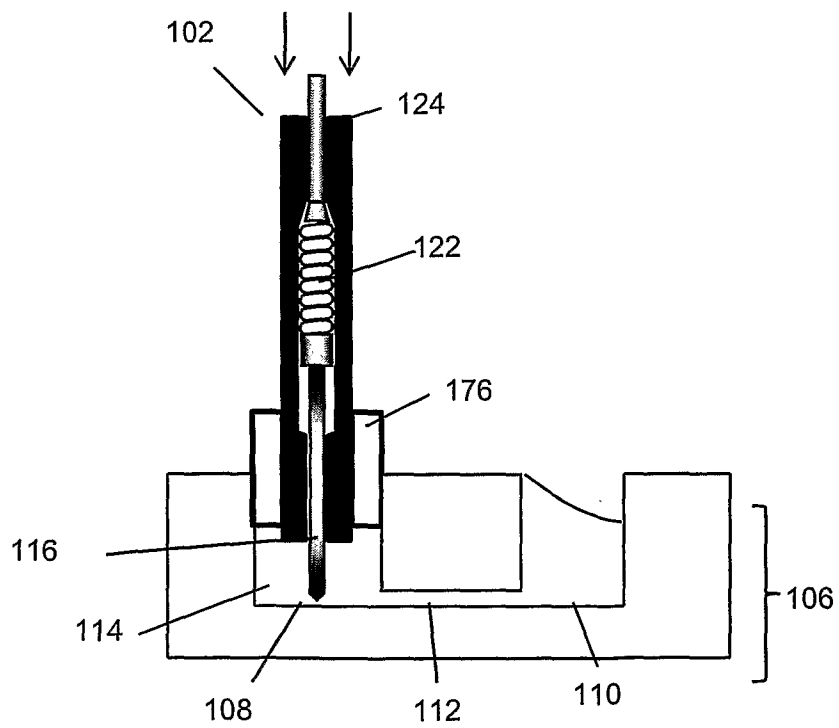


Figure 8A'

Figure 8B

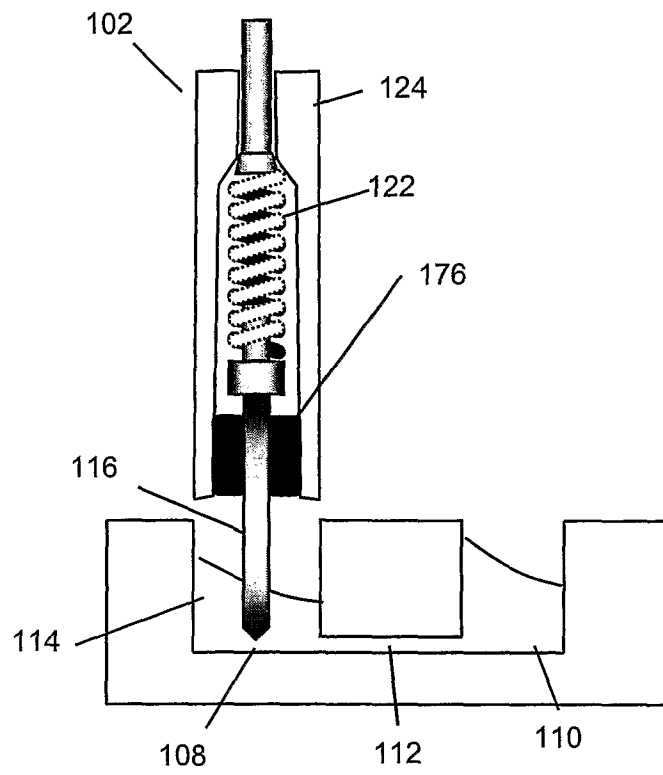


Figure 8B'

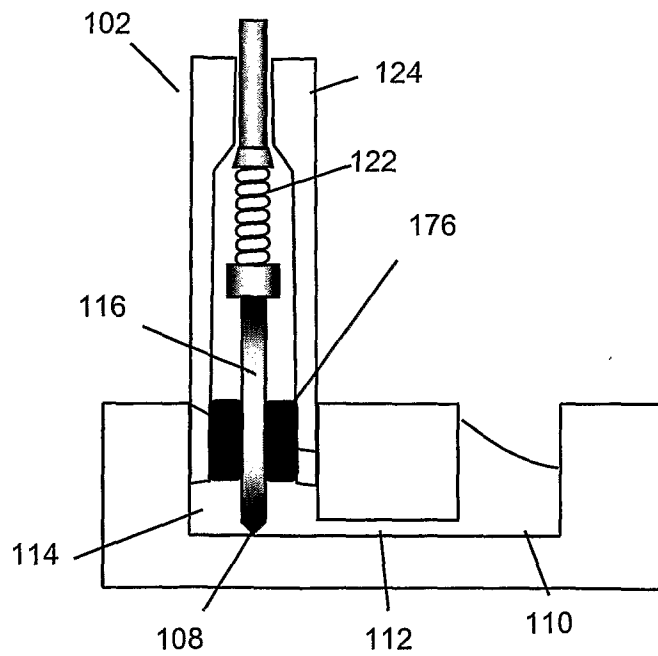


Figure 8C

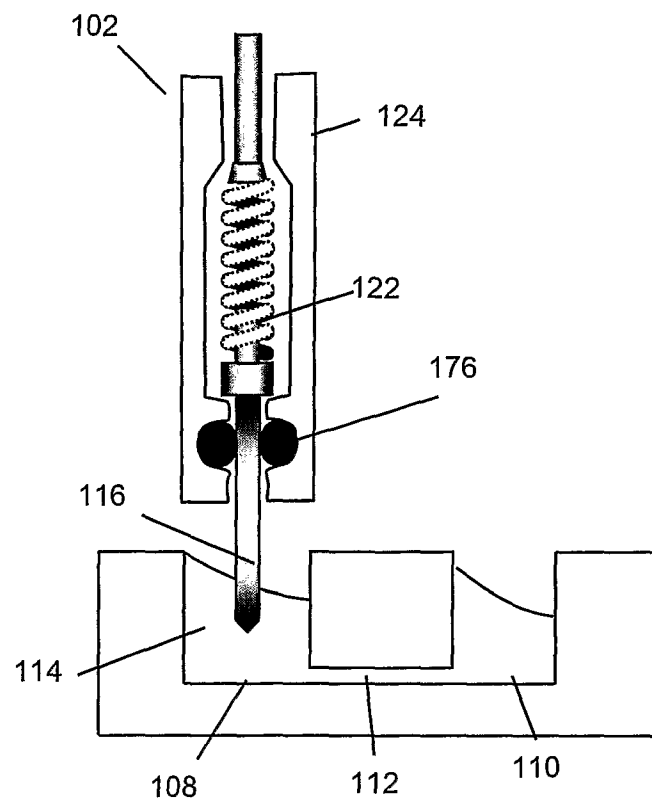
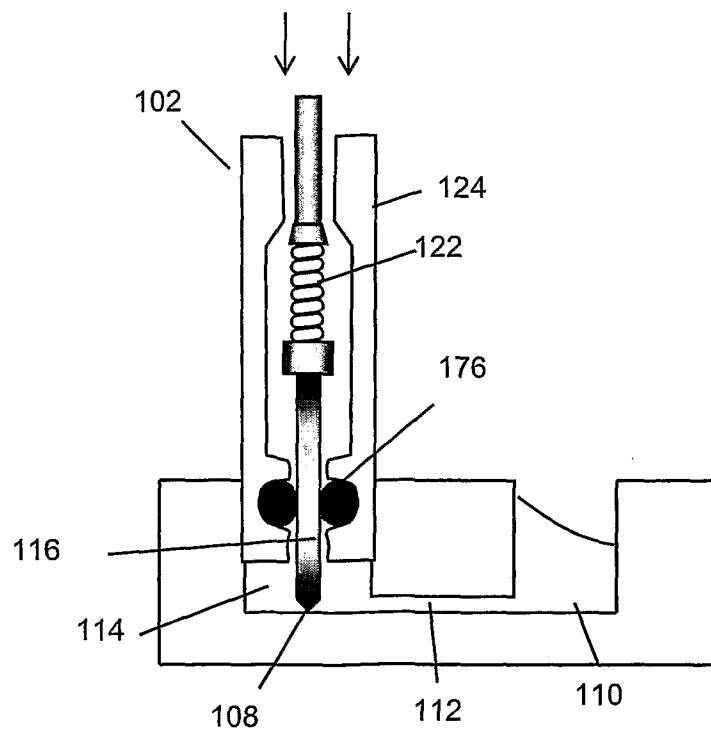


Figure 8C'



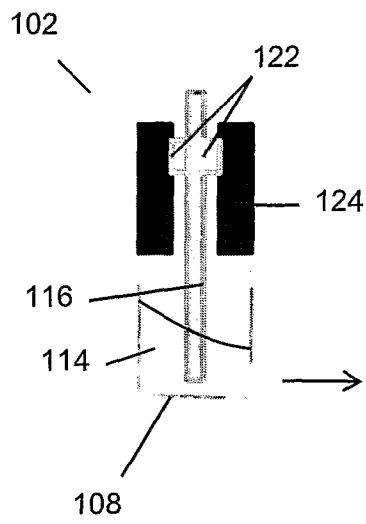


Figure 9A

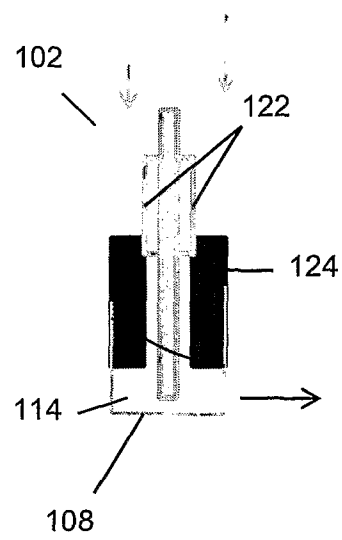


Figure 9B

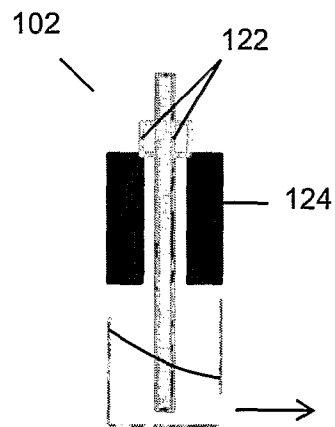


Figure 10A

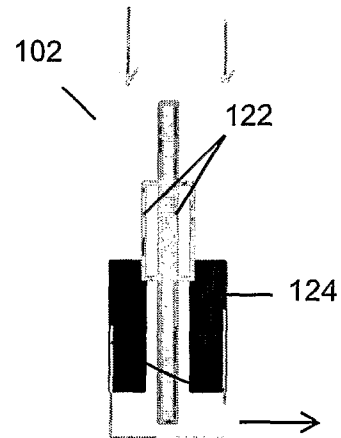


Figure 10B

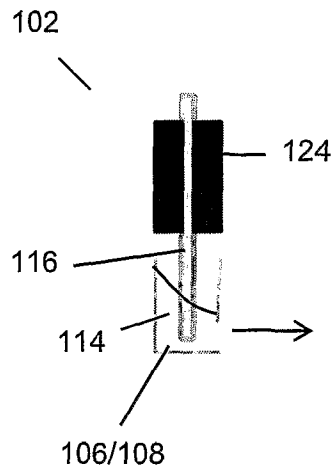


Figure 11A

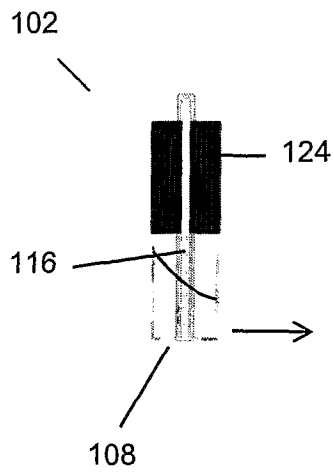


Figure 11B

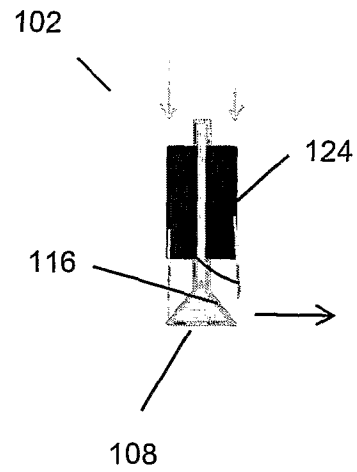


Figure 11C

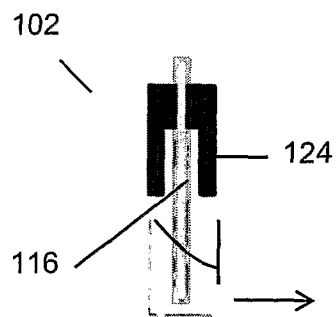


Figure 12

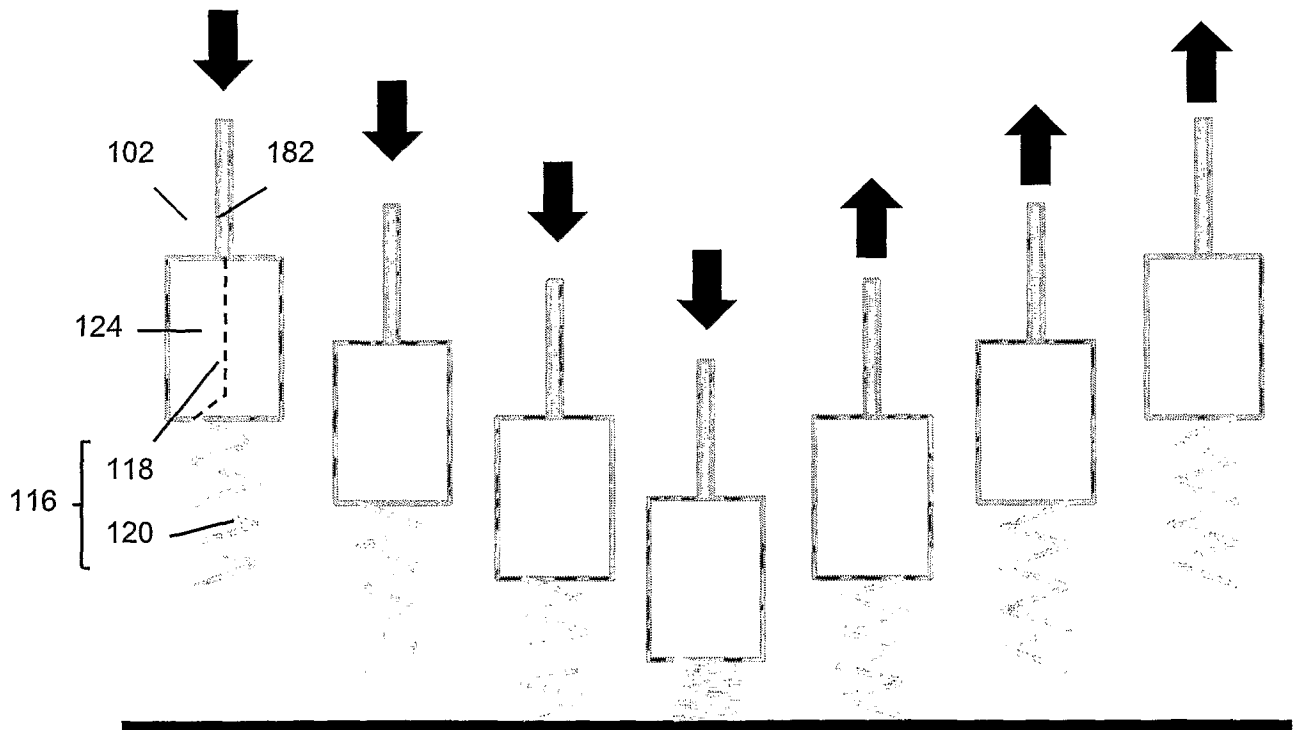


Figure 13

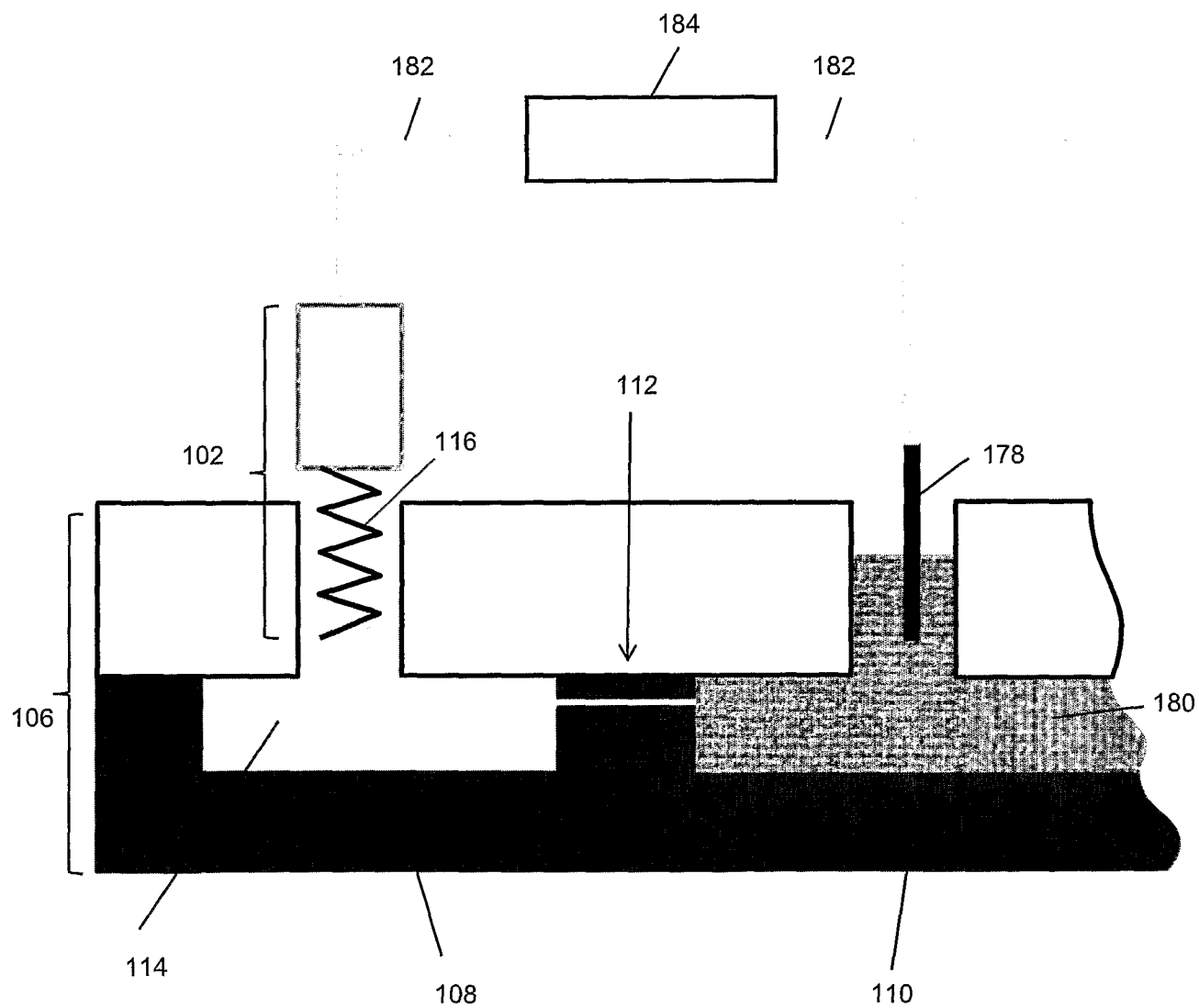


Figure 14A

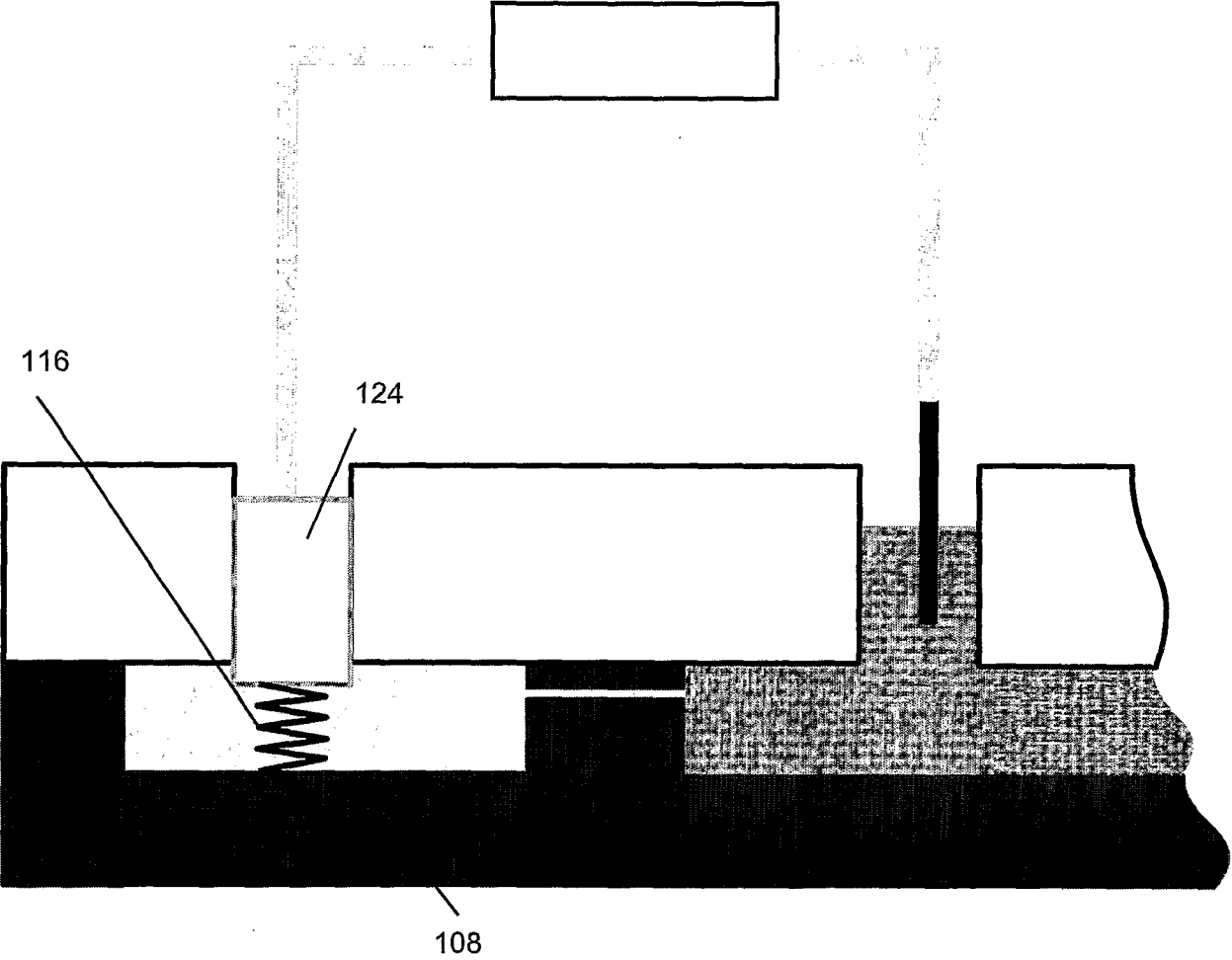


Figure 14B

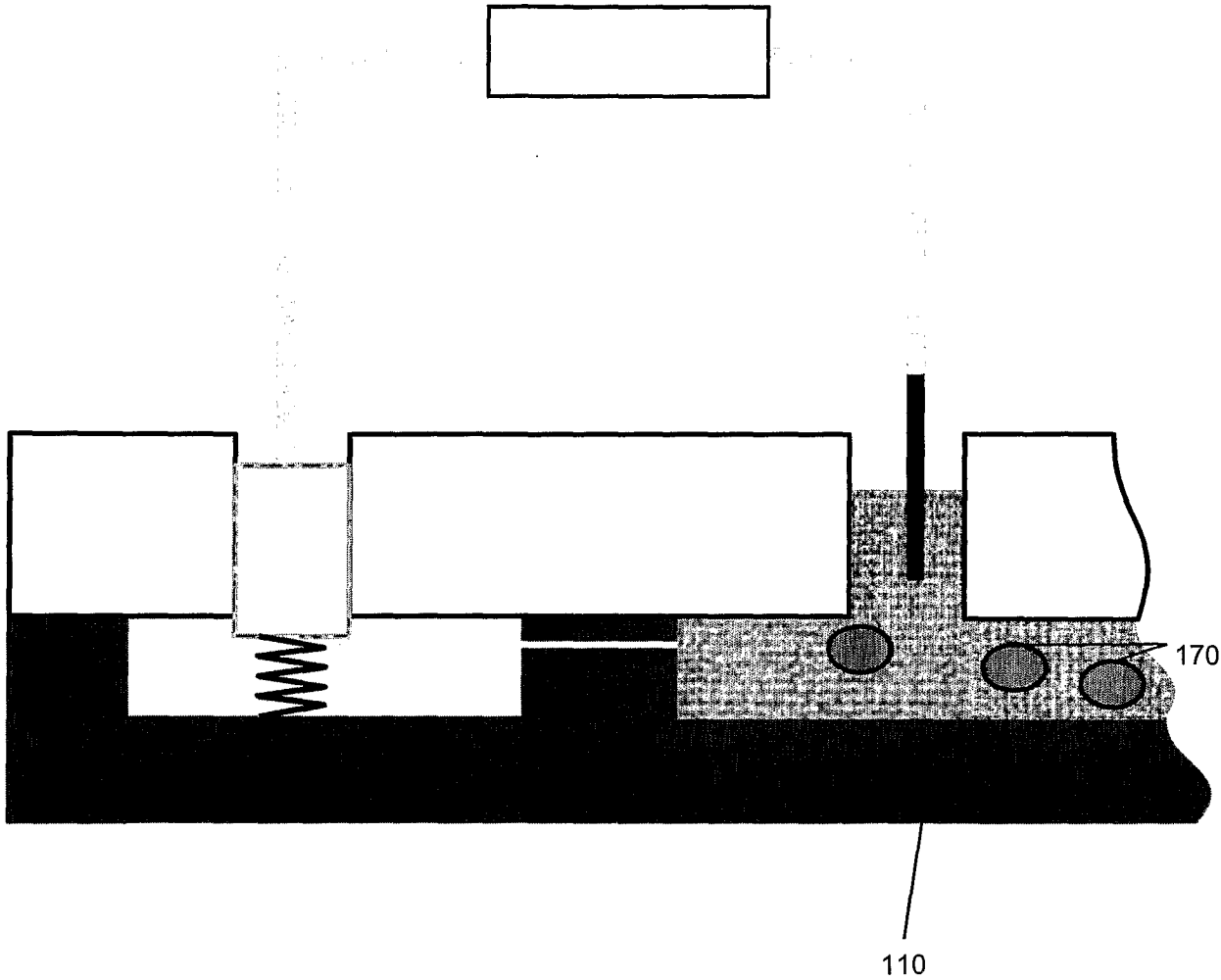
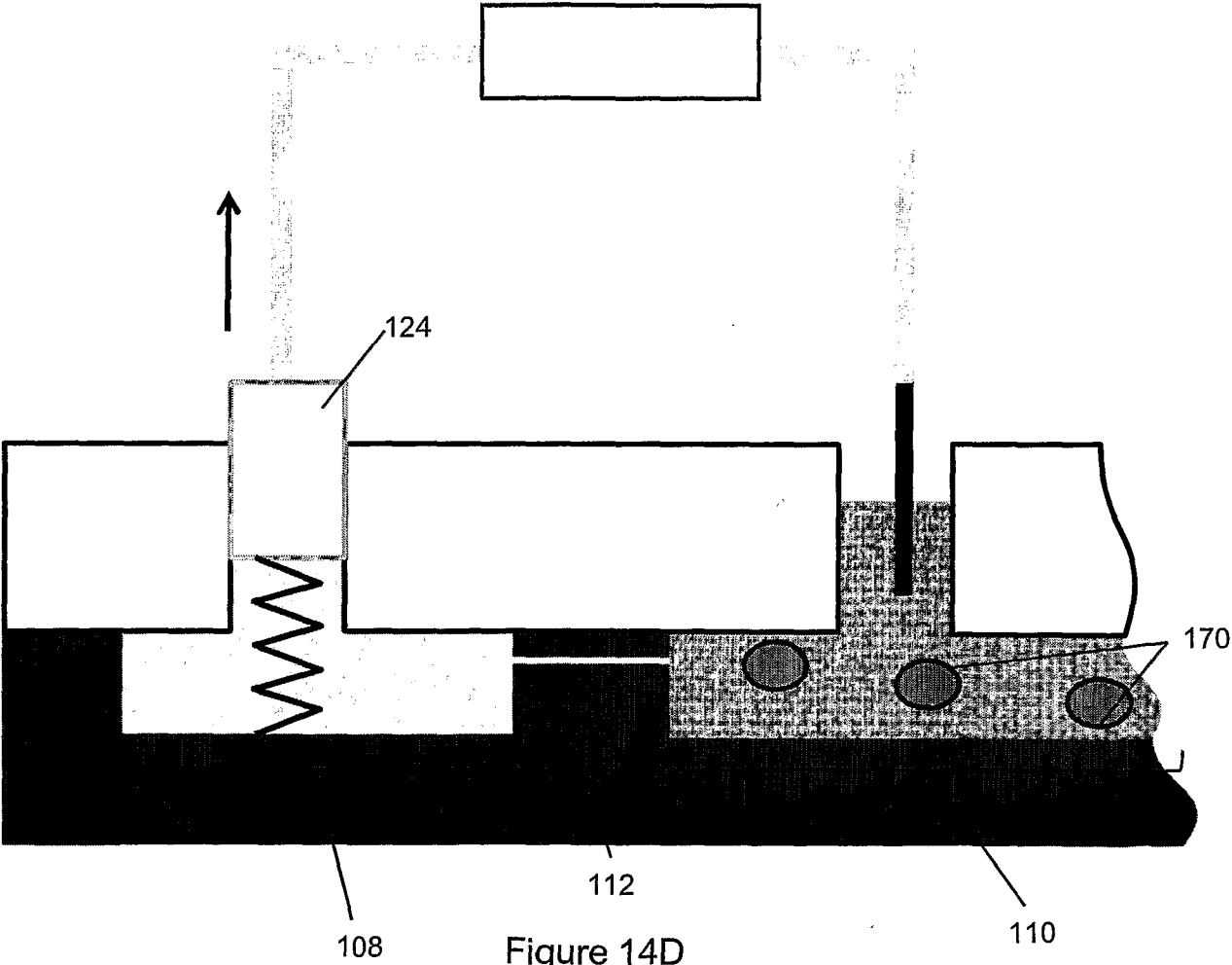


Figure 14C



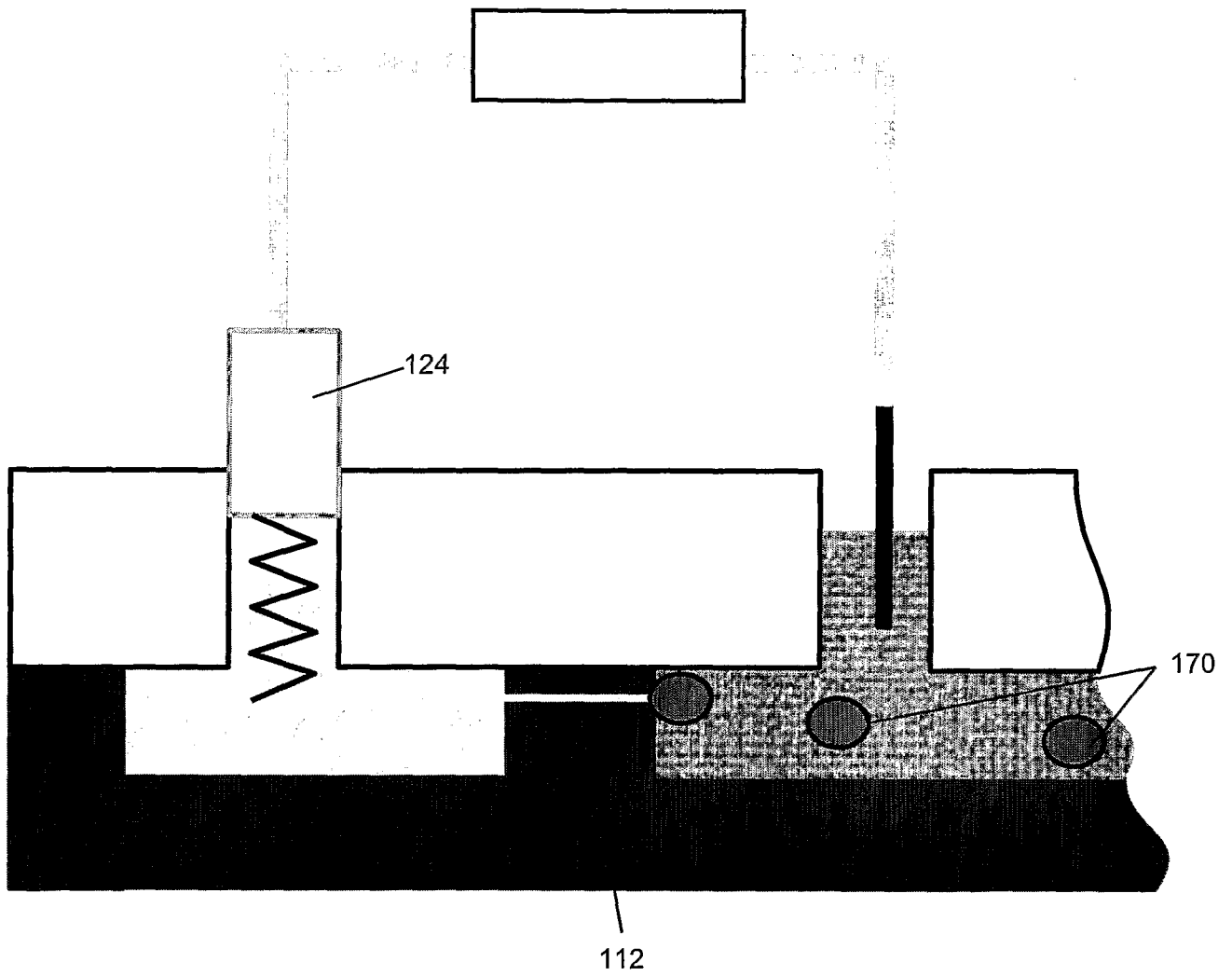


Figure 14E

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG2010/000064

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl.

B01L 3/00 (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI/EPODOC/INSPEC & keywords (microtitre, capillary, electrode, seal, plunger, spring and similar terms); Espacenet & keywords (well, microfluidic, electrode); USPTO & keywords (microwell, microfluid, electrode, seal, channel, spring and similar terms); GOOGLE & keywords (microfluid, electrode, seal spring, capillary, microplate and similar terms)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2005/0054028 A1 (TEICH et al) 10 March 2005 See abstract and figs 1 and 2	
A	WO 2005/039772 A2 (SCHWARTZ) 6 May 2005 See abstract and fig 4A	
A	US 2009/0236226 A1 (YUEN) 24 September 2009 See abstract	
A	WO 2007/026232 A2 (MCGILL UNIVERSITY) 8 March 2007 See abstract and fig 1	



Further documents are listed in the continuation of Box C



See patent family annex

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

01 April 2010

Date of mailing of the international search report

08 APR 2010

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/SG2010/000064

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member			
US	2005054028	CN	1867819	CN	101506643
		EP	2041551	US	7276351
		US	7638321	US	2007087401
		WO	2005026701	US	2008014571
WO	2005039772	EP	1635948	WO	2008008149
		US	7185551	US	6805015
US	2009236226	US	2004231437	US	2004231438
		WO	2009117147	WO	2004105950
WO	2007026232	US	2009149334		
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.					
END OF ANNEX					