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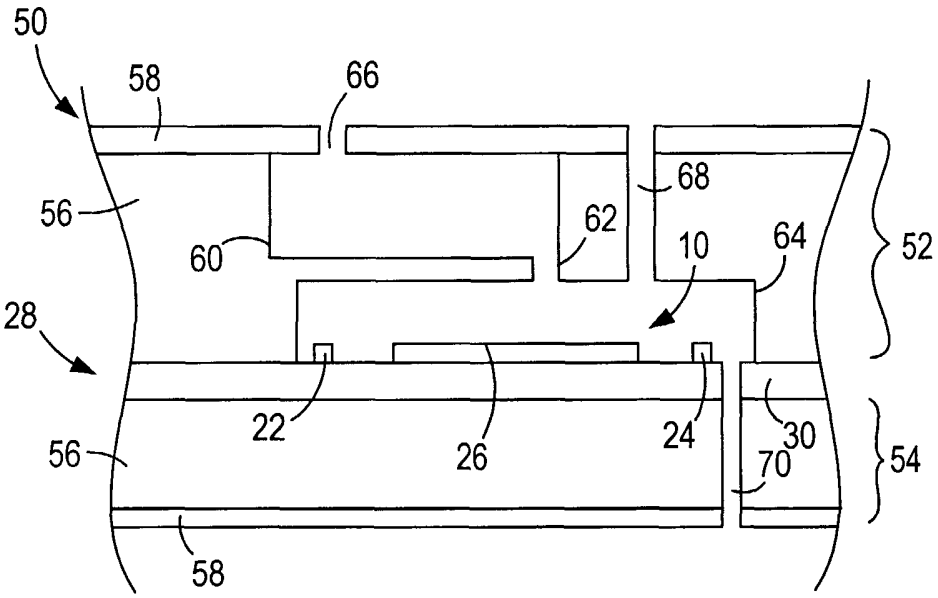
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(54) **Title:** SYSTEM FOR DETECTION OF A COMPONENT IN A LIQUID



(57) **Abstract:** The system includes a liquid transport structure (50) configured to hold a sensor (10) for detecting one or more components in a liquid. The liquid transport structure (50) includes a reservoir (60) configured to hold a liquid within the liquid transport structure (50) and a channel (62) configured to transport a liquid held in the reservoir (60) to a sensor (10) held by the liquid transport structure (50).

WO 2004/011922 A1

SYSTEM FOR DETECTION OF A COMPONENT IN A LIQUID

RELATED APPLICATIONS

[01] This application claims priority to provisional patent application serial number 60/399,058 filed on July 26, 2002, entitled "Assay System Employing a Cartridge" and incorporated herein in its entirety.

BACKGROUND

FIELD OF THE INVENTION

[02] The invention relates to assay equipment. More particularly, the invention relates to a system having a liquid transport structure for use with assay equipment.

BACKGROUND OF THE INVENTION

[03] A variety of assays have been developed for detecting the presence of one or more target agents in a liquid. This liquid is often prepared from a sample that is believed to have the target agent. The sample must often be transported from a site where the sample is obtained to a laboratory where the assay is performed. An undesirable amount of time is often associated with transporting the sample to the laboratory. As a result, there is a need for an assay system that can be performed in the field.

SUMMARY OF THE INVENTION

[04] The invention relates to an apparatus for use with assay equipment. The apparatus includes a liquid transport structure having a reservoir configured to hold a liquid within the liquid transport structure. The apparatus includes an outlet channel configured to transport a liquid held in the reservoir to a chamber within the liquid transport structure.

[05] Another embodiment of the apparatus includes a liquid transport structure configured to hold a sensor for detecting one or more components in a liquid. The liquid transport structure includes a reservoir configured to hold a liquid within the liquid transport structure and a channel configured to transport a liquid held in the reservoir to a sensor held by the liquid transport structure. The liquid transport structure can also include an inlet channel extending from an external side of the liquid transport structure to the reservoir.

[06] In some instances, the liquid transport structure includes a first member positioned over the sensor and a second member positioned under the sensor. The first member and/or the second member can include a base and a cover. The base and the cover can each define a portion of the reservoir.

[07] The liquid transport structure can be removably coupled with an interface system that provides liquid communication between the reservoir and one or more tubes. In some instances, the liquid transport structure is configured to be clamped between two or more members of the interface system.

[08] The liquid transport structure can hold a sensor structure that includes the sensor positioned on a sensor support. In some instances, the sensor structure is configured to be removed from the liquid transport structure. The sensor structure can include a plurality of sensors positioned on the sensor support. Further, the liquid transport structure can define a plurality of reservoirs that are each configured to hold a liquid within the liquid transport structure. The liquid transport structure can also include a plurality of channels that are each configured to transport a liquid from a reservoir to a sensor on the sensor structure.

[09] The sensor can include a plurality of electrodes positioned on the sensor support. The electrodes can include a reference electrode and a counter electrode that are each spaced apart from a working electrode.

[010] The invention also relates to a sensor having an electrode support with a first support region spaced apart from a second support region. One or more electrodes are positioned on the first support region and one or more of the electrodes positioned on the second support region. In some instances, a working electrode is positioned on the second

support region, a reference electrode is positioned on the first support region and a counter electrode is positioned on the first support region.

[011] The invention also relates to a method for performing an assay. The method includes changing the pressure on a liquid stored in a reservoir of a liquid transport structure. The pressure is changed such that at least a portion of the liquid flows from the reservoir onto a sensor held by the liquid transport structure. The pressure can be changed by increasing pressure in an inlet channel extending from an external side of the liquid transport structure to the reservoir and/or by reducing pressure in an outlet channel extending from the reservoir to a chamber formed over the sensor.

[012] Another embodiment of the method includes applying one or more liquids to a sensor such that a target agent bonds to the sensor along with one or more non-target agents. The sensor is configured to detect a component in a liquid and includes two or more electrodes positioned on a sensor support. The method also includes removing non-target agents from the sensor. Removing the non-target agents can include flowing a liquid across the sensor. The liquid can be flowed across the sensor so as to generate a shear flow pattern on the sensor. In some instances, a liquid transport structure defines a chamber over the sensor and flowing the liquid across the sensor includes flowing the liquid through the chamber.

BRIEF DESCRIPTION OF THE FIGURES

[013] Figure 1A is a topview of a sensor configured to detect a component in a liquid.

[014] Figure 1B is a sideview of the sensor taken in the direction of the arrow labeled A in Figure 1A.

[015] Figure 1C is a cross section of the sensor taken at the line labeled B in Figure 1A.

[016] Figure 1D illustrate a sensor structure having the sensor illustrated in Figure 1A through Figure 1C bonded to a sensor support.

[017] Figure 1E is a cross section of the sensor structure taken along a line extending between the brackets labeled A in Figure 1D.

[018] Figure 2A is a topview of another embodiment of a sensor structure.

[019] Figure 2B is a cross section of the sensor structure taken along the line labeled A in Figure 2A.

[020] Figure 2C is a cross section of the sensor structure taken along the line labeled B in Figure 2A.

[021] Figure 3 is a topview of a sensor structure having a plurality of sensors on a sensor support.

[022] Figure 4 is a topview of a sensor having a rectangular perimeter.

[023] Figure 5A illustrates a drop of a liquid formed constrained over the working electrode of a sensor.

[024] Figure 5B illustrates a drop of a liquid formed constrained over the working electrode, the reference electrode and the counter electrode of a sensor.

[025] Figure 6 illustrates a sensor structure having a sensor formed on a sensor support. The sensor support includes a well shaped so as to constrain a liquid over the sensor.

[026] Figure 7A is a topview of a liquid transport system configured to hold a sensor structure. The liquid transport system includes a reservoir and is configured to transport a liquid from the reservoir to a sensor included on the sensor structure.

[027] Figure 7B is a sideview of the liquid transport structure taken in the direction of the arrow labeled A in Figure 7A.

[028] Figure 7C is a cross section of the liquid transport structure taken along the line labeled B in Figure 7A.

[029] Figure 7D is a cross section of a liquid transport structure having a reservoir positioned below the sensor structure.

[030] Figure 7E is a cross section of a liquid transport structure having a reservoir positioned over the sensor structure and a reservoir positioned under the sensor structure.

[031] Figure 7F is a topview of a portion of a liquid transport structure having a plurality of reservoirs configured to transport a liquid to a single sensor.

[032] Figure 8 is a cross section of an embodiment of a liquid transport structure having a common chamber over a plurality of sensors.

[033] Figure 9A is a cross section of the liquid transport structure shown in Figure 7C where the first member and the second member each have a one-piece construction.

[034] Figure 9B is a cross section of a liquid transport structure having a second member that serves as the sensor support.

[035] Figure 9C is a cross section of a liquid transport structure where the first member and the second member each have a one-piece construction and where the second member serves as a sensor support.

[036] Figure 9D is a cross section of a liquid transport structure that does not include a second member.

[037] Figure 10A is a cross section of a liquid transport structure having inlet channels sealed by a sealing mechanism. Each sealing mechanism can be operated so as to unseal and re-seal an inlet channel.

[038] Figure 10B is the liquid transport structure illustrated in Figure 10A after one of the inlet channels has been unsealed.

[039] Figure 10C is a cross section of a liquid transport structure having inlet channels sealed by a sealing mechanism. A common chamber is defined over a plurality of sensors.

[040] Figure 11A is a cross section of a liquid transport structure having a diaphragm obstructing an inlet channel.

[041] Figure 11B is a cross section of a liquid transport structure having an instrument moved into contact with the diaphragm of Figure 11A.

[042] Figure 11C is a cross section of a liquid transport structure having a diaphragm obstructing a vent channel. The diaphragm includes one or more openings through which a fluid can flow

[043] Figure 11D is a cross section of a liquid transport structure having an instrument moved into contact with the diaphragm of Figure 11C.

[044] Figure 11E is a cross section of a liquid transport structure having a diaphragm positioned so as to obstruct a plurality of channels.

[045] Figure 11F is a cross section of a liquid transport structure having a reservoir. A diaphragm is positioned so as to cover the reservoir.

[046] Figure 11G is a cross section of a liquid transport structure having an instrument moved into contact with the diaphragm of Figure 11F.

[047] Figure 12 is a cross section of a liquid transport structure having a reservoir with an outlet channel. An obstruction is positioned so as to obstruct the outlet channel.

[048] Figure 13A is a cross section of a liquid transport structure configured to generate a liquid flow across a plurality of sensors. The liquid transport structure includes channels that each have a port in a lateral side of an assay chamber within the liquid transport structure.

[049] Figure 13B is a cross section of a liquid transport structure having a channel with one port on a upper side of the liquid transport structure and another port positioned in a lateral side of an assay chamber positioned within the liquid transport structure.

[050] Figure 13C is a cross section of a liquid transport structure configured to generate a liquid flow across a plurality of sensors. The liquid transport structure includes a channel extending through an upper sdie of the liquid transport structure.

[051] Figure 13D is a cross section of a channel configured to serve as a nozzle.

[052] Figure 14A illustrates an outlet channel configured to direct a liquid flowing from the outlet channel onto the working electrode of a sensor.

[053] Figure 14B illustrates an outlet channel configured to direct a liquid flowing from the outlet channel onto the working electrode, the reference electrode and the counter electrode of a sensor.

[054] Figure 15A is a cross section of a liquid transport structure having an assay chamber without a sensor.

[055] Figure 15B is a cross section of a liquid transport structure having an assay chamber without a sensor and an assay chamber with a sensor.

[056] Figure 16A is a topview of an interface system configured to serve as an interface between a liquid transport structure and pressure control devices such as pumps, vacuums and valves.

[057] Figure 16B is a sideview of the interface system looking in the direction of the arrow labeled A in Figure 16A.

[058] Figure 16C is a sideview of a liquid transport structure positioned between the first interface member and the second interface member of Figure 16B.

[059] Figure 16D is a cross section of the interface member taken along the line labeled B in Figure 16A.

[060] Figure 16E is a cross section of the interface member illustrated in Figure 16A taken between the lines labeled C. The interface member of Figure 16E is shown coupled with the first member of the liquid transport structure of Figure 7C.

[061] Figure 17A is a sideview of a liquid transport structure positioned between the first interface member and the second interface member of an interface system configured for in conjunction with sealing mechanisms for sealing inlet channels on a liquid transport structure.

[062] Figure 17B is a bottomview of the interface system illustrated in Figure 17A.

[063] Figure 17C is a cross section of the interface system taken along the line labeled A in Figure 17B.

[064] Figure 18A is a sideview of assay equipment for use with a liquid transport structure that serves as a cartridge that can be incorporated into and removed from the assay equipment.

[065] Figure 18B is a cross sectional view of the assay equipment shown in Figure 18A.

[066] Figure 18C is a cross section of assay equipment that is suitable for use with a liquid transport structure constructed according to Figure 10A through Figure 10C.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[067] The invention relates to a liquid transport structure for use with an assay. The liquid transport structure holds one or more sensors for the detection of a component in a liquid. A suitable sensor is an electrochemical sensor including a plurality of electrodes formed on a sensor support. These sensors can have a compact size that is suitable for use with small volumes of liquid.

[068] The liquid transport structure can include inlet channels that each extend from an outside surface of the liquid transport structure to a reservoir located inside of the holder. The liquid transport structure can also include a plurality of outlet channels that are each configured to carry a liquid from a reservoir to a sensor held within the liquid transport structure. Liquids that are to be employed during an assay can be stored in each of the reservoirs or delivered into the reservoirs from an outside source. Each liquid can be transported onto the sensor at the desired time. The ability to store these solutions in the reservoir allows the liquid transport structure to be used in the field.

[069] The liquid transport structure can be interfaced with assay equipment such as pumps, vacuums and valves for controlling the flow of liquid from the reservoirs. The liquid transport structure can be constructed so as to be easily coupled with the assay equipment and easily removed from the assay equipment. As a result, different liquid transport structures can be used with the assay equipment. Accordingly, the liquid transport system provides a wide range of flexibility.

[070] Figure 1A through Figure 1C illustrate an example of a sensor 10 configured to detect a component in a liquid. Figure 1A is a topview of the sensor 10 and Figure 1B is a sideview of the sensor 10 shown in Figure 1A taken in the direction of the arrow labeled A. Figure 1C is a cross section of the sensor 10 shown in Figure 1A taken at the line labeled B.

[071] The sensor 10 includes a plurality of electrodes 12 positioned on an electrode support 14. The electrode support 14 includes a first support region 16 spaced apart from a second support region 18. One or more tether members 20 immobilize the position of the

first support region 16 relative to the second support region 18. Although the first support region 16 is shown as surrounding the second support region 18, the first support region 16 need not surround the entire second support region 18.

[072] A reference electrode 22 and a counter electrode 24 are spaced apart from one another on the first support region 16. A working electrode 26 is formed on the second support region 18. A portion of the working electrode 26 extends from the second support region 18 across a tether member 20 to the first support region 16. As will be illustrated below, the portion of the working electrode 26 positioned on the first support region 16 can serve as a contact pad.

[073] The sensor 10 can be constructed such that the largest dimension of the working electrode 26 is less than 1 μm, 10 μm, 50 μm, 100 μm, 1 mm or 10 mm. Suitable widths for the counter electrode 24 and the reference electrode 22 include, but are not limited to, widths less than 1 μm, 10 μm, 100 μm, 500 μm, 0.1 mm, 1 mm or 5 mm. Suitable dimensions for the gap between the working electrode 26 and the reference electrode 22 and/or between the working electrode 26 and the counter electrode 24 include, but are not limited to, gaps less than 0.1 μm, 10 μm, 50 μm, 200 μm, 0.5 mm or 2 mm. These dimensions can provide for a sensor 10 having a compact size that is suitable for use in on site assay equipment.

[074] Suitable materials for the sensor 10 support include, but are not limited to, plastics, polymers, glass, silicon substrates and metals. Suitable material for the working electrode 26 include, but are not limited to, gold, silver, copper, platinum, chromium, aluminum, titanium, nickel and conducting polymers. Suitable methods for forming the electrodes 12 on the electrode support 14 include, but are not limited to, lift-off processes with photolithography, thin film deposition with shadow mask and thin film foil pressing.

[075] Figure 1D and Figure 1E illustrate a sensor 10 structure employing the sensor 10 illustrated in Figure 1A through Figure 1C. Figure 1D is a topview of the sensor 10 structure. Figure 1E is a cross section of the sensor structure 28 taken along a line extending between the brackets labeled A in Figure 1D.

[076] The sensor structure 28 includes the sensor 10 illustrated in Figure 1A through Figure 1C bonded to a sensor support 30. Suitable materials for the sensor support 30 include, but are not limited to, plastics, polymers, glass, silicon and metals. A suitable method for bonding the sensor 10 to the sensor support 30 includes, but is not limited to, gluing, ultrasonic bonding, taping, welding and pressing. Electrical conductors 32 provide electrical communication between pads 34 positioned at a side of the sensor structure 28 and pads positioned adjacent to the sensor 10. The pads adjacent to the sensor 10 are in electrical communication with the electrodes. For instance, the pads adjacent to the sensor 10 can be wire bonded to the electrodes 12. The pads 34 at the side of the sensor structure can be connected to a coupler (not shown) to provide electrical communication between the electrodes 12 and electronics for operating the sensor 10. Alternatively, the pads 34 can be directly coupled with wires that provide electrical communication between the sensor 10 and the electronics. Suitable conductors 32 include, but are not limited to, metal traces formed on the sensor support 30 using integrated circuit manufacturing techniques or printed circuitry techniques.

[077] Figure 2A through Figure 2C illustrate another embodiment of a sensor structure 28. Figure 2A is a topview of the sensor structure 28 and Figure 2B is a cross section of the sensor structure 28 shown in Figure 2A taken along the line labeled A. Figure 2C is a cross section of the sensor structure 28 shown in Figure 2A taken along the line labeled B.

[078] The electrodes 12 of a sensor 10 are formed directly on the sensor support 30. Accordingly, the sensor support 30 serves as the electrode support 14 disclosed with respect to Figure 1A through Figure 1C. Electrical conductors 32 provide electrical communication between each of the electrodes 12 and a pad 34. The electrodes 12, the conductors 32 and the pads 34 can be formed on the sensors 10 support using the thin film deposition and photo-lithography techniques employed in integrated circuit manufacturing.

[079] Although Figure 1A through Figure 2C illustrate the sensor structure 28 as having a single sensor 10, a sensor structure 28 can include a plurality of sensors 10 as illustrated in Figure 3. The sensors 10 can be arranged in an array on the sensor structure 28. Each of the sensors 10 includes a working electrode 26, a reference electrode 22 and a counter electrode 24. Electrical conductors 32 provide electrical communication between each of

the electrodes 12 and a pad 34 positioned at a side of the sensor structure 28. Although each of the pads 34 is shown as being positioned along the same side of the sensor structure 28, the pads 34 can be positioned on different sides of the sensor structure 28.

[080] Although the working electrode 26 is shown above as having a round shape, the working electrode 26 can have a variety of other shapes including, but not limited to, rectangular shapes, triangular shapes and wedge shapes as illustrated in Figure 4.

[081] During operation of a sensor 10, one or more liquids are transported onto the sensor 10. In some instances, a liquid positioned on the sensor structure 28 is washed off the sensor structure 28 and replaced with a different liquid. A liquid transported onto the sensor structure 28 can be confined to the working electrode 26 in the shape of a drop 36 as shown in Figure 5A or can be formed over each of the electrodes 12 as shown in Figure 5B.

[082] The sensors 10 described above can be operated as electrochemical sensors 10. For instance, the one or more liquids transported onto a sensor 10 are selected so as to bond a target agent to the sensor 10 and/or to the sensor support 30. Examples of target agents include, but are not limited to, DNA strands, proteins, small molecules and cells. A target DNA strand can be bonded to the sensor 10 by bonding a DNA strands with a complementary region to the sensor 10 and then transporting onto the sensor 10 a liquid containing the target DNA strand. Further, bonding to the sensor 10 antibodies that specifically bind to the target cell and then transporting onto the sensor 10 a liquid containing the target cell can serve to bond a target cell to the sensor 10. As noted above, one or more liquids are transported onto the sensor 10 so as to bond the target agent to the sensor 10 and/or to the sensor support 30. Examples of methods for bonding various components to the sensor 10 and/or the sensor support 30 are described in U.S. patent application serial number 09/848,727, filed on May 3, 2001, entitled "Biological Identification System with Integrated Sensor Chip" and incorporated herein in its entirety.

[083] Once the target agent has been bonded to the sensor 10, a sample to be tested for the presence of the target agent is prepared by transporting onto the sensor 10 a liquid contains one or more first components that interact with the target agent so as to produce a second component in the sample. In some cases, the target agent can be modified by a

signal agent to react with the first component. The sample is tested by applying a potential between the working electrode 26 and the reference electrode 22 while monitoring current passing through a circuit that includes the working electrode 26, the sample and the counter electrode 24. The potential applied between the working electrode 26 and the reference electrode 22 is raised to a level sufficient to cause electron transfer between the working electrode 26 and second component that diffuses from the target agent to the working electrode 26. In some case, the electron transfer between the target agent and the working electrode 26 can be monitored. The electron transfer allows current to flow through the circuit. A current flowing through the working electrode 26 and the counter electrode 24 indicates that the target agent is present in the sample while the lack of current indicates that the component is not present in the sample. Because the first component interacts with the target agent to produce the second component in the sample, the presence of the second component in the liquid indicates the presence of the target agent. In some instances, the direct electron transfer between the target agent and the working electrode 26 is monitored instead of monitoring the secondary components.

[084] Because the sensors 10 illustrated above can be operated as electrochemical sensors 10, coulometric, amperometric and/or voltametric methods can be employed to quantify the concentration of the target agent in the sample.

[085] The sensor 10 described above can be operated using other methods. For instance, the target agent can also be the component that diffuses to the sensor 10 and transfers electrons with the working electrode 26.

[086] A variety of mechanisms are available for constraining a liquid to the working electrode 26 or over each of the electrodes 12. For instance, when the surface of working electrode 26 is elevated relative to the sensor support 30 as shown in Figure 5A, the surface tension of the liquid can serve to confine the drop 36 to the working electrode 26. Further, when the surface of the counter electrode 24 and the surface of the reference electrode 22 are elevated relative to the sensor support 30 as shown in Figure 5B, the surface tension of the liquid can serve to confine the drop 36 within the perimeter of the reference electrode 22 and the counter electrode 24. In some cases, the surface of working

electrode 26 is suspended over the sensor support 30 or isolated to employ surface tensions to confine the liquid on the surface of the working electrode 26.

[087] Elevating one or more electrodes 12 relative to a sensor support 30 can be achieved by selecting an electrode support 14 with the desired thickness. Alternatively, a trench can be etched between the working electrode 26 and the reference electrode 22, between the working electrode and the counter electrode 24, around the outside of the reference electrode 22 and/or around the outside of the counter electrode 24. When the sensor structure 28 is constructed as shown in Figure 2A through Figure 2C, the electrodes 12 can be formed with sufficient thickness to elevate the drop relative to the sensor support 30 and/or a recess can be formed in the sensor support 30 adjacent to the electrode 12. When a surface of an electrode 12 is to be elevated so as to constrain a liquid to the electrode 12, a suitable height for the surface of an electrode 12 includes, but is not limited to, heights greater than .5 μm, 10 μm, 500 μm and 5 mm.

[088] Other mechanisms are available for constraining a liquid to a sensor 10. For instance, all or a portion of the upper surface of the sensor support 30 can be hydrophobic. In some instances, the portion of the upper surface between the reference electrode 22 and the working electrode 26 and between the counter electrode 24 and the working electrode 26 is hydrophobic. An aqueous liquid transported onto the working electrode 26 will remain constrained on the working electrode 26 until enough liquid is transported onto the working electrode 26 to overcome the hydrophobic nature of the upper surface and cross over the gap between the working electrode 26 and the reference electrode 22 and/or the gap between the working electrode and the counter electrode 24. Accordingly, the hydrophobic nature of the upper surface can serve to constrain a drop of the liquid to the working electrode 26.

[089] When the portion of the upper surface located outside of the counter electrode 24 and the reference electrode 22 is also hydrophobic, an aqueous liquid transported onto the sensor structure 28 is driven onto the reference electrode 22, the counter electrode 24 and the working electrode 26. Accordingly, the hydrophobic nature of the upper surface can serve to constrain a drop of the liquid to the reference electrode 22 and the counter electrode 24.

[090] A variety of techniques can be employed to create a hydrophobic sensor support 30. For instance, the sensor support 30 can be constructed of a hydrophobic medium such as most plastics and polymers. Alternatively, the sensor support 30 can be constructed of a medium having a hydrophobic coating or treatment. Glass and silicon are examples of media that are suitable for use with hydrophobic coating.

[091] In some instances, the exposed surfaces of the working electrode 26, the reference electrode 22 and/or the counter electrode 24 are hydrophilic. The hydrophilic nature of the electrodes 12 serves to draw the liquid onto the electrodes 12. Accordingly, the hydrophilic nature of the electrodes 12 can serve to constrain liquid to the working electrode 26, the reference electrode 22 and/or the counter electrode 24.

[092] A variety of techniques can be employed to create one or more hydrophilic electrodes 12. For instance, an electrode 12 can be coated with a hydrophilic medium. As an example, a working electrode 26 constructed of gold can have a protein coating.

[093] The sensor support 30 can include a well as shown in Figure 6. The well can serve to constrain the liquid to a particular region of the sensor structure 28. The working electrode 26 can cover the bottom and sides of the well or only a portion of the well. Alternatively, the working electrode 26 can extend from inside the well to outside the well. In some instances, the reference electrode 22 and the counter electrode 24 are also positioned in the well.

[094] A sensor structure 28 can be included in a liquid transport structure 50 for use in transporting a liquid to one or more sensors 10 included on the sensor structure 28. Figure 7A through Figure 7C illustrate an example of a liquid transport structure 50 including a sensor structure 28. Figure 7A is a topview of a liquid transport structure 50. Figure 7B is a sideview of the liquid transport structure 50 taken in the direction of the line labeled A in Figure 7A. Figure 7C is a cross section of the liquid transport structure 50 taken along the line labeled B in Figure 7A.

[095] The liquid transport structure 50 includes a first member 52 and a second member 54 configured to hold the sensor structure 28. The first member 52 and the second member 54 each include a base 56 and a cover 58. A suitable material for the first member 52 and

the second member 54 includes, but is not limited to, acrylic plastics and polymers. In some instances, the liquid transport structure 50 has a compact size that is suitable for use in the field. For instance, the liquid transport structure 50 can have a volume less than 26 cubic inches, less than 16 cubic inches, 4 cubic inches or 1 cubic inch. Examples of suitable dimensions include, but are not limited to, a block that is about 2 inch by 1 inch by 0.5 inch, 2 inch by 2 inch by 1 inch or 4 inch by 4 inch by 1 inch.

[096] The liquid transport structure 50 can employ a variety of mechanisms for immobilizing the components of the liquid transport structure 50 relative to one another. For instance, registration or alignment pins (not shown) can extend through the liquid transport structure 50 to keep the various components immobilized relative to one another. Each pin can extend through first member 52, the sensor structure 28 and the second member 54. The use of pins allows the liquid transport structure 50 components to be separated from one another although other mechanisms may permanently immobilize the various components of the liquid transport structure 50. Additionally or alternatively, the components of the liquid transport structure 50 can be immobilized using techniques such as ultrasonic bonding, welding and gluing with registration and alignment geometry on each component. Although the liquid transport structure 50 is shown as having a substantially block shape structure, the liquid transport structure 50 can have a variety of different shapes.

[097] The portion of the sensor structure 28 having the pads 34 extends from the liquid transport structure 50. As a result, the sensor structure 28 can be interfaced with a coupler that connects the sensor structure 28 to electronics configured to operate each sensor 10 so as to detect a component in the liquid.

[098] The first member 52 can include one or more reservoirs 60. Each reservoir 60 is configured to hold a liquid to be transported to one or more sensors 10 located on the sensor structure 28. The cross section shown in Figure 7C illustrates the relative positions of a reservoir 60 and a sensor 10 positioned on the sensor structure 28. The dashed line in Figure 7A shows the approximate location of the reservoir 60 within the first member 52. The base 56 of the first member 52 defines a portion of the reservoir 60 and the cover 58 of the first member 52 defines a portion of the reservoir 60. An inlet channel 66 extends

through the cover 58 to the reservoir 60. Suitable volumes for the reservoir include, but are not limited to, volumes less than 1μL, 100 μL or 10 mL and/or volumes greater than 1 nL, 10μL or 1mL.

[099] The sensor structure 28 and the first member 52 define an assay chamber 64 over the sensor 10. An outlet channel 62 extends from the reservoir 60 to the assay chamber 64 through the first member 52. In some instances, the outlet channel 62 is sized so the surface tension of a liquid in the reservoir 60 prevents the liquid from flowing out of the reservoir 60 under the action of gravity. A vent channel 68 extends through the first member 52 to the assay chamber 64. The vent channel 68 can be employed to vent the assay chamber 64 when liquid flows into and/or out of the assay chamber 64. Additionally, a waste channel 70 extends from the assay chamber 64 through the sensor structure 28 and through the second member 54. The waste channel 70 can be employed as an outlet for excess liquid or as an outlet for wash fluids when a liquid is washed off a sensor 10.

[0100] During operation of the liquid transport structure 50, a positive pressure is applied to a liquid in the reservoir 60 so as to transport the liquid through the outlet channel 62 into the assay chamber 64. The pressure can be sufficient to transport the liquid through the outlet channel 62, into the assay chamber 64 and onto the sensor 10. The positive pressure can be generated by increasing the pressure in the inlet channel 66 and/or by sealing the waste channel 70 while decreasing the pressure in the vent channel 68.

[0101] The reservoir 60 can be positioned below the sensor structure 28 as shown in Figure 7D. The base 56 of the second member 54 defines a portion of the reservoir 60 and the cover 58 of the second member 54 defines a portion of the reservoir 60. An inlet channel 66 extends through the cover 58 to the reservoir 60. A sensor 10 is positioned in an assay chamber 64 defined by the sensor structure 28 and the first member 52. An outlet channel 62 extends from the reservoir 60 to the assay chamber 64 through the base 56 of the second member 54 and through the sensor structure 28. During operation of a liquid transport structure 50 constructed according to Figure 7D, a positive pressure is applied to a liquid in the reservoir 60 so as to transport the liquid through the outlet channel 62 into the assay chamber 64. The positive pressure can be generated by increasing the pressure in

the inlet channel 66 and/or by sealing the waste channel 70 while decreasing the pressure in the vent channel 68. The volume of liquid transported into the assay chamber 64 can be sufficient to form a drop of the liquid on the working electrode 26. In some instances, the volume of liquid transported through the outlet channel 62 is sufficient to form a drop over the working electrode 26, the counter electrode 24 and the reference electrode 22 or to fill the assay chamber.

[0102] Each reservoir 60 can include more than one outlet channel 62 extending to an assay chamber 64. Increasing the number of outlet channels 66 can reduce the amount of pressure that is require to drive a liquid out of a reservoir 60 an into that assay chamber 64. In some instances, different outlet channels can extend from the same reservoir to different assay chambers.

[0103] The liquid transport structures 50 illustrated above can be combined to provide a liquid transport structure 50 having a reservoir 60 positioned over the sensor structure 28 and a reservoir 60 positioned under the sensor structure 28 as illustrated in Figure 7E.

[0104] The first member 52 and/or the second member 54 can include a plurality of reservoirs 60 configured to transport a liquid to a single sensor 10. For instance, Figure 7F is a topview of a portion of a liquid transport structure 50. The dashed line labeled B illustrates the location of a sensor 10 in the liquid transport structure 50. The dashed lines labeled A each illustrate the location of a reservoir 60 configured to transport a liquid onto the working electrode 26. The lines labeled C each illustrate the location of an outlet channel 62 associated with one of the reservoirs 60. Constructing the liquid transport structure 50 such that the first member 52 and/or the second member 54 include a plurality of reservoirs 60 configured to transport a liquid to a sensor 10 can increase the number of liquids that can be transported onto a single sensor 10.

[0105] Although Figure 7A through Figure 7F illustrate the liquid transport structure 50 employed in conjunction with a sensor structure 28 according to Figure 2A through Figure 2C, the liquid transport structure 50 can be employed with a sensor structure 28 according to Figure 1D and Figure 1E.

[0106] Figure 8 is a cross section of another embodiment of a liquid transport structure 50. The first member 52 defines a common assay chamber 64 over a plurality of sensors 10. The first member 52 includes a vent channel 68. The second member 54 includes a plurality of reservoirs 60. Each reservoir 60 includes an outlet channel 62 configured to transport a liquid onto a particular sensor 10. Each sensor 10 can receive a liquid from more than one reservoir 60.

[0107] An inlet channel 66 extends from each reservoir 60. Before operation of the liquid transport structure 50, each inlet channel 66 can be maintained at a same pressure that is less than or equal to the pressure in the vent channel 68 to prevent flow of a liquid from a reservoir 60 into the assay chamber 64. During operation of the liquid transport structure 50, a liquid from a particular reservoir 60 can be transported onto a particular sensor 10 by increasing the pressure in the inlet channel 66 of that reservoir 60 above the pressure in the vent channel 68. The relative pressure can be increased by increasing the pressure in an inlet channel 66 and/or by reducing the pressure in the vent channel 68.

[0108] In some instances, the first member 52 and/or the second member 54 are not constructed with a base 56 and a cover 58. For instance, the first member 52 and/or the second member 54 can have a one-piece construction. Figure 7D illustrates the first member 52 constructed as a single piece. Further, Figure 9A is a cross section of the liquid transport structure 50 shown in Figure 7C where the first member 52 and the second member 54 each have a one-piece construction. In some instances, the first member 52 and/or the second member 54 are constructed by immobilizing various components of the liquid transport structure relative to one another using techniques such as gluing, ultrasonic bonding, taping, welding and pressing.

[0109] In some instances, the sensor structure 28 is not independent of the liquid transport structure 50. For instance, the second member 54 can serve as the sensor support 30 or the sensor support 30 can be constructed to serve as the second member 54. Figure 9B is a cross section of a liquid transport structure 50 having a second member 54 that serves as the sensor support 30. Figure 9C is a cross section of a liquid transport structure 50 where the first member 52 and the second member 54 each have a one-piece construction and where the second member 54 serves as a sensor support 30.

[0110] In some instances, the liquid transport structure 50 does not include a second member 54. Figure 9D is a cross section of a liquid transport structure 50 that does not include a second member 54. A liquid can be transported from the reservoir 60 onto the sensor 10 by increasing the pressure in the inlet channel 66.

[0111] Many of the liquid transport structures 50 above are shown as having both a vent channel 68 and a waste channel 70. In some instances, the vent channel 68 also serves as a waste channel 70 and the liquid transport structure 50 does not include a waste channel 70. In some instances, the waste channel 70 also serves as a vent channel 68 and the liquid transport structure 50 does not include a vent channel 68.

[0112] As noted above, the liquid transports structures can be operated by controlling the pressure of one or more inlet channels 62 and one or more vent channels 68. Figure 10A through Figure 10B illustrate a system for controlling pressure in one or more inlet channels 62 and one or more vent channels 68. Figure 10A is a cross section of a liquid transport structure 50 before a liquid is transported from a reservoir into an assay chamber. Each of the inlet channels 62 is sealed with a sealing mechanism 72 that can be operated so as to unseal and re-seal an inlet channel 66. A vacuum can be pulled on each of the vent channels 68 so the pressure in the assay chambers 64 is reduced below the ambient pressure. During operation of the liquid transport structure 50, a liquid from a particular reservoir 60 can be transported onto a particular sensor 10 by unsealing the inlet channel 66 in liquid communication with the particular channel. Figure 10B is the liquid transport structure 50 illustrated in Figure 10A after one of the inlet channels 62 has been unsealed. The pressure differential between the inlet channel 66 and the vent channel 68 draws the liquid from the reservoir 60 onto the sensor 10 as illustrated by the arrow labeled A in Figure 10B. In some instances, the sealing mechanism 72 can be moved so as to re-seal the inlet channel 66 after the desired amount of liquid has been transported onto the sensor 10. Re-sealing the inlet channel 66 allows the liquid from another reservoir 60 in liquid communication with the same assay chamber 64 to be transported onto the same sensor 10.

[0113] A suitable sealing mechanism 72 is illustrated in Figure 10A and Figure 10B. Each sealing mechanism 72 includes a rod that can be moved into contact with the liquid transport structure 50 so as to seal an inlet channel 66. The rod can also be moved away

from the liquid transport structure 50 so as to unseal an inlet channel 66. In some instances, the rod or the liquid transport structure 50 can include a gasket mechanism (not illustrated) positioned so as to form an airtight seal at the interface of the rod and the liquid transport structure 50. For instance, an O-ring can be seated on the rod such that the O-ring is positioned so as to surround an inlet channel 66 when the rod is moved into contact with the liquid transport structure 50.

[0114] Although Figure 10A and Figure 10B illustrate sealing mechanisms configured to seal inlet channels 62 by covering the opening of the inlet channel 66, a sealing mechanism can be constructed such that a portion of the sealing mechanism extends into the inlet channel 66 so as to plug liquid flow through the inlet channel 66. A gasket mechanism is often not required when a sealing mechanism is constructed so as to extend into the inlet channel 66.

[0115] As shown in Figure 10C, the principle illustrated in Figure 10A and Figure 10B can be extended to a liquid transport structure 50 constructed according to Figure 8. During operation of the liquid transport structure 50, a vacuum can be pulled on the vent channel 68 to reduce the pressure in the common assay chamber 64 relative to the ambient pressure. A liquid from a particular reservoir 60 can be transported onto a particular sensor 10 by unsealing the inlet channel 66 in liquid communication with the particular channel. The pressure differential between the common assay chamber 64 and the unsealed vent channel 68 draws the liquid from the reservoir 60 onto the sensor 10.

[0116] Although the principle of sealing and unsealing the inlet channels 62 are taught in the context of a liquid transport structure 50 having reservoirs 60 positioned under the sensors 10, the same principles can be applied to a liquid transport structure 50 having reservoirs 60 positioned over a sensor 10 as shown in Figure 7C or to a liquid transport structure 50 having one or more reservoirs 60 positioned over a sensor 10 and one or more reservoirs 60 positioned under a sensor 10 as shown in Figure 7E.

[0117] The liquid transport structures shown above can include a diaphragm 74 obstructing an inlet channel 66. For instance, Figure 11A is a cross sectional view of a liquid transport structure 50 having a diaphragm 74 obstructing an inlet channel 66. Although the diaphragm 74 is shown positioned over a port of the inlet channel 66, the

diaphragm 74 can be positioned in the inlet channel 66. Suitable materials for a diaphragm 74 include, but are not limited to, latex, rubbers, silicon rubbers and polymers. A suitable method of immobilizing a diaphragm 74 relative to the liquid transport structure 50 includes, but is not limited to, gluing, ultrasonic bonding, taping, welding, epoxying and pressing.

[0118] In some instances, a diaphragm is flexible. A flexible diaphragm 74 can be operated so as to control pressure on liquids within a liquid transport structure 50. For instance, an instrument 76 can be employed to drive the diaphragm 74 further into the inlet channel as shown in Figure 11B. When the diaphragm is substantially impermeable to fluids, the movement of the diaphragm 74 into the inlet channel increases the pressure within the inlet channel 66 and can drive a liquid from the reservoir into the assay chamber 64.

[0119] Although the diaphragm 74 of Figure 11A is shown as obstructing an inlet channel 66, a diaphragm 74 can be employed to obstruct other channels on the liquid transport structure 50. For instance, a diaphragm 74 can be employed to obstruct a waste channel 70 and/or a vent channel 68.

[0120] The diaphragm 74 can include one or more openings through which the fluid can flow. Example openings include, but are not limited to, pores, slits, holes, apertures. The size and number of the one or more openings can control the pressure required to drive a fluid through the diaphragm. For instance, reducing the size and/or number of the one or more openings can increase the pressure required to drive the fluid through the diaphragm. Suitable diaphragms having openings include, but are not limited to, passive valves, pinch holes, septa, filters and membranes.

[0121] A diaphragm 74 having one or more openings through which a fluid can flow can be employed to control pressure in the assay chamber 64. For instance, Figure 11C is cross section of a liquid transport structure 50 having a diaphragm 74 obstructing a vent channel 68. The one or more openings allow fluid in the assay chamber 64 to be vented through the vent channel 68 as shown by the arrow labeled A. An instrument 76 can be moved into contact with the diaphragm 74 to seal the vent channel 68. For instance, the arrow labeled A in Figure 11D illustrates the instrument 76 shown in Figure 11C moved

into contact with the diaphragm 74. The instrument can seal the one or more openings in the diaphragm 74 or can close the one or more openings.

[0122] Although the above diaphragms are portrayed as being flexible, the diaphragm can be rigid.

[0123] The liquid transport structure can include a plurality of diaphragms 74. Different diaphragms 74 can obstruct different channels. Different diaphragms 74 can be positioned on different sides of the liquid transport structure 50. A single diaphragm 74 can obstruct more than one channel as illustrated in Figure 11E. In some instances, the diaphragm 74 is layer of material that extends across a side of the liquid transport structure 50. The layer of material can include one or more openings aligned with channels that are not to be obstructed.

[0124] In some instances, a diaphragm 74 can be positioned so as to cover a reservoir 60. For instance, Figure 11F is a cross section of a liquid transport structure 50. A diaphragm 74 extends across the top of a reservoir 60 so as to seal the top of the reservoir 60 to liquids within the reservoir 60. An instrument 76 can be employed to drive the diaphragm 74 into the reservoir 60 as shown in Figure 11G. The movement of the diaphragm 74 into the reservoir 60 can drive a liquid from the reservoir 60 into the assay chamber 64. In some instances, the diaphragm 74 can extend across a side of a base so the diaphragm 74 serves as a cover 58 for a base of the first member or for a base of the second member.

[0125] One or more outlet channels 62 of a liquid transport structure can include an obstruction 78 as illustrated in Figure 12. Figure 12 is a cross section of a liquid transport structure having an obstruction 78 positioned over the outlet channel 62. Although the obstruction 78 is shown positioned over a port of the outlet channel 62, the obstruction 78 can be positioned in the outlet channel 62. Suitable materials for an obstruction 78 include, but are not limited to, latex, rubbers, silicon rubbers and polymers. A suitable method for immobilizing an obstruction 78 relative to the liquid transport structure includes, but is not limited to, gluing, ultrasonic bonding, taping, welding, epoxying and pressing.

[0126] The obstruction 78 can serve to constrain a liquid in a reservoir 60 by increasing the pressure required to drive a liquid from the reservoir 60 into the assay chamber 64. For instance, the obstruction 78 can include one or more openings through which the liquid can flow. Example openings include, but are not limited to, pores, slits, holes, apertures. The size and number of the one or more openings can control the pressure required to drive a liquid from the reservoir into the assay chamber. For instance, reducing the size and/or number of the one or more openings can increase the pressure required to drive the liquid into the assay chamber 64. A suitable obstruction 78 includes, but is not limited to, passive valves, pinch holes, septa, filters and membranes.

[0127] The liquid transport structure 50 can include one or more channels 86 configured to flow a liquid across one or more sensors 10 held in a liquid transport structure 50. Figure 13A is a cross section of a liquid transport structure 50 configured to generate a shear flow across a plurality of sensors 10. Channels 86 are formed in the liquid transport structure 50 such that ports of different channels 86 are located on opposing lateral sides 88 of the assay chamber 64. Flowing a liquid through the channel 86 labeled A to the channel 86 labeled B causes the liquid to flow through the assay chamber 64 as shown by the arrow labeled C. The liquid can be flowed so as to generate a flow pattern that is substantially parallel to the upper surface of the working electrode 26. For instance, the liquid can be flowed through the assay chamber 64 so as to generate a shear pattern at the sensors 10.

[0128] Although Figure 13A illustrates a plurality of sensors 10 positioned in the assay chamber 64, the channels 86 can be employed in conjunction with a liquid transport structure 50 having a single sensor positioned in an assay chamber 64.

[0129] One of more of the channels 86 can be constructed to have a port positioned on the upper side of the liquid transport structure 50 and/or on the lower side of the liquid transport structure 50. For instance, Figure 13B is a cross section of a liquid transport structure 50 having a channel 86 with one port on the upper side of the liquid transport structure 50 and another port on the lateral side 88 of the assay chamber 64. Having a port on the upper side of the liquid transport structure 50 or on the lower side of the liquid transport structure 50 allows the channel 86 to be accessed using the same mechanisms as other channels with ports on the same side of the liquid transport structure 50.

[0130] One of more of the channels 86 can be constructed without a port positioned in the upper side of the assay chamber. For instance, Figure 13B is a cross section of a liquid transport structure 50 having a channel 86 with a port on the upper side of the assay chamber. The channel allows the liquid to be flowed onto a sensor 10 from over the sensor 10 as illustrated by the arrow labeled A. Alternatively, the direction of the liquid flow can be reversed. Although not illustrated, a channel 86 can be constructed with a port positioned in the lower side of the assay chamber. As a result, the liquid can be flowed up into the assay chamber.

[0131] The flow of a liquid across a sensor can reduce noise associated with operation of the liquid transport structure 50. As noted above, a target agent is generally bonded to the surface of the sensor 10 or to the sensor support 30 during operation of a sensor 10. Non-specific binding of other agents to the sensor 10 and/or the sensor support 30 can act as a source of noise. Non-target agents are generally bound with less affinity or weaker bond than the target agent. As a result, the flow of a liquid across the sensors can cause the non-target agents to detach while the target agents remain intact. The ability to detach these non-target agents from the sensor 10 and/or from the sensor support 30 can serve to reduce the noise associated with operation of the sensors 10.

[0132] A channel 86 can be configured to act as a nozzle. Figure 13D is a cross section of a liquid transport structure 50 having a channel 86 configured to serve as a nozzle. The cross sectional area of the channel decreases up to the port. The nozzle can increase the speed of the liquid flow into the assay chamber and can accordingly increase the force of the liquid on the non-target agents. As a result, the nozzle structure can remove additional non-target agent from the sensor.

[0133] Although Figure 13 illustrates a single channel 86 through opposing lateral sides 88 of the liquid transport structure 50, a lateral side 88 of the liquid transport structure 50 can include more than one channel 86. Further, the channel 86 can be formed in more that two of the lateral sides 88.

[0134] The outlet channels 66 of the liquid transport structures 50 shown above can be constructed so as to provide a particular flow of liquid onto a sensor 10. For instance, when a reservoir 60 is positioned below a sensor 10, the outlet of an outlet channel 62 can

be angled toward the working electrode 26 as shown in Figure 14A. The angle of the outlet channel 62 can enhance the flow of a liquid onto the working electrode 26 as illustrated by the arrow labeled A. The outlet channel 62 can also flare toward the working electrode 26 and the reference electrode 22 or toward the working electrode 26 and the counter electrode 24 as illustrated in Figure 14B. The outlet channel 62 illustrated in Figure 14B facilitates the flow of the liquid over the working electrode 26 and the counter electrode 24 as shown by the arrow labeled B.

[0135] When a reservoir 60 is positioned under the sensors 10, the above illustrations show the outlet of the outlet channel 62 positioned between the working electrode 26 and the reference electrode 22 or between the working electrode 26 and the counter electrode 24. However, the outlet of the outlet channel 62 can be positioned elsewhere relative to the sensor 10. For instance, the outlet can be positioned between the reference electrode 22 and the counter electrode 24. Alternatively, the outlet can be positioned such that the outlet and the working electrode 26 are on opposite sides of the reference electrode 22. Further, the outlet can be positioned such that the outlet and the working electrode 26 are on opposite sides of the reference electrode 22.

[0136] The liquid transport structures illustrated above need not include sensors. For instance, the liquid transport structures illustrated above can be assembled without a sensor structure. As a specific example, Figure 15A illustrates the liquid transport structure of Figure 7C assembled without a sensor structure. The assay chamber 64 can serve as a mixing chamber. For instance, liquids can be transported into the assay chamber from different reservoirs 60. Accordingly, the liquids from different reservoirs are mixed together in the assay chamber 64. When one or more channels include a diaphragm 74, the diaphragm 74 can be manipulated so as to agitate and further mix the liquids in the mixing chamber. The pressure in the mixing chamber can be increased so as to drive the mixed liquids through the waste channel 70 where the mixed liquids can be employed in other applications.

[0137] The liquid transport structure 50 can include one or more assay chambers 64 that serve as a mixing chamber and one or more assay chambers 64 having one or more sensors. For instance, Figure 15B is a cross section of a liquid transport structure 50

having a plurality of assay chambers 64. Sensors 10 are arranged on the sensors structure 28 such that a sensor 28 is present in one assay chamber 64 but is not present in another assay chamber 64. The assay chamber 64 that does not include a sensor can be operated as a mixing chamber.

[0138] As noted above, a liquid is transported from a reservoir 60 into an assay chamber by generating a pressure differential across a reservoir 60. The pressure in a channel can be controlled with the use of pressure sources such as pumps and vacuums. Figure 16A through Figure 16E illustrate an interface system 90 that can be employed to provide liquid communication between each reservoir 60 and a pump and/or a vacuum. Figure 16A is a topview of an interface system 90 configured to be employed with a liquid transport structure 50. Figure 16B is a sideview of the interface system 90 illustrated in Figure 16A looking in the direction of the arrow labeled A. The interface system 90 includes a first interface member 92 and a second interface member 94. Figure 16C is a sideview of a liquid transport structure 50 positioned between the first interface member 92 and the second interface member 94 of Figure 16B. Figure 16D is a cross section of the interface member seen in Figure 16A taken along the line labeled B. Figure 16E is a cross section of the interface member illustrated in Figure 16A taken between the lines labeled C. The interface member of Figure 16E is shown coupled with the first member 52 of the liquid transport structure 50 of Figure 7C.

[0139] The liquid transport structure 50 can be interfaced with assay equipment by clamping the liquid transport structure 50 between interface members as shown in Figure 16C. The interface between the first liquid transport structure 50 member and an interface member is shown in Figure 16E. A suitable material for construction of the interface members includes, but is not limited to, acrylic plastics. The interface members include one or more lumens 96 configured to be aligned with the channels 98 on the adjacent liquid transport structure 50 member. The channels 98 with which the lumens 96 are aligned can include inlet channels, outlet channels, vent channels and waste channels. Each lumen 96 includes a narrow section and a broad section. A connector 104 is inserted into the broad section of the lumen 96. A suitable material for construction of the connector 104 includes, but is not limited to, metals, hard plastics and polymers. The

connector 104 includes a flange 105. A gasket mechanism 106 such as an O-ring is positioned between the interface member and the flange 105. The gasket mechanism 106 serves to seal the connection between the connector 104 and the interface member.

[0140] The interface members also include recesses 108 configured to seat a gasket mechanism 106 around the opening of a lumen 96. A suitable gasket mechanism 106 includes, but is not limited to, an O-ring. As is evident in Figure 16E, the gasket mechanism 106 seated in the recesses 108 seals the connection between the liquid transport structure 50 member and the interface member.

[0141] The connectors 104 can each be coupled with a tube 110 as illustrated in Figure 16B, and Figure 16E. Although a single connector 104 is shown as being coupled with a tube 110, a plurality of the connectors 104 can be coupled with a tube 110. In some instances, each of the connectors 104 is coupled with a tube 110. The narrow section of the lumen 96 extends through the connector 104 and the tube 110. Additionally, the narrow section of the lumen 96 is aligned with a channel 98 through the liquid transport structure 50 member. Accordingly, liquid from the tube 110 can flow from or into the channel 98 in the liquid transport structure 50 member. As a result, the interface system 90 serves to provide liquid communication between the tubes 110 and channels 98 in the liquid transport structure 50. The assay equipment can include vacuums and/or pumps in liquid communication with the tubes 110. The vacuums and/or pumps can be employed to control the pressures in the various channels 98 of the liquid transport structure 50. The assay equipment can include valves in communication with the tubes 110. Each valve can be employed to stop liquid flow through a tube 110, to allow liquid flow through a tube 110 or to control the flow rate of liquid through a tube 110.

[0142] Figure 17A through Figure 17C illustrate an interface system 90 for use with a liquid transport structure 50 constructed in accordance with Figure 10A through Figure 10C. Figure 17A is a sideview of a liquid transport structure 50 positioned between the first interface member 92 and the second interface member 94 of an interface system 90. Figure 17B is a bottomview of the interface system 90 illustrated in Figure 17A. Figure 17C is a cross section of the interface system 90 taken along the line labeled A in Figure 17B.

[0143] The interface system 90 can be employed with a liquid transport structure 50 constructed according to Figure 10C. Accordingly, the first member 52 of the liquid transport structure 50 can include a single vent channel 68. Hence, the first interface member 92 is illustrated with a single connector 104 for providing liquid communication between a tube 110 and the vent channel 68.

[0144] The second interface member 94 includes a plurality of guide lumens 114. The guide lumens 114 are positioned such that each of the guide lumens 114 is aligned with an inlet channel 66 when the second interface member 94 is positioned adjacent to the liquid transport structure 50. The sealing mechanisms can be moved within the guide lumens 114 as illustrate by the arrow labeled A. Each guide lumen 114 guides the movement of the sealing mechanism relative to the liquid transport structure 50. For instance, when a sealing mechanism is employed to seal an inlet channel 66, the guide lumen 114 guides the movement of the sealing mechanism into contact with the liquid transport structure 50.

[0145] The interface system 90 of Figure 17A through Figure 17C can be employed with a liquid transport structure according to Figure 11A through Figure 11G. For instance, the liquid transport structure can include one or more diaphragms 74 positioned as shown in Figure 11A through Figure 11G. The guide lumens 114 can be configured to guide the movements of the implements 76 into contacted with the diaphragms 74.

[0146] In some instances an interface member will not include any lumens. For instance, when a member of the liquid transport structure 50 does not include any channels, the adjacent interface member need not include any lumens. As a result, the adjacent interface member can be a slab.

[0147] In some instances, the liquid transport structure 50 serves as a cartridge that can be easily incorporated into and removed from assay equipment including equipment such as the pumps, vacuums, valves and/or electronics discussed above. Figure 18A is a sideview of assay equipment for use with a liquid transport structure 50 that serves as a cartridge. Figure 18B is a cross sectional view of the assay equipment shown in Figure 18A.

[0148] The illustrated assay equipment includes a frame 116 with a base 118 and an upper body 120. The upper body 120 can be moved relative to the base 118 as illustrated by the

arrow labeled A. The base 118 holds the second interface member 94 while the upper body 120 holds the first interface member 92. The liquid transport structure 50 is configured to be coupled with the frame 116 during operation of the assay system and can be removed from the frame 116. The liquid transport structure 50 can be coupled with the frame 116 by positioning the liquid transport structure 50 on the second interface member 94 and lowering the upper body 120 toward the base 118 until the liquid transport structure 50 is clamped between the first interface member 92 and the second interface member 94 as shown in Figure 18A. The liquid transport structure 50 can be removed from the frame 116 by moving the upper body 120 away from the base 118 and removing the liquid transport structure 50 from the second interface member 94.

[0149] When the liquid transport structure 50 is coupled with the frame 116, the sensors 10 can be in electrical communication with electronics (not shown) for operating the sensors 10. This electrical communication can be achieved by inserting the pads 34 of the chip into a port that provides electrical communication between the sensors 10 and the electronics before or after the liquid transport structure 50 is coupled with the assay equipment.

[0150] The upper body 120 of the frame 116 and/or the lower body of the frame 116 can include a chamber 122 where various equipment is positioned. For instance, a chamber 122 can hold the pumps, vacuums, valves and/or electronics discussed above. Alternatively, the pumps, vacuums, valves and/or electronics can be located outside of the frame 116. The electronics can operate the pumps, vacuums and valves so as to create the desired pressure in the channels of the liquid transport structure 50. Accordingly, the electronics can control the transport of the liquid from a reservoir into the assay chamber.

[0151] Figure 18C is a cross section of assay equipment that is suitable for use with a liquid transport structure 50 constructed according to Figure 10A through Figure 10C. The base 118 holds a second interface member 94 constructed according to Figure 17C. The base 118 also holds a plurality of sealing mechanisms extending through the second interface member 94. Each sealing mechanism 72 is coupled with an actuator 126 configured to independently move each sealing mechanism 72 through the associated guide lumen 114. A suitable actuator 126 includes, but is not limited to, a stepped motor, a

linear actuator or a bubble actuator. Electronics (not shown) can control the actuators. For instance, the electronics can engage a particular actuator to move a sealing mechanism through the associated guide lumen 114 and unseal an inlet channel 66. Accordingly, the electronics can control the transport of the liquid from the liquid transport structure 50 onto a sensor 10.

[0152] The sealing mechanisms shown in Figurer 18C can be replaced with the instruments discussed in Figure 11A through Figure 11G. Accordingly, the actuator 126 can be employed to move the instrument 76 into contact with a diaphragm on the liquid transport structure.

[0153] Although the first interface member and the second interface member are shown as being independent of the frame, the first interface member and/or the second interface member can be integrated into the frame.

[0154] Although the liquid transport structure is illustrated above as being constructed from a first member and a second member, the first member and the second member can be formed into a single piece. As a result, the liquid transport structure can have a one-piece construction or a multi-piece construction.

[0155] Although the liquid transport structure is disclosed in the context of a particular sensor embodiment, the liquid transport structure can be employed other sensor types and constructions. For instance, the liquid transport structure can be employed with sensors other than electrochemical sensors. Further, the sensor need not be limited to detection of biological agents and can be a sensor for the detection of other agents such as chemicals and particulates, electrolytes and molecules.

[0156] Other embodiments, combinations and modifications of this invention will occur readily to those of ordinary skill in the art in view of these teachings. Therefore, this invention is to be limited only by the following claims, which include all such embodiments and modifications when viewed in conjunction with the above specification and accompanying drawings.

CLAIMS

What is claimed is:

1. An apparatus for use with an assay, comprising:

a liquid transport structure configured to hold a sensor for detecting one or more components in a liquid, the liquid transport structure having;

a reservoir configured to hold a liquid within the liquid transport structure; and

an outlet channel configured to transport a liquid held in the reservoir to a sensor held by the liquid transport structure.

2. The apparatus of claim 1, wherein the liquid transport structure is configured to hold a plurality of sensors.

3. The apparatus of claim 1, further comprising:

a sensor structure held by the liquid transport structure, the sensor structure having one or more sensors for detecting a component in a liquid.

4. The apparatus of claim 3, wherein

the sensor structure includes a plurality of sensors;

the reservoir is one of a plurality of reservoirs configured to hold a liquid within the liquid transport structure; and

the liquid transport structure includes a plurality of channels that are each configured to transport a liquid from a reservoir to a sensor.

5. The apparatus of claim 4, wherein the liquid transport structure defines a common chamber over a plurality of the sensors.

6. The apparatus of claim 1, wherein the liquid transport structure includes an inlet channel extending from an external side of the liquid transport structure to the reservoir.

7. The apparatus of claim 6, wherein a diaphragm obstructs the inlet channel.

8. The apparatus of claim 7, wherein the diaphragm is impermeable to liquids.

9. The apparatus of claim 8, wherein the diaphragm is flexible.

10. The apparatus of claim 1, wherein the outlet channel includes an obstruction positioned so as to obstruct the outlet channel.

11. The apparatus of claim 10, wherein the obstruction includes one or more openings through which the liquid in the reservoir can flow.

12. The apparatus of claim 1, wherein the liquid transport structure is substantially block shaped.

13. The apparatus of claim 1, wherein the liquid transport structure has a volume less than 16 cubic inches.

14. The apparatus of claim 1, wherein the liquid transport structure is configured to be coupled with and removed from an interface system, the interface system providing liquid communication between the reservoir and a tube.

15. The apparatus of claim 14, wherein the liquid transport structure is configured to be clamped between two or more members of the interface system.

16. The apparatus of claim 1, wherein the liquid transport structure defines an assay chamber over the sensor.

17. The apparatus of claim 16, wherein at least one channel extends from an external side of the liquid transport structure to a lateral side of the assay chamber.

18. The apparatus of claim 17, wherein the at least one channel includes a nozzle.

19. The apparatus of claim 16, wherein a channel extends from the assay chamber to an external side of the liquid transport structure.

20. The apparatus of claim 18, wherein a diaphragm obstructs the channel.

21. The apparatus of claim 19, wherein the diaphragm includes one or more openings through which a fluid can flow.

22. The apparatus of claim 1, wherein the liquid transport structure includes a first member positioned over the sensor and a second member positioned under the sensor.

23. The apparatus of claim 22, wherein at least one member includes a base and a cover, the cover and the base each defining a portion of the reservoir, the member being selected from a group consisting of the first member and the second member.

24. The apparatus of claim 1, wherein the sensor includes a plurality of electrodes positioned on a sensor support.

25. The apparatus of claim 24, wherein the electrodes include a reference electrode and a counter electrode that are each spaced apart from a working electrode.

26. The apparatus of claim 25, wherein each of the electrodes are positioned on an electrode support bonded to the sensor support.

27. The apparatus of claim 26, wherein the electrode support includes a first support region spaced apart from a second support region, one or more of the electrodes positioned on the first support region and one or more of the electrodes positioned on the second support region.

28. An apparatus for use with an assay, comprising:

a liquid transport structure having a reservoir configured to hold a liquid within the liquid transport structure; and

an outlet channel configured to transport a liquid held in the reservoir to a chamber within the liquid transport structure.

29. The apparatus of claim 28, wherein

the reservoir is one of a plurality of reservoirs configured to hold a liquid within the liquid transport structure; and

the liquid transport structure includes a plurality of channels that are each configured to transport a liquid from a reservoir to the chamber.

30. The apparatus of claim 28, wherein the liquid transport structure includes an inlet channel extending from an external side of the liquid transport structure to the reservoir.

31. The apparatus of claim 30, wherein a diaphragm obstructs the inlet channel.

32. The apparatus of claim 31, wherein the diaphragm is impermeable to liquids.

33. The apparatus of claim 28, wherein a channel extends from the chamber to an external side of the liquid transport structure.

34. The apparatus of claim 33, wherein a diaphragm obstructs the channel.

35. The apparatus of claim 34, wherein the diaphragm includes one or more openings through which a fluid can flow.

36. The apparatus of claim 28, wherein the outlet channel includes an obstruction positioned so as to obstruct the outlet channel.

37. The apparatus of claim 36, wherein the obstruction includes one or more openings through which the liquid in the reservoir can flow.

38. The apparatus of claim 28, wherein the liquid transport structure is substantially block shaped.

39. The apparatus of claim 28, wherein the liquid transport structure has a volume less than 16 cubic inches.

40. The apparatus of claim 28, wherein a plurality of channels extend from an external side of the liquid transport structure to a lateral side of the chamber.

41. A sensor, comprising:

an electrode support including a first support region spaced apart from a second support region;

one or more electrodes positioned on the first support region; and

one or more of the electrodes positioned on the second support region.

42. The sensor of claim 41, wherein one or more tethers connect the first support region to the second support region.

43. The sensor of claim 41, wherein a portion of an electrode on the second support region extends across a tether onto the first support region.

44. The sensor of claim 41, wherein the first support region substantially surrounds the second support region.

45. The sensor of claim 41, wherein a plurality of electrodes are positioned on the first support region and a single electrode is positioned on the second support region.

46. The sensor of claim 41, wherein a working electrode is positioned on the second support region, a reference electrode is positioned on the first support region and a counter electrode is positioned on the first support region.

47. The sensor of claim 46, wherein the working electrode has more surface area than the counter electrode and more surface area than the reference electrode.

48. The sensor of claim 41, wherein a gap between the first support region and the second support region does not exceed 2 mm.

49. The sensor of claim 41, wherein the electrode support is one of a plurality of electrode supports positioned on a sensor support.

50. A method for performing an assay, comprising:

changing the pressure on a liquid stored in a reservoir of a liquid transport structure so as to transport at least a portion of the liquid from the reservoir into a chamber within the liquid transport structure.

51. The method of claim 50, wherein changing the pressure on the liquid includes increasing pressure in an inlet channel extending from an external side of the liquid transport structure to the reservoir.

52. The method of claim 50, wherein increasing pressure in the inlet channel includes advancing a diaphragm obstructing the inlet channel from a first position to a position further in the inlet channel.

53. The method of claim 50, further comprising:

repeatedly advancing a diaphragm obstructing the inlet channel from a first position to a position further in the inlet channel so as to agitate the liquid transported onto the sensor after transporting the liquid onto the sensor.

54. The method of claim 50, wherein changing the pressure on the liquid includes reducing pressure in an outlet channel extending from the reservoir to the chamber.

55. The method of claim 50, wherein a sensor is positioned in the chamber and the at least a portion of the liquid is transported onto the sensor, the sensor being configured to detect a component in a liquid.

56. The method of claim 56, further comprising:

applying a potential between a working electrode and a reference electrode of the sensor while monitoring current passing through a circuit that includes the working electrode, the liquid and a counter electrode of the sensor.

57. A method for performing an assay, comprising:

applying one or more liquids to a sensor such that a target agent bonds to the sensor along with one or more non-target agents, the sensor configured to detect a component in a liquid and including two or more electrodes positioned on a sensor support; and

removing agents from the sensor such that the portion of the non-target agents removed is larger than the portion of target agents that are removed.

58. The method of claim 57, wherein removing agents from the sensor includes flowing a liquid across the sensor.

59. The method of claim 58, wherein the liquid is flowed across the sensor so as to generate a shear flow pattern on the sensor.

60. The method of claim 59, wherein a liquid transport structure defines a chamber over the sensor and flowing the liquid across the sensor includes flowing the liquid through the chamber.

61. The method of claim 59, wherein the chamber includes lateral sides and the liquid is flowed from a channel in one lateral side of the chamber to a channel in another lateral side of the chamber.

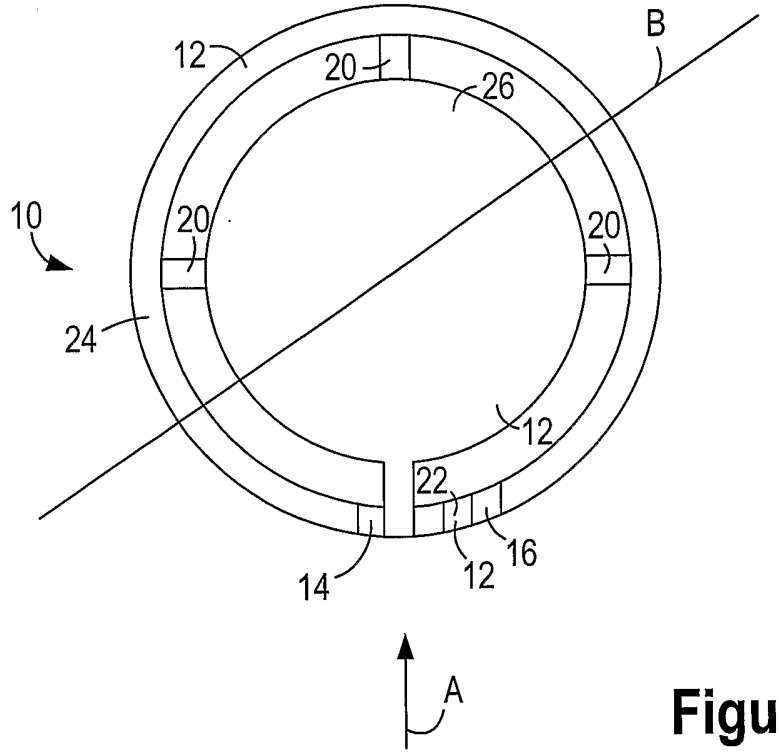


Figure 1A

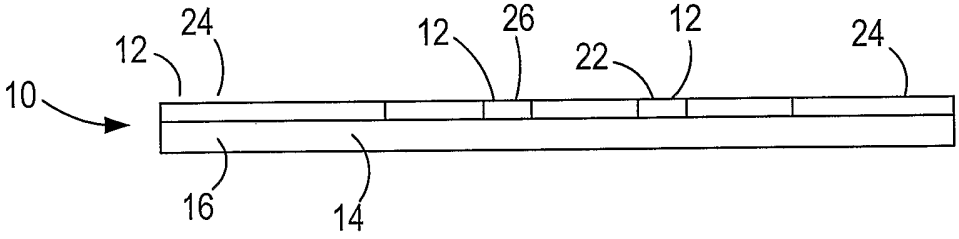


Figure 1B

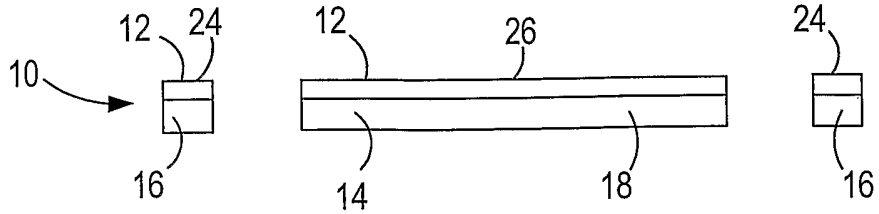


Figure 1C

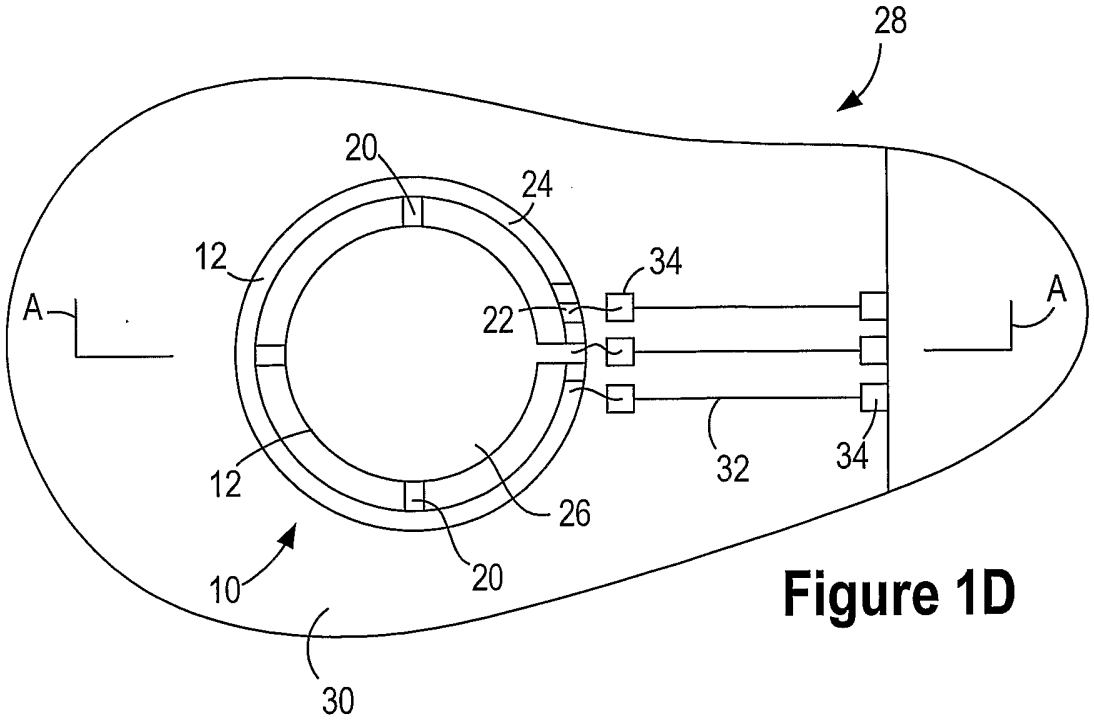


Figure 1D

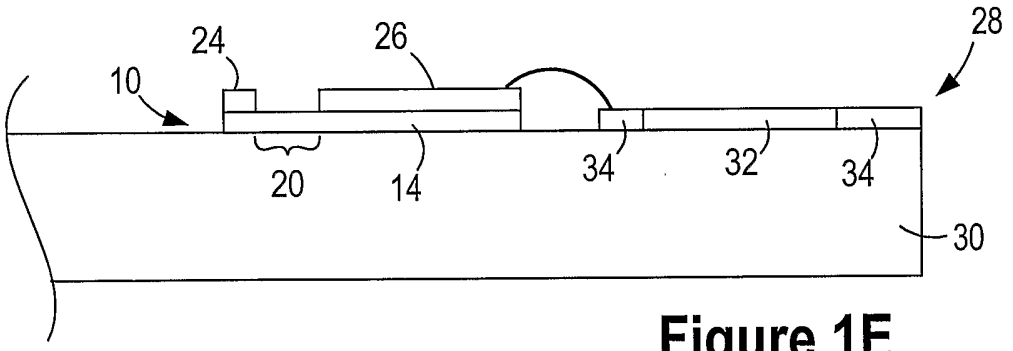


Figure 1E

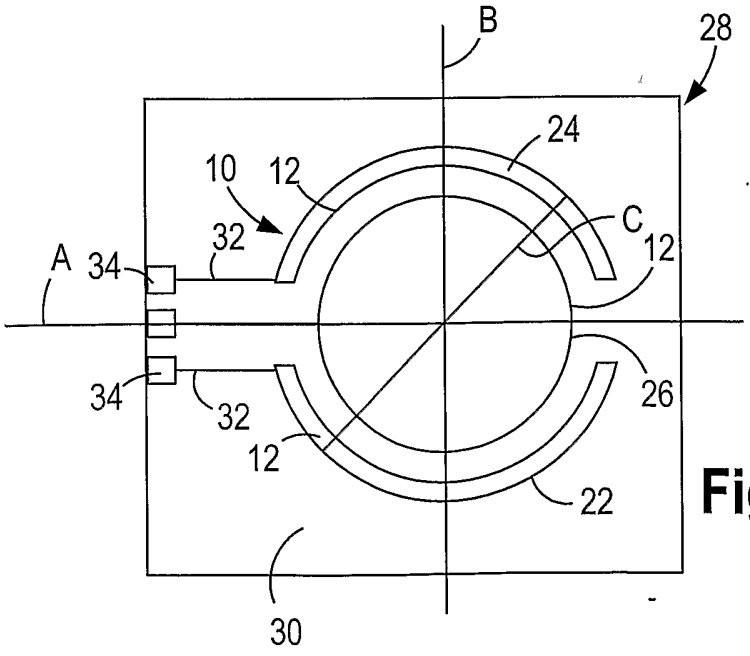


Figure 2A

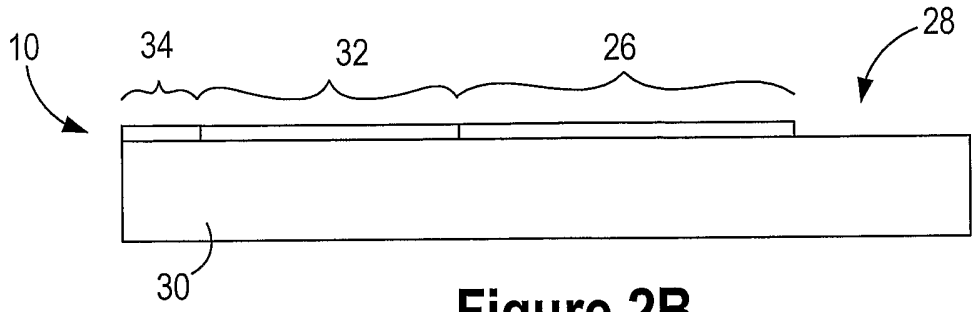


Figure 2B

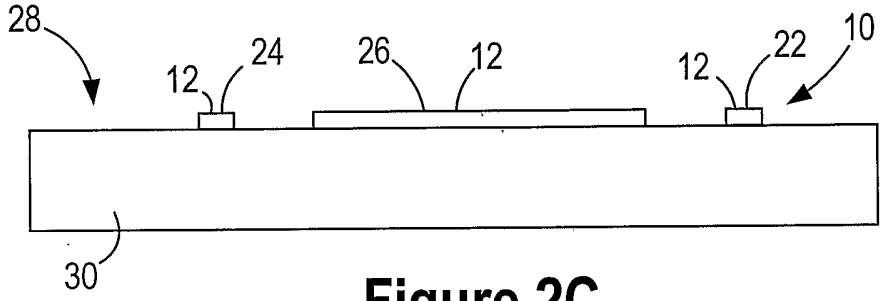


Figure 2C

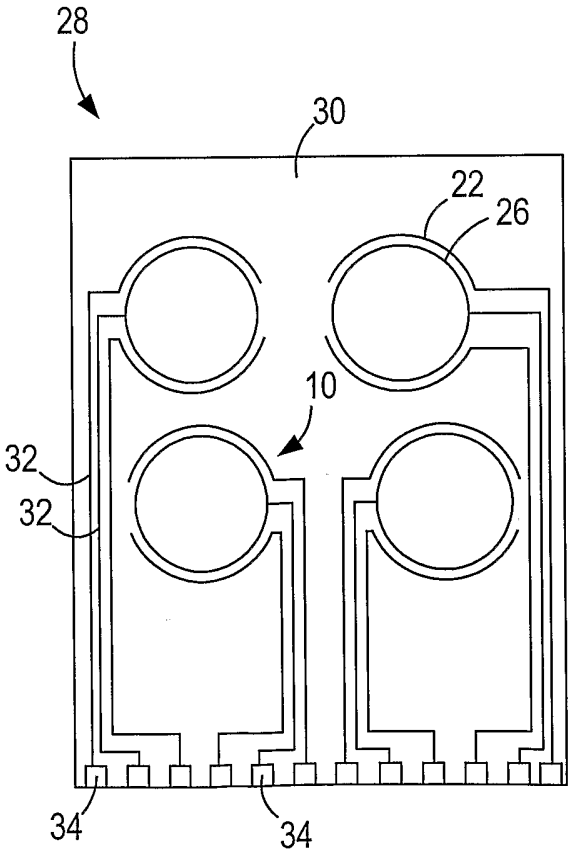


Figure 3

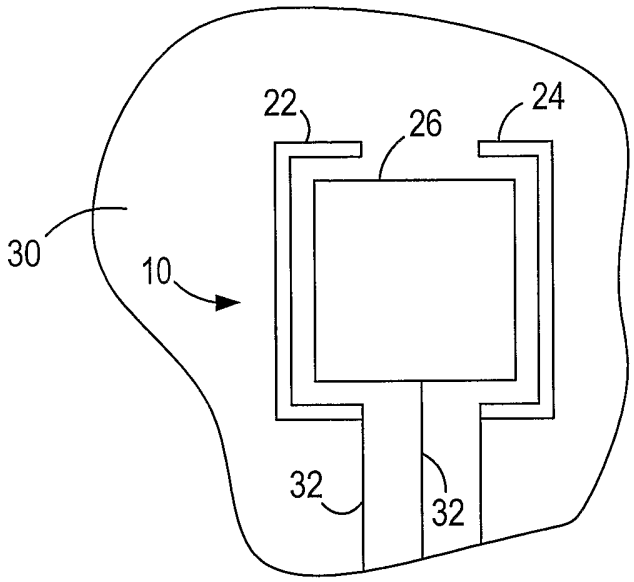


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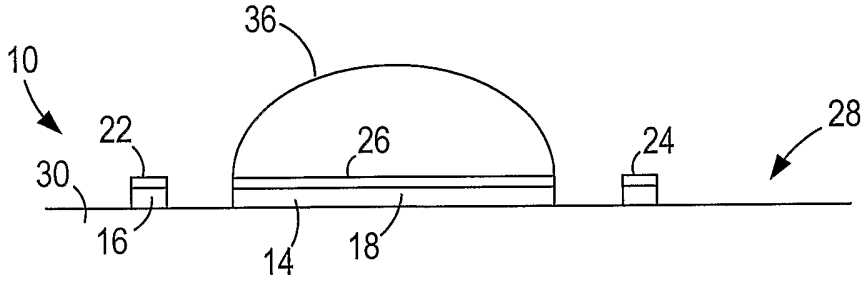


Figure 5A

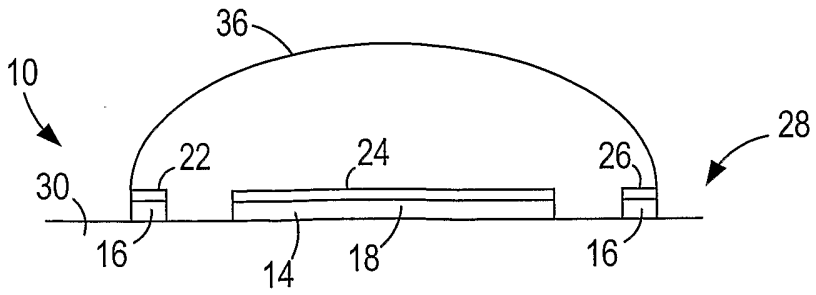


Figure 5B



Figure 6

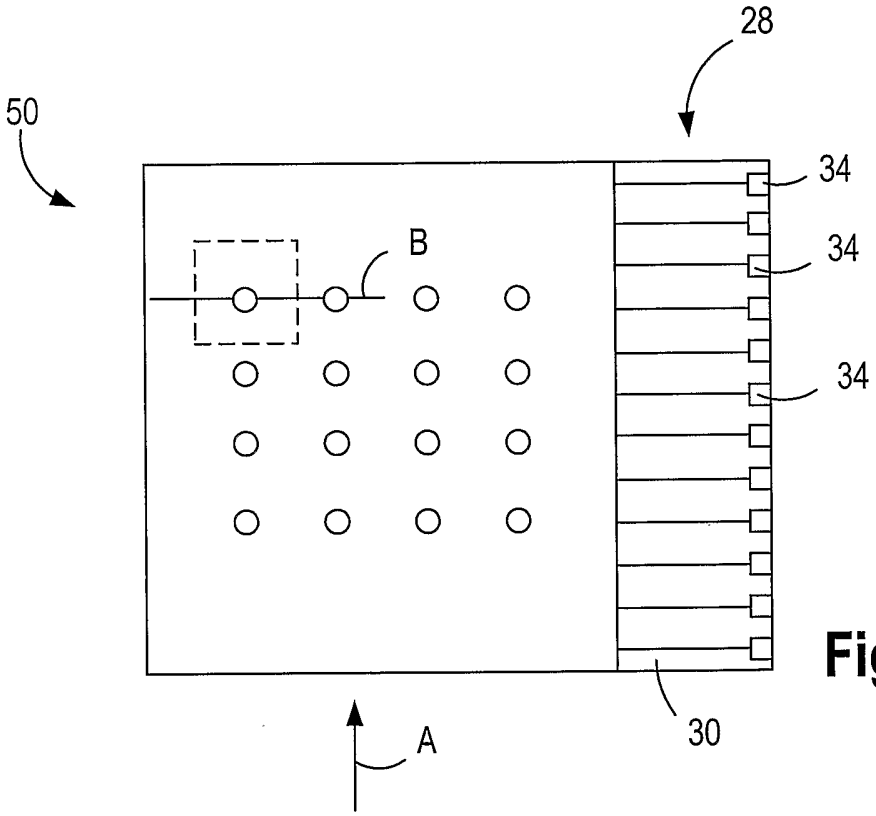


Figure 7A

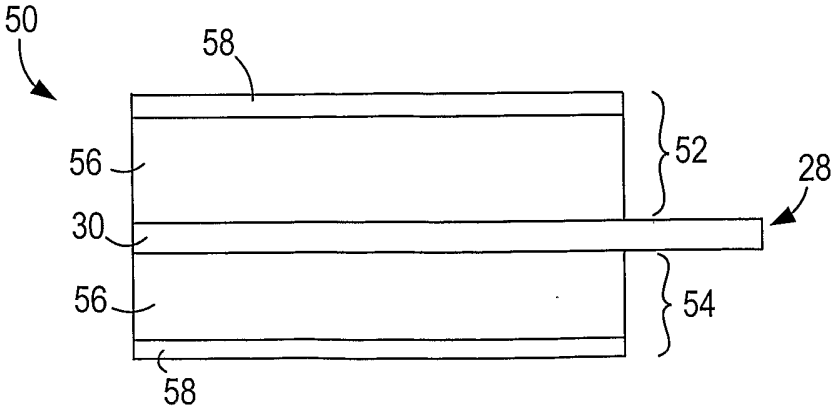


Figure 7B

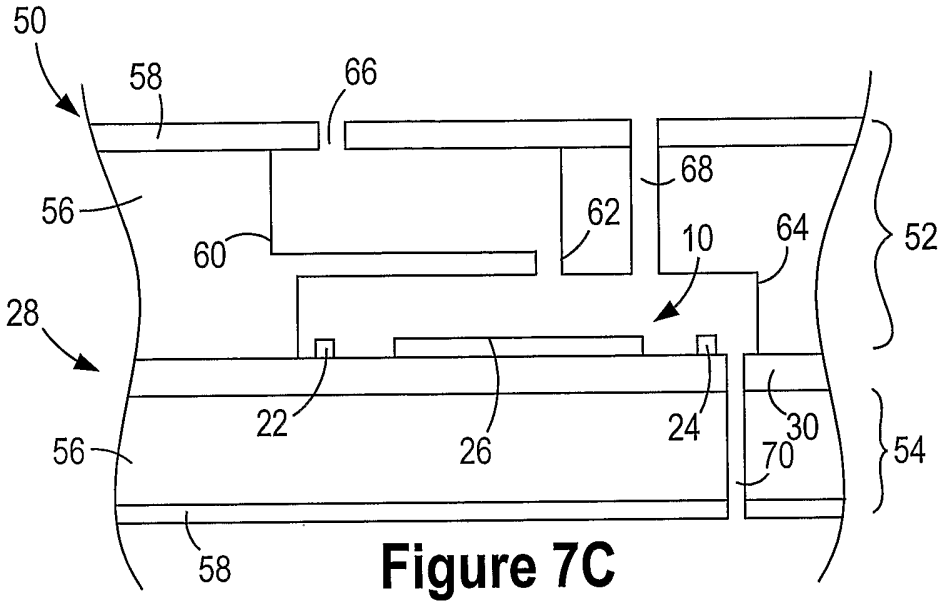


Figure 7C

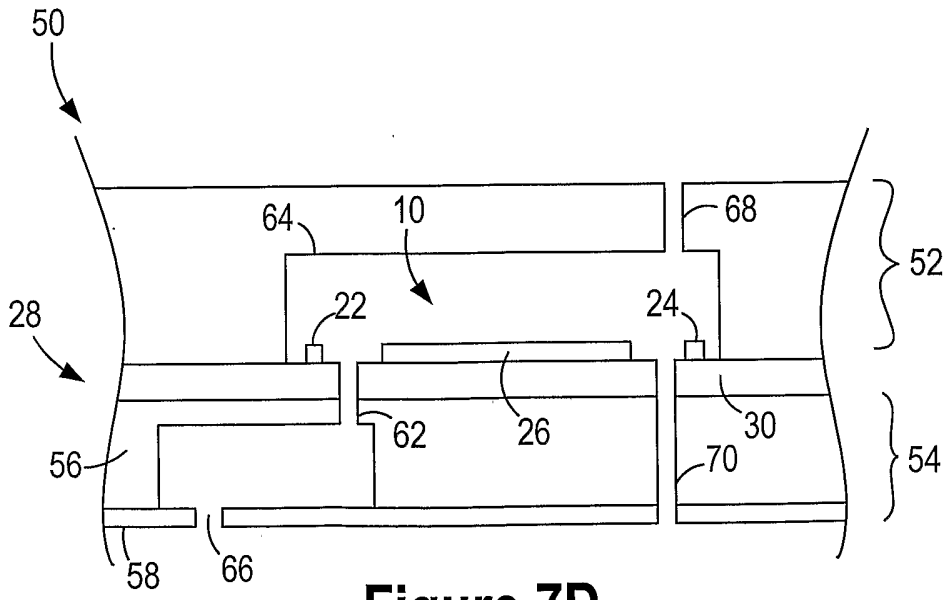


Figure 7D

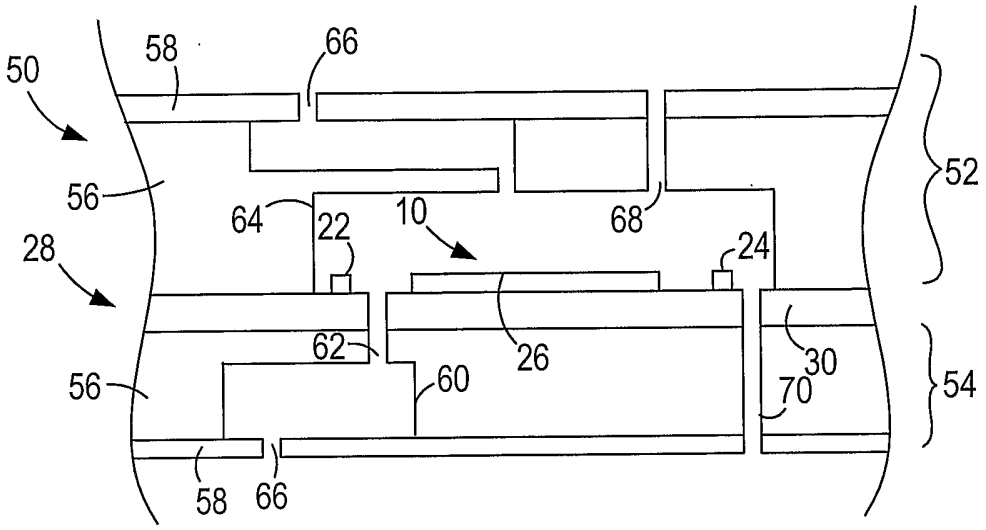


Figure 7E

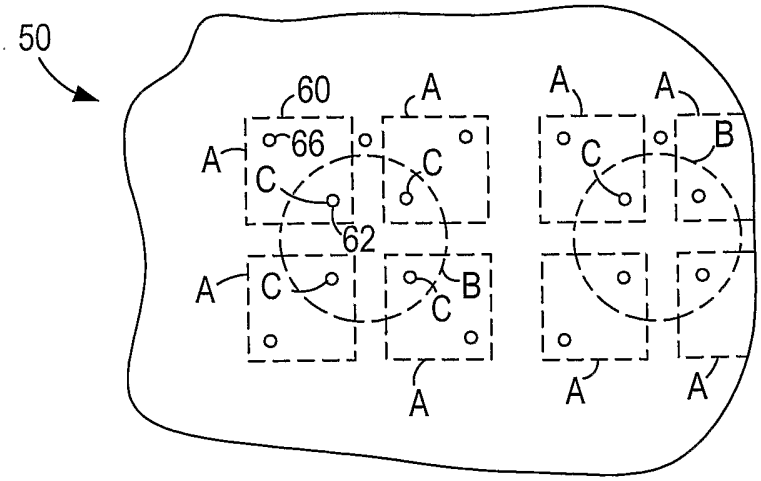


Figure 7F

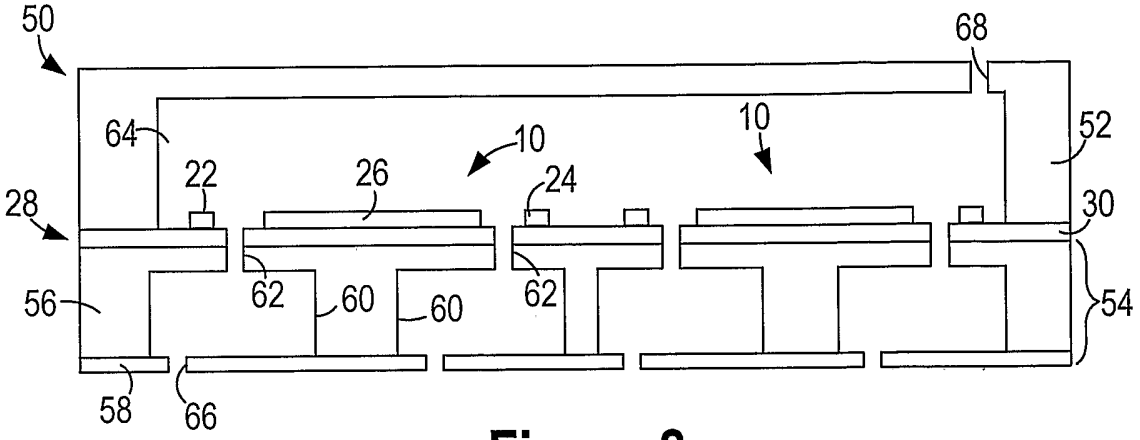


Figure 8

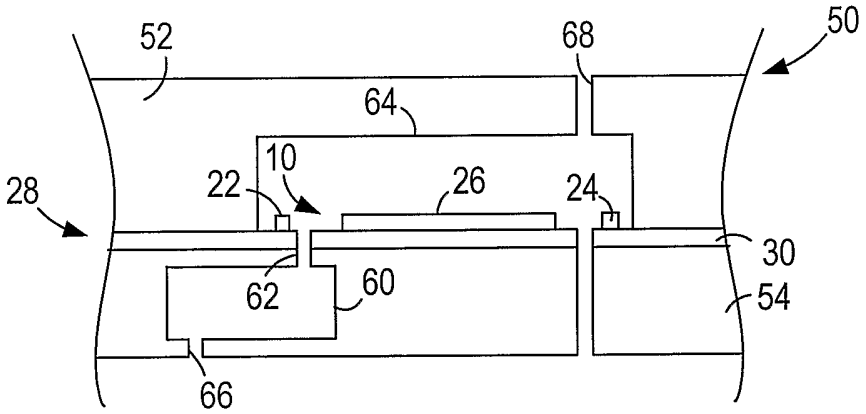


Figure 9A

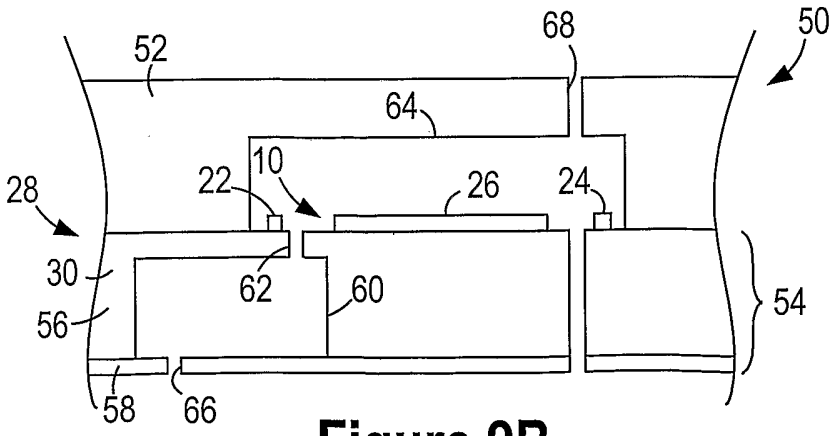


Figure 9B

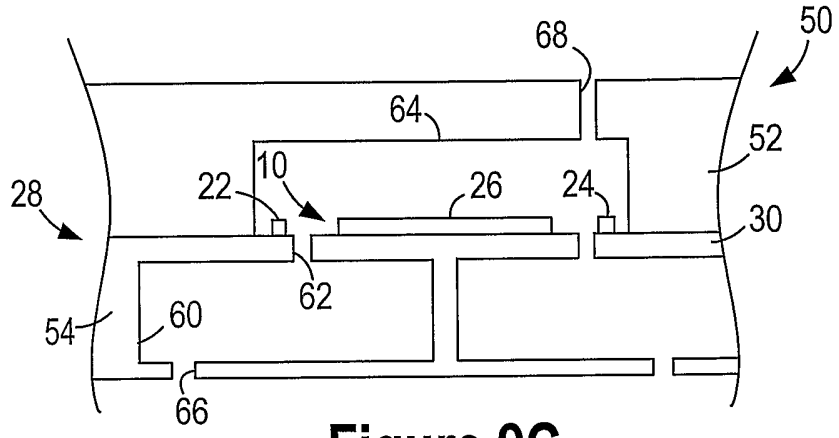


Figure 9C

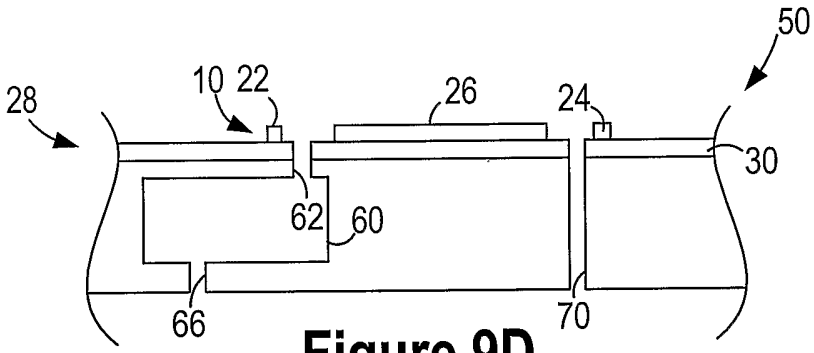


Figure 9D

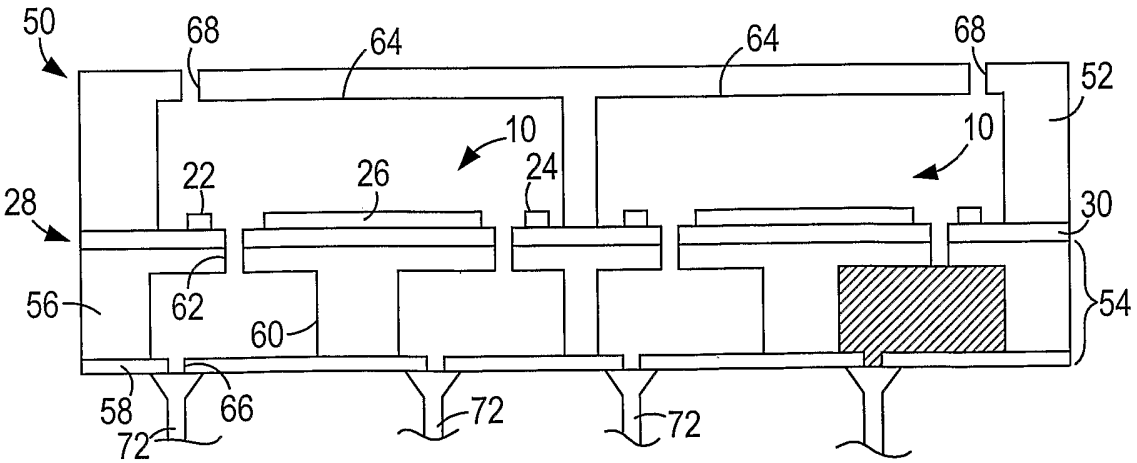


Figure 10A

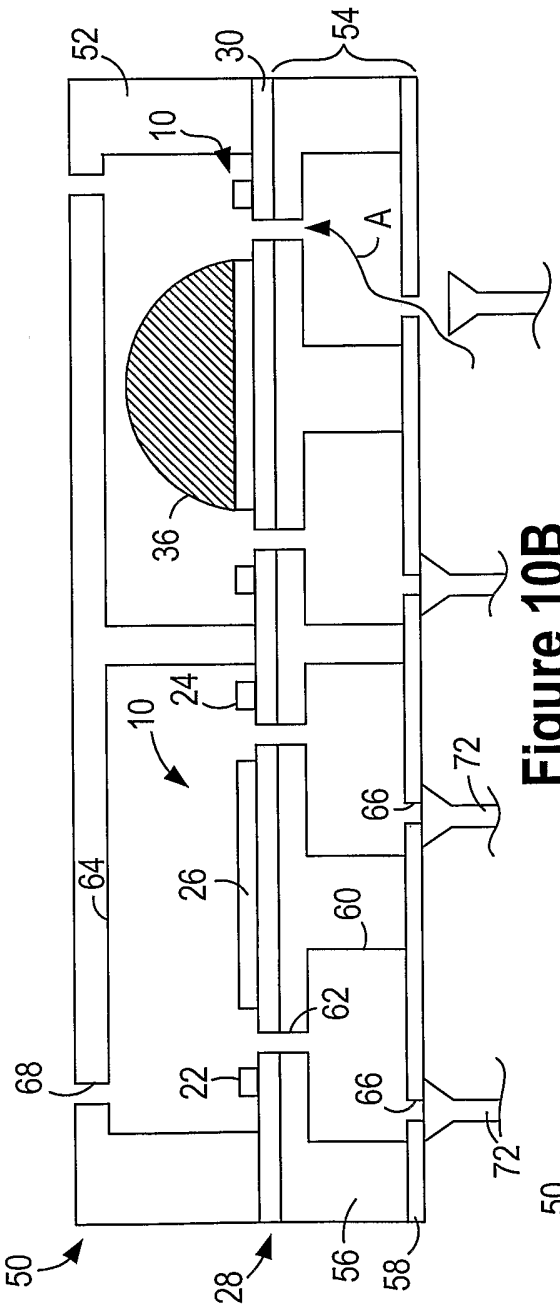


Figure 10B

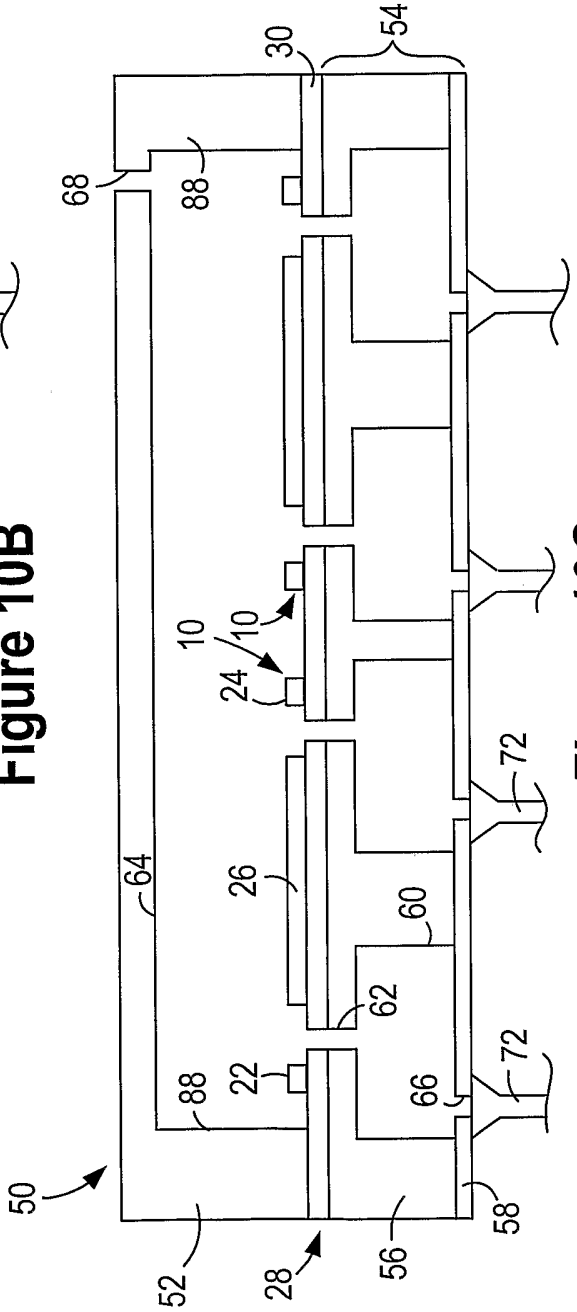


Figure 10C

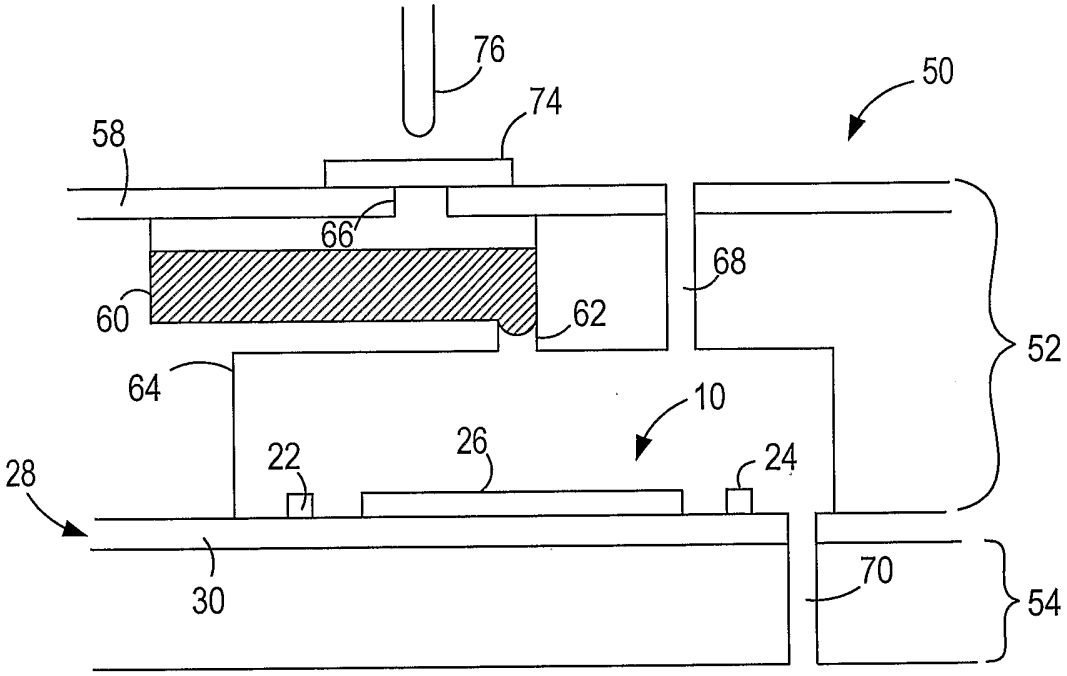


Figure 11A

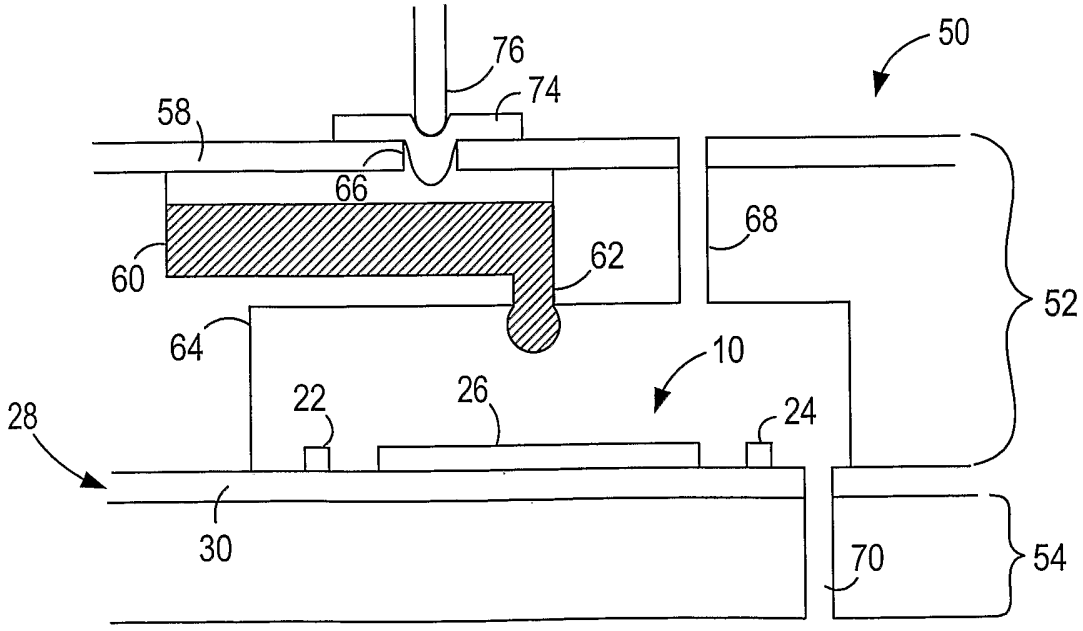


Figure 11B

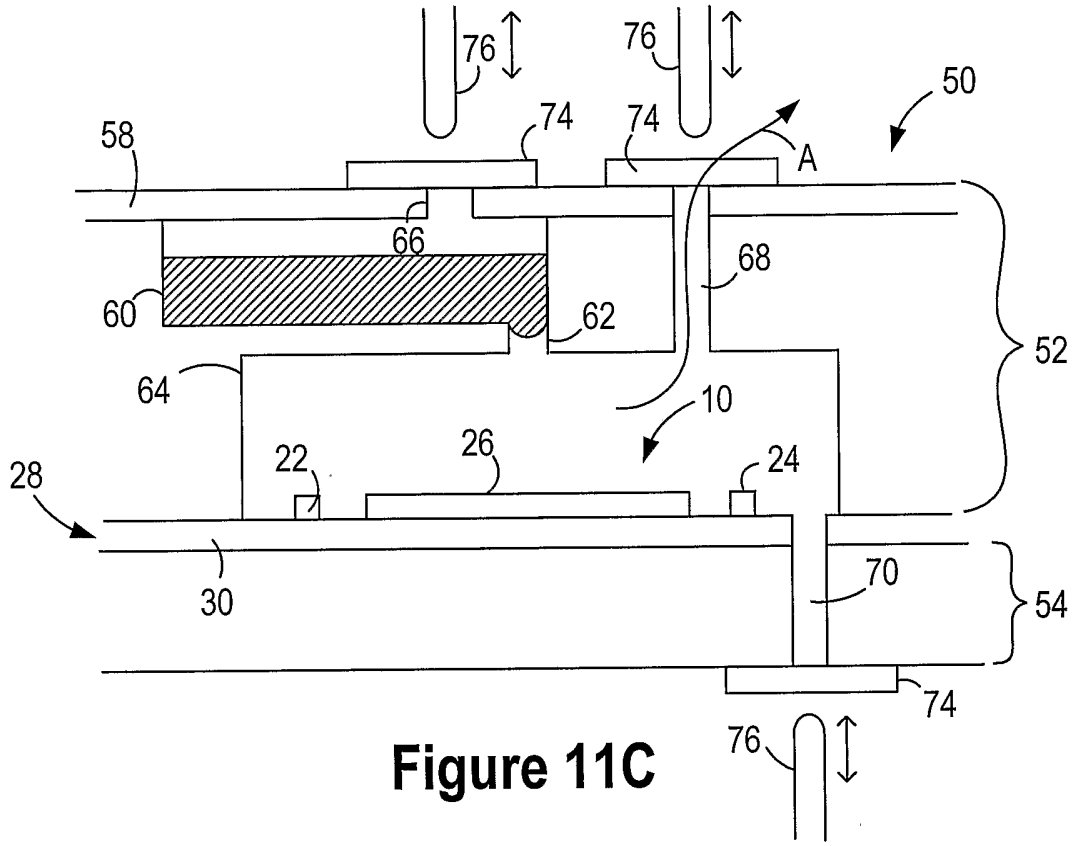


Figure 11C

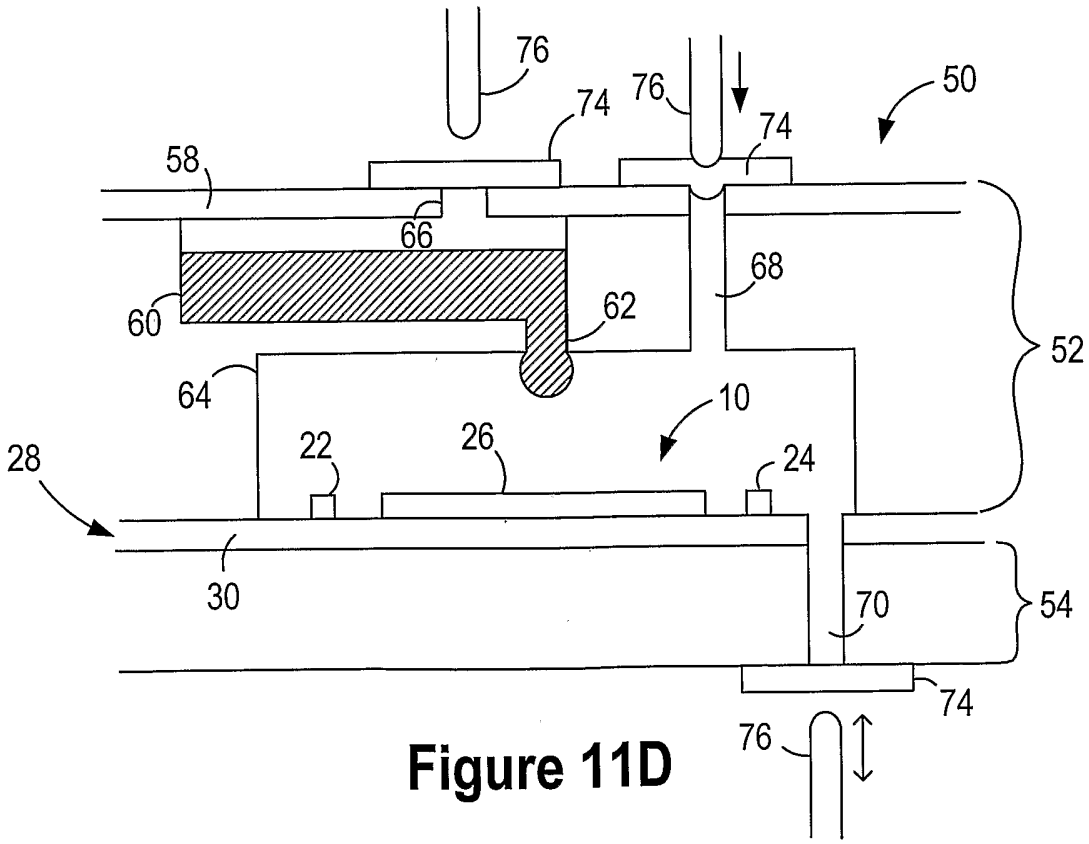


Figure 11D

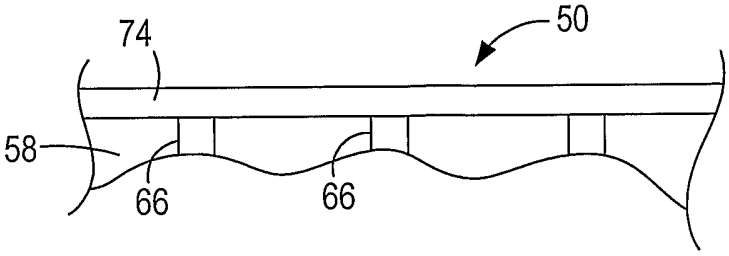


Figure 11E

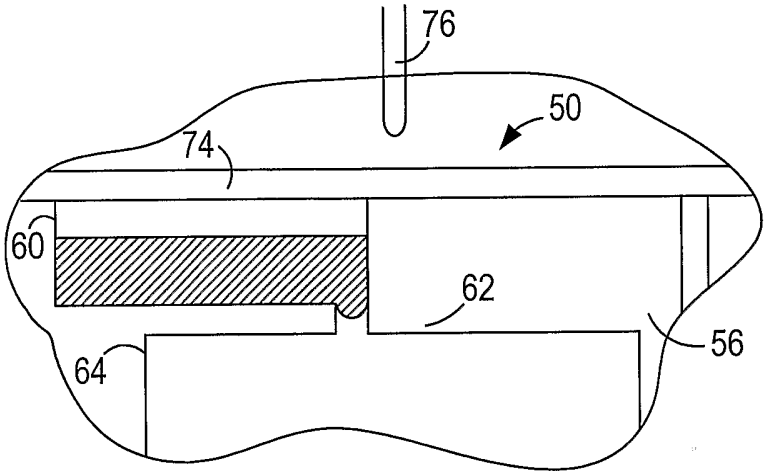


Figure 11F

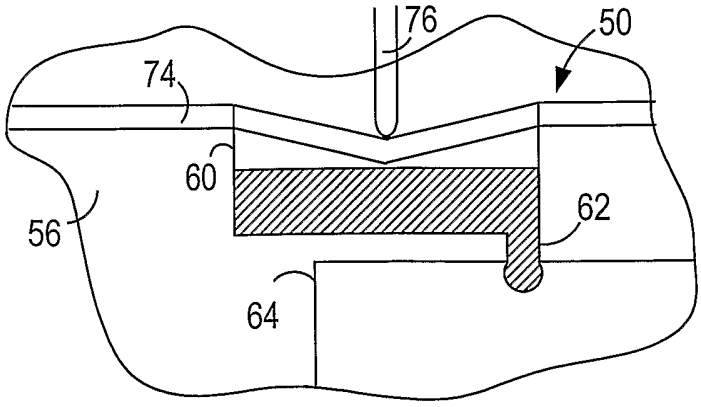


Figure 11G

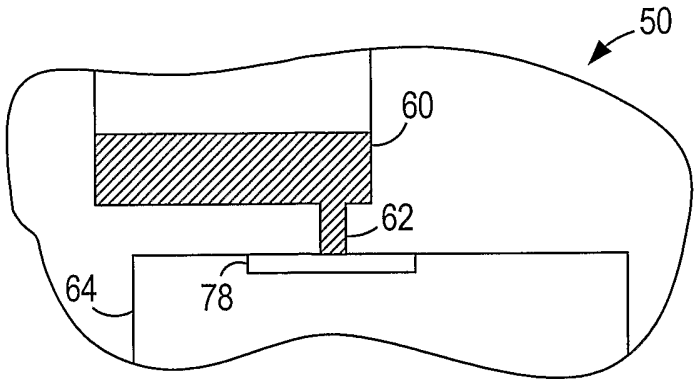


Figure 12

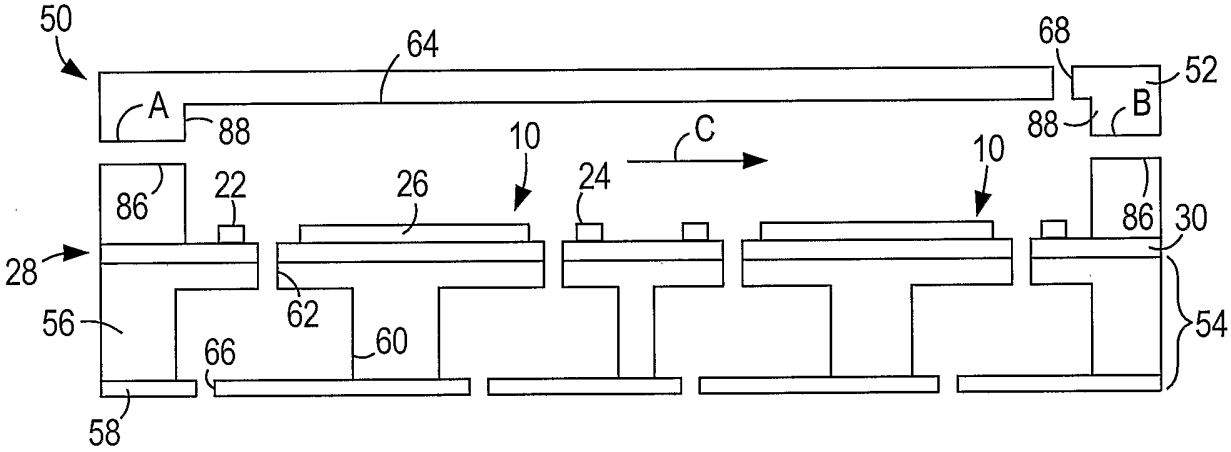


Figure 13A

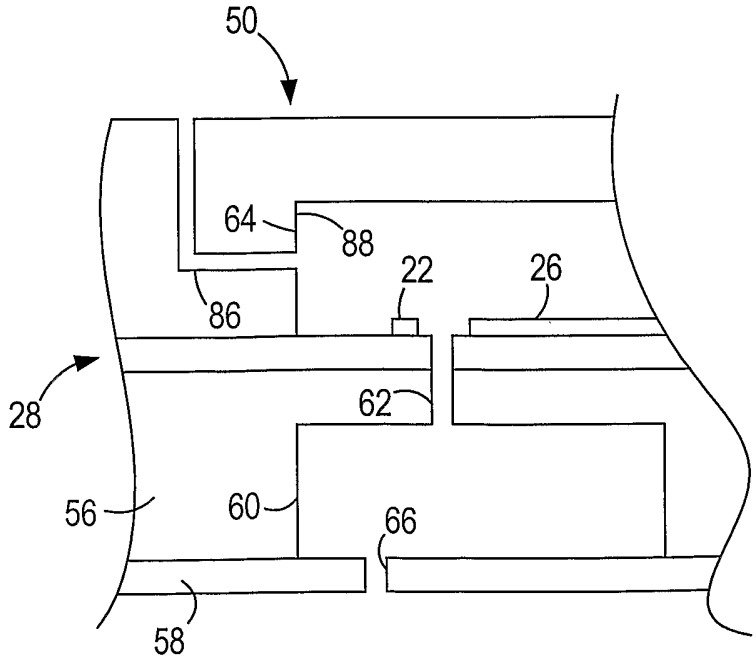


Figure 13B

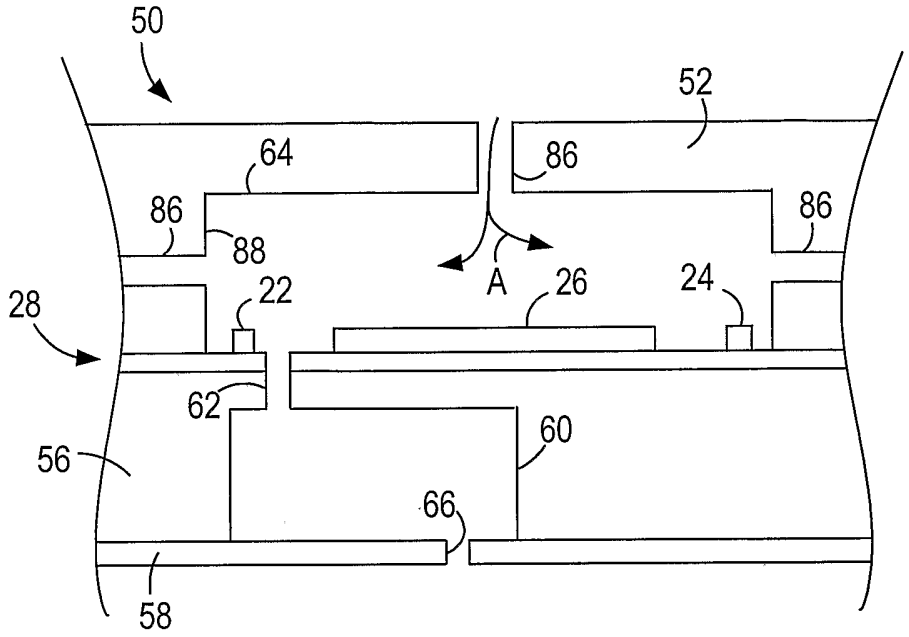


Figure 13C

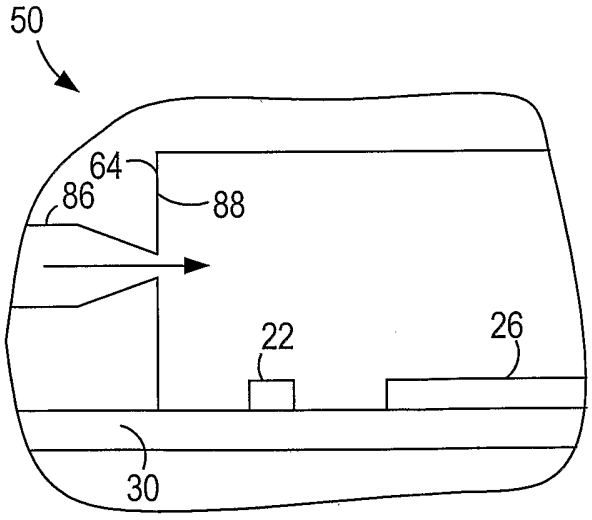


Figure 13D

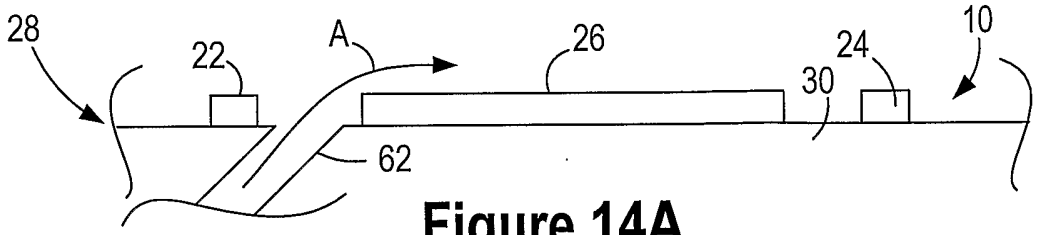


Figure 14A

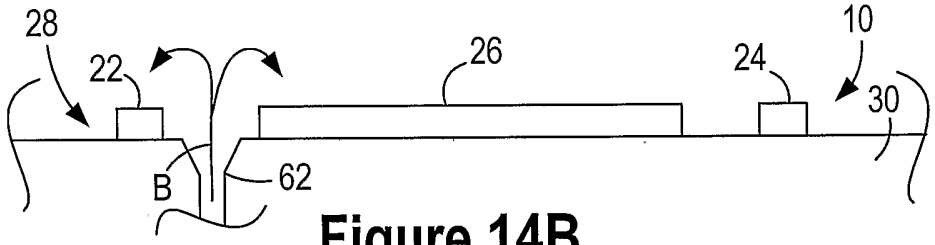


Figure 14B

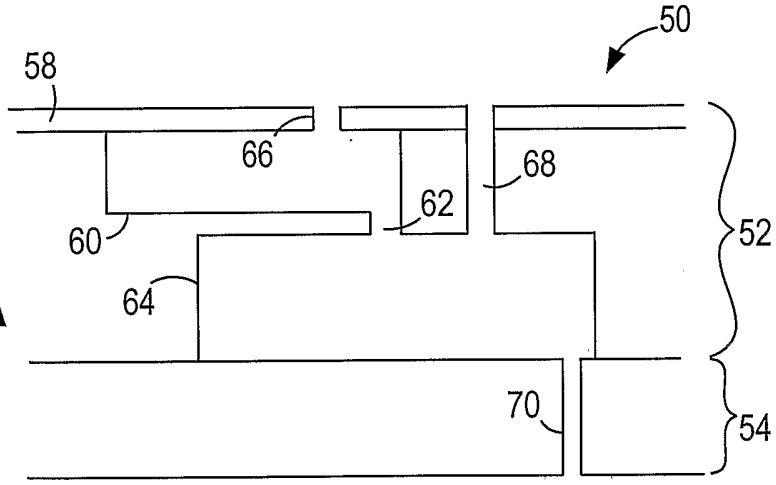


Figure 15A

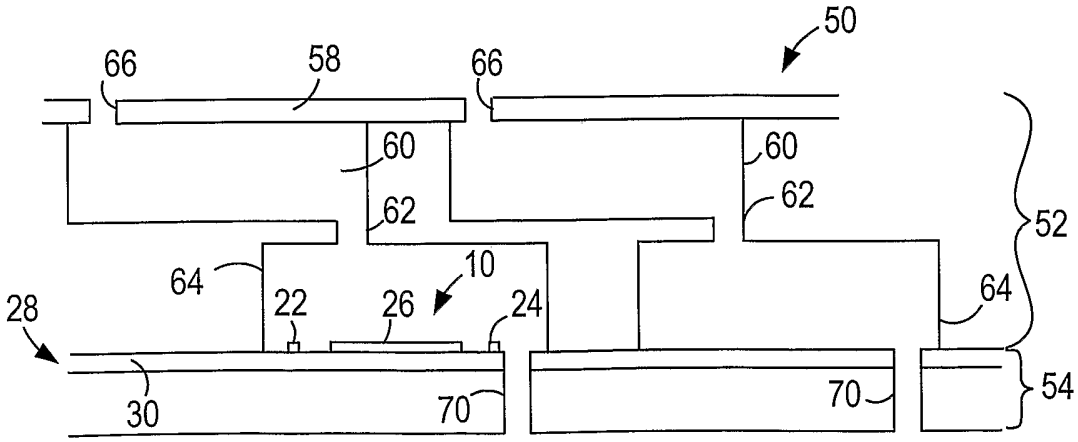


Figure 15B

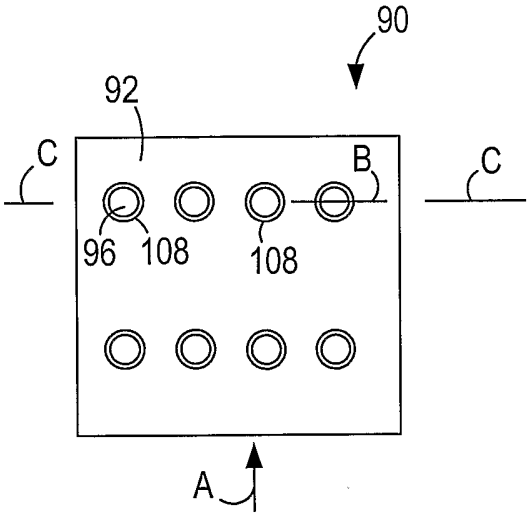


Figure 16A

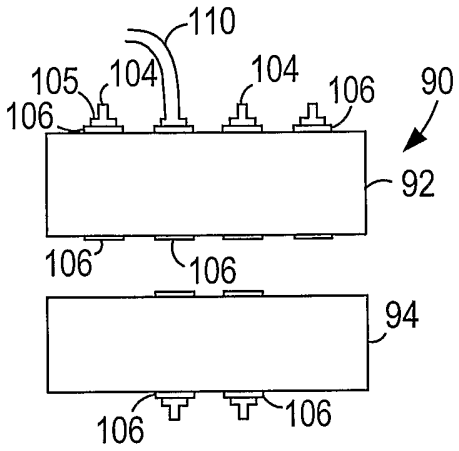


Figure 16B

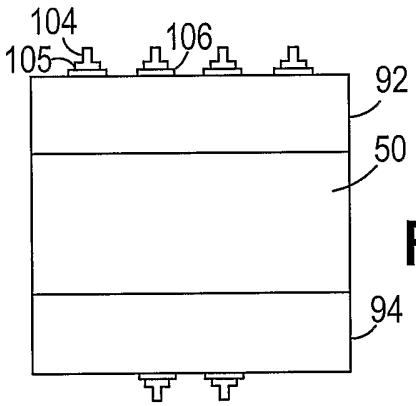


Figure 16C

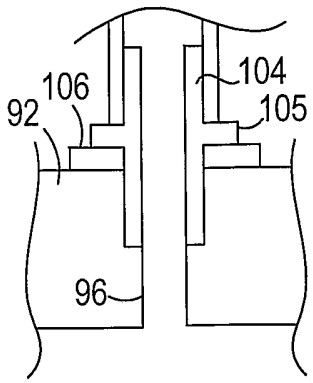


Figure 16D

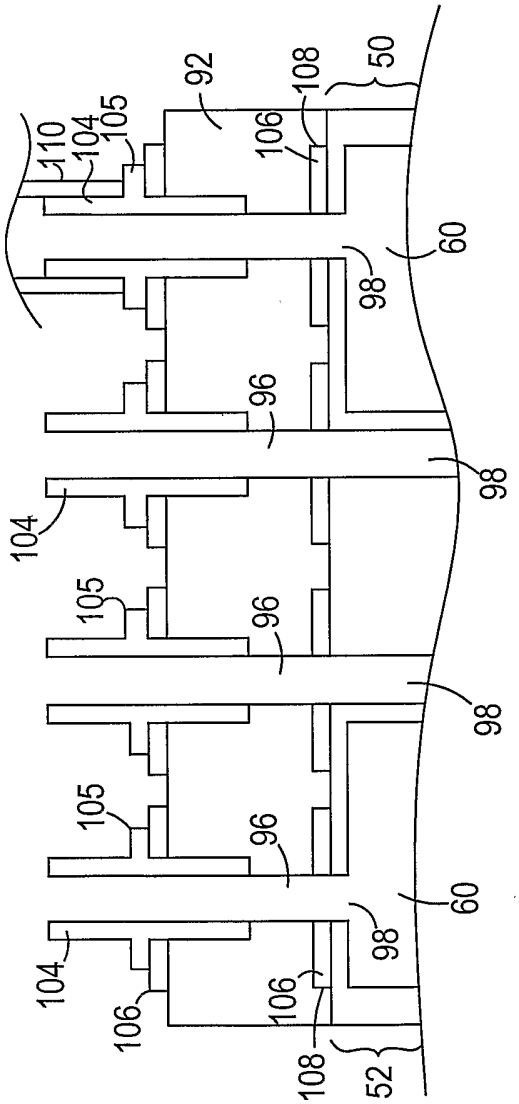


Figure 16E

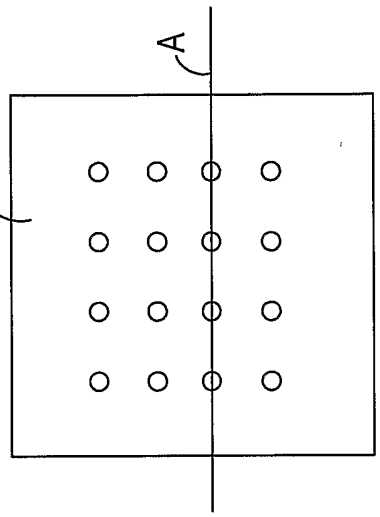


Figure 17B

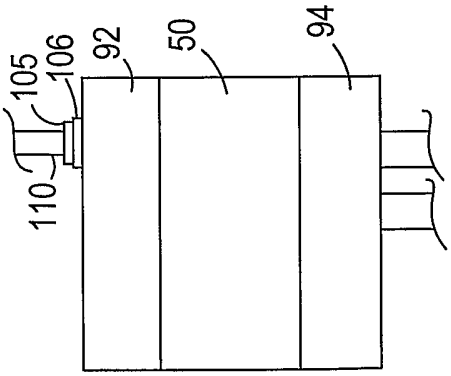


Figure 17A

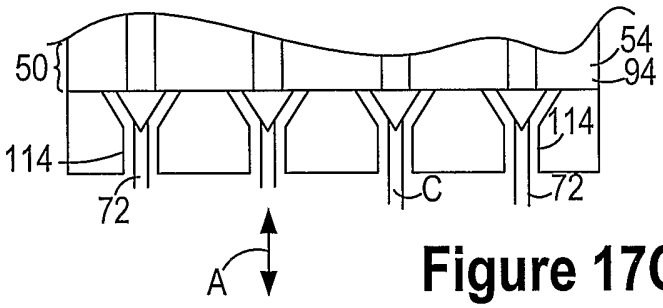


Figure 17C

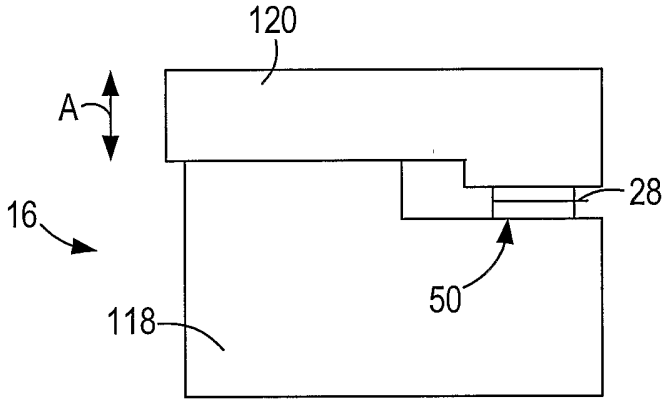


Figure 18A

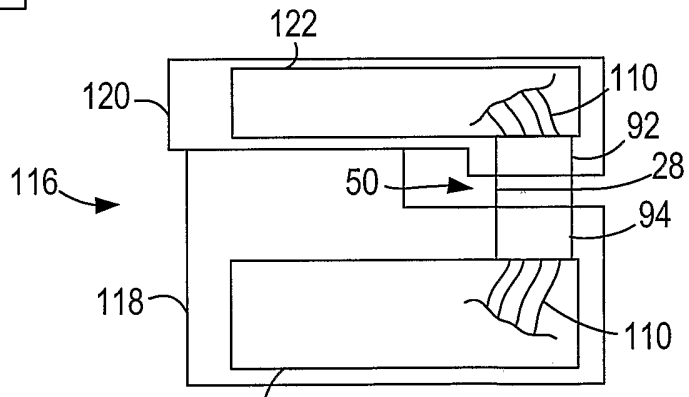


Figure 18B

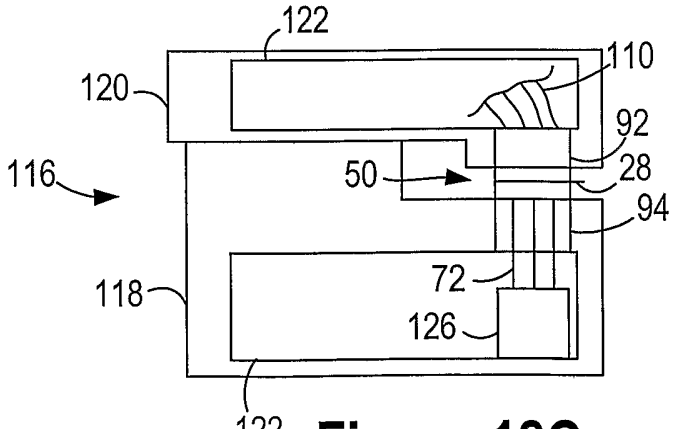


Figure 18C

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/39809

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N 27/403; B01L 3/02
US CL : 204/403.01,409; 422/58,100,102

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)
U.S. : 204/403.01,409; 422/58,100,102

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 4,426,451 A (COLUMBUS) 17 January 1984 (17.01.1984), fig. 1, 2, col. 1, lines 40-45, col. 4, line 5 through col. 6, line 49.	1-6,10-19, 22,23, 28-30, 33, 36-40 --- 7-9, 20, 21, 24-27, 31, 32, 34, 35
Y	US 6,117,290 A (SAY et al) 12 September 2000 (12.09.2000), fig. 1, 3, 4, col. 6, lines 54-64 and col. 9, line 28 through col. 10, line 16.	7-9,20,21,24-27, 31, 332, 34, 35
A	US 4,323,536 A (COLUMBUS) 06 April 1982 (06.04.1982), see entire document.	1-40
A	US 6,331,439 B1 (CHERUKURI et al) 18 December 2001 (18.12.2001), see entire document	1-40

☐ 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

"E" earlier application or patent published on or after the international filing date

"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)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"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

"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

"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

"&" document member of the same patent family

Date of the actual completion of the international search
09 April 2003 (09.04.2003)

Date of mailing of the international search report
28 APR 2003

Name and mailing address of the ISA/US
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Nam Nguyen
Telephone No. 703-308-0661

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/39809

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-40

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-40, drawn to liquid transport structure for use with assay.

Group II, claim(s) 41-49, drawn to a sensor having support regions for the electrodes.

Group III, claim(s) 50-56, drawn to a method of moving fluid through a liquid transport structure.

Group IV, claim(s) 57-61, drawn to method of applying target agent to a sensor.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature of groups I and III is a liquid transport structure not required of groups II or IV. The special technical feature of group II is an electrode support not required for groups I, III, and IV. The special technical feature of group IV is the application of target agents to sensor not required of groups I-III. Although groups I and III share a special technical feature, the special technical feature linking the two inventions (i.e. the liquid transport structure) is either obvious over or anticipated by US Patent 4,426,451. Accordingly, the liquid transport structure does not provide a contribution over the prior art, and no general inventive concept exists between groups I and III. Therefore, holding of lack of unity is proper.