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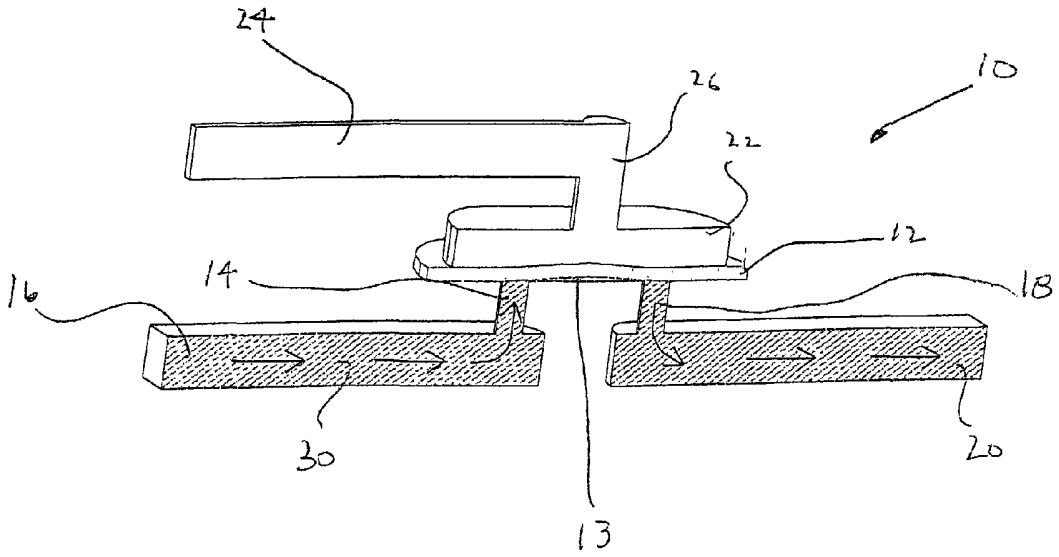
(54) Title: PNEUMATIC VALVE INTERFACE FOR USE IN MICROFLUIDIC STRUCTURES



(57) Abstract: A pneumatic valve for use in laminated plastic microfluidic structures. This zero or low dead volume valve allows flow through microfluidic channels for use in mixing, dilution, particulate suspension and other techniques necessary for flow control in analytical devices.

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PNEUMATIC VALVE INTERFACE FOR USE IN MICROFLUIDIC STRUCTURES

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application claims benefit from U.S. provisional Patent Application Serial No. 60/281,114, filed April 3, 2001, which application is incorporated herein by reference.

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates generally to microscale devices for performing analytical testing and, in particular, to a valve interface for use in laminated microfluidic structures.

2. Description of the Prior Art

Microfluidic devices have recently become popular for performing analytical testing. Using tools developed by the semiconductor industry to miniaturize electronics, it has become possible to fabricate intricate fluid systems which can be inexpensively mass produced. Systems have been developed to perform a variety of analytical techniques for the acquisition of information for the medical field.

Microfluidic devices may be constructed in a multi-layer laminated structure where each layer has channels and structures fabricated from a laminate material to form microscale voids or channels where fluids flow. A microscale channel is generally defined as a fluid passage which has at least one internal cross-sectional dimension that is less than 500 μm and typically between about 0.1 μm and about 500 μm. The control and pumping of fluids through these channels is affected by either external pressurized fluid forced into the laminate, or by structures located within the laminate.

U.S. Patent No. 5,716,852 teaches a method for analyzing the presence and concentration of small particles in a flow cell using diffusion principles. This patent, the disclosure of which is incorporated herein by reference, discloses a channel cell system for detecting the presence of analyte particles in a sample stream using a laminar flow channel having at least two inlet means which provide an indicator stream and a sample stream, where the laminar flow channel has a depth sufficiently small to allow laminar flow of the streams and length sufficient to allow diffusion of particles of the analyte into the indicator stream to form a detection area, and having an outlet out of the channel to form a single mixed stream. This device, which is known at a T-Sensor, may contain an external detecting means for detecting changes in the indicator stream. This detecting means may be provided by any means known in the art, including optical means such as optical spectroscopy, or absorption spectroscopy of fluorescence.

U.S. Patent No. 5,932,100, which patent is also incorporated herein by reference, teaches another method for analyzing particles within microfluidic channels using diffusion principles. A mixture of particles suspended in a sample stream enters an extraction channel from one upper arm of a structure, which comprises microchannels in the shape of an "H". An extraction stream (a dilution stream) enters from the lower arm on the same side of the extraction channel and due to the size of the microfluidic extraction channel, the flow is laminar and the streams do not mix. The sample stream exits as a by-product stream at the upper arm at the end of the extraction channel, while the extraction stream exits as a product stream at the lower arm. While the streams are in parallel laminar flow in the extraction channel, particles having a greater diffusion coefficient (smaller particles such as albumin, sugars, and small ions) have time to diffuse into the extraction stream, while the larger particles (blood cells) remain in the sample stream. Particles in the exiting extraction stream (now called the product stream) may be analyzed without interference from the larger particles. This microfluidic structure, commonly known as an "H-Filter," can be used for extracting desired particles from a sample stream containing those particles.

Several types of valves are commonly used for fluid management in flow systems. Flap valves, ball-in-socket valves, and tapered wedge valves are a few of the valve types existing in the macroscale domain of fluid control. However, in the microscale field, where flow channels are often the size of a human hair (approximately 100 microns in diameter), there are special needs and uses for valves which are unique to microscale systems, especially microfluidic devices incorporating fluids with various concentrations of particulates in suspension.

Special challenges involve mixing, dilution, fluidic circuit isolation, and anti-sediment techniques when employing microscale channels within a device. The incorporation of a simple compact microfluidic valve within microscale devices addresses these potential problems while maintaining high density of fluidic structure within the device, and eliminating the need for active valve actuation in many cases.

Many different types of valves for use in controlling fluids in microscale devices have been developed. U.S. Patent No. 4,895,500, which issued on January 23, 1990, describes a silicon micromechanical non-reverse valve which consists of a cantilever beam extending over a cavity and integrally formed with the silicon wafer such that the beam can be shifted to control flow within channels of the microfluidic structure.

U.S. Patent No. 5,443,890, which issued August 22, 1995 to Pharmacia Biosensor AB, describes a sealing device in a microfluidic channel assembly having first and second flat surface members which when pressed against each other define at least part of a microfluidic channel system between them.

U.S. Patent No. 5,593,130, which issued on January 14, 1997 to Pharmacia Biosensor AB, describes a valve for use in microfluidic structures in which the material fatigue of the flexible valve membrane and the valve seat is minimized by a two-step seat construction and the fact that both the membrane and the seat are constructed from elastic material.

U.S. Patent No. 5,932,799, which issued August 3, 1999 to YSI Incorporated, teaches a microfluidic analyzer module having a plurality of channel forming laminate layers which are directly bonded together without adhesives, with a valve containing layer directly adhesivelessly bonded over the channel containing layers and a flexible valve member integral with the valve layer to open and close communication between feed and sensor channels of the network.

U.S. Patent No. 5,962,081, which issued October 5, 1999 to Pharmacia Biotech AB, describes a method for the manufacturer of polymer membrane-containing microstructures such as valves by combining polymer spin deposition methods with semiconductor manufacturing techniques.

U.S. Patent No. 5, 977,355, which issued on October 26, 1999 to Xerox Corporation, describes a valve array system for microdevices based on microelectro-mechanical systems (MEMS) technology consisting of a dielectric material forming a laminate which is embedded within multiple laminate layers.

U.S. Patent No. 6,068,751, which issued on May 30, 2000, describes a microfluidic delivery system using elongated capillaries that are enclosed along one surface by a layer of malleable material which is shifted by a valve having a electrically-powered actuator.

SUMMARY OF THE INVENTION

It is therefore an object of the present invention to provide an efficient valve suitable for use in a microfluidic system.

It is a further object of the present invention is to provide a microfluidic valve which can be integrated into a cartridge constructed of multi-layer laminates.

It is a further object of the present invention is to provide an array of microfluidic valves which can be integrated into a cartridge constructed of multi-layer laminates.

These and other objects of the present invention will be more readily apparent in the description and drawings which follow.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective view of a microfluidic valve according to the present invention;

FIG. 2 is a fragmentary cross-sectional view of an alternative valve according to the present invention;

FIG. 3 is a fragmentary cross-sectional view of the valve of FIG. 2 shown in its activated position;

FIG. 4 is a fragmentary top view, partly in phantom, of the valve of FIG. 2;

FIG. 5 is a fragmentary cross-sectional view of another alternative valve according to the present invention;

FIG. 6 is a fragmentary cross-sectional view of the valve of FIG. 5 shown in its activated position;

and FIG. 7 is a perspective view of an array which uses valves according to the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

A basic zero dead volume valve according to the present invention is shown in FIG. 1. Referring now to FIG. 1, a valve generally indicated at 10 consists of a membrane layer 12 which covers a flat surface 13 coupled to an input channel 14, which is connected to a flow channel 16 and also an output channel 18 connected to a flow channel 20. Above layer 12 is an air chamber 22 which is coupled to a pneumatic source 24 by a short air channel 26. In operation, zero dead volume valve 10 works as follows: a liquid 30 enters channel 16 and travels into channel 14 where it contacts membrane layer 12. Under atmospheric conditions within air chamber 22, membrane lines flat against surface or seat 13, causing liquid 30 to stop in channel 14. However, if the fluid pressure within channel 14 exceeds the elastic force contained in membrane 13, membrane 13 will bulge out into chamber 22, allowing liquid 30 to pass under membrane 13 and flow out through channel 18 and into channel 20, as shown by the arrows in FIG. 1. Valve 10 shown in FIG. 1 may operate as a zero volume valve, as it is a normally closed valve in which sufficient fluid pressure moves the membrane away from its sealing position to open with only atmospheric pressure within chamber 22.

When in operation within a microfluidic circuit, pneumatic pressure within channel 24 is used to open and close valve 10. If it is desirable to keep valve 10 in its closed position, positive air pressure is applied through source 24 into channel 26, when it fills air chamber 22, which forces membrane 12 against seat 13. It has been found that applying +10 psi air pressure within source 24 will

adequately keep valve 10 closed. It is desirable to open valve 10, a negative pressure of -55 mm Hg creates a vacuum within chamber 22 to completely lift membrane 12 away from seat 13 to allow liquid 30 to travel from channel 14 across surface 13 out of channel 18. Pressure from source 24 can also be varied to vary the flow through valve 10.

FIGS. 2-4 show an alternate embodiment in which a valve 40 is constructed as a normally open valve. Referring now to FIG. 2, a latex rubber diaphragm membrane 50 is held between two spacing layers 54 of a laminated microfluidic structure. Valve 40 is fabricated from a series of laminar sheets 60 which are preferably MYLAR® or a similar plastic sheet. Channels are constructed within valve 40 by cutout spaces within spacing layers 54 between sheets 60. In FIG. 2 is in its relaxed state, which allows liquid to enter a flow inlet 62, and pass through a channel 64 into a lower chamber 66 below membrane 50. The liquid can flow out of valve 40 from chamber 66 through a channel 68 and out through a flow outlet 70. Flow through valve 40 is controlled by pneumatic pressure which is supplied by a valve air supply channel 72 through a channel 74 into an upper chamber 76.

Operation of valve 40 is clearly shown in FIG. 3. Referring now to FIG. 3, sufficient air pressure is supplied via channel 72 through channel 74 and into upper chamber 76. This pressure forces membrane 50 to flex downwardly into lower chamber 66, blocking channels 64 and 68, preventing fluid flow between inlet 62 and outlet 70.

FIGS. 5 and 6 show another embodiment of the valve of the present invention. Referring now to FIG. 5, which shows the normal "on" state of the valve, a valve 80 is constructed from a pair of laminar MYLAR® sheets 82 which are separated by a series of spacing layers 84. Channels are formed in spacing layers 84 by cutout sections which form a flow structure. A flexible membrane 86 is held between two spacing layers 84 in its relaxed state. A fluid input channel 90 is connected to channel 92 and to an upper chamber 94. A fluid output chamber 96 is also coupled to upper chamber 94. A pneumatic supply channel 98 is connected to a lower chamber 100. In its normal inactivated state, valve 80 is "on," allowing liquid to flow from inlet 90 to outlet 96. When it is desirable to turn valve 80 "off," sufficient air pressure is supplied to supply channel 98, filling lower chamber 100 with pressurized air and forcing membrane 86 upwardly into upper chamber 94, sealing scaling channel 92 such that the flow passage from inlet 90 to outlet 96 is blocked, closing valve 80, as can be seen in FIG. 6.

FIG. 7 shows an array 110 in which a plurality of valves 80 can be constructed. Array 110 includes a plurality of input air ports 112 along with a plurality of input fluid ports 114. Each of valves 80 can be selectively operated to control fluid flow through a microfluidic device. Such an array of microfluidic valves can be integrated into a cartridge constructed of multi-layer laminates, and can be used to control multiple parallel fluidic processes, or a single process at multiple locations in a microfluidic circuit. Such a system may have applications in drug discovery processes, or in the analysis of multiple samples.

While the present invention has been shown and described in terms of preferred embodiments thereof, it will be understood that this invention is not limited to any particular embodiment and that changes and modifications may be made without departing from the true spirit and scope of the invention as defined in the appended claims.

What is claimed is:

1. A device for controlling flow in microfluidic devices comprising:

a first substrate having at least one microfluidic structure manufactured therein;

a first flexible sheet placed on top of at least a portion of said microfluidic structure; and

means for creating a pressure differential onto said first flexible sheet such that a portion of said sheet moves in relationship to said microfluidic structure wherein the cross-section of said microfluidic structure is altered at least in one dimension such that the fluid resistance in said microfluidic structure is altered.

2. The device of claim 1 further comprising a second microfluidic structure on the opposite side of said first flexible sheet for transmitting pressure through air or fluid flow onto a specific location of said first flexible sheet such that a portion of said sheet moves in relationship to said microfluidic structure such that the cross-section of said microfluidic structure is altered at least in one dimension such that the fluid resistance in said microfluidic structure is altered.

3. A device for controlling flow in microfluidic devices, comprising:

a first substrate having at least one microfluidic structure manufactured therein;

a first flexible sheet placed on top of a at least a portion of said microfluidic structure; and

means for creating pressure onto multiple, individually addressable locations on said first flexible sheet such that one or more potions of said sheet move in relationship to said microfluidic structure such that the cross-section of said microfluidic structure is altered at least in one dimension in one or more

locations such that the fluid resistance in said microfluidic structure is altered in one or more locations such that fluid flow through said microfluidic structure can be directed or altered.

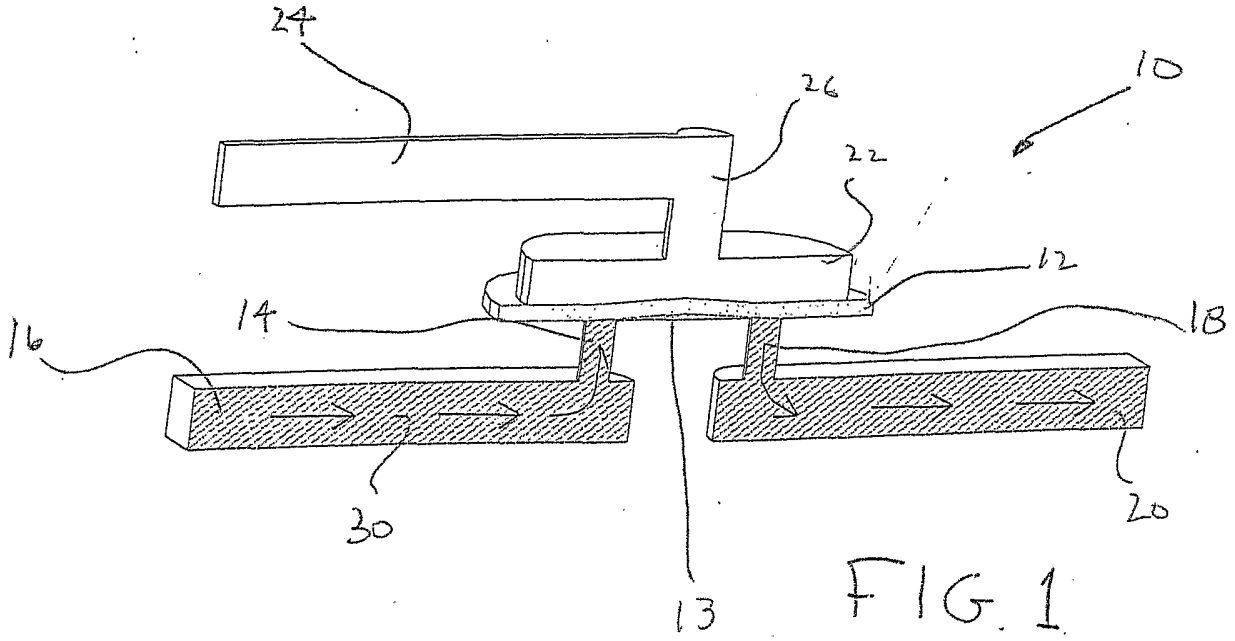

FIG. 1

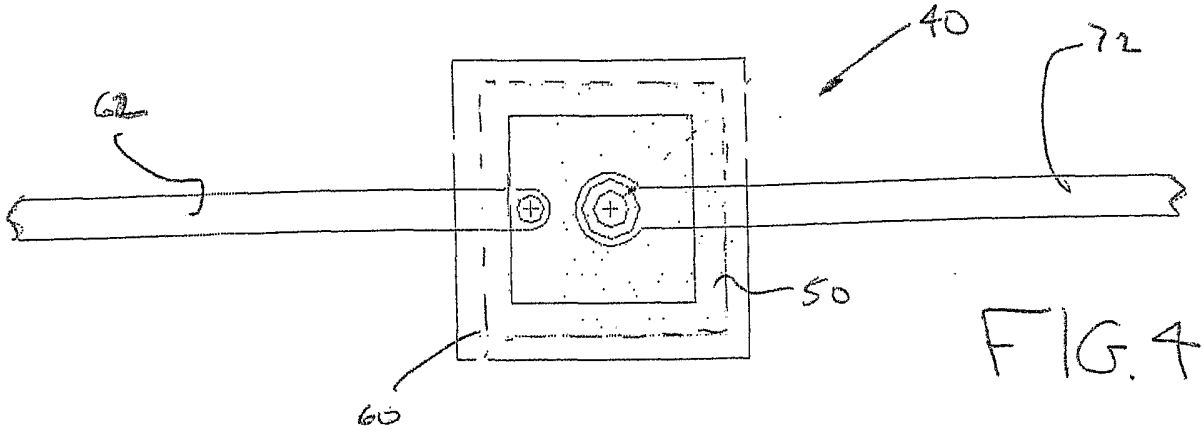

FIG. 4

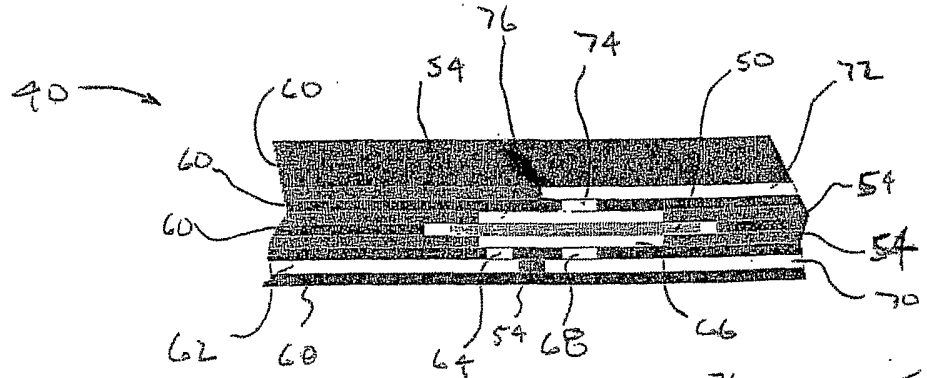

FIG. 2

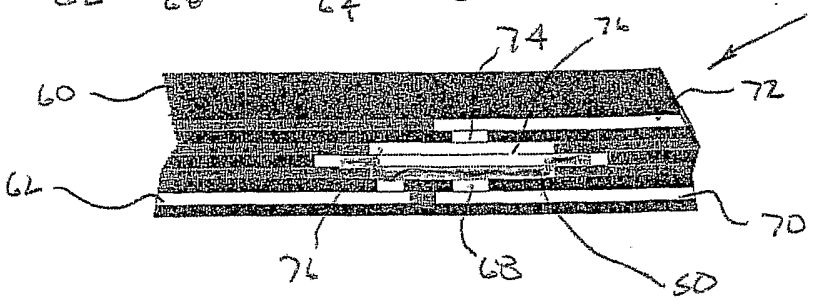

FIG. 3

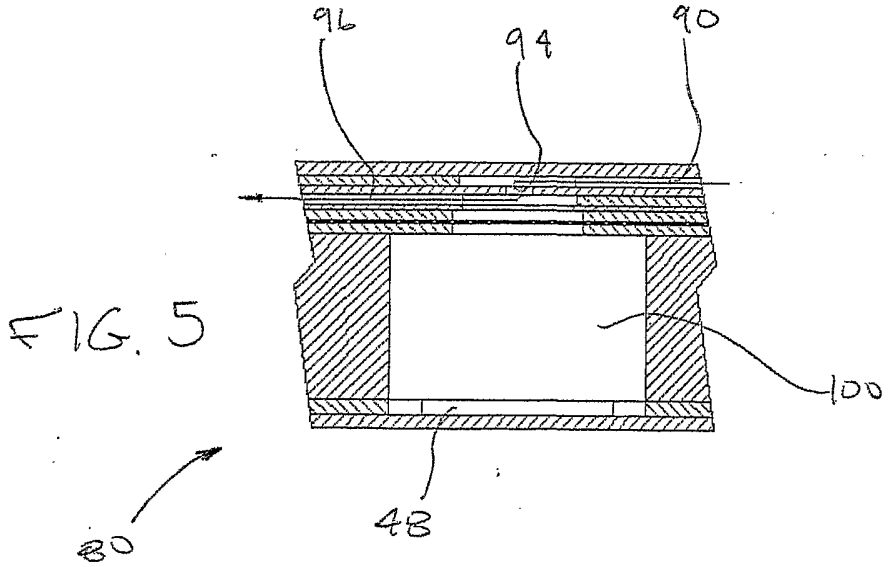

FIG. 5

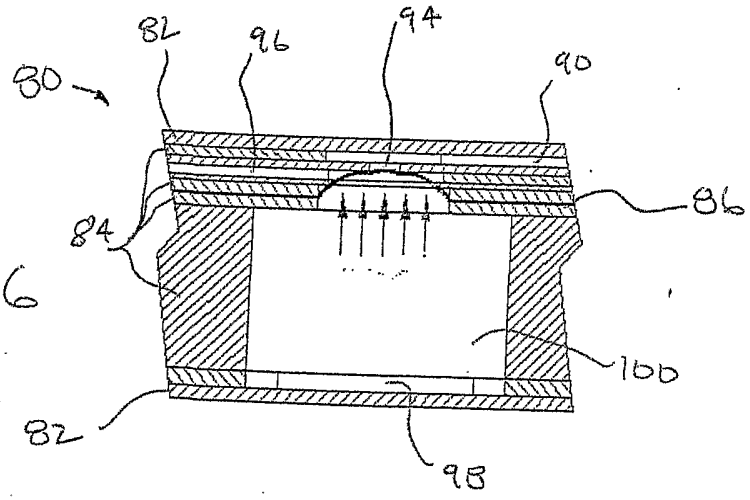

FIG. 6

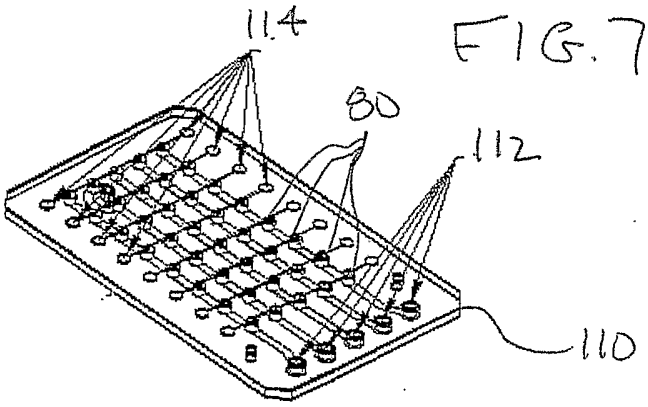

FIG. 7