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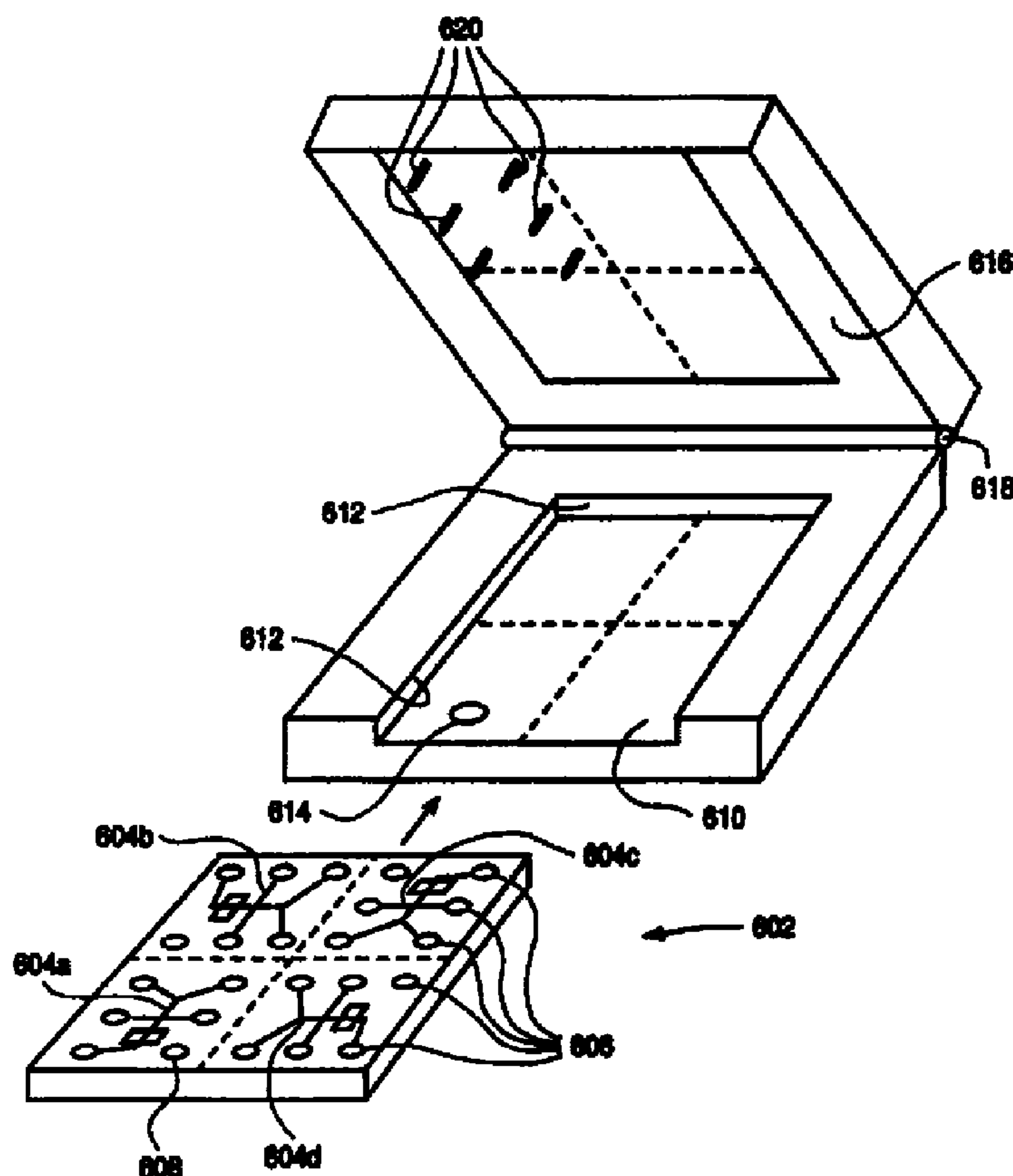
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(54) Titre : INTERFACES AMELIOREES DE DETECTEUR/CONTROLEUR POUR SYSTEMES MICROFLUIDIQUES

(54) Title: IMPROVED CONTROLLER/DETECTOR INTERFACES FOR MICROFLUIDIC SYSTEMS



(57) Abrégé/Abstract:

The present invention is generally directed to improved methods, structures and systems for interfacing microfluidic devices with ancillary systems that are used in conjunction with such devices. These systems typically include control and monitoring systems (620) for controlling the performance of the processes carried out within the device, e.g., monitoring and controlling environmental conditions and monitoring results of the processes performed, e.g., detection.

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(54) Title: IMPROVED CONTROLLER/DETECTOR INTERFACES FOR MICROFLUIDIC SYSTEMS (57) Abstract The present invention is generally directed to improved methods, structures and systems for interfacing microfluidic devices with ancillary systems that are used in conjunction with such devices. These systems typically include control and monitoring systems (620) for controlling the performance of the processes carried out within the device, e.g., monitoring and controlling environmental conditions and monitoring results of the processes performed, e.g., detection.		

IMPROVED CONTROLLER/DETECTOR INTERFACES FOR MICROFLUIDIC SYSTEMS

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BACKGROUND OF THE INVENTION

Despite the advancements in the fields of
15 microfluidics, microfabrication and the like, there remains a
fundamental problem with the implementation of these
technologies in achieving their full potential. Specifically,
although microfluidic systems are readily applicable to high
throughput, low volume, automatable chemical and biochemical
20 analyses and syntheses, many of the advantages gained through
the use of microfluidic systems are lost through the lack of
interfacing systems that are capable of functioning at the
horizons of these microfluidic systems. For example, one of
the major advantages of these microfluidic systems is the
25 ability to perform operations using extremely small fluid
volumes, thereby requiring smaller amounts of potentially
valuable reagents and/or samples. However, although a
microfluidic system may be capable of operating with fluid
volumes in the nanoliter range, the lack of fluid handling
30 systems capable of delivering such volumes to these
microfluidic systems renders this advantage substantially
unrealized. Specifically, the user is still required to
utilize reagents and/or samples in the 1 to 10 μ l range.

One example of a fluidic interface which addresses
35 these problems, namely, the introduction of samples and other
fluids into microfluidic analytical systems, is described in
commonly assigned U.S. Patent No. 5,779,868, issued July 14,

1998.

In brief, the described system includes an electropipettor interfaced with the channels of a microfluidic device, for electrokinetically introducing very small volumes of samples or other materials into the microfluidic device.

In addition to fluidic interfaces, microfluidic systems also require additional device:world interfaces, including an interface between the device and the detection, sensing or monitoring means that are utilized with the system. Also required are interfaces between the device and the systems that control the operation of the device, such as systems that control fluid direction and transport within the device, and/or environmental conditions present within or around the device, and the like.

Microfluidic devices previously described in the literature have generally included only crude device:world interfaces which severely limited or eliminated a substantial proportion of the promised benefits of microfluidic systems, including automatability, ease of use, low volume and high throughput, which have been the goals of these systems.

Accordingly, there exists a need in the art for improved interfaces between microfluidic devices and the ancillary systems that are utilized with these microfluidic systems, such that these microfluidic systems can realize a greater proportion of their promised benefits. The present invention provides a solution to many of these and other problems.

SUMMARY OF THE INVENTION

The present invention generally provides improved methods, apparatuses and systems for interfacing microfluidic devices with the various systems used in conjunction with these devices, such as electrical control and monitoring systems, and the like. These improved interfaces provide microfluidic systems that are easier to use, e.g., "user friendly," are more readily automatable, and as a result, have higher throughputs than previously described analytical systems.

In a first aspect, the present invention provides a microfluidic device, comprising:

a body structure comprising an upper layer, a bottom layer, and a plurality of intersecting microscale channels;

5 one or more first ports within the upper layer and in fluidic communication with the plurality of intersecting microscale channels;

one or more second ports comprising a thin, flat electrode surface within the upper layer, wherein the one or more second ports are blocked from fluidic communication with the one or more first ports; and

10 an electrical interface component in electrical communication with the one or more first ports and the one or more second ports.

Each of the ports is in fluid communication with at least one of the plurality of intersecting channels. An electrical controller comprises a
15 plurality of electrical leads, each of the leads being operably coupled to a power source, where the electrical controller concomitantly delivers a voltage to each of the plurality of electrical leads. An interface structure permits the separate and removable coupling of each of the electrical leads with each of the plurality of ports, whereupon each of the leads is in electrical
20 communication with a fluid disposed in each of the ports. The interface structure often includes a cover having at least a first surface, and a plurality of electrode pins mounted thereon, the electrode pins being oriented for insertion into the plurality of ports, each of the electrode pins being electrically coupled to a separate one of the electrical leads. Optionally, the interface
25 structure further comprises a base adapted for receiving the microfluidic device, wherein an edge of the cover is attached to the base by a hinge, whereby the cover is capable of being rotatably closed over the microfluidic device mounted on the base, to insert the plurality of pins into the plurality of ports. In a further alternate aspect, the body of the device is planar in
30 structure, and the electrical interface structure comprises a plurality of electrical contact pads disposed along the at least one edge of the microfluidic device, each of the electrical contact pads being electrically coupled to at

least one of the plurality of ports, and each of the plurality of electrical leads is positioned to contact a separate one of the plurality of contact pads.

Alternatively, the electrical leads are disposed within a slot and oriented whereby each of the electrical leads contacts a separate one of the plurality of electrical contact pads, when the portion of the bottom layer extending beyond the top layer is inserted into the slot.

The present invention also provides a microfluidic device, comprising:

10 a body structure comprising an upper layer, a bottom layer, and a plurality of intersecting microscale channels;

one or more ports comprising a thin, flat electrode surface within the upper layer, wherein the one or more ports are positioned such that the ports are not in fluid communication with the plurality of intersecting microscale channels; and

15 an electrical interface component in electrical communication with both the plurality of intersecting microscale channels and the one or more ports.

20 In still another aspect, the present invention provides an electrically controlled microfluidic system, comprising:

a microfluidic device comprising a body structure, a plurality of microscale channels disposed in the body structure, a plurality of ports disposed in the body structure, and a plurality of electrical contact pads disposed along at least one edge of the body structure, wherein each of the plurality of ports is in fluid communication with at least one of the plurality of microscale channels, and wherein each of the plurality of electrical contact pads is electrically coupled to at least one of the plurality of ports; and an electrical control device comprising a base adapted for receiving the microfluidic device; an electrical interface array comprising a cover having at least a first surface and a plurality of electrical contacts mounted thereon, the

electrical contacts being oriented to contact the plurality of electrical contact pads; and a plurality of electrical leads, each of the leads being electrically coupled to the plurality of electrical contacts and operably coupled to a power source, wherein an edge of the cover is attached to the base, whereby the

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cover is capable of being rotatably closed over the microfluidic device mounted on the base, to contact the plurality of electrical contacts on the cover with the plurality of electrical contact pads on the body structure.

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Preferably, at least three electrical interface elements will be provided in the form of rigid electrodes. These electrodes can ideally extend from the structure into the fluid in the ports of the microfluidic device. The base of the structure may be coupled together using a hinge or other mechanical coupling arrangement, and the base will often fittingly receive the microfluidic device. This arrangement can be used to maintain alignment between a large number of very small ports of the microfluidic device and the electrodes of the interface, thereby allowing complex microfluidic devices to be easily removed and replaced.

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5 In yet another aspect, the present invention provides a
microfluidic device comprising a body structure having a port (for receiving
fluid) and an interior portion. The interior portion defines a plurality of
intersecting microscale channels. The interior portion blocks communication
between the channels and the port. An electrical interface component
10 electrically couples the fluid in the port to the channels, or to ports in fluid
communication with the channels.

 In yet another aspect, the invention provides a microfluidic
device comprising a body structure including an upper layer and a bottom
15 layer. The body structure has an interior portion defining first and second
intersecting microscale channels. The first channel has an un-intersected
terminus. The upper layer includes first and second ports therethrough. The
first port is disposed at the terminus of the first channel. The interior portion
blocks fluid communication between the first port and the second port. An
20 electrically conductive film is disposed between the first and second layers.

The film electrically couples a first fluid in the first port with a second fluid in the second port. These advantageous structures allow electrically potentials
5 to be applied to a sample fluid by inserting an electrode into a fluidically isolated port containing saline or the like. The

film (or other electrical conductor) need not be disposed between the layers. For example, alternative embodiments may include conductors overlaid over the upper layer (i.e., bridging between ports). Regardless, as compared to systems in which electrodes are directly inserted into each sample, the invention provides a reduced risk of cross-contamination when replacing one microfluidic device with another.

Preferably, electrodes of the interface structure will extend into ports containing an electrolyte. The electrolyte can be electrically coupled, in turn, to a sample fluid within a sample port using a thin film conductor deposited between the layers of the microfluidic body structure, typically using any of the thin film deposition techniques developed for production of integrated circuits, recording media or the like. The use of fluid to couple an electrode to the film enhances the reliability of the electrical connection and avoids damage to the film when the electrode is moved between a coupled position and a de-couple position.

In a still further aspect, the invention provides the use of an interface to connect a microfluidic device to an electrical controller. The interface has a structure that includes a plurality of fixed electrodes disposed thereon. The electrodes are operably coupled to the electrical controller. The fixed electrodes are positioned on the structure to be inserted into a plurality of ports on the microfluidic device when the structure is moved from a first position to a second position.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 schematically illustrates one embodiment of a microfluidic device fabricated from a plurality of laminated or bonded parts, for use in accordance with the methods and systems of the present invention.

Figure 2A illustrates one embodiment of an improved electrical interface between a microfluidic device and electrical controller. Figure 2B

illustrates an alternate configuration for the cover element of the interface shown in Figure 2A.

Figure 3 illustrates a further embodiment of an electrical interface between a microfluidic device and an electrical controller. Figure 3A illustrate the interface components present on a microfluidic device from a top view, while Figures 3B and 3C illustrate the device from the side and perspective views, in combination with a complementary interface element from an electrical controller.

Figures 4A-4D illustrate an alternate embodiment of a microfluidic device incorporating an electrical interface array. Figure 4A shows an alternate structure of a microfluidic device, while Figures 4B-4D illustrate the device with an optional coupler assembly from various perspectives.

Figure 5 illustrates a substrate wafer from which a number of microfluidic devices incorporating the electrical interface array shown in Figure 4 are manufactured.

Figure 6 illustrates a microfluidic system incorporating interface elements on the device and controller which are in communication when the device is inserted into the controller in any of a number of fixed or predetermined orientations.

Figure 7 schematically illustrates an electrical coupling arrangement in which a substantially rigid electrode pin mates with a thin, flat electrode surface.

Figure 8 schematically illustrates an alternative coupling arrangement in which a substantially rigid electrode pin is electrically coupled to a thin, flat electrode using an electrolyte to avoid damage to the flat electrode during coupling.

Figures 9A and B illustrate a microfluidic device having ports which are in electrical continuity with fluid sample ports, but which are not in fluid continuity with the sample ports so as to avoid cross-

contamination of samples when the microfluidic device is removed and replaced from the interface structure.

DESCRIPTION OF THE PREFERRED EMBODIMENT

5 The present invention is generally directed to improved methods, structures and systems for interfacing microfluidic devices with ancillary systems that are used in conjunction with such devices. These systems typically include fluid
10 handling systems for delivering fluids to a microfluidic device, e.g., sampling systems, control and monitoring systems for monitoring the processes carried out by the microfluidic devices and for controlling the performance of those processes, e.g.,
15 controlling internal fluid transport and direction, monitoring and controlling environmental conditions and monitoring results of the processes performed, e.g., detection.

 In a first general aspect, the present
20 invention provides electrically controlled microfluidic systems which have improved interfaces between the device itself and the electrical controlling system. Such systems include a microfluidic device made up of a body structure which
25 includes an interior portion and an exterior portion. The devices include a plurality of intersecting channels disposed within, and typically defined by, the interior portion of the body structure. Typically, such microfluidic devices also include a
30 plurality of ports disposed in the body structure, communicating the exterior portion of the device with the interior portion of the device, where the ports are in fluid communication with one or more of the plurality of intersecting microscale channels.

35 As used herein, the term "microscale" or "microfabricated" generally refers to structural elements or features of a device which have at least one fabricated dimension in the range of from about

0.1 μm to about 500 μm . Thus, a device referred to as being microfabricated or microscale will include at least one structural element or feature having such a dimension. When used to describe a fluidic element, such as a passage, chamber or conduit, the terms "microscale," "microfabricated" or "microfluidic" generally refer to one or more fluid passages, chambers or conduits which have at least one internal cross-sectional dimension, e.g., depth, width, length, diameter, etc., that is less than 500 μm , and typically between about 0.1 μm and about 500 μm . In the devices of the present invention, the microscale channels or chambers preferably have at least one cross-sectional dimension between about 0.1 μm and 200 μm , more preferably between about 1 μm and 100 μm , and often between about 1 μm and 20 μm . Accordingly, the microfluidic devices or systems prepared in accordance with the present invention typically include at least one microscale channel, usually at least two intersecting microscale channels, and often, three or more intersecting channels disposed within a single body structure. Channel intersections may exist in a number of formats, including cross or "four-way" intersections, "T" intersections, or any number of other structures whereby at least two channels are in fluid communication.

The body structure of the microfluidic devices described herein is typically fabricated from a number of discrete elements which, when assembled, form or define the integrated microscale channels and chambers of the microfluidic devices. Typically, the body structure comprises an aggregation of two or more separate layers which when appropriately mated or joined together, form the body structure of the microfluidic device of the invention, e.g., containing the channels and/or chambers described herein. Typically, the microfluidic devices described herein will comprise a top portion, a bottom portion, and an

interior portion, wherein the interior portion substantially defines the channels and chambers of the device.

Figure 1 illustrates a two-layer body structure for the microfluidic device 10. In preferred aspects, the bottom portion of the device 12 comprises a solid substrate that is substantially planar in structure, and which has at least one substantially flat upper surface 14. A variety of substrate materials may be employed as the bottom portion. Typically, because the devices are microfabricated, substrate materials will be selected based upon their compatibility with known microfabrication techniques, e.g., photolithography, wet chemical etching, laser ablation, air abrasion techniques, injection molding, embossing, and other techniques. The substrate materials are also generally selected for their compatibility with the full range of conditions to which the microfluidic devices may be exposed, including extremes of pH, temperature, salt concentration, and application of electric fields. Accordingly, in some preferred aspects, the substrate material may include materials normally associated with the semiconductor industry in which such microfabrication techniques are regularly employed, including, e.g., silica based substrates, such as glass, quartz, silicon or polysilicon, as well as other substrate materials, such as gallium arsenide and the like. In the case of semiconductive materials, it will often be desirable to provide an insulating coating or layer, e.g., silicon oxide, over the substrate material, and particularly in those applications where electric fields are to be applied to the device or its contents.

In additional preferred aspects, the substrate materials will comprise polymeric materials, e.g., plastics, such as polymethylmethacrylate (PMMA), polycarbonate, polytetrafluoroethylene (TEFLON™),

polyvinylchloride (PVC), polydimethylsiloxane (PDMS), polysulfone, and the like. Such polymeric substrates are readily manufactured using available microfabrication techniques, as described above, or from microfabricated masters, using well known molding techniques, such as injection molding, embossing or stamping, or by polymerizing the polymeric precursor material within the mold (See U.S. Patent No. 5,512,131). Such polymeric substrate materials are preferred for their ease of manufacture, low cost and disposability, as well as their general inertness to most extreme reaction conditions. Again, these polymeric materials may include treated surfaces, e.g., derivatized or coated surfaces, to enhance their utility in the microfluidic system, e.g., provide enhanced fluid direction, e.g., as described in U.S. Patent No. 5,489,402, issued November 23, 1999.

The channels and/or chambers of the microfluidic devices are typically fabricated into the upper surface of the bottom substrate or portion 12, as microscale grooves or indentations 16, using the above described microfabrication techniques. The top portion or substrate 18 also comprises a first planar surface 20, and a second surface 22 opposite the first planar surface 20. In the microfluidic devices prepared in accordance with the methods described herein, and as noted above, the top portion also includes a plurality of apertures, holes or ports 24 disposed therethrough, e.g., from the first planar surface 20 to the second surface 22 opposite the first planar surface.

The first planar surface 20 of the top substrate 18 is then mated, e.g., placed into contact with, and bonded to the planar surface 14 of the bottom substrate 12, covering and sealing the grooves

and/or indentations 16 in the surface of the bottom substrate, to form the channels and/or chambers (i.e., the interior portion) of the device at the interface of these two components. The holes 24 in the top portion of the device are oriented such that they are in communication with at least one of the channels and/or chambers formed in the interior portion of the device from the grooves or indentations in the bottom substrate. In the completed device, these holes function as reservoirs for facilitating fluid or material introduction into the channels or chambers of the interior portion of the device, as well as providing ports at which electrodes may be placed into contact with fluids within the device, allowing application of electric fields along the channels of the device to control and direct fluid transport within the device.

These devices may be used in a variety of applications, including, e.g., the performance of high throughput screening assays in drug discovery, immunoassays and genetic analysis for research and diagnostic applications, and the like. As such, the devices described herein, often include multiple sample introduction ports or reservoirs, for the parallel or serial introduction and analysis of multiple samples. Alternatively, these devices may be coupled to a sample introduction port, e.g., a pipettor, which serially introduces multiple samples into the device for analysis. Examples of such sample introduction systems are described in e.g., U.S. Patent Nos. 6,046,056 issued April 14, 2000; 5,880,071 issued March 9, 1999.

In preferred aspects, the electrically controlled microfluidic devices, methods and systems described herein, employ electrokinetic material

transport systems, and preferably, controlled electrokinetic material transport systems. As such, the microfluidic systems of the present invention typically include an electrical control system, for
5 controlling and/or monitoring the processes being carried out by the microfluidic device. In at least one aspect, the electrical control system includes a plurality of electrical leads, each of the leads being operably coupled to a power source, whereby the
10 electrical control system is capable of concomitantly delivering voltages to each of the plurality of electrical leads. Examples of preferred power sources are described in e.g., U.S. Patent No. 5,800,690 issued September 1, 1998.

15 The systems of the present invention also include an electrical interface array, permitting each of the electrical leads to be separately, and preferably, removably coupled to each of the plurality
20 of ports on the microfluidic device, whereupon each of the leads is placed in electrical communication with a fluid that is disposed in each of the ports.

As used herein, "electrokinetic material transport systems" include systems which transport and
25 direct materials within an interconnected channel and/or chamber containing structure, through the application of electrical fields to the materials, thereby causing material movement through and among the channel and/or chambers, i.e., cations will move
30 toward the negative electrode, while anions will move toward the positive electrode.

Such electrokinetic material transport and direction systems include those systems that rely upon the electrophoretic mobility of charged species within
35 the electric field applied to the structure. Such systems are more particularly referred to as electrophoretic material transport systems. Other electrokinetic material direction and transport

systems rely upon the electroosmotic flow of fluid and material within a channel or chamber structure which results from the application of an electric field across such structures. In brief, when a fluid is placed into a channel which has a surface bearing charged functional groups, e.g., hydroxyl groups in etched glass channels or glass microcapillaries, those groups can ionize. In the case of hydroxyl functional groups, this ionization, e.g., at neutral pH, results in the release of protons from the surface and into the fluid, creating a concentration of cations at near the fluid/surface interface, or a positively charged sheath surrounding the bulk fluid in the channel. Application of a voltage gradient across the length of the channel, will cause the positively charged sheath to move in the direction of the voltage drop, i.e., toward the negative electrode.

"Controlled electrokinetic material transport and direction," as used herein, refers to electrokinetic systems as described above, which employ active control of the voltages applied at multiple, i.e., more than two, electrodes. Rephrased, such controlled electrokinetic systems concomitantly regulate voltage gradients applied across at least two intersecting channels. Controlled electrokinetic material transport is described in Published PCT Application No. WO 96/04547, to Ramsey.

In particular, the preferred microfluidic devices and systems described herein, include a body structure which includes at least two intersecting channels or fluid conduits, e.g., interconnected, enclosed chambers, which channels include at least three unintersected termini. The intersection of two channels refers to a point at which two or more channels are in fluid communication with each other, and generally encompasses "T" intersections, cross intersections, "wagon wheel"

intersections of multiple channels, or any other channel geometry where two or more channels are in such fluid communication. An unintersected terminus of a channel is a point at which a channel terminates not as a result of that channel's intersection with another channel, e.g., a "T" intersection. In preferred aspects, the devices will include at least two intersecting channels having at least three unintersected termini. In a basic cross channel structure, where a single horizontal channel is intersected and crossed by a single vertical channel, controlled electrokinetic material transport operates to controllably direct material flow through the intersection, by providing constraining flows from the other channels at the intersection. For example, assuming one was desirous of transporting a first material through the horizontal channel, e.g., from left to right, across the intersection with the vertical channel. Simple electrokinetic material flow of this material across the intersection could be accomplished by applying a voltage gradient across the length of the horizontal channel, i.e., applying a first voltage to the left terminus of this channel, and a second, lower voltage to the right terminus of this channel, while applying no voltage to the top and bottom termini of the vertical channel. However, this type of material flow through the intersection results in a substantial amount of diffusion at the intersection, resulting from the natural diffusive properties of the material being transported in the medium used, at the intersection.

In controlled electrokinetic material transport, the material being transported across the intersection is constrained by low level current from the side channels, e.g., the top and bottom channels. This is accomplished by applying a slight voltage gradient along the path of material flow, e.g., from the top or bottom termini of the vertical channel,

toward the right terminus. The result is a "pinching" of the material flow at the intersection, which prevents the diffusion of the material into the vertical channel. The pinched volume of material at the intersection may then be injected into the vertical channel by applying a voltage gradient across the length of the vertical channel, i.e., from the top terminus to the bottom terminus. In order to avoid any bleeding over of material from the horizontal channel during this injection, a low level of current is directed back into the side channels, resulting in a "pull back" of the material from the intersection.

In addition to pinched injection schemes, controlled electrokinetic material transport is readily utilized to create virtual valves which include no mechanical or moving parts. Specifically, with reference to the cross intersection described above, flow of material from one channel segment to another, e.g., the left arm to the right arm of the horizontal channel, can be efficiently regulated, stopped and reinitiated, by a controlled flow from the vertical channel, e.g., from the bottom arm to the top arm of the vertical channel. Specifically, in the 'off' mode, the material is transported from the left arm, through the intersection and into the top arm by applying a voltage gradient between the left and top termini. A constraining flow is directed from the bottom arm to the top arm by applying a similar voltage gradient along this path (between the bottom terminus and the top terminus). Metered amounts of material are then dispensed from the left arm into the right arm of the horizontal channel by switching the applied voltage gradient from left to top, to left to right. The amount of time and the voltage gradient applied dictates the amount of material that will be dispensed into the right arm of the horizontal channel, in this manner.

Although described for the purposes of illustration with respect to a four-way or cross intersection, these controlled electrokinetic material transport systems can be readily adapted for more complex interconnected channel networks, e.g., arrays of interconnected parallel channels. Similarly, although electrodes are generally placed into electrical contact with the termini of the various channels in the system, electrodes may also be placed in electrical contact with intermediate points in the channels, depending upon the nature of the operation being performed.

In the simplest embodiment, the electrical interface array which provides at least one component of the overall electrical interface or connection between the electrical controller and the plurality of ports on the microfluidic device, comprises a series of electrode pins, each of which is appropriately positioned for insertion into each of the plurality of ports on the device. In at least one embodiment, such electrodes are fixedly mounted on the surface of a planar cover element. The cover element is then placed over the surface of the device which includes the ports disposed therein, e.g., the top substrate, whereupon the electrodes are inserted into the ports. In preferred aspects, the cover element is provided as the cover of a hinged chamber, well, cavity or recessed region into which the microfluidic device is inserted. The cover element, or a housing in which the cover element is mounted, is preferably connected to the edge of the chamber via a hinge along one edge of the cover element, such that the cover element may simply be rotated on the hinge into the closed position, whereupon the electrodes are placed into the ports. This "clam-shell" structure permits simple and rapid interfacing of microfluidic devices with electrical control systems. The clam-shell also helps to secure the microfluidic device against additional

elements of the overall system, e.g., heating blocks, heat sinks, optical systems, etc., to ensure the most efficient interfacing of the device with these components. Additionally, the cover element, or the entire clam-shell portion of the system is readily interchangeable with different covers having different electrode pin configurations, permitting adaptation to devices which have alternate port configurations. Examples of such interchangeable systems are described in commonly assigned U.S. Patent No. 5,955,028 issued September 21, 1999.

Figure 2A provides an illustration of cover element 202, which has a plurality of electrode pins 204 disposed thereon. The pins are oriented on the surface of the cover element such that they will communicate with the ports 24 of the microfluidic device 10, when the cover element is placed over the top surface of the device. Each of electrode pins 204 is electrically coupled to one of the electrical leads from the electrical controller (not shown). Typically, this connection is via electrical circuitry from each separate pin, extending through the rear portion of the cover element 202 to connect to each separate electrical lead on the controller, however, in some cases, multiple electrodes may be coupled to the same electrical lead, e.g., where two electrodes are intended to provide the same voltage level at two different ports of the device. Alternatively, the circuitry from each electrode pin is connected to one port of a multi-port connector, e.g., at the rear portion of the cover, to which is coupled a complementary multi-port connector from the controller, which connector includes electrical connections to the various electrical leads from the controller. These multi-port connectors are generally commercially available, and are readily connected to

the various electrical leads on the controllers and the electrodes present in the cover. As shown, the cover element 202 is connected to a separate structural element or base 206, which includes a nesting well, cavity or recessed region 208 disposed therein. The cover 202 is connected to the base 206 via hinge 210. The microfluidic device 10 is inserted into the nesting well 208. Arrows 212 illustrate the direction of rotation of the cover element 202. After inserting a microfluidic device into the nesting well 208, the hinged cover element is rotated down on the hinge 210 until the electrode pins 204 are in contact with fluid that is contained within the ports 24 of the device, and in fluid communication with the channels and/or chambers of the device. The use of this type of interface permits the user to simply insert the microfluidic device 10 into the nesting well and close the cover, whereupon the device is interfaced with the electrical controller. It will be readily appreciated that microfluidic devices of varied sizes, shapes and configurations may be inserted into a given interface (e.g., base and cover) through the incorporation of the device into a uniformly sized adapter plate. The use of such adapter plates for interfacing differently sized or differently configured microfluidic devices with a particular controller element is described in greater detail in U.S. Patent Application No. 5,955,028 issued September 21, 1999.

As shown in Figure 2A, the electrode pins 24 are oriented in a grid format, e.g., in columns and rows. Although a single column or row of electrodes may be provided in accordance with the present invention, e.g., as described in greater detail herein, typically, such gridded arrays of electrodes will be at least two rows and at least two columns of electrodes, i.e., 2X2. In preferred aspects, the

gridded array of electrodes will comprise at least two columns of electrodes and at least three rows of electrodes. In many embodiments, the gridded array may include at least four columns and at least four rows of electrodes (e.g., a 4X4 gridded array). Although it is not required, in order to promote uniformity, the spacing between the rows and columns of the electrode array is preferably equal, e.g., each probe is equidistant from the adjacent probes in the same column and row. By arranging the electrode pins as a gridded array of electrodes, one is able to standardize the electrode format, and provide microfluidic systems having a matching, e.g., complementary, port format. In particular, because one can create a wide variety of channel geometries for performing a given fluidic operation within a microfluidic device, the operations performed within the interior portion of a microfluidic device, e.g., within the channels and chambers, often have little influence on the orientation of the ports on the surface of the device, and consequently, the electrodes for interfacing with those ports. As such, orientation of the electrodes, and complementary ports in a gridded format permits the utilization of a standard electrode/device interface, regardless of the operation for which the device will be used.

Where fluids are contained within relatively small areas, e.g., in the reservoirs of the devices of the present invention, such systems can often produce a certain amount of water vapor, which vapor is particularly localized at or near the ports of the microfluidic device. This vapor generation is increased where temperatures of the fluids are elevated, e.g., when applying substantial electrical currents through these fluids. Condensation of these vapors as liquid, e.g., on the surface of the microfluidic device and/or the surface of the cover element, can result in an electrical connection being

made between two or more neighboring or adjacent electrode pins, across the surface of the device or the cover element, e.g., a shorting out of the electrodes. As such, it is generally desirable to either prevent this condensation, or, in the event of such condensation, prevent the formation of the electrical connection between adjacent electrodes across the external surfaces of the device. As such, in preferred aspects, the microfluidic systems are provided with a barrier between adjacent electrodes when they are inserted into the ports of the device. Preferably, the barrier forms a liquid tight seal between adjacent ports and/or electrodes. These barriers may be fabricated or placed onto the surface of the cover element, or alternatively, on the surface of the microfluidic device, e.g., as a gasket.

One example of such a liquid tight barrier structure is shown in Figure 2B, which illustrates an alternative embodiment of the cover element 202. As shown, the barrier is a part of the cover element 202. In particular, raised regions 220 are provided on the surface of the cover element 202, between the various electrode pins 204 that are disposed thereon. The raised regions are of such height as to permit insertion of each of the electrode pins into its respective port of a microfluidic device and contact the fluid therein, while the raised regions securely contact the surface of the microfluidic device, providing a fluid tight seal between the ports/electrodes of the system. The raised regions 220 are optionally provided as a separate part 222, e.g., as shown, which is mated, bonded or otherwise attached to the surface of the cover element 202, or are fabricated into the surface of the cover element 202. In preferred aspects, these raised regions, or the cover element as a whole, are either fabricated from or coated with a hydrophobic material, e.g., a polymer such as polytetrafluoroethylene (TEFLON™), to

provide additional fluid sealing capabilities when these regions are contacted with the top surface of the microfluidic device. In alternative aspects, the barrier may be provided in whole or in part, on the surface of the microfluidic device which includes the ports. For example, a hydrophobic coating is optionally provided on the top surface of the device, or alternatively, gasket-like structures are provided upon the surface of the device, e.g., fabricated upon or mated with that surface. When the cover element 202 is placed over the surface of the device to interface the electrical controller with the ports of the device, these gasket-like structures provide a fluid tight barrier between the neighboring or adjacent ports/electrodes. Again, the height of these structures is such that the electrodes are in electrical contact with the fluids disposed in the ports, when the cover element is placed over the device. Typically, such electrodes will range in length of from about 1 mm to about 10, from their tips to the point at which they are attached to the cover element. The electrodes may be fixedly mounted in the cover, or alternatively, may be spring mounted, to maintain the electrode in optimal communication with the port, or fluids therein, and to prevent damage to the electrodes or the microfluidic devices upon closing the cover. Although the barrier is generally described as including raised regions, it will be readily apparent that the cover element may be provided with recessed regions 224 surrounding each of the various electrode pins. Recessed regions 224 are generally provided extending from around the electrodes to the near edge of the cover. In addition to presenting a potential fluid barrier between adjacent electrodes, the recessed region provides an air passage or vent from each port to the surrounding environment, permitting escape of fluid vapors, gases and the like, which can adversely effect the operation

of the system, either through condensation, pressure effects or otherwise.

In optional embodiments, the electrical interface array comprises a plurality of electrical contact pads that are electrically coupled to each of the various ports of the microfluidic device. These electrical contact pads are generally disposed along at least one edge of the microfluidic device. These electrical contact pads typically comprise a small electrically conductive surface which is contacted by the electrical leads of the electrical controller. In such cases, the electrical lead will generally include a mechanism for maintaining the electrical lead in contact with the contact pads, when the leads are placed in contact with the electrical interface array, e.g., a pressure contact or wiping contact. Such mechanisms are typically included within commercially available electrical connectors, which are readily adaptable for use with the electrical leads of the controller. Each of the electrical leads is then positioned, e.g., within the coupler, to contact a separate one of the electrical contact pads on the device.

An example of a microfluidic device incorporating this type of electrical interface array is illustrated in Figure 3. This figure illustrates the device from a top view (3A), end view (3B) and perspective view (3C). As shown, the device 10 is fabricated in a layered format from at least two separate planar elements, a top substrate 22 and a bottom substrate 12 (Fig. 3B). The bottom substrate 12 has an extended portion 302, which extends beyond the top substrate along at least one edge. A plurality of electrical contact pads 304 are provided upon this extended portion 302. Typically, these contact pads 304 are fabricated from an appropriately conductive material and are deposited upon the exposed surface of the extended portion of the lower substrate

using well known deposition methods, e.g., chemical vapor deposition, sputtering, thermal or E beam evaporation, electroplating, and the like. The individual traces and pads are then defined with a photolithographic lift-off technique. Each of the electrical contact pads is electrically coupled, via wires or circuitry 306, to a separate one of the various ports 24 that are disposed through the top substrate of the device 22. Typically, this circuitry 306 is deposited upon the upper surface 14 of the bottom substrate 12 prior to the bonding of the bottom substrate 12 to the top substrate 22. In this situation, it will be appreciated that the circuitry 306 is sufficiently thin as to permit complete bonding of the two substrate layers, i.e., to prevent leakage of fluidic elements within the interior portion of the device. Sufficiently thin circuitry is generally less than about 1500 Å thick, preferably between about 500 and 1400 Å thick, and is generally deposited upon the upper surface of the bottom substrate using any of the above described methods.

In preferred aspects, the circuitry 306 is comprised of sufficiently durable material to prevent its degradation, particularly at the metal/fluid interface, e.g., the point at which the electrode contacts the fluid contained within the ports or channels of the microfluidic device, under the elevated voltages and currents applied across that circuitry, as well as the elevated temperatures that may be involved in the process of bonding substrates together. In particular, the thin circuitry utilized in the devices described herein will often be subjected to relatively high currents and voltages which are typically passed through to fluid containing channels. Further, in the case of devices fabricated from thermally bonded substrate layers, this fabrication can include bonding temperatures in the range of 500 to 1400°C, and typically from about 500

to about 800°C. In particular, some metals that are commonly utilized in the patterning of electrical circuitry on solid substrates, such as pure chrome and pure titanium, are subject to substantial oxidation under conditions of thermal bonding, e.g., using the temperatures described above.

By way of example, electrodes comprising a gold conductive layer on a chrome adhesion layer, patterned on a glass substrate, showed substantial degradation following the thermal bonding process (extensive discoloration, indicative of substantial oxidation), and were unable to withstand application of normal operating currents. Similarly, electrodes comprised of a gold conductive layer on a titanium adhesion layer were capable of withstanding the thermal bonding process, but peeled and disappeared under the normal operating current densities of approximately 50 mA/cm².

Accordingly, in preferred aspects, the devices of the present invention include circuitry that has a thickness less than 1500 Å, and preferably, between about 800 and about 1400 Å, but which circuitry is capable of withstanding normal current ranges applied through the circuitry without substantially degrading, i.e., greater than 1 μA, preferably in the range of 10 to about 1000 μA. In the case of the devices of the present invention, this circuitry is thus capable of withstanding current densities greater than 10 μA/cm², preferably greater than 0.1 mA/cm², more preferably greater than 0.5 mA/cm², and still more preferably, greater than 1 mA/cm². In some applications, the circuitry is capable of withstanding greater than 5 mA/cm², more preferably, greater than 10 mA/cm², often greater than 50 mA/cm², and in certain instances, greater than 100 mA/cm², without being substantially degraded at the metal/fluid interface. Further, the circuitry described herein is also typically capable of

withstanding bonding temperatures greater than 500°C, and preferably between about 500 and 1400°C, without being substantially degraded during the thermal bonding process.

5 An electrode that is not "substantially degraded" as that phrase is used herein, refers to an electrode that has lost less than 20% of either its thickness (as measured by profilometry), or its current carrying capacity (as measured by change in
10 impedance). Preferably, such electrodes will lose less than 10% and more preferably, less than 5% of their thickness or current carrying capacity.

 Generally, the circuitry will include a conductive layer that includes one of the metals
15 selected from tungsten, palladium, ruthenium, iridium, osmium or rhodium. In preferred aspects, the conductive layer comprises tungsten as at least one element of the conductive layer (also referred to herein as an electrode, electrical circuitry or
20 electrical conduit). The tungsten containing portion of the electrical circuitry may be provided as the adhesion layer or as the entire electrical layer. By "tungsten containing" is meant a metal layer that may be entirely tungsten or a tungsten alloy or amalgam.
25 In preferred aspects, the tungsten containing layer is titanium/tungsten alloy. This alloy is typically primarily, e.g., greater than 50% tungsten, preferably, greater than 70% tungsten, and more preferably, greater than 80% tungsten.

30 In particularly preferred aspects, the electrical circuitry includes a titanium/tungsten adhesion layer with a platinum overlay (Pt/TiW), where the adhesion layer is in the range of approximately 50 to 600 Å thick, preferably about from about 300 to 500
35 Å thick, while the platinum layer is in the range of approximately 400 to 1200 Å thick, preferably from about 700 to about 1100 Å thick. Electrical circuitry comprised of this material, and which falls within the

preferred thickness ranges, has demonstrated an ability to withstand both the high temperatures of the bonding process as well as the high current densities applied in the microfluidic systems described herein.

5 More conventional electrical circuitry compositions, e.g., gold/chrome (Au/Cr), platinum/chrome (Pt/Cr), and the like, showed substantial degradation under these conditions, and particularly at the fluid/metal interface.

10 Figures 3B and 3C illustrate the interfacing of the microfluidic device shown in Figures 3A, with the electrical leads from the electrical controller. As shown, the microfluidic device 10 may be readily inserted into an appropriately sized slot 310 on a
15 multi-port coupler 312. Within the slot 310, is a series of electrical contacts 314 or leads, which are electrically coupled to the electrical controller (not shown). Each contact is positioned within the slot 310 to separately contact each of the electrical
20 contact pads 304 on the device 10. Each of these contacts is typically a flexible contact, e.g., flexibly mounted within the slot 310, whereby when the extended region 302 of the device 10 is inserted into the slot 310, each of the electrical contacts in the
25 slot is pressed against its corresponding electrical contact pad 304 on the device 10.

 In a related embodiment, the electrical interface array is optionally disposed along more than one edge of the microfluidic device. This is
30 accomplished in a similar manner as provided in Figure 3, except that the bottom substrate extends beyond more than one edge of the top substrate, providing extended regions along several or all edges of the microfluidic device. In one preferred aspect, the
35 extended portion of the bottom substrate is provided by the presence of recessed regions of the top substrate, exposing portions of the surface of the bottom substrate upon which electrical contact pads

are disposed. An example of a device incorporating this alternative structure for an electrical interface array is illustrated in Figures 4A-4D.

As shown, in Figure 4A, the device 10 is again fabricated with a layered construction, including a top substrate 22 and a bottom substrate 12, where the top substrate includes a plurality of ports 24 disposed therethrough, providing access to the channels/chambers in the interior portion of the device (not shown). A plurality of recessed regions 402 are provided along the edges of the top substrate 22. When the top substrate is mated with the bottom substrate, these recessed regions in the top substrate leave portions or regions 404 of the surface of the bottom substrate exposed. The electrical contact pads, as previously described, are deposited in these exposed regions, providing access points for connection to the electrical leads from the electrical controller. Again, these contact pads are electrically coupled to the various ports 24 of the device 10, e.g., via appropriate circuitry.

In the case of the device shown in Figure 4A, interfacing the device with the electrical controller is optionally carried out by any one of the methods described above. For example, a cover element, e.g., a clam-shell as shown in Figure 2, is used to interface the device with the controller. In this instance, the electrode pins, or optionally, corresponding, flexible electrical contacts, mounted on the cover element, are positioned to contact and are preferably contacted with or pressed against the electrical contact pads in the recessed regions of the top substrate of the device, e.g., through the inclusion of a pressure or wiping contact.

In an alternate aspect, the device shown in Figure 4A is inserted into a complementary coupler assembly which contains the electrical leads from the controller, or appropriate interface circuitry for

interfacing each electrical contact pad on the device with one of the leads. Each lead or portion of interfacing circuitry, is appropriately positioned within the coupler assembly to contact a separate electrical contact pad on one edge of the device. This alternate construction is illustrated in Figures 4B, 4C and 4D. In particular, Figure 4B shows the microfluidic device 10 and the coupler assembly 410. The coupler assembly includes a main body portion 412 which has an opening 414 disposed through it, which opening is adapted to receive the device 10. As shown, this opening includes protruding portions 416 along the inner edge of the opening, which extend into the opening and are positioned and shaped to mate with the recessed regions 402 on the device 10. Electrical circuitry, in the form of an electrical interface pin 418, is mounted on the bottom surface of each of these protruding portions of the adapter whereby the electrical interface pin will contact the electrical contact pad disposed on the exposed surface 404 within the recessed regions 402 of the device. Each electrical interface pin extends out from the coupler assembly so as to provide a connection point at which the pin may be coupled to an appropriate electrical lead from the controller. As shown in Figures 4B-4D, each pin 418 is angled, e.g., at a 90° angle, so that it contacts the contact pad in a recessed region on the device in a horizontal orientation, but extends out the bottom surface of the coupler assembly 410 in a vertical orientation, past the device 10. Further, each electrical interface pin is also recessed, or disposed within a slot, on the bottom surface of the protruding portion and interior edge of the opening in the coupler assembly's body structure. This permits a snug fit between the device and the coupler assembly.

The overall device/coupler assembly is particularly advantageous in providing a microfluidic system that is readily interfaced with an electrical

controller, simply by plugging the overall device/coupler into an appropriately configured electrical connection. In some aspects, the orientation of the electrical interface pins extending from the bottom of the device/coupler assembly, is the same as that orientation used in conventional integrated circuits, e.g., dual in-line orientation, thereby providing ready access to commercial sources for many of the interfacing components.

Figures 4C and 4D illustrate perspective and end views of the microfluidic device/coupler assembly in its assembled form. Figure 4D illustrates the mating of the device 10 with the coupler assembly 410, from an end view, showing the contact between the electrical interface pins 418 and the contact pads on the exposed surface 404 in the recessed regions of the device. Although shown as a removable part, the coupler assembly is optionally provided attached to the microfluidic device, e.g., via an adhesive, or acoustically welded.

In addition to providing simple interfacing between the microfluidic device and the electrical controller, the electrical interface array shown in the device of Figures 4A-4D also provides advantages in terms of ease of manufacturing. In particular, preferred methods of fabricating microfluidic devices, as described above, are readily adapted to the fabrication of devices employing these structures. In particular, as noted previously, the microfluidic devices of the present invention are preferably manufactured from larger substrate wafers or plates which are bonded together to form an aggregate plate or wafer containing a number of devices as a single unit, produced in a single process. These devices are then separated from the larger wafer or plate into individual devices.

The recessed regions in the top substrate are provided by providing extra rows and columns of

holes or ports in the top substrate wafer, between those holes or ports that are required to provide fluid access to the channels in the interior portion of the device. The individual devices are then
5 separated from the larger aggregate wafer or plate, by scribing or sawing through the middle of the holes or ports that are within these extra rows and columns. This is illustrated in Figure 5, which shows a substrate wafer or plate 500 from which several
10 individual devices 10 are produced. The top substrate wafer or plate 500 includes the various ports 24 required for fluid access to the channels and chambers of each individual device. However, The substrate wafer or plate also includes additional rows and
15 columns of ports 502, which serve to form the recessed regions of the top substrate in each device. Cut or scribe lines 506 illustrate the pattern of separating the individual devices from the larger wafer or plate, whereby each device will be provided with these
20 recessed regions along each edge of each device.

In addition to providing substantially more user friendly systems, the improved interfaces described herein also provide a number of additional advantages. In one example, the devices incorporating
25 these improved interfaces are fabricated as multi-device units, e.g., a single body structure incorporating two discrete and separate channel networks or microfluidic systems therein. In such cases, each separate system, e.g., each channel
30 network, includes a separate interface array as described above. These interface arrays may be coupled with corresponding control elements for simultaneous or tandem operation, or optionally, can be rotated within a single control unit for successive
35 operation.

In this latter mode, the microfluidic device includes a first interface component on the body structure capable of delivering energy to the first

channel network, and a second interface component on the body structure capable of delivering energy to the second channel network. Although the instant invention is generally described in terms of transmission of electrical energy to each of the channel networks from a controller unit, interface arrays for transmission of other types of energy are also contemplated. For example, interface arrays for transmission of heat energy, light or other electromagnetic radiation, pressure, and the like, are optionally incorporated into the systems described herein.

As noted above, the overall system described herein, also includes a controller unit which includes an energy source such as an electrical power supply as described above, although, again, light sources, heat sources, pressure sources and the like are also contemplated. The controller includes a first surface adapted for mounting the body structure of the microfluidic device thereon. Typically, this surface includes appropriate structural elements, e.g., alignment pins, holes, grooves, slots, tabs, walls or the like, which are complementary and correspond to like structures on the body of the device, such that the body structure of the device mounted on the surface is maintained in one of at least two fixed orientations, and preferably, at least four different orientations. The surface region of the controller also includes at least a third interface component which is operably coupled to the energy source, e.g., via electrical circuitry, optical trains, pressure conduits and the like. This third interface component is typically oriented on the controller surface such that it is in communication with the first interface component on the body structure when the device is mounted in one orientation, and in communication with the second interface component on the body structure of the device when the device is mounted on the

controller in the second orientation. When the interface component on the controller is in communication with the interface components on the body structure, it is capable of transmitting the energy from the energy source to those interface components and their respective channel networks.

In the case of the use of electrical energy, e.g., in controlling and directing electrokinetic flow within each of the channel networks of the device, the interface components present on the device's body structure and on the controller typically incorporate any of the previously described electrical interface structures. For example, the interface component on the controller typically includes multi-port electrical couplers, electrode pin arrays, and the like, while the interface component present on the device is the complementary structure, e.g., the electrical contact pads, or port/reservoir arrays described above.

In the case of the use of light energy, the interface array on the body structure of the device typically comprises an optically transparent window which is capable of transmitting the light energy to or from one or more of the channels in each separate channel network. The interface component on the controller typically includes appropriate optics for directing the light energy from the light source in the controller unit to the window.

Although described in terms of the transmission of energy from the controller to the channel networks of the device via the interface component on the controller, through the interface component on the body of the device, the present invention also envisions the flow of energy in the opposite direction, i.e., the transmission of energy from the respective channel networks through the interface components on the body structure, and the receipt of this energy by the interface component on

the controller. In this mode of operation, the controller typically includes energy detection systems for detecting energy, e.g., signals, originating from the respective channel networks. Examples of such energy or signals include optical signals, such as fluorescent, chemiluminescent or colorimetric signals, thermal signals, or electrical signals, such as in the determination of resistances or voltages within the channel networks, or other potentiometric or amperometric signals relating to the chemical environment within the channels.

An illustration of an embodiment of the interchanging interfacing systems described herein is shown in Figure 6. As shown, the body structure 602 of the device includes within its interior portion, four separate channel networks 604a, 604b, 604c and 604d. Each of the four separate channel networks includes a first interface component in the form of a plurality of ports 606 in fluid communication with that channel network. Each channel network also includes an optical detection window 608 disposed over one of the channels in each of the channel networks. The controller includes a mounting surface 610 which includes retaining walls 612 for maintaining the body structure in one of four fixed orientations when it is inserted into the controller. The mounting surface includes a first interface component in the form of optical detector 614, which is oriented on the mounting surface 610 such that it is disposed adjacent to the optical detection window on one of channel networks 604a-d, e.g., 604a when the device is inserted into the controller in the orientation shown. As shown the controller also includes a cover element 616 coupled to the mounting surface via hinge 618. The cover element 616 includes an additional interface component in the form of an array of electrode pins 620, which electrode pins are electrically coupled to an electrical controller, e.g., as described above.

The electrode array is oriented on the cover such that when the cover element is closed over the body structure inserted into the controller, the electrode pins are inserted into the ports of one of the channel networks, e.g., into channel network 604a in the orientation shown.

Inserting the body structure into the controller in a first orientation presents the interface components of one channel network to the interface components of the controller. Rotation of the body structure 602 in the horizontal plane, e.g., 90 degrees, then presents the interface components of a second channel network 604b to the interface components of the controller. This type of rotatable structure permits one to load fluids, samples and the like into a number of separate device/channel networks, which are then subject to successive analysis etc., simply by rotating the body structure and reinserting it into the controller. This greatly reduces the amount of time required to perform a large number of particular analyses or other fluidic manipulations on samples and the like.

Referring now to Figure 7, it will often be advantageous to provide electrical coupling between the interface system and the microfluidic channels without directly contacting sample fluids with an electrode of the interface system. For example, when a first microfluidic device is to be removed from its clamshell interface structure and replaced with an alternate microfluidic device with different fluids, the use of electrodes which extend first into the fluids of the first device, and then into the fluids of the second device poses a risk of cross-contamination. Additionally, as the fluid samples may include corrosive agents, there is some risk of electrode degradation over time.

To avoid cross-contamination and degradation of the interface electrical components when using

corrosive fluids, the microfluidic devices of the present invention may include thin, flat electrodes or pads 702 which are electrically coupled to the fluids within the channel system, but which extend outside the channel system so that at least a portion of the flat electrode surface is not in fluid continuity with the intersecting channels. Electrical coupling between the clamshell interface structure and the thin, flat electrode may optionally be provided by simply having an electrode pin of the clamshell cover extend down so as to be in direct contact with the flat electrode of the microfluidic device when the cover is in the closed position, as shown in Figure 7.

Unfortunately, direct contact electrical coupling between a thin, flat electrode on the microfluidic device and a pin extending from the clamshell cover can have significant disadvantages. Specifically, the pin electrodes may be substantially rigid structures. If such a rigid pin electrode extends too far from the cover, the pin will advance beyond the initial point of contact. As the distal tip of pin electrode 704 advances against a thin, film electrode 702, large stresses can be generated. These stress can cause failure of the electrical contact due to fracture of the flat electrode 702, breakage of the pin electrode 704, or piercing of a surface coating, electrode film, bonding layer, or the underlying microfluidic device body structure. However, if rigid pin 704 does not advance far enough to provide contact between the pin and the flat electrode 702, the electrical coupling between these structures will be unreliable. Hence, it would be beneficial to provide alternative coupling arrangements which offered greater reliability, without excessively tight tolerances, complex contact biasing mechanisms, or the like.

As illustrated in Fig. 8, in order to provide reliable and compliant electrical coupling of

a thin film, flat electrode 802 with a rigid pin electrode 804, a microfluidic device body 806 includes a fluidically isolated port 808 containing an electrolyte solution 810. When pin electrode 804 extends into electrolyte 810, the electrolyte can provide complaint electrical coupling between the thin, flat electrode 802 and pin without damage to either. This provides a highly efficient electrical coupling with relatively loose tolerances, as pin electrode 804 need not even be in contact with the thin (and sometime mechanically delicate) flat electrode 802.

Pin 804 will often comprise a conductive metal, typically comprising, e.g., platinum, gold, titanium, or the like, and ideally comprising platinum. Pin electrode 804 will generally be rigidly affixed to the rotatable cover of a clam shell interface system as described above, but may alternatively be mechanically coupled to the microfluidic device support base by a wide variety of detachable, sliding, pivoting, and/or linear joints so as to maintain alignment between the pin electrode and port 808. Pin 804 will generally have a length in the range from about 2mm to about 10mm inches, and a diameter from about 50 μ m to about 2mm. Other dimensions, outside these ranges, may also be useful in certain situations.

Thin, flat electrode 802 may be fabricated from an appropriately conductive material, and will often be disposed at least in part between the layers of a multi-layer microfluidic device body structure. For example, thin, flat electrodes may be provided by depositing an appropriately conductive material upon an upper surface of a lower substrate layer prior to bonding the upper and lower substrate layers together. A variety of well known deposition methods might be employed, including chemical vapor deposition, sputtering, thermal or E beam evaporation,

electroplating, and the like. The electrode and electrode coupling circuitry may again be defined with a photographic lift-off technique. As was also described above, port 808 may be formed by bonding the upper and lower substrate layers together after forming an opening through the upper layer. The upper and lower layers are aligned during bonding so as to electrically expose flat electrode 802 within the opening of port 808.

Thin flat electrode 802 may comprise any of the electrode and/or circuitry materials described above. Ideally, flat electrode 802 will comprise structures similar to the circuitry described above with reference to Figs. 3A-C.

Electrolyte 810 is fluidically isolated from the sample fluids in the channel system by the structure of the microfluidic device. Hence, there is little or no danger of cross-contamination when pin electrode 804 is removed from port 808, the microfluidic device is removed and replaced by an alternative device having a different fluid sample to be tested, and pin 804 is advanced into the coupling port of that other device. Hence, electrolyte 810 may comprise a wide variety of alternative fluids.

Electrolyte 810 will preferably be non-corrosive so as to allow long term use of pin electrode 804 with minimal degradation. Suitable electrolyte fluids may include saline, conductive buffer, KCl, NaCl, or the like.

An exemplary microfluidic device including fluidically isolated electrical coupling ports is illustrated schematically in Figure 9A, and in more detail in Figure 9B. Microfluidic device 900 again has a substrate body 902 defining a plurality of intersecting microfluidic channels 904. Ports 24 are often disposed at unintersected termini of the channel system, and fluids within the channel system be

transported electrokinetically by applying voltages to the fluids within these ports, as described above.

To provide electrical coupling with the fluid in ports 24, sealed ports 808 are in electrical continuity with ports 24, but are not in fluid continuity with the channel system. To provide this electrically continuity, thin, flat electrodes 802 extend between isolated ports 808 and terminal ports 804. Hence, the electrode material defines an inter-port conductor 906. To efficiently electrically couple the fluids within the ports, flat electrodes 802 will typically have a surface area of between about $100\mu\text{m}^2$ and 20mm^2 within each of ports 808 and ports 24. Inter-port conductor 906 will typically have a width which is substantially greater than its thickness, the width typically allowing the conductor to withstand the normal current densities described above. As no fluid coupling is provided between isolated ports 808 and 24, inter-port conductors 906 are generally the only electrical coupling provided between the fluids contained therein.

25

Although the present invention has been described in some detail by way of illustration and example for purposes of clarity and understanding, it will be apparent that certain changes and modifications may be practiced within the scope of the appended claims.

30

WHAT IS CLAIMED IS:

1. A microfluidic device, comprising:
a body structure comprising an upper layer, a bottom layer, and a plurality of
5 intersecting microscale channels;
one or more first ports within the upper layer and in fluidic
communication with the plurality of intersecting microscale channels;
one or more second ports comprising a thin, flat electrode
surface within the upper layer, wherein the
10 one or more second ports are blocked from fluidic communication with the
one or more first ports; and
an electrical interface component in electrical communication
with the one or more first ports and the one or more second ports.
- 15 2. A microfluidic device, comprising:
a body structure comprising an upper layer, a bottom layer, and
a plurality of intersecting microscale channels;
one or more ports comprising a thin, flat electrode surface within
the upper layer, wherein the one or more ports are positioned such that the
20 ports are not in fluid communication with the plurality of intersecting
microscale channels; and
an electrical interface component in electrical communication
with both the plurality of intersecting microscale channels and the one or more
ports.
- 25 3. The microfluidic device of claim 2, wherein the plurality of
intersecting microscale channels further comprises one or more alternate
ports in fluid communication with an unintersected terminus of the plurality of
intersecting microscale channels.

4. The microfluidic device of claim 3, wherein the electrical interface component is in electrical communication with the one or more alternate ports.

5 5. The microfluidic device of claims 1 or 2, wherein the one or more second ports of claim 1 or the one or more ports of claim 2 further comprises an electrolytic solution.

6. The microfluidic device of claim 5, wherein the electrolytic
10 solution comprises a saline solution.

7. The microfluidic device of claims 1 or 2, wherein the electrical interface component couples a first fluid in the one or more first ports of claim 1 or the one or more alternate ports of claim 2 with a second fluid in the one
15 or more second ports of claim 1 or the one or more ports of claim 2.

8. The microfluidic device of claim 7, wherein the first fluid comprises a sample fluid, and the second fluid comprises an electrolyte.

9. The microfluidic device of claims 1 or 2, wherein the electrical interface component is disposed between the upper layer and the bottom layer of the body structure.

10. The microfluidic device of claim 9, wherein the electrical
25 interface component comprises an electrically conductive film.

11. The microfluidic device of claims 1 or 2, wherein the electrical interface component comprises one or more conductors overlaid over the upper layer of the body structure.

30

12. The microfluidic device of claims 1 or 2, wherein the electrical

interface component comprises a plurality of electrical interface components, wherein each member of the plurality of electrical interface components extends from an associated unintersected terminus of a microchannel to one of the one or more second ports of claim 1 or to one of the one or more ports
5 of claim 2.

13. A microfluidic system comprising:
the microfluidic device of any one of claims 1 through 12;
an electrical controller to communicate with an energy
10 source; and
an interface structure comprising a support base, a rotatable cover, and at least one electrode, and wherein the at least one electrode is rigidly affixed to the rotatable cover, and extends from the interface structure to the microfluidic device when the microfluidic device is placed in the support
15 base and the rotatable cover is closed.

14. The microfluidic system of claim 13, wherein the electrical controller comprises a plurality of electrical leads and an additional interface component that operably couples the electrical controller to the energy
20 source.

15. The microfluidic system of claim 13, wherein the electrical controller further includes the energy source.

25 16. The microfluidic system of claim 14, wherein the additional interface component comprises one or more of electrical circuitry, optical trains, and pressure conduits.

30 17. The microfluidic system of claim 13, wherein the at least one electrode is positioned on the rotatable cover to contact the second ports or the ports of claims 1 through 12, when the microfluidic device is placed in the support base and the rotatable cover is closed.

18. The microfluidic system of claim 13, wherein the at least one electrode is positioned on the rotatable cover to contact both the first ports and second ports, or both the ports and alternate ports, of claims 1 through 5 13, when the microfluidic device is placed in the support base and the rotatable cover is closed.

19. An electrically controlled microfluidic system, comprising:
a microfluidic device comprising a body structure, a plurality of microscale
10 channels disposed in the body structure, a plurality of ports disposed in the body structure, and a plurality of electrical contact pads disposed along at least one edge of the body structure, wherein each of the plurality of ports is in fluid communication with at least one of the plurality of microscale channels, and wherein each of the plurality of electrical contact pads is
15 electrically coupled to at least one of the plurality of ports; and
an electrical control device comprising a base adapted for receiving the microfluidic device; an electrical interface array comprising a cover having at least a first surface and a plurality of electrical contacts mounted thereon, the electrical contacts being oriented to contact the plurality of electrical contact
20 pads; and a plurality of electrical leads, each of the leads being electrically coupled to the plurality of electrical contacts and operably coupled to a power source, wherein an edge of the cover is attached to the base, whereby the cover is capable of being rotatably closed over the microfluidic device mounted on the base, to contact the plurality of electrical contacts on the
25 cover with the plurality of electrical contact pads on the body structure.

20. The microfluidic system of claim 19, wherein the edge of the cover is attached to the base by a hinge.

30 21. The microfluidic system of claim 19, wherein the electrical control system concomitantly delivers a voltage to each of the plurality of electrical leads.

22. The microfluidic system of claim 19, wherein the body structure comprises a top substrate and a bottom substrate, wherein a portion of the bottom substrate extends beyond the top substrate along at least one edge of the body structure, wherein the plurality of microscale channels are disposed between the top layer and the bottom substrate, wherein the plurality of ports are disposed through the top substrate, and wherein the electrical contact pads are disposed in the portion of the bottom substrate that extends beyond the top substrate.

10

23. The microfluidic system of claim 22, wherein the top substrate comprises a plurality of recessed regions along at least one edge of the body structure, exposing the extended portion of the bottom substrate; and wherein the electrical contact pads are disposed within the plurality of recessed regions.

15

24. The microfluidic system of claim 23, wherein the top substrate comprises the plurality of recessed regions along two edges of the body structure, and wherein the plurality of electrical contact pads are disposed in the plurality of recessed regions.

20

25. The microfluidic system of claim 23, wherein the electrical interface array further comprises a main body portion, an opening dispersed in the main body portion, and protruding portions positioned and shaped to mate with the plurality of recessed regions on the top substrate of the microfluidic device.

25

26. The microfluidic system of claim 19, wherein each of the plurality of electrical contact pads is electrically coupled to at least one of the plurality of ports by electrical circuitry disposed between the top substrate and the bottom substrate.

30

27. The microfluidic system of claim 26, wherein the electrical circuitry comprises circuitry capable of withstanding current densities greater than $10 \mu\text{A}/\text{cm}^2$.

5 28. The microfluidic system of claim 26, wherein the electrical circuitry has a thickness between about 800 and about 1400 Ångströms.

29. The microfluidic system of claim 26, wherein the electrical circuitry comprises a conductive layer selected from the group consisting of
10 tungsten, palladium, ruthenium, iridium, osmium and rhodium.

30. The microfluidic system of claim 26, wherein the electrical circuitry comprises a titanium/tungsten alloy.

15 31. The microfluidic system of claim 30, wherein the electrical circuitry comprises an adhesion layer that comprises the titanium/tungsten alloy, and an overlay that comprises platinum.

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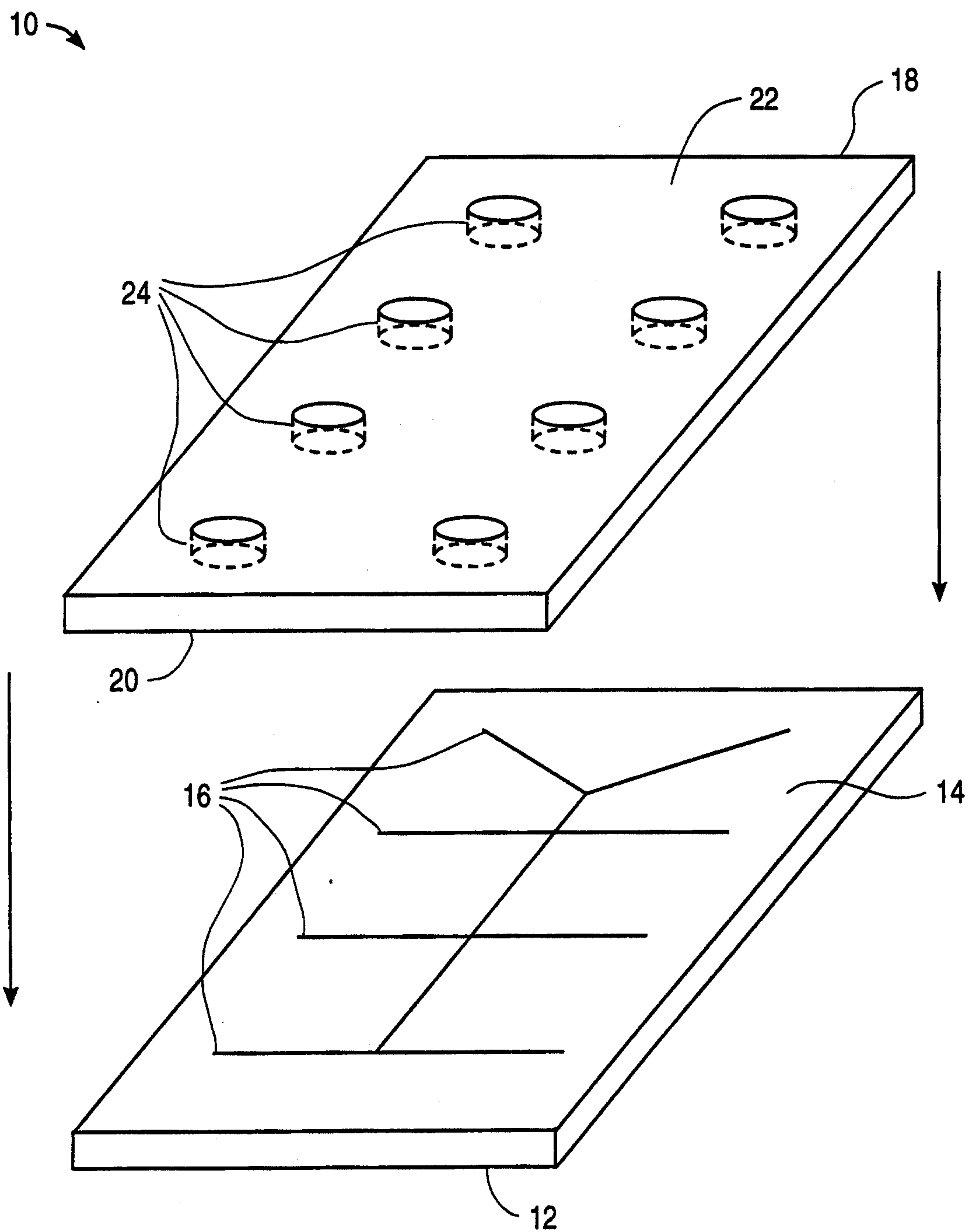


FIG. 1

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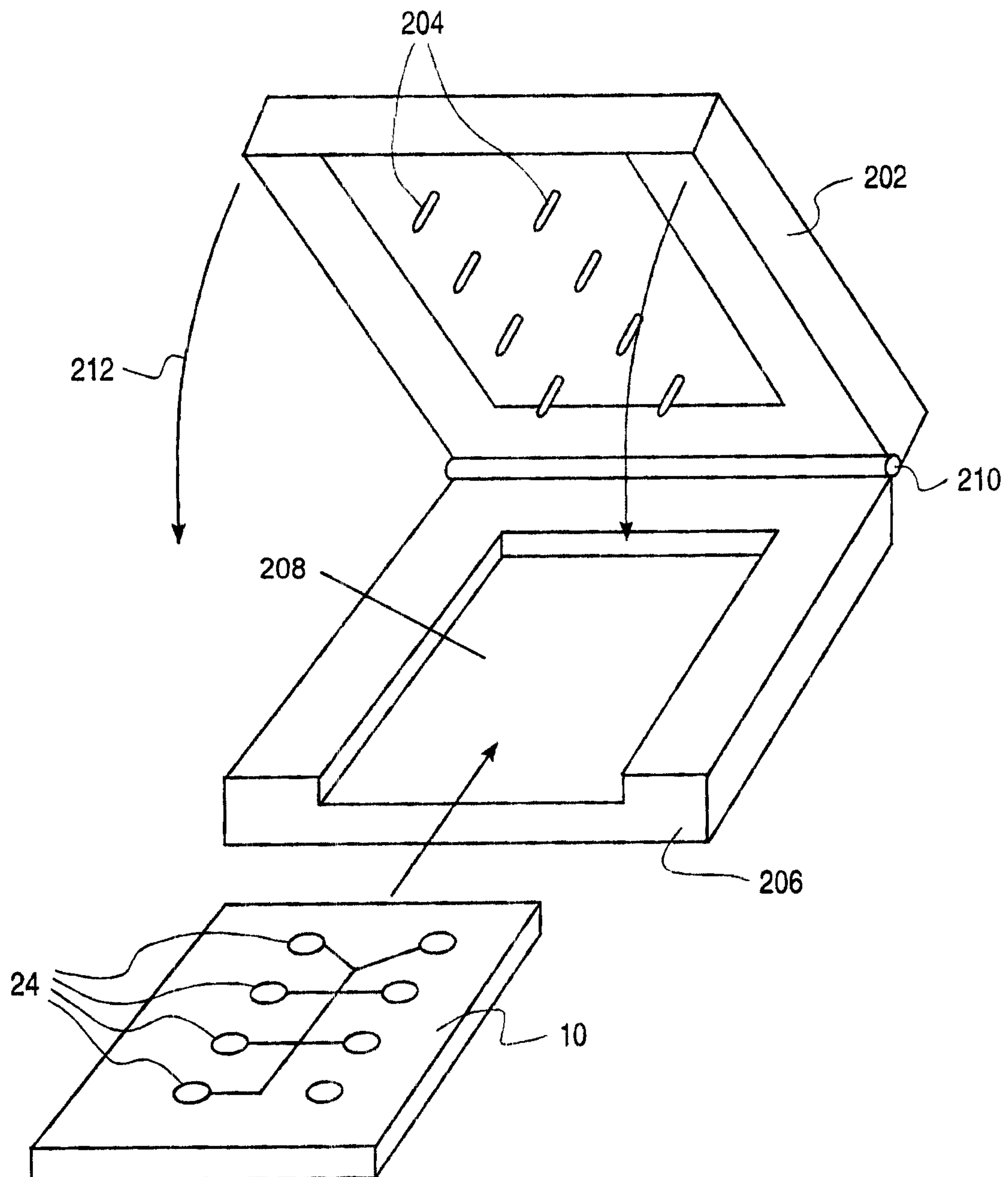


FIG. 2A

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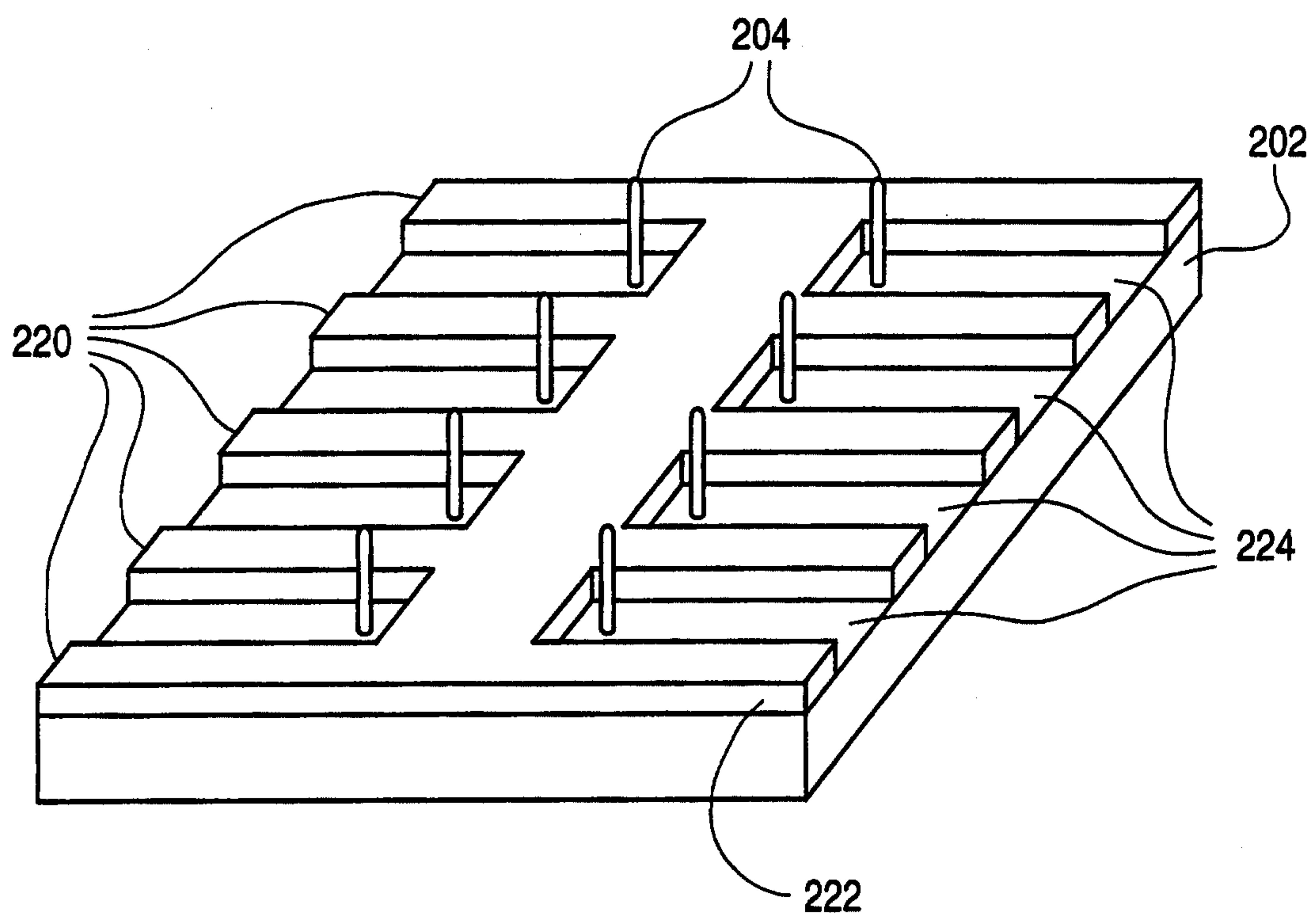
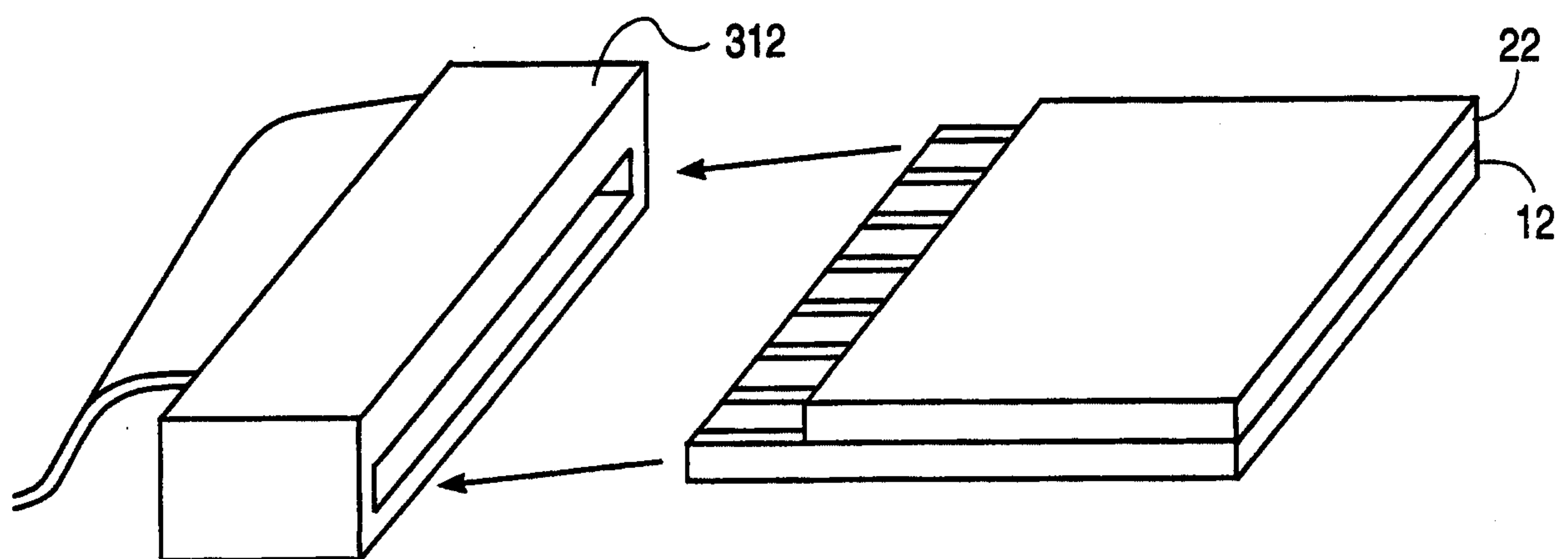
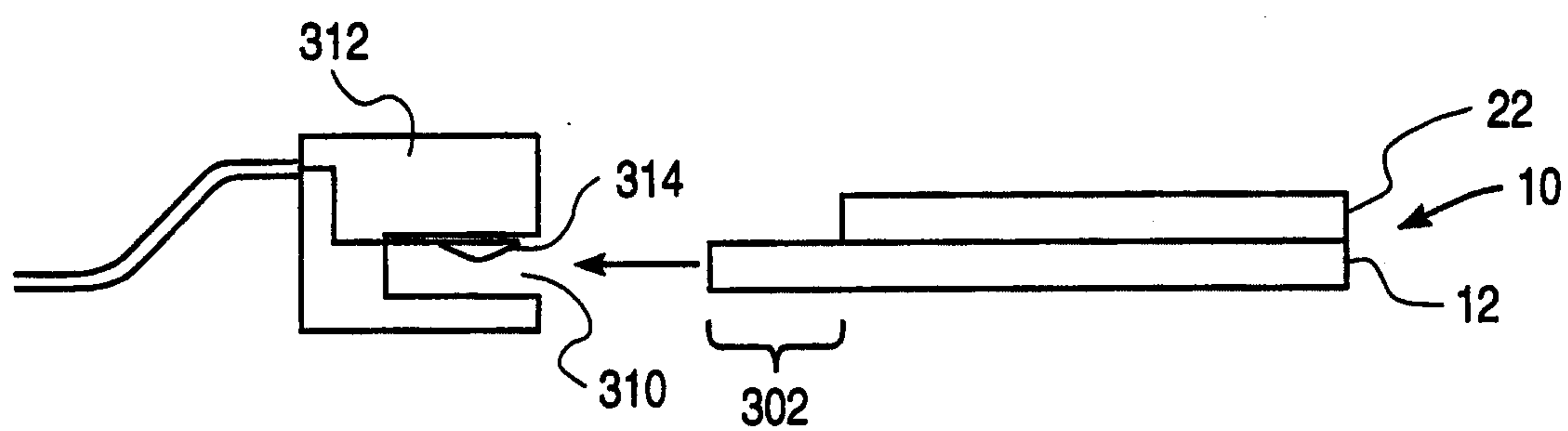
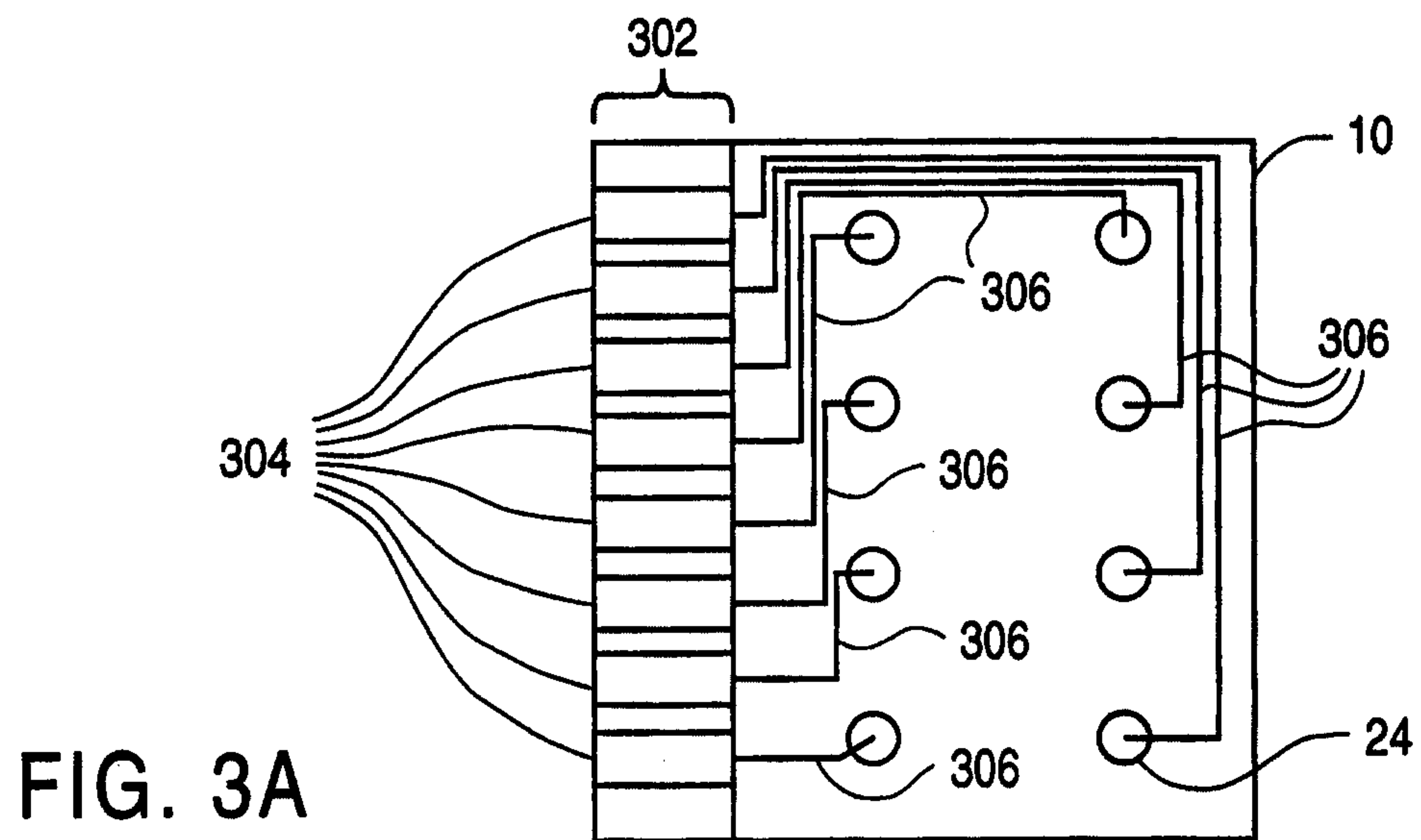


FIG. 2B

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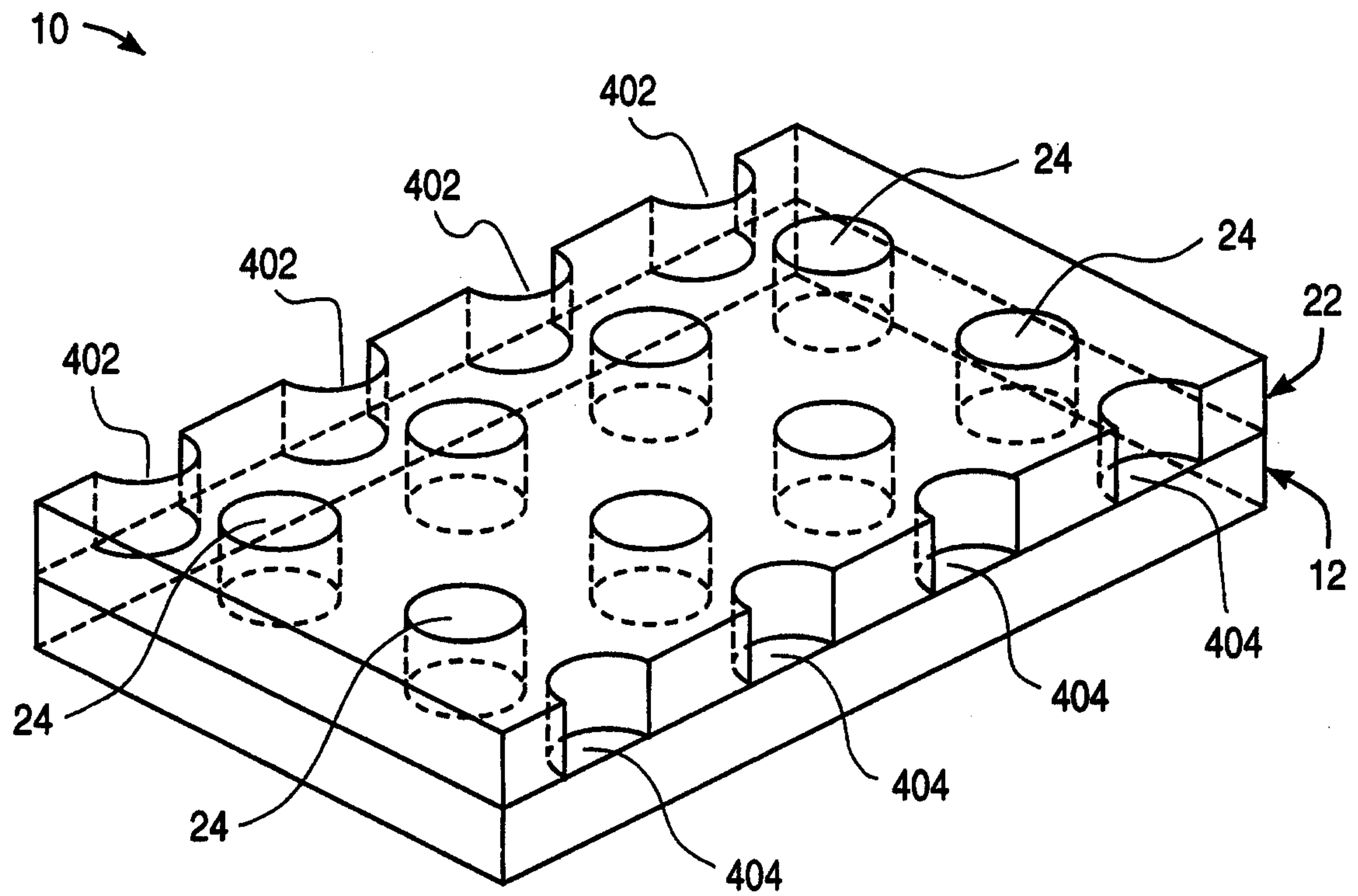


FIG. 4A

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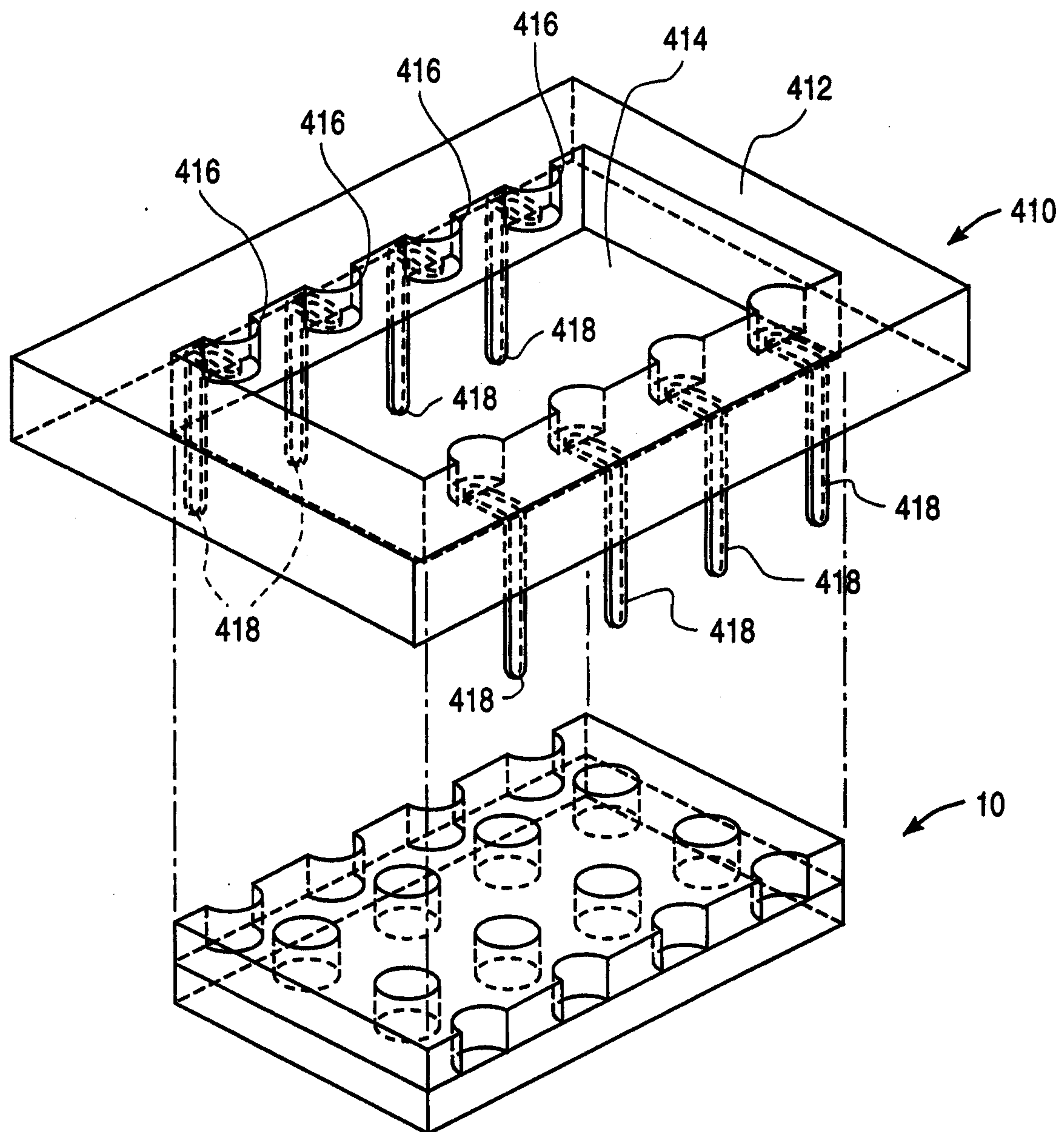


FIG. 4B

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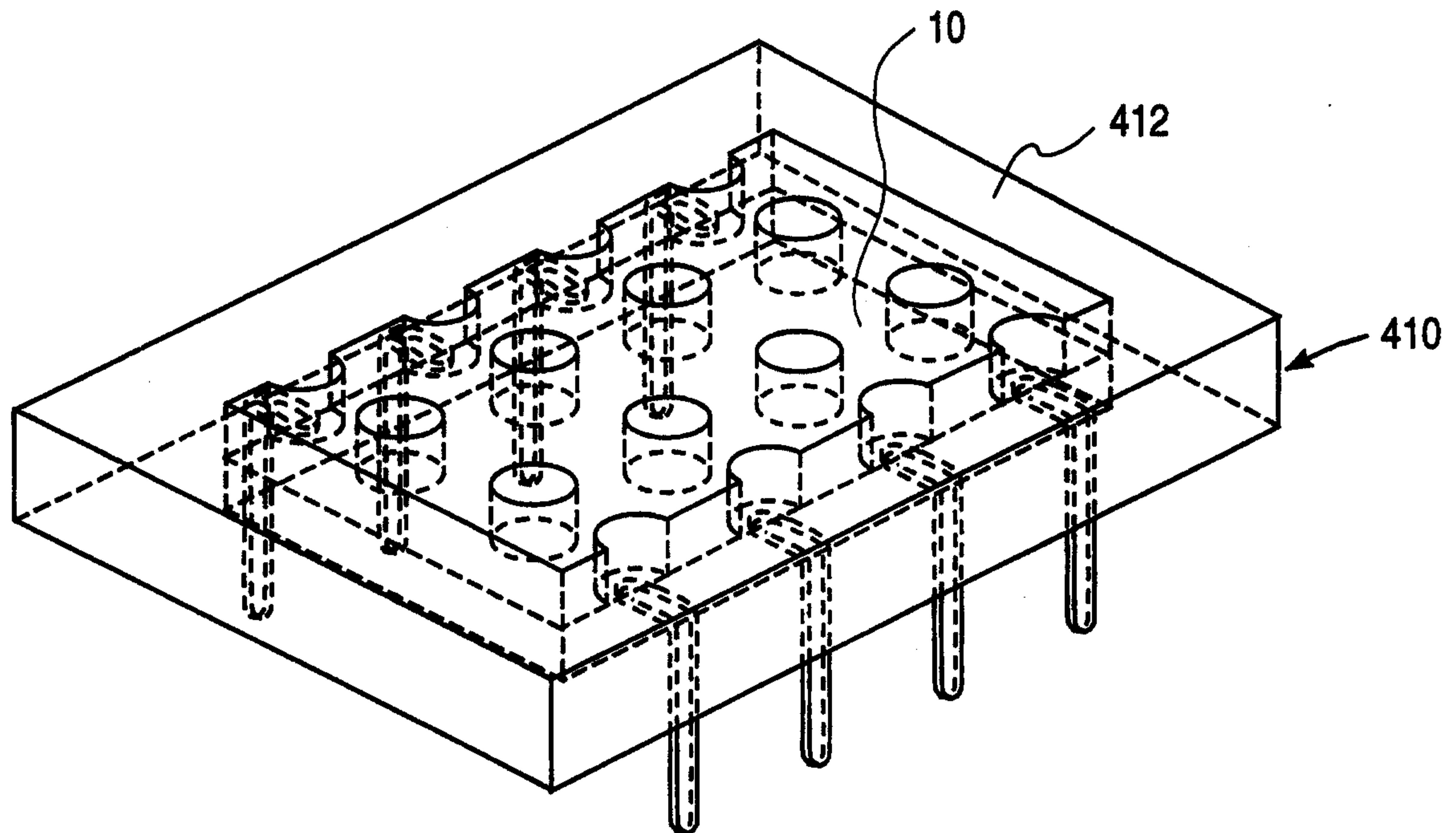


FIG. 4C

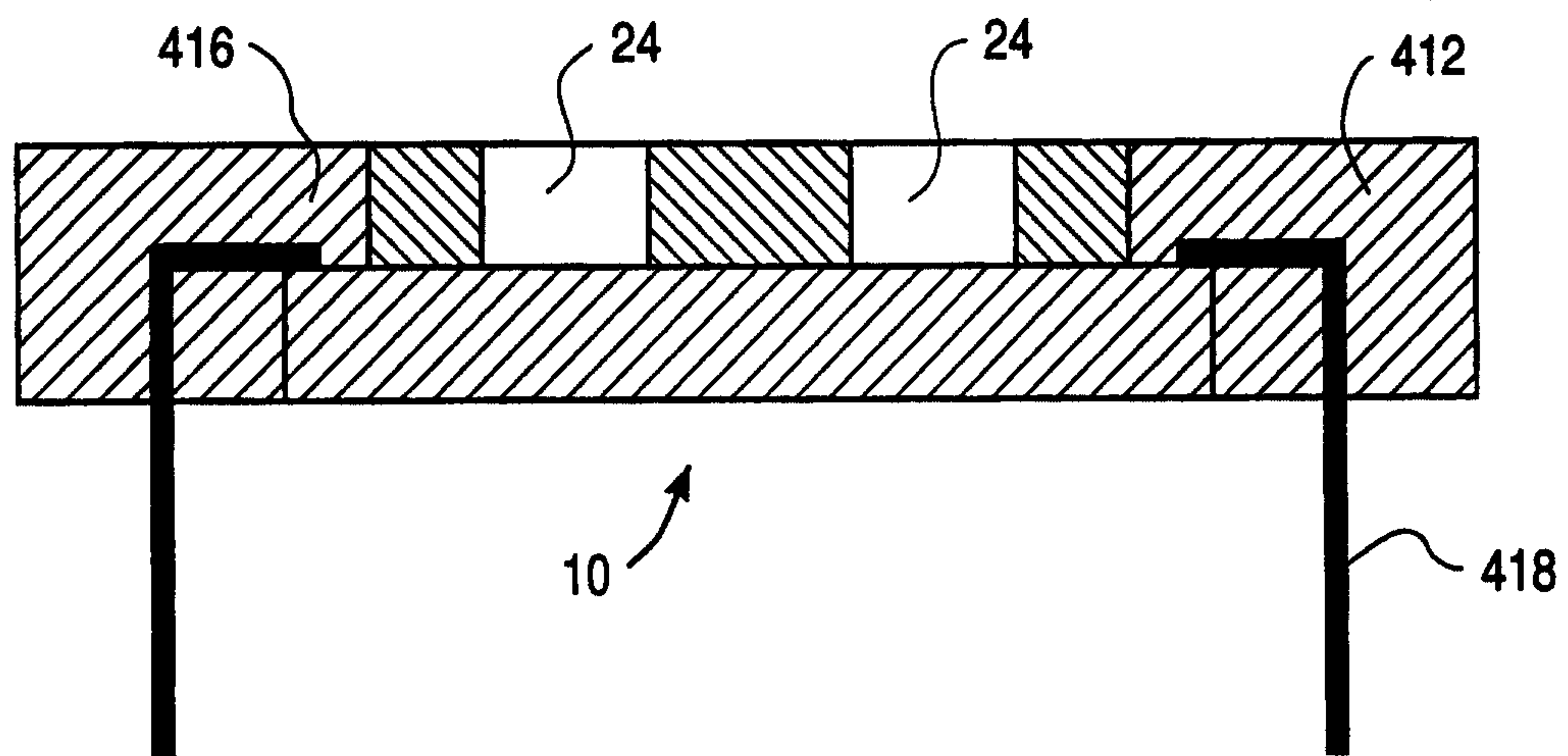


FIG. 4D

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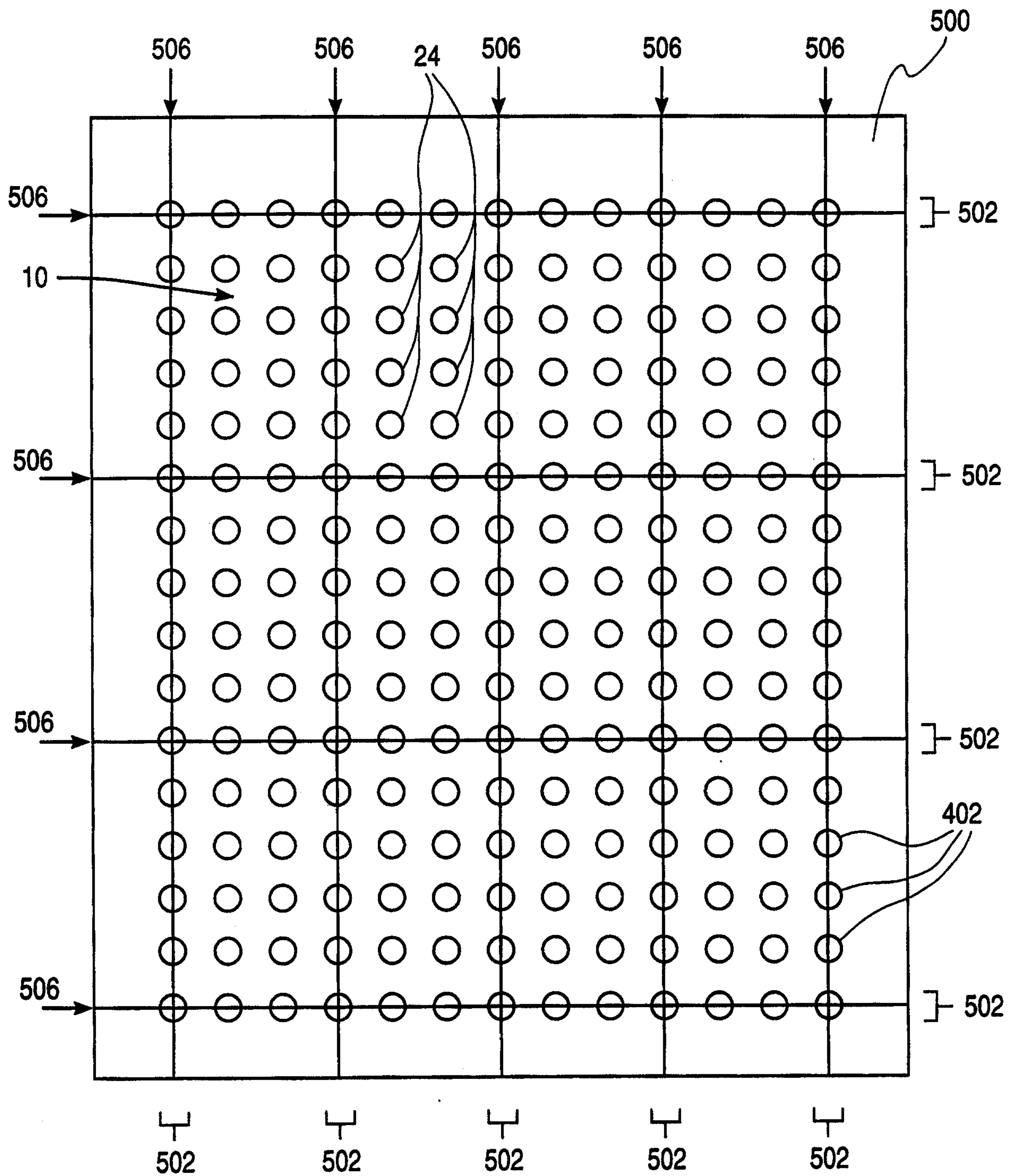


FIG. 5

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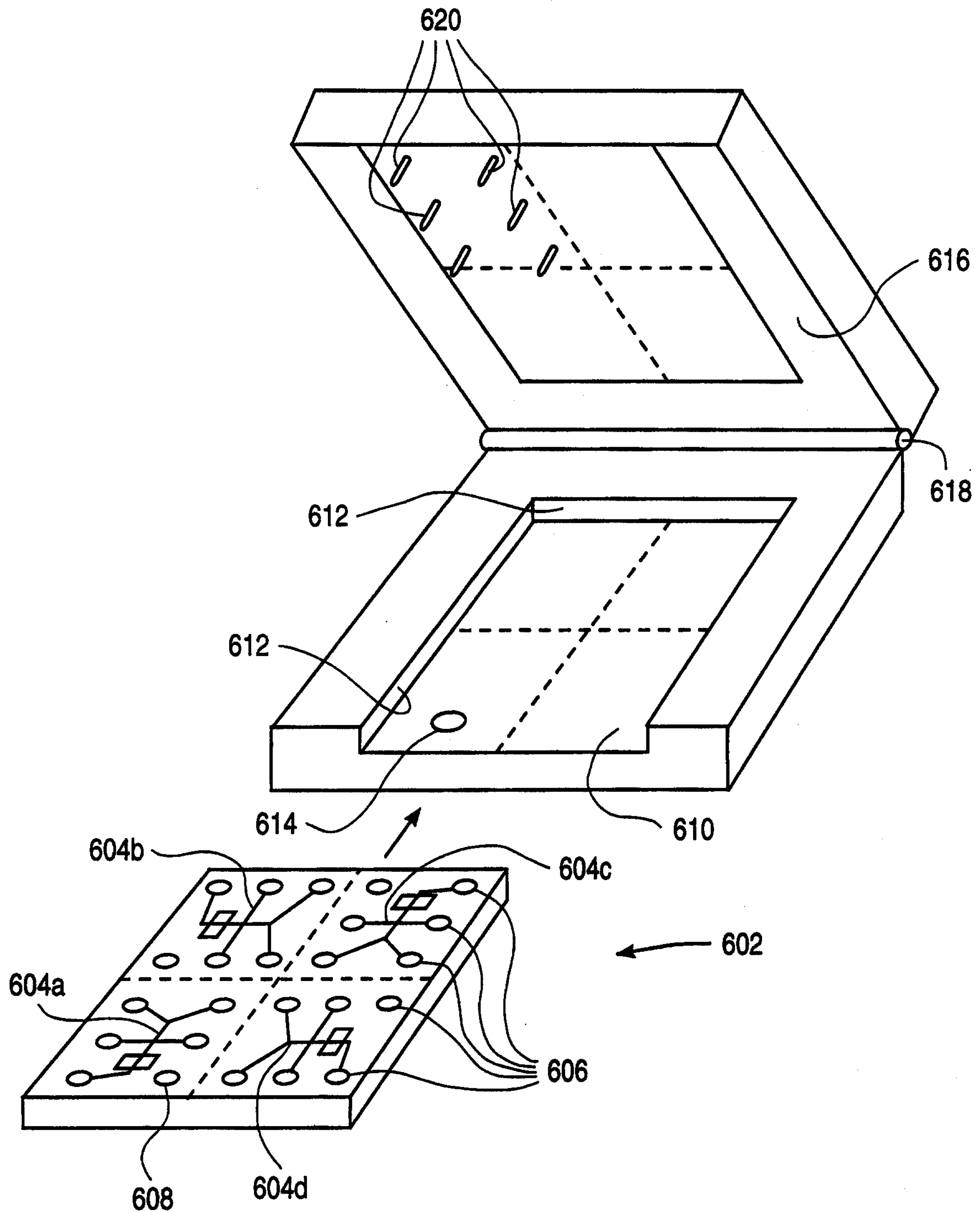


FIG. 6

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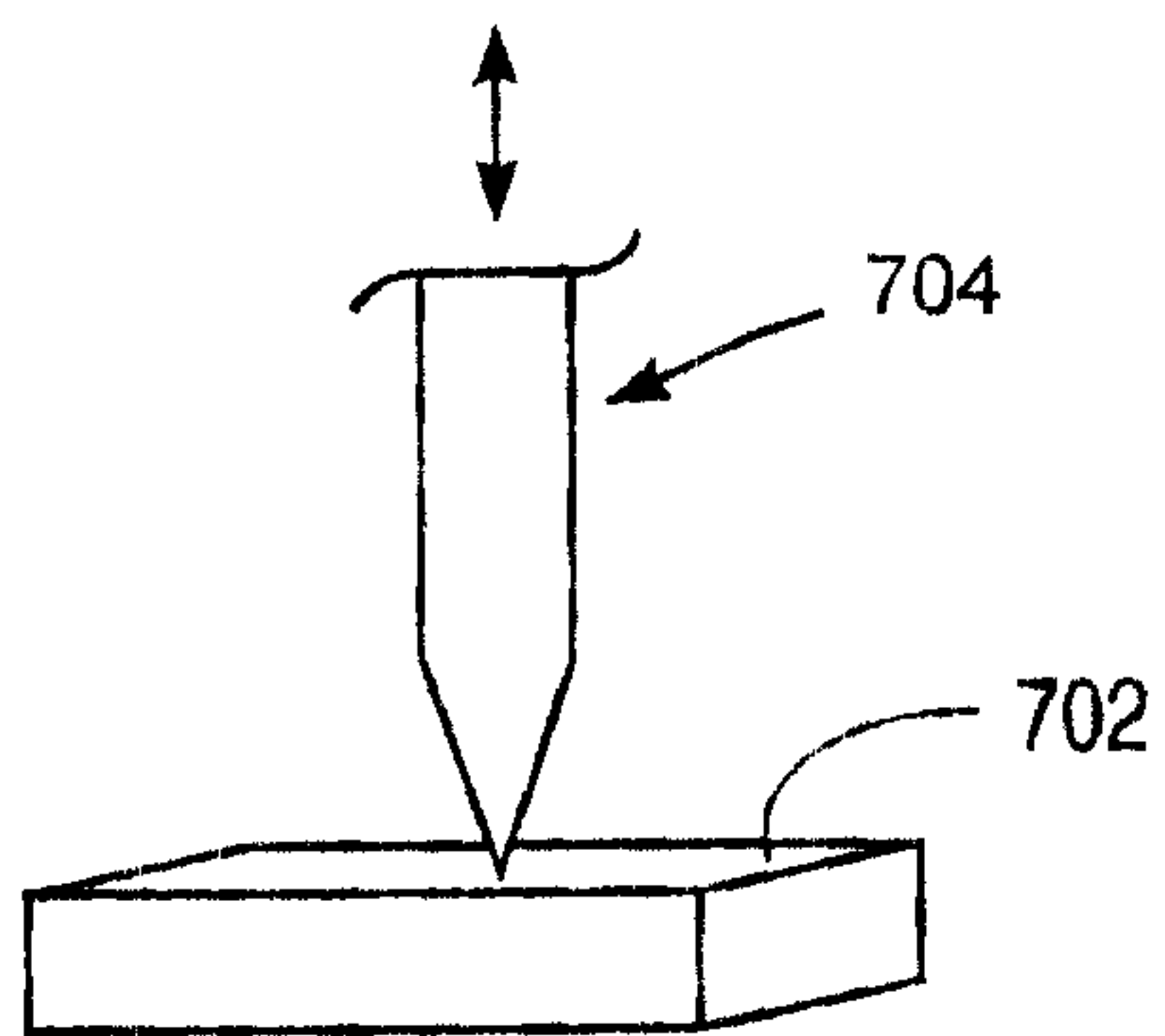


FIG. 7

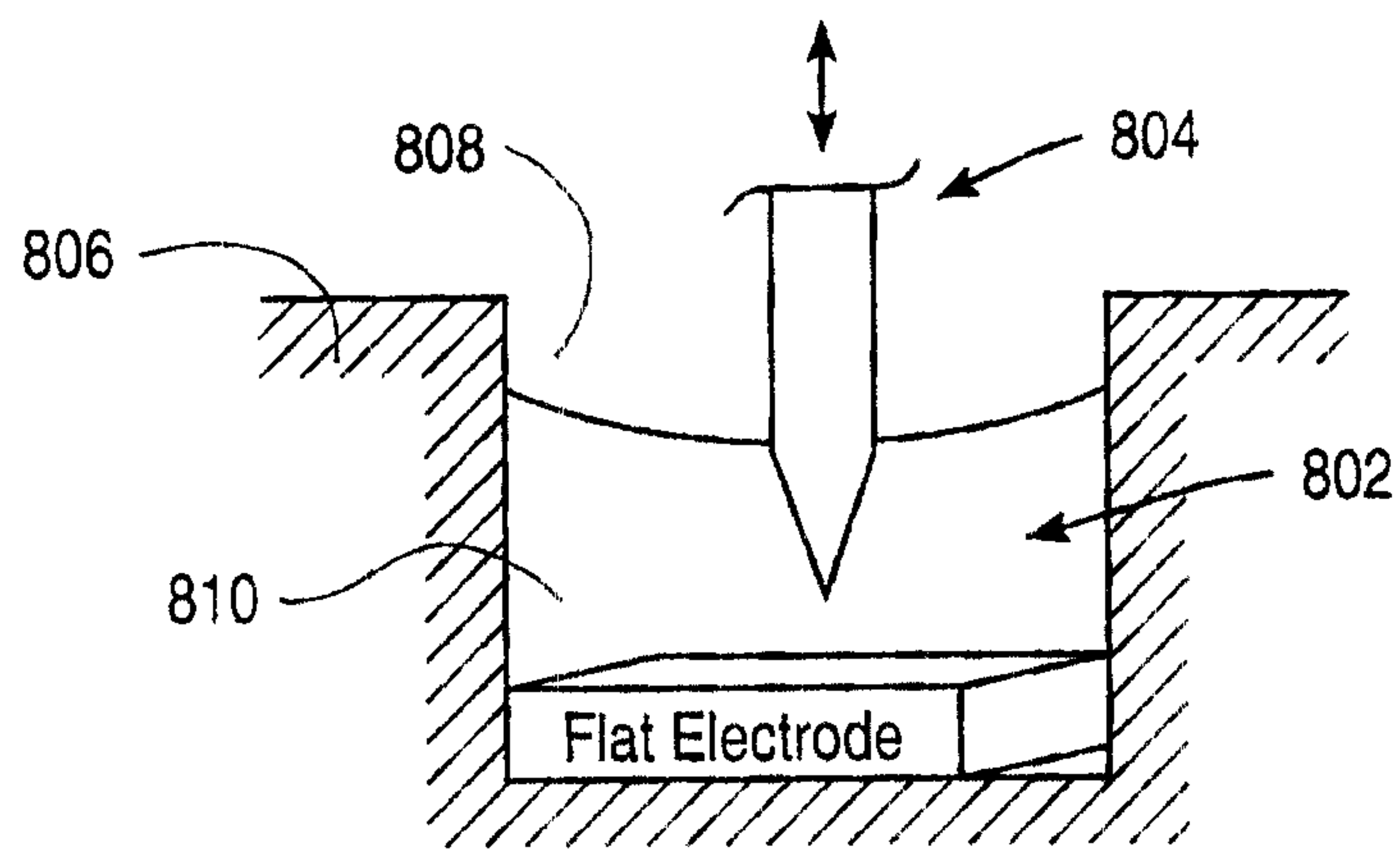


FIG. 8

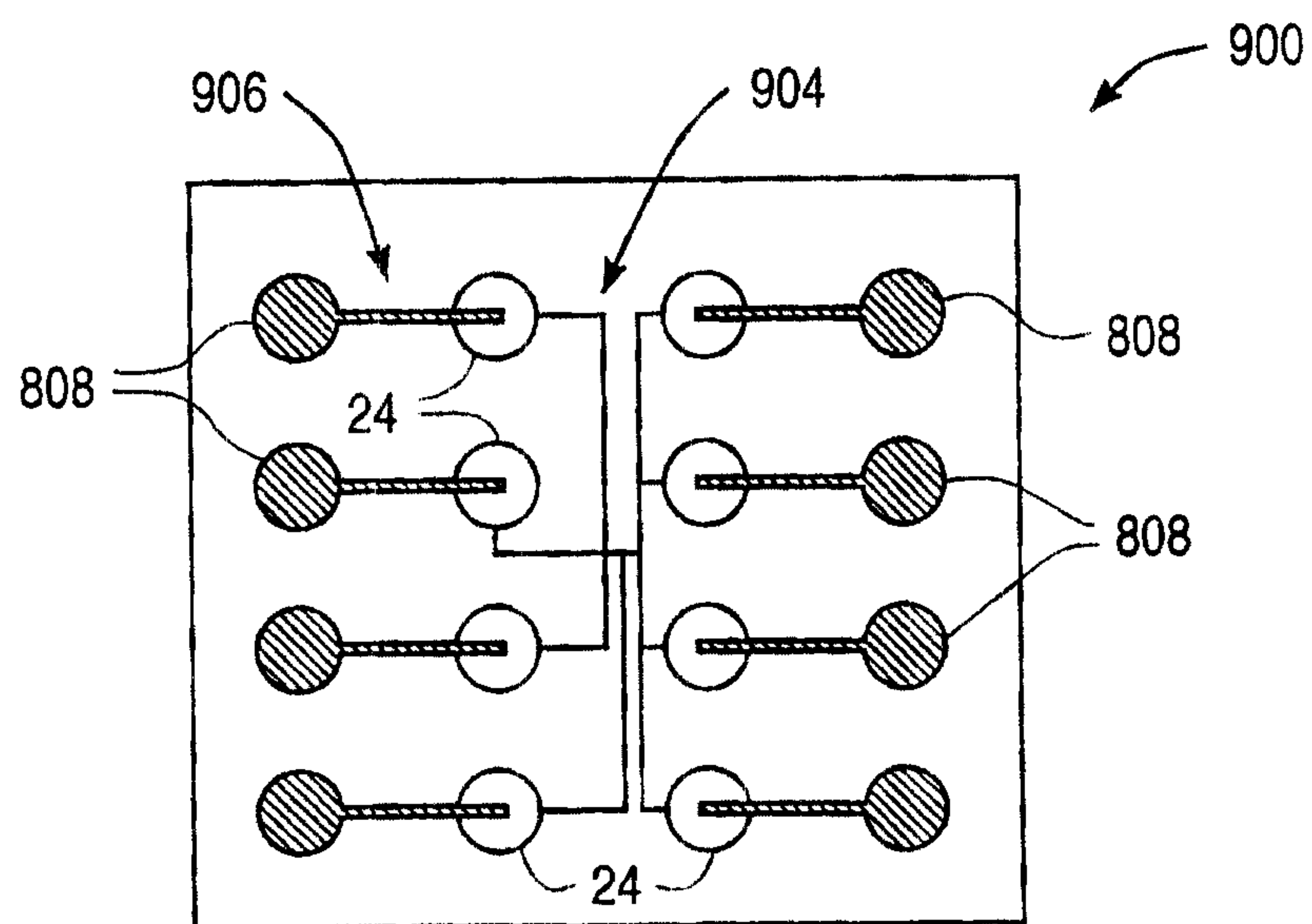


FIG. 9A

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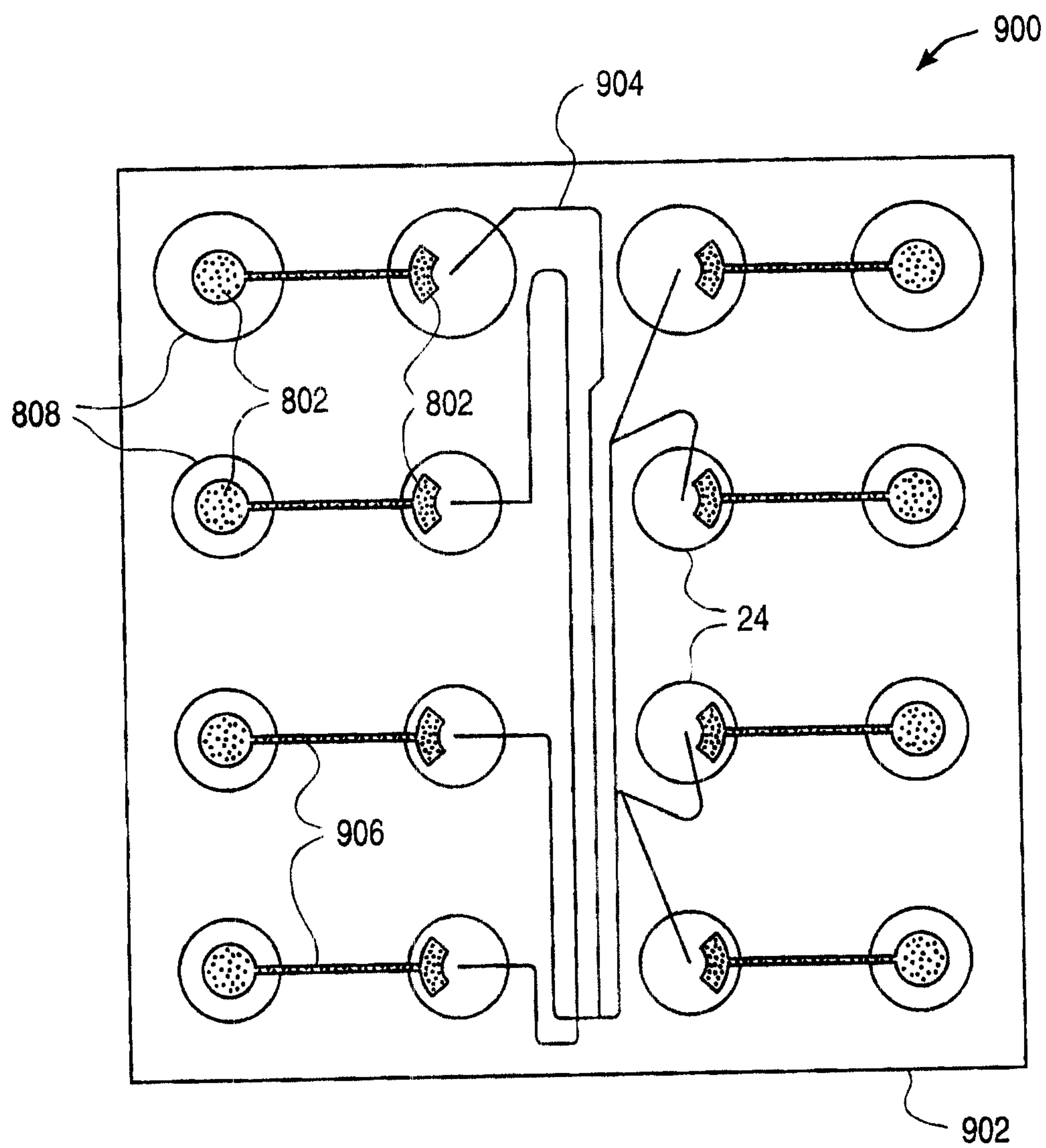


FIG. 9B

