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(54) **Title:** BIOSENSOR WITH LASER-SEALED CAPILLARY SPACE AND METHOD OF MAKING

(57) **Abstract:** A test strip or biosensor comprising a base substrate on which an electrode system is formed. One or more laminate layers overlie the base substrate to form a sample-receiving chamber in which a reagent is deposited. An opening is provided from the sample-receiving chamber to the exterior of the biosensor. The layers and the base substrate are laser welded to secure the biosensor. One of the layer and base substrate is light transmissive to allow laser welding at the interface therebetween. The biosensor may be formed from a series of continuous webs that are subsequently sliced to form individual biosensors.

Roche Diagnostics GmbH & F. Hoffmann La Roche AG

BIOSENSOR WITH LASER-SEALED CAPILLARY SPACE AND METHOD OF MAKING

The present invention relates generally to the testing of body fluids for concentration of analytes and more particularly to a test strip or biosensor for such testing.

Test strips are often used to measure the presence and/or concentrations of selected analytes in test samples. For example, a variety of test strips are used to measure glucose concentrations in blood to monitor the blood sugar level of people with diabetes. These test strips include a reaction chamber into which a reagent composition has been deposited. Current trends in test strips require smaller test samples and faster analysis times. This provides a significant benefit to the patient, allowing the use of smaller blood samples that can be obtained from less sensitive areas of the body. Additionally, faster test times and more accurate results enable patients to better control their blood sugar level.

In connection with smaller sample volumes, it is known to provide test strips having a sufficiently small reaction chamber such that sample fluid is drawn therein by capillary action, which is a phenomenon resulting from the surface tension of the sample fluid and the thermodynamic tendency of a liquid to minimize its surface area. For example, U.S. Patent No. 5,141,868 discloses a test strip having a cavity sized sufficiently small to draw sample liquid therein by capillary action. The cavity is defined by two parallel plates spaced about 1 mm apart by two epoxy strips extending lengthwise along lateral sides of the plates. The cavity is open at both ends, one of which receives the sample, and the other of which allows air to escape. The cavity includes an electrode structure and carries a coating of a material appropriate to the test to be performed by the test strip.

Various other test strip designs include capillary cavities that draw sample fluid therein and include vent openings to allow air to escape. As one should appreciate, capillary channels in current test strip designs are typically very small and are continually being designed smaller to reduce the amount of sample needed for testing. However, the smaller the capillary entrance width, the more difficult it becomes to accurately apply (or "target") a small sample volume to the capillary of the test strip. Targeting is even more important in segments of the demographic with impaired vision and/or reduced dexterity because it is more difficult for this segment to accurately align their fingers with the dosing edge of a test strip. Furthermore, the sample fluid sometimes undesirably hesitates before being drawn into the capillary, a phenomenon referred to as "dose hesitation." It would be desirable to overcome the difficulties associated with small capillaries in test strip design.

A limitation of electrochemical methods of measuring the concentration of a chemical in blood is the effect of confounding variables on the diffusion of analyte and the various active ingredients of the reagent. Examples of limitations to the accuracy of blood glucose measurements include variations in blood composition or state (other than the aspect being measured). For example, variations in hematocrit (concentration of red blood cells) can effect the signal generation of a blood sample. The utility of a reported blood glucose response after a short test time is questionable in applications where the results are not compensated for other sample variables or interferents such as hematocrit and temperature.

With respect to hematocrit in blood samples, prior art methods have relied upon the separation of the red blood cells from the plasma in the sample, by means of glass fiber filters or with reagent films that contain pore-formers that allow only plasma to enter the films, for example. Separation of red blood cells with a glass fiber filter increases the size of the blood sample required for the measurement, which is contrary to test meter customer expectations. Porous films or membranes are only partially effective in reducing the hematocrit effect, and must be used in combination with increased delay time and/or specialized measurement techniques to achieve the desire accuracy. Thus, it is desirable to manufacture a biosensor that is capable of reducing hematocrit interference in an easy, simple, and cost-effective manner.

Adhesives are typically used to join or seal together various layers of test strips. For high volume production of test strips, adhesives can be a significant cost both as a raw material and especially with respect to manufacturing costs. For instance, several manufacturing processes can be detrimentally affected by the adhesives. As an example, slitters, which are used to cut a web to form the strips, can be gummed up over time as a result of a build up of adhesive sawdust. As a result, the slitters must be shut down periodically for cleaning. This periodic interruption of production results in lower production rates. Thus, it is desirable to manufacture test strips in an inexpensive manner.

A first aspect of the present invention concerns a biosensor that includes a base substrate and at least one cover layer overlying the base substrate. The base substrate and the cover layer cooperate to define a sample-receiving chamber therebetween. A reagent is positioned within the sample-receiving chamber. The base substrate and the cover layer further cooperate to provide an opening for the sample-receiving chamber along an edge of the biosensor. The base substrate and the cover layer are laser welded to define the sample-receiving chamber.

A further aspect concerns a biosensor that includes a base substrate and a cover layer. One or more laser welds in cooperation with the base substrate and the cover layer define a micro-capillary chamber sized to reduce hematocrit interference in a blood sample. A reagent is disposed within the micro-capillary chamber to analyze the blood sample.

Another aspect concerns a biosensor that includes a spacer positioned between the base substrate and the cover layer for further defining the sample-receiving chamber. The spacer and base substrate are laser welded and the cover layer and spacer are laser welded, simultaneously or sequentially. A reagent is positioned within the sample-receiving chamber.

Still yet another aspect concerns a method in which a reagent is deposited on a base substrate. The base substrate and a cover layer and optionally a spacing layer are laser welded together to form a sample-receiving chamber of a biosensor that contains the reagent.

For a better understanding of the invention, its advantages, and objectives obtained therefrom, reference should be made to the drawings and to the accompanying description, in which there is illustrated and described preferred embodiments of the invention.

Referring now to the drawings, wherein like reference numerals and letters indicate corresponding structure throughout the several views:

FIG. 1 is a flow diagram for a biosensor manufacturing technique that utilizes laser welding according to one embodiment.

FIG. 2 is an exploded view of a biosensor web assembled in accordance with the technique illustrated in FIG. 1.

FIG. 3 is an enlarged view of a first biosensor laser welded in accordance with the technique illustrated in FIG. 1.

FIG. 4 is an enlarged view of a second biosensor laser welded in accordance with the technique illustrated in FIG. 1.

FIG. 5A is a flow diagram for a biosensor manufacturing technique that utilizes laser welding according to another embodiment.

FIG. 5B is a flow diagram for a biosensor manufacturing technique that utilizes laser welding according to yet another embodiment.

FIG 5C is a flow diagram for a biosensor manufacturing technique that utilizes laser welding according to yet another embodiment.

FIG. 6 is an exploded view that shows a spacer layer being applied to a web of base substrate material.

FIG. 7A is a bilaminate biosensor.

FIG. 7 B is a diagrammatic view of a laser welding system for a trilaminate biosensor.

FIG. 8 is a cross-sectional view of a drum assembly used in the laser welding system in FIG. 7.

FIG. 9 is a perspective view of the drum assembly in FIG. 8.

FIG. 10 is a front view of a variation of the laser welding system in FIG. 7.

FIG. 11 is an enlarged perspective view of the laser welding system in FIG. 10.

FIG. 12 is a top view of a first tri-laminate biosensor.

FIG. 13 is a top view of a second tri-laminate biosensor.

FIG. 14 is an exploded view of the first tri-laminate biosensor in FIG. 12.

FIG. 15 is a perspective view of a roll of a base substrate web.

FIG. 16 is an enlarged view of the base substrate web in FIG. 15.

FIG. 17 is a perspective view of a roll of a spacer web.

FIG. 18 is an enlarged view of the spacer web in FIG. 17.

FIG. 19 is a perspective view of a roll of a cover layer web.

FIG. 20 is an enlarged view of the cover layer web in FIG. 19.

FIG. 12 is a top view of a laminate that includes the spacer web of FIG. 17 overlaying the base substrate web of FIG. 15 during assembly.

FIG. 22 is a top view of the cover layer web of FIG. 19 overlaying the laminate of FIG. 21 during assembly.

FIG. 23 is a top view of the laminate of FIG. 22 that shows laser weld regions.

FIG. 24 is a top view of a web of biosensors resulting from the laminate in FIG. 23.

FIG. 25 is an exploded view of a third tri-laminate biosensor.

FIG. 26 is a top view of the third tri-laminate biosensor that shows its laser welded regions.

For the purposes of promoting an understanding of the principles of the invention, reference will now be made to the specific embodiments illustrated herein and specific language will be used to describe the same. It will nevertheless be understood that no limitation of the scope of the invention is thereby intended. Any alterations and further modifications in the described processes or devices, and any further applications of the principles of the invention as described herein, are contemplated as would normally occur to one skilled in the art to which the invention relates.

Biosensors and methods for their manufacture are generally known. More specifically, biosensors and methods for their manufacture that are suited for the present invention are known from US 2005/0019212 A1 (published on January 27, 2005). Specific reference is made to paragraphs [0048] to [0249] and figures 1 to 19 C of this published U.S. patent application, where biosensors and methods generally suited for the present invention are disclosed in detail.

While the biosensors and methods disclosed in US 2005/0019212 A1 are described with specific emphasis on electrochemical embodiments, the present invention is not limited to electrochemical systems, sensors and methods. Rather, the methods and biosensors of the present invention can also be used in connection with optical sensing technologies as generally known in the art.

Laser Sealed Manufacturing Technique

As discussed in the Background section above, adhesives for high volume production of test strips can be a significant cost both as a raw material and especially with respect to manufacturing costs. Instead of using adhesive, various techniques will be described below in which the laminate structures of the test strips are laser welded together. Test strips can be manufactured in an efficient and cost effective manner with these laser welding techniques. For example, the material costs associated with adhesives can be significantly reduced or even eliminated altogether. In addition, manufacturing issues created by the use of adhesives can be lessened or eliminated. As noted before, when adhesives are used to bond together the various layers and components of the test strip, adhesive sawdust can gum up on slitters that are used to cut the test strips. As a result, the slitters need to be shut down periodically for routine cleaning and maintenance, thereby lowering production rates. With the laser welding technique described herein, the issues associated with adhesives can be significantly reduced or even eliminated. Although the focus of the discussion for this technique will be forming capillary channels via laser welding, it should be recognized other components of test strips can be joined together via laser welding. For instance, as will be described below, all of the layers of the test strip can be laser welded together, thereby eliminating the need for adhesives. This adhesive free test strip can be for example achieved by lasing over most or all of the surface area of the laminate structure, or with spot welds spaced thereupon.

For purposes of the present invention, the underlying principle of laser welding two laminate layers together is that for any given type of laser, there are clear (or transparent) materials that will not absorb the energy of the laser (which as a result passes therethrough) and black (or absorptive) materials that will absorb this energy. As will be explained in further detail below, it is important to note that the terms “clear” and “black” refer to the laser-energy absorption characteristics of the materials, and not necessarily to the translucence, opacity or color thereof. It is desirable that these adjacent clear and black materials be essentially the same chemically as well as physically (e.g. same or nearly the same polymer base, same or nearly the same melting point). To seal two layers together, the laser is directed at the clear layer of a bi-laminate set up. The energy of the laser passes through the clear layer and is absorbed by the black layer. The black layer then melts and the heat from that physical reaction in turn melts the clear layer. The melted portions then mix and cool, leaving a weld. If the clear and black layers are significantly different in chemical and/or physical properties, this mixing may not be robust, thereby leaving a weak or otherwise insufficient weld.

The melting of the layers does not typically occur through the entire thickness of either layer. That is, the black layer is typically only melted to a certain depth therein for a given laser energy. Nevertheless, more than two layers can be laser welded together, either sequentially or simultaneously. As an example, three layers can be laser welded together to create a tri-laminate structure. For a tri-laminate set up, the laser can be directed at the outer layers individually, which can be done simultaneously or in sequence, depending on the configuration of the laser equipment and the webs of the laminates. For example, a first clear layer can be laser welded to a first side of a middle black layer, followed by turning the structure over for laser welding a second clear layer to a second side of the middle black layer. Alternatively, two lasers may be employed on generally opposite sides of the structure to laser weld the first and second clear layers to the black layer simultaneously (or nearly so). As a result, in a tri-laminate set up, both of the outer layers are typically clear, while the middle layer is black.

Notwithstanding the foregoing, it is possible for the black layer to be melted through its entire thickness in order to weld to the clear layers on opposite sides simultaneously, provided that the thickness of that layer is sufficiently thin or the energy of the laser is sufficiently high. In that case, a tri-laminate strip can be made in a single laser shot aimed at a clear outer layer that is welded to a black middle layer which in turn welds to a black or clear outer layer on the back side relative to the laser.

As also mentioned in the Background section, variations in hematocrit levels can affect the generated signal for a blood sample, and thus, it is desirable to manufacture a biosensor that is capable of reducing hematocrit interference in an easy, simple, and cost-effective manner. It has been found that physical separation via a microcapillary significantly reduces hematocrit. The microcapillary also reduces the required sample volume, which is desirable for consumers. However, due to the small dimensions involved with microcapillaries, there is a need for tight dimensional control during manufacturing. It was discovered that microcapillaries can be produced with high throughput, at low cost, and with tight tolerance control via laser welding. With laser welding, microcapillaries having volumes from 20 nl to 200 nl (or even smaller) can be produced in an efficient, consistent, and cost-effective manner. The micro-capillaries manufactured with this technique obviate the need for expensive surface-treated foils by utilizing the reagent as the hydrophilic modifier. Usually, these micro-capillaries for separating hematocrit are created when a bi-laminate structure is used in the test strip.

The principle is that red blood cells are relatively large, and thus if a capillary is formed by sealing two layers together that are held loosely together during the lasing sequence, the capillary height is high enough to allow fluid to enter via capillary action but is too low for red blood cells to enter. Thus, red blood cells congregate at the inlet of the micro-capillary channel. To further facilitate dosing in such a micro-capillary channel, a concave cutout of the top layer can be made such that the strip is contacted like a top-dosing strip but the reaction site is within the capillary channel.

A flow diagram 600 in FIG. 1 illustrates one example of a laser welding technique according to one embodiment that can be incorporated into the biosensor manufacturing technique described with reference to FIGS. 5-19 of US 2005/0019212 A1. It should be appreciated that this laser welding technique can be incorporated into other biosensor manufacturing processes besides the one described with reference to FIGS. 5-19 of US 2005/0019212 A1. For example, it should be recognized that this laser welding technique should not be limited to the specific embodiments described herein such as ablated electrodes, slot die coated reagent layers, etc. That is, this laser welding technique can be adapted for other types test strips such as those with printed electrodes, dispensed reagents, vent holes, etc. Generally speaking, instead of using an adhesive, laser welds are used to secure the chamber cover layer 240 (cf. FIG. 12 of US 2005/0019212 A1) to the rest of the biosensor in the illustrated technique. The technique can be used to produce test strips via a continuous and/or discrete manufacturing process. For instance, large volumes of biosensors can be mass- produced with this technique via a continuous web process. Alternatively, individual test strips can be manufactured via the laser welding technique described herein.

In stage 602, the sets of electrodes 182, traces 184, and contact pads 186 (cf. FIG. 7 of US 2005/0019212 A1) are formed in the manner as described above. In one example, gold or other noble metal is sputtered or vapor deposited onto one side of a thin, clear electrode support foil that forms the base substrate 12. The support foil in selected embodiments can be about 200 μm thick, and the support foil can be for example a clear polycarbonate (PC) or polyester (PET) foil. To assist in the laser welding process, which will be described in detail below, the support foil can be clear or transparent relative to the type of radiation used in the laser welding, but as should recognized the foil can be opaque or semi-transparent in other embodiments. The now metallized surface or film 170 is laser ablated to form the electrodes 182, traces 184, and contact pads 186 along with other features, as is depicted in FIG. 7 of US 2005/0019212 A1. Again, it should be recognized that the electrodes 182 can be manufactured via other techniques.

As noted before, the reagent layer 190 can be formulated so as to be hydrophilic, thereby eliminating the need for expensive surface-treated cover foils. During stage 604 (FIG. 1), the reagent layer 190 is deposited (and dried, if necessary). For example, an electromagnetic bellows (EMB) technique can be used which permits highly precise deposition of reagent to only where it is needed. EMB dispensing products are commercially available from Fluilogic OY of Espoo, Finland. Similarly, in other embodiments, laser printing, ink jet printing, laser ink jet printing, or even laser ablative techniques can be used, such as those described in WO 2007/033079 A2 to Home Diagnostics, Inc.. The reagent layer 190 for laser welding is typically discontinuous with one or more separate discrete sections. For instance, the reagent layer 190 in an embodiment depicted in FIG. 2 can be in the form of discrete reagent pads or sections deposited over the electrodes 182. Between the reagent pads 190, there are uncovered sections 605 that are not covered by the reagent. These uncovered sections 605 provide a clean contact surface between the base substrate web 188 and the chamber cover layer or web 240 for facilitating laser welding between layers. Any reagent present between the clear and black layers at the weld locations can tend to shade or block absorption of the laser energy on the absorptive or black layer. This in turn can tend to weaken the resulting weld between the layers and/or prevent proper sealing between the layers. The above-mentioned electromagnetic bellows technique is one suitable embodiment to create these discrete reagent pads 190 and uncovered sections 605, thereby minimizing the risk of the reagent weakening the welds through contamination. It is contemplated that trace amounts of the reagent 190 can be present at sections 605 to such a minor extent so as to not significantly affect weld strength and seal of the laser weld. It is also envisioned that sections 605 can be colored and/or treated in such a manner so as to promote laser welding as well. For example, sections 605 can be colored so as to absorb laser energy to promote laser welding , or sections 605 can be transparent so as to allow the laser energy to pass through in order to heat other surfaces, such as for example the chamber cover layer 240. A person of ordinary skill in the art will appreciate that whether the base substrate web 188 or cover layer 240 is the clear layer and black layer respectively is a matter of design choice, and the claims attached hereto shall not be limited (except as specifically recited) as to which structural element is clear versus black. Any specific reference or description in this regard is for exemplary purposes only.

As can be seen in the FIG. 2 exploded view, the spacing layer (cf. 196 of FIG. 10 of US 2005/0019212 A1) has been eliminated. Instead, the chamber cover layer (second layer) 240 is directly attached to the base substrate web (first layer) 188. Generally, the chamber cover layer 240 is flat, and to form the sample receiving (micro-capillary) chamber 24, in certain embodiments the chamber cover layer 240 may be embossed in stage 606 to form channel indentations 607. The channel indentations 607 are spaced apart so as to coincide with the electrodes 182 and reagent 190 for the individual test strips. It should be appreciated that the channel indentations 607 can be formed in other manners besides through embossing, such as by stretching, folding, or otherwise deforming the chamber cover layer 240, for example. Moreover, the channel indentations 607 can be created during creation of the chamber cover layer 240 such that the channel indentations 607 are integral with the chamber cover layer 240. It is further contemplated that channel indentations 607 can be formed by applying additional components to the chamber cover layer 240, such as extra layers.

Stage 606 in other embodiments can be optional such that the channel indentations 607 are not required. For example, a chamber cover layer 240 without channel indentations 607 can be attached somewhat loosely to the web of base substrate material 188 in a manner such that a small gap is possible between the cover layer 240 and base substrate 188 that forms the sample receiving chamber 24. The two layers are laser sealed together without a spacer and without the channel embossed in the cover. Instead, the layers are brought together generally loosely and laser sealed. This allows for the formation of a rather thin capillary channel which can be used for hematocrit separation. As noted before, red blood cells are relatively large, and thus if a capillary is formed by sealing two layers together that are held loosely together during laser welding, the capillary height is high enough to allow fluid to enter via capillary action but is too low for red blood cells to enter. Thus, red blood cells congregate at the inlet of the capillary channel. In one form, the chamber cover layer 240 is slackened during attachment so as to create rather large sample receiving channels 24, but in other forms, the chamber cover layer 240 can be taut such that the sample receiving chambers 24 are relatively thin so as to minimize sample sizes as well as enhance hematocrit separation. It should be recognized that stage 606 can occur in a different order than is illustrated in FIG. 1. For example, stage 606 can occur before, during, and/or in between stages 602 and 604.

In stage 608, the chamber cover layer 240 is laser welded to the web of base substrate material 188. As mentioned previously, laser welding can produce micro-capillaries with high throughput, at low cost, and with tight tolerance control. Due to their small size, micro-capillaries in turn can reduce hematocrit interference.

As should be recognized, a device that produces any particles or electromagnetic radiation in a coherent state is considered a laser. In most cases, "laser" refers to a source of coherent photons, i.e. light or other electromagnetic radiation. As should be appreciated, the word "light" in the acronym Light Amplification by Stimulated Emission of Radiation (laser) is typically used in the expansive sense, as photons of any energy; it is not limited to photons in the visible spectrum. As a result, there are X-ray lasers, infrared lasers, ultraviolet lasers, and the like. For example, a microwave equivalent to an optical laser is commonly called a "maser", but it should be recognized that for the purposes of discussion herein that masers are considered a type of laser. Although this technique will be described with reference to optical or near-optical-type lasers, it should be appreciated that other types of lasers can be used to weld the various layers together. In one particular form, the laser used for laser welding is an infrared (IR), solid-state laser. The laser that performs laser welding in stage 608 can be a continuous-type laser or a pulse-type laser. In one embodiment, the laser welding machine is of a type commercially available from Leister Process Technologies of Sarnen, Switzerland, but of course, other types of laser welders can be used.

When referring to the optical properties of the various layers during discussion of laser welding, the optical properties are in reference to the type of laser being used. For example, when a layer is transparent (or even translucent) in optical light but absorptive in ultraviolet light, the layer will be referred to as absorptive (or black) when an ultraviolet laser is used and transparent when an optical laser is used. To aid the reader in understanding this technique, the word "black" may be used herein to refer to a laser absorptive layer even when the layer in reality might not be actually black when viewed by an individual, but for instance, it might be another color or shade, such as grey, brown, etc. In a similar fashion, the term "clear" may at times be used herein to refer to laser transmissive layers that are transparent or translucent with respect to the laser beam such that the laser beam (at least in part) is able to pass through the layer. In general, during the laser welding of the various layers, one of the layers is more transmissive of the laser beam than at least one of the other layers and at least one of the other layers is more absorptive of the laser energy. This is distinguishable from certain known laser welding techniques in which the layers can be any material, where one layer is transmissive and the other layer is first coated with a substance designed to absorb the laser energy and adhere or otherwise weld the layers together. A commercial example is the CLEARWELD® process provided by Gentex Corporation of Simpson, Pennsylvania. In the present design, however, there is no need for coating a substance on any layer, and in most embodiments, this is generally a materials and manufacturing cost intended to be avoided.

When a layer is more absorptive than other layers, such as when a layer is black and the other layers are clear for an optical-type laser, the laser beam passes through the transmissive (clear) layers and is absorbed by the absorptive (black) layers. The resulting heat generated by the absorption of the laser beams melts all or part of the absorptive layer. The heat of the absorptive layer then melts the clear layer. The melted portions then mix and cool, leaving a weld. As noted before, if the clear and absorptive layers have significantly different chemical and/or physical properties, this mixing may not be robust, thereby leaving a weak or otherwise insufficient weld.

The chamber cover layer 240 can be laser welded to the reagent cover layer 188 in a number of manners. Looking at FIG. 3, the chamber cover layer 240 is spaced apart from a vent member 610 that covers the electrodes 182 and traces 184 so as to create the vent opening 34. As depicted, the chamber cover layer 240 is welded along weld lines 612 along the periphery of the end of test strip 614 as well as along the sample-receiving chamber 24. Like before, the ends of the test strips 614 can be trimmed along trim lines 262, and the individual test strips 614 can be separated along separation lines 264. After trimming, the weld lines 612 at least in part remain attached to the test strips so as to prevent body fluid from bypassing the sample-receiving chambers 24 during sampling.

During welding, the laser energy shines through a transparent (or semi-transparent/transmissive) layer and is absorbed by an absorptive layer, relative to the laser beam used, so as to create the heat that melts all or portions of the layers, thereby creating the weld lines 612. In one embodiment, the cover layer 240 is generally absorptive of and the base substrate web 188 is generally transparent relative to the laser energy utilized for welding. The cover layer 240 in one particular example is black (0.5% carbon black), and the web 188 is clear. Although the cover layer 240 generally absorbs the energy of the laser, the cover layer 240 in some forms can be visually transparent if a non-visible light laser beam is used. When the cover layer 240 is optically transparent (or semitransparent/translucent), the cover layer 240 can form a visualization window for determining fill sufficiency. In this embodiment, the laser beam is applied to the web side 188. When the beam is applied, the beam shines through the base substrate web 188, and the cover layer 240, which is opaque, absorbs the laser beam energy. The heat generated by the absorption of the laser beam energy causes the cover layer 240 and the web 188 to melt. Once cooled, the cover layer 240 and the web 188 fuse together along the weld lines 612 to create a strong, fluid tight seal. As mentioned above, the channel indentations 607 along with the weld lines 612 in one embodiment help to define the sample-receiving chamber 24, but in other embodiments, it is contemplated that the channel indentations 607 can be optional.

In an alternative embodiment, the cover layer 240 is generally transparent (transmissive), and the base substrate web 188 is generally absorptive (black). The laser beam in this embodiment is applied through the transparent cover layer 240 and absorbed by the absorptive web 188. The energy absorbed by the web 188 causes the web 188 and cover layer 240 to melt and fuse together at the weld lines 612. When the cover layer 240 is transparent in visible light, the cover layer 240 can be used to form a visualization window.

With the previously described embodiments, the laser beam is applied to a single side, but the laser beam in other embodiments can be applied to both sides either simultaneously or consecutively. For instance, both the cover layer 240 and the base substrate web 188 can be black, and laser beams are applied to the cover layer 240 and the web 188 at the same time in generally opposite relation. Moreover, the various layers do not need to be uniformly absorptive or transparent. In other words, the transmissive properties can vary at numerous locations on a layer. As one example, only a section of the layers that are intended to be welded are made absorptive, while other parts are made reflective or configured to scatter light so as to inhibit welding in areas that should not be welded, such as inside the sample-receiving chamber 24. It should be recognized that the various layers in whole or in part can be made absorptive of laser energy on a temporary or permanent basis, such as by applying an opaque ink to one or more of the layers. It is envisioned that a graphics label can be printed on or applied to the cover layer 240 as well as to other components. Various masking techniques can be used as well during laser welding to prevent or promote laser welding in various areas.

If so desired, other components can be attached via laser welding. For example, the vent member 610 can be attached via laser welding. Moreover, the vent member 610 can be attached before, during, or after the cover layer 240 is laser welded to the web 188. Laser welding can be used in conjunction with other forms for securing the various layers. For example, an adhesive can be used to secure a layer on a temporary basis before a laser weld permanently secures the layer. Once assembled, the test strips or sensors 614 are individually punched and packaged in the manners as described above. Alternatively, the sensors 614 can remain attached together to create a sensor tape for a multiple-test meter cartridge. Like the previous embodiments, the sensors 614 are punched or otherwise cut in such a manner that the sample receiving chamber 24 opens along an end edge of the test strip 614 for end dosing purposes.

FIG. 4 illustrates an alternate embodiment in which a cover layer or foil 616 stretches from the sample-receiving chamber 24 to near the contact pads 186 so as to cover the electrodes 182 and traces 184. Like the previous embodiment, the cover layer 616 is laser welded to the base substrate web layer 188 to create a two-layer or bi-laminate design. The web 188 and the cover layer 616 can be colored in the same manner as described above. That is, the layers can be alternately transparent and absorptive such that one of the layers allows the laser beam to pass through, while the other layer absorbs the laser beam. Instead of having weld lines 612 of the type illustrated in FIG. 3, the cover layer 616 in FIG. 4 has weld areas 618 that define the sample-receiving chambers 24. Vent openings 620 for venting air from the sample-receiving chambers 24 can be punched or otherwise formed in the cover layer 616. Optionally, a body cover 234 (cf. FIG. 12 of US 2005/0019212 A1) of the type described above can be attached over the cover layer 616 so as to partially cover the vent openings, thereby providing a fill indicator line. Once assembled, individual sensors 622 can be detached and packaged for individualized use, or the sensors 622 can remain attached in a sensor tape for a multiple-test meter cartridge.

It should be appreciated that laser welding can be used in a three (or more) layer sensor configuration as well, like the one illustrated in FIGS. 10-13 of US 2005/0019212 A1. Instead of using adhesive, the base substrate web 188, spacing layer 196, and cover layer 240 are secured together via laser welding. Other components, like the body cover 234, can be laser welded in place as well. A flow diagram 624 in FIG. 5A illustrates a technique for laser welding the three layers together to form a tri-laminate structure. In stage 626, the sets of electrodes, traces, and contact pads (cf. 182, 184, 186 FIG. 7 of US 2005/0019212 A1) are formed in a manner such as is described above. In one example, gold is vapor deposited onto one side of a thin, clear electrode support foil that forms the base substrate (electrode support substrate). The support foil in selected embodiments can be about 200 μm thick, and the support foil can be for example a clear polycarbonate (PC) or polyester (PET) foil. The now metallized surface or film is laser ablated to form the electrodes, traces, and contact pads along with other features, as is depicted in FIG. 7 of US 2005/0019212 A1 (cf. numerals 170, 182, 184, 186). It should be appreciated that the electrode patterns can be formed in other manners, such as via printing techniques, etc.

In stage 628, the reagent layer (cf. 190 in FIG. 8 of US 2005/0019212 A1) is deposited over the electrodes on web in any suitable manner as described above with sufficient precision and definition so as to avoid leaving any more than trace amounts of reagent between base substrate and spacer layer at any location intended for laser welding. In one embodiment, between reagent pads, there are uncovered sections 605 that are not covered by the reagent. As should be recognized, the reagent layer 190 can be deposited in other manners as well.

Turning to FIG. 6, spacing (second) layer 196, which has pre-capillaries 220a, 220b, 220c, etc., is applied to the web of base substrate material 188 in stage 630 and the layers are laser welded. The spacing layer 196 is approximately 100 μm thick PC or PET foil in one embodiment, but it should be appreciated that the cover layer 240 can have a different thickness and/or be made from different kinds of materials in other embodiments. However, even in this case, it is helpful that the various layers generally share similar chemical and physical properties so as to ensure adequate weld strength. In one example, the spacing layer 196 has a thickness that is high enough to allow fluid to enter via capillary action but is too low for red blood cells to enter, thereby enhancing hematocrit separation.

In stage 632, the cover layer 240 along with the body cover 234 is applied to the assembly 230 formed by the spacing layer 196 and web 188, as is depicted in FIG. 12 of US 2005/0019212 A1, and is laser welded thereto. In one embodiment, the cover layer 240 is approximately 100 μm thick PC or PET foil. However, it should be understood that the cover layer 240 can have a different thickness and/or be made from different materials. Once the three layers are laser welded together, they create assembly 260, which is illustrated in FIG. 13 of US 2005/0019212 A1. In one embodiment, the web of base substrate material 188 and cover layer 240 are generally clear or transparent, and the spacing layer 196 is generally black (0.5% wt./wt.).

In order to avoid particularly stringent tolerances in depositing the reagent layer 190 on the base substrate web 188 only within the dimensions of the to-be-defined capillary channel, in one embodiment (see flow diagram in FIG. 5B) the spacing layer 196 is applied to the base substrate web 188 (with the electrode patterns already formed thereon) and laser welded together prior to depositing the reagent layer 190. The cover layer 240 is then applied to the spacing layer 196 and laser welded together to create assembly 260. Thus the progression of stages is 626, 630, 628, 632. For a diagrammatic view of one possible continuous process embodiment of this progression, see FIG. 7B.

During laser welding according to FIGS. 5A and 5B, laser beams are applied to the web 188 and the cover layer 240 in a sequential fashion in order to laser weld the layers together. In other embodiments, however, the three layers can be laser welded generally simultaneously (see FIG. 5C). Thus, in stages 630a and 632a, the spacing layer 196 is applied to base substrate web 188 (with a formed electrode pattern and a reagent layer dispensed thereon in a sufficiently precise and defined pattern) and the cover layer 240 is applied to the spacing layer 196. In stage 634, the three layers are laser welded together generally simultaneously. As noted above, this can be achieved in at least two different ways. First, the three layers having been brought together may be laser welded as a result of multiple lasers applying laser beams to both sides in generally opposite relation. Second, the three layers having been brought together may be laser welded by a single laser configured to weld the three layers together at one time, wherein the spacing layer 196 comprises the more absorptive or black layer and one or the other of the cover layer 240 and base substrate web 188 comprises the transmissive or clear layer, wherein the other of layer 240 and web 188 may be either clear or black.

In the previously described examples, the web 188 and cover layer 240 were clear, and the spacing layer 196 was absorptive or black. However, other color combinations can be used. As an example, the web 188 can be black or more absorptive in comparison to the spacing 196 and cover 240 layers, which can be generally clear or more transmissive. After the spacing layer 196 is applied to the web 188 in stage 630, the spacing layer 196 is laser welded to the web 188. Once the spacing layer 196 is welded, the spacing layer 196 can be made less transmissive such as by printing a dark ink onto the spacing layer 196 or otherwise darkening the spacing layer 196 so as to promote laser welding of the cover layer 240. The relatively clear cover layer 240 is then laser welded to the now darkened spacing layer 196.

Various systems can be used for performing the above-discussed laser welding techniques. An example of laser welding system 640 for forming a bi-laminate biosensor will now be initially described with reference to FIG. 7A, which shows a diagrammatic view of the laser welding system 640. FIG. 7B shows a diagrammatic view of a laser welding system for forming a tri-laminate biosensor that will be described in greater detail below. As can be seen, the laser welding system 640 in FIG. 7A includes a cover supply reel 642 that supplies a cover layer web 644 that forms the chamber cover layer 240 and a base or substrate supply reel 646 that supplies substrate web 648 that forms the electrode support base substrate web layer 188. In the depicted embodiment, the cover layer web 644 is generally a black or laser absorptive layer, and the substrate web 648 is generally a clear or laser transmissive layer. However, it should be recognized that the properties of these webs can be reversed. That is, the cover layer web 644 can be generally clear, and the substrate web 648 can be black in other embodiments. In such a case, it should be recognized that the positions of the webs relative to the laser need to be swapped such that the laser is able to be absorbed by the black web. In the illustrated embodiment, the cover layer web 644 does not include any type of embossing so that the formed capillary channel is very thin so as to promote hematocrit separation, but in other embodiments, the cover layer web 644 can include embossing. The substrate web 648 in the depicted embodiment includes electrodes and deposited reagent. Along each web 644, 648, supply brakes or servodrives 650 control the tension and/or speed of the webs 644, 648 so that they remain properly synchronized for the laser welding process. If servodrives are used instead of brakes to control the unwinding speed of the reels 642, 646 at location 650, tension sensors will be typically required for both the input and output webs. Linear web guides 652 are used to guide the webs 644, 648 in the system 640.

The two webs 644, 648 are laser welded together at laser welding section 654. As can be seen in FIG. 7A, the laser welding section 654 includes a press roller 656 and a drum assembly 658. FIG. 8 illustrates a cross-sectional view of an embodiment of the drum assembly 658, and FIG. 9 shows a perspective view. With reference to FIG. 8, the drum assembly 658 generally includes a servomotor 660, a flexible coupling 662, a mask spindle 664, a bearing spacer 666, a mask wheel 668, and an acrylic wheel 670. The servomotor 660 is coupled to the mask spindle 664 through flexible connection 662. Opposite the servomotor 660, the mask wheel 668 is attached to the mask spindle 664, and the acrylic wheel 670 surrounds the mask wheel 668. The acrylic wheel 670, which freely rotates due to the bearing spacer 666, provides a contact surface for the substrate web 648 against the drum assembly 658. It should be appreciated that the acrylic wheel 670 can be made from other optically transparent materials besides acrylic. The bearing spacer 666 provides rotational support to the mask spindle 664 as the servomotor 660 rotates the mask wheel 668. As depicted, the mask wheel 668 has a series of mask sections 672 that mask various areas of the webs 644, 648 during laser welding. Each mask section includes a laser mask aperture 674 that defines the laser welded areas on the webs 644, 648. During operation, a laser is disposed inside the mask wheel 668, and the laser shines one or more laser beams through the laser apertures 674 so as to form a laser weld between the webs 644, 648 that coincides with the shape of the laser aperture 674. By rotating the mask wheel 668, the webs 644, 648 are able to be laser welded together in a high speed fashion. The laser apertures 674 in the depicted embodiment are physical openings in the mask wheel 668, but in other embodiments, the laser apertures 674 can be in the form of optically transparent sections. In the illustrated embodiment, the laser apertures are U-shaped so as to generally coincide with the laser welded section that surrounds the capillary channel of the biosensor. It should be recognized that, depending on the desired shape of the laser weld, the laser apertures can be shaped differently in other embodiments.

Referring again to FIG. 7A, a high-speed laser sensor 676 is disposed along the substrate web 648 just prior to the laser welding section 654. The high speed laser sensor 676 measures the speed and/or determines the relative position of the substrate web 648 by visualizing the electrodes on the substrate web 648. It should be appreciated that the position of the electrodes (or other components) and/or speed can be indirectly detected through target markings on the substrate web 648. With the laser sensor 676, the servomotor 660 of the drum assembly 658 is able to synchronize the rotation of the mask wheel 668 with the movement of the substrate web 648. This ability to synchronize rotation of the mask wheel 668 helps to ensure that the laser apertures 674 are properly positioned over the substrate web 648 during welding so as to avoid accidentally welding the wrong area. If possible, the laser sensor 676 should be placed close to drum assembly 658 to minimize the effect of stretching of the substrate web 648. In one particular example, the laser sensor 676 is an Aromat UZF321 Photometric Sensor (Panasonic Electric Works Corporation), but it should be understood that other types of sensors can be used.

At the laser welding section 654, the webs 644, 648 are squeezed between the press roller 656 and the drum assembly 658. A laser within the mask wheel 668 directs a laser beam towards the pressed together webs 644, 648. The laser beam shines through the laser apertures 674 as they rotate into position, while the mask wheel 668 masks the rest of the webs 644, 648 from the laser beam. Given that the substrate web 648 is clear, the laser beam from the laser aperture shines through the substrate web 648 and is absorbed by the black (or absorptive) cover web 644. The resulting heat causes the webs 644, 648 to melt and fuse together to form a welded biosensor web 678. Located downstream from the laser welding section 654, an inspection camera 680 inspects the biosensor web 678 for any defects as well as maintains process control. In one form, the inspection camera 680 is charge-coupled device (CCD) camera, but it can include other types of inspection devices. Downstream from the laser welding section 654, a master servodrive 682 maintains generally constant web speed, and the welded biosensor web 678 is wrapped around a rewind reel 684. The servodrives as well as other motors in the laser welding system 640 can come from various sources, such as from Rockwell Automation (Allen-Bradley).

FIG. 10 illustrates a front view of one variation to the laser welding system 640 described above with reference to FIG. 7A. FIG. 11 shows an enlarged perspective view of the laser welding section 654. Like before, the laser welding system 640 includes the cover supply reel 642, the substrate supply reel 646, supply servodrive 650, the laser welding section 654 with press roller 656 along with drum assembly 658, the master servodrive 682, and the rewind reel 684. FIG. 10 further illustrates a laser generator 686 disposed inside the drum assembly 658 for generating the laser beam and a laser adjustment mechanism coupled to the laser generator 686 for adjusting the relative position of the laser generator 686. Control/power systems 690 that are operatively coupled to the laser generator and other components of the system are also shown in FIG. 10. These control/power systems 690 are used to power and control the components of the system, such as the laser generator 686. A press roller actuator 692 is attached to the press roller 656 for actuating the press roller 656. Supply 694 and discharge 696 rollers are oriented in a triangular pattern relative to the drum 658 so as to guide the webs through the laser welding section in taut manner. The laser welding process in the system of FIG. 10 occurs in generally the same fashion as described above.

A laser welding process for a tri-laminate biosensor using similar techniques, principles and systems is illustrated in FIG. 7B. The laser welding system 698 in FIG. 7B shares numerous components in common with the laser welding system of FIG. 7A. For the sake of brevity and clarity, these common components will not be described in detail below, but please refer to their description above. One additional component of interest illustrated in FIG. 7B is reagent dispenser 699, which is used to dispense the reagent in a manner consistent with the discrete dispensing requirements set forth above.

FIG. 12 illustrates a top view of a first embodiment of a tri-laminate biosensor or test strip 700 that can be manufactured using the above-described laser welding techniques, and FIG. 13 shows a second embodiment of a tri-laminate biosensor or test strip 702 that can also be manufactured using the above-described laser welding techniques. As can be seen, both biosensors 700, 702 have a similar configuration with the exception of the electrode structure. The biosensor 700 in FIG. 12 has electrodes 704 that enter through the lateral sides of a sample or capillary chamber 706; whereas, the electrodes 708 of the FIG. 13 biosensor 702 enter through the end of the sample chamber 706. Both types of biosensors 700, 702 are laser welded together in the same fashion. For the sake of brevity and clarity, a technique for laser welding these tri-laminate biosensors will be described with reference to the FIG. 12 biosensor 700, but the same laser welding technique can be easily applied to manufacture the FIG. 12 biosensor 702.

FIG. 14 depicts an exploded view of the first tri-laminate biosensor 700, which includes a clear base substrate 710, a clear top substrate or cover layer 712, and a black capillary substrate or spacer layer 714. Again, it should be recognized that the various clear and black layers can be different in other embodiments. The base substrate 710 has electrodes 704, and at the sample chamber 706, the electrodes 704 are at least in part covered with a reagent. The spacer layer 714 has an opening 716 that along with the base substrate 710 and cover layer 712 form the sample chamber 706.

As alluded to before, the various layers of the biosensor 700 are typically supplied in rolls or reels so that the biosensor can be manufactured via a continuous process. FIG. 15 shows a perspective view of one such roll 718 of a base substrate web 720 that has a plurality of base substrates 710, which is shown in an enlarged view in FIG. 16. FIG. 19 shows a perspective view of a roll 728 that supplies a cover layer web 730, which is shown in an enlarged view in FIG. 20. A roll 722 in FIG. 17 supplies a spacer web 724 that forms the spacer layer 714 in the biosensor 700. Looking at FIG. 18, which shows an enlarged view of the spacer web 724, a plurality of sample cavity openings 726 that eventually form the spacer opening 716 are defined in the spacer web 724. It will be appreciated, however, that instead of openings 726 being pre-formed on spacer web 724, they may be provided just prior to the spacer web 724 being introduced to the base substrate web 720 in order to ensure that the openings 726 are properly positioned over the electrodes 704 at the required location for the sample chamber 706. With reference to FIG. 7B, a punching or cutting device (not shown) may be provided about spacer web 724 proximal to linear web guides 652 and servodrives 650. Sensors at drum assembly 658 may be configured to provide feedback to a controller controlling the rate of punching/cutting of openings 726 by the cutting device. Such sensors, for example, may determine the actual distance between electrodes 704 in adjacent biosensors in the web 720, and indicate to the controller appropriate locations for the openings 726 to be provided. As may be appreciated, this is an additional means for ensuring proper synchronization of all the webs being assembled for a tri-laminate embodiment of the present invention.

Turning to FIG. 21, the spacer web 724 is positioned to cover the end of the base substrate web 720 that contains the working, counter, and/or reference electrodes along with the reagent. The spacer web 724 is aligned with base substrate web 720 so that the sample cavity openings are aligned with the appropriate electrodes and reagent so as to form the sample cavity 706. With reference to FIG. 22, the cover layer web 730 is aligned slightly offset from the end of the sample cavity openings 726 so as to form vent openings 732 that are used to vent air from the sample cavities 706 when fluid is collected. In the illustrated embodiment, both the base substrate web 720 and the cover layer web 730 are clear, while the spacer web 724 is black. During laser welding, the laser beams shine through the clear base substrate 720 and cover 730 webs, and the laser beams are absorbed into the black spacer web 724. The resulting heat melts and fuses together the webs. FIG. 23 shows a top view of the U-shaped laser sealed region 734 that surrounds the sample chamber 706. Again, it should be recognized that that the laser sealing of the substrate web 720 and the cover layer web 730 to the spacer web 724 can occur simultaneously or sequentially. The excess web material is cut off along cutoff line 736 to arrive at a web of biosensors 700, which is shown in FIG. 24.

FIG. 25 illustrates a perspective view of a biosensor 740 according to another embodiment that is laser welded together in a manner similar to the technique described above, with a few minor exceptions noted below. Like before, the biosensor 740 includes a base substrate 742, the cover layer 712, and the spacer layer 714 that forms sample chamber 706. As can be seen, the base substrate 742 has an electrode structure 744 that slightly differs from the previously described one. Turning to FIG. 26, like the previous embodiment, the black spacer web 724 that forms the spacer layer 714 and the clear cover layer web 730 that forms the cover layer 712 are layered across a base substrate web 746 that forms the base substrate 742. The end edges of the base substrate web 746, the spacer web 724, and the cover layer web 730 are respectively indicated by lines 748, 750, and 752 in FIG. 26. The excess web material is removed at cut-off line 754 to form the opening of the sample chamber 706. One notable distinction, when compared to the weld pattern 734 in FIG. 23, the biosensor 740 in FIG. 26 is different. As can be seen, the weld pattern 756 in FIG. 26 stretches in a continuous manner.

While preferred embodiments incorporating the principles of the present invention have been disclosed hereinabove, the present invention is not limited to the disclosed embodiments. Instead, this application is intended to cover such departures from the present disclosure as come within known or customary practice in the art to which this invention pertains and which fall within the limits of the appended claims.

The following is a list of preferred embodiments of the invention:

1. A biosensor, comprising:
a base substrate,
at least one cover layer overlying the base substrate, wherein the base substrate and the cover layer cooperate to define a sample-receiving chamber;
one of the base substrate and the cover layer being more transmissive than the other;
a reagent positioned within the sample-receiving chamber;
the base substrate and the cover layer providing an opening for the sample-receiving chamber along an edge therebetween; and
at least one laser weld joining the base substrate to the cover layer to form the sample-receiving chamber.

2. The biosensor according to embodiment 1, further comprising an electrode formed on the base substrate.

3. The biosensor according to embodiment 2, wherein the electrode is a laser ablated electrode.

4. The biosensor according to embodiment 1, wherein the less transmissive one is black in color.

5. The biosensor according to embodiment 1, wherein the one that is more transmissive is substantially clear.

6. The biosensor according to embodiment 1, wherein the base substrate is substantially clear and the cover layer is substantially black.

7. The biosensor according to embodiment 1, wherein the base substrate is substantially black and the cover layer is substantially clear.

8. The biosensor according to embodiment 1, further comprising a spacing layer over the base substrate, the cover layer overlying the spacing layer, the at least one laser weld comprising at least one laser weld joining the base substrate to the spacing layer and at least one laser weld joining the spacing layer to the cover layer, wherein the base substrate, the spacing layer and the cover layer so joined form the sample receiving chamber.

9. The biosensor according to embodiment 8, wherein the cover layer and the base substrate are more transmissive than the spacing layer.

10. The biosensor according to embodiment 9, wherein:
the base substrate is substantially clear,
the spacing layer is black, and
the cover layer is substantially clear.

11. The biosensor according to embodiment 1, further comprising a spacing layer laser welded between the base substrate and the cover layer to define the sample receiving chamber.

12. The biosensor according to embodiment 11, further comprising:
a body cover attached to the spacing layer; and
the body cover being spaced apart from the cover layer to define a vent slot for venting air from the sample receiving chamber.

13. The biosensor according to embodiment 12, wherein the body cover is laser welded to the spacing layer.

14. The biosensor according to embodiment 1, wherein the reagent is hydrophilic.

15. The biosensor according to embodiment 1, wherein at least the cover layer has a channel indentation to form the sample-receiving chamber.

16. The biosensor according to embodiment 1, wherein at least one of the base substrate and cover layer are formed from polycarbonate.

17. The biosensor according to embodiment 1, wherein at least one of the base substrate and cover layer are formed from polyester.

18. The biosensor according to embodiment 1, wherein the cover layer defines a vent opening positioned to vent air from the sample receiving chamber.

19. The biosensor according to embodiment 1, wherein the base substrate and the cover layer being laser welded around at least a portion of the periphery of the sample-receiving chamber

20. The biosensor according to embodiment 1, wherein the base substrate and the cover layer have laser weld areas where the base substrate and the cover layer are welded together.

21. The biosensor according to embodiment 1, wherein the sample-receiving chamber has a volume of between about 20 and about 200 nL.

22. A biosensor, comprising:
a base substrate;
a cover layer;
one or more laser welds in cooperation with the base substrate and the cover layer defining a micro-capillary chamber sized to reduce hematocrit interference in a blood sample; and
a reagent disposed within the micro-capillary chamber to analyze the blood sample.

23. The biosensor of embodiment 22, wherein the one or more lasers welds directly weld the cover layer to the base substrate.

24. The biosensor of embodiment 22, further comprising a spacer laser welded between the base substrate and the cover layer to define the micro-capillary chamber.

25. The biosensor of embodiment 22, wherein the base substrate has one or more electrodes for analyzing the blood sample.

26. The biosensor of embodiment 22, wherein one of the base substrate and the cover layer is more absorptive of laser energy than the other at the one or more laser welds.

27. A method, comprising:
depositing a reagent on a base substrate; and
laser welding together the base substrate and a cover layer to form a sample-receiving chamber of a biosensor that contains the reagent.

28. The method of embodiment 27, further comprising:
forming a vent that communicates with the sample-receiving chamber.

29. The method of embodiment 27, wherein:
one of the base substrate and the cover layer is more transparent than the other; and
said forming the sample-receiving chamber includes laser welding through the one that is more transparent by directing a laser beam through the one that is more transparent.

30. The method of embodiment 29, wherein:
the base substrate is substantially transparent relative to the laser beam;

the cover layer is configured to substantially absorb the laser beam; and
said forming the sample-receiving chamber includes shining the laser beam through the base substrate and against the cover layer.

31. The method of embodiment 27, further comprising:
wherein the cover and base substrates have a common, co-extensive edge; and
forming an opening for the sample-receiving chamber along the co-extensive edge of the base substrate and cover layer.

32. The method of embodiment 27, further comprising:
providing continuous webs of the base substrate and the cover layer;
wherein said laser welding includes laser welding together the continuous webs of the base substrate and the cover layer to form a laminate, wherein the laminate includes multiple sample-receiving chambers containing the reagent; and
forming an opening for each sample-receiving chamber along an edge of at least one of the base substrate and cover layer.

33. The method of embodiment 32, wherein said laser welding includes:
rotating a rotary-type mask as the continuous webs of the base substrate and the cover layer move thereby, wherein the rotary-type mask includes a plurality of mask apertures; and
shining a laser beam through at least one of the mask apertures to form a laser weld between the continuous webs.

34. The method of embodiment 33, further comprising:
synchronizing speed of the web of the base substrate with the rotary mask so that the mask apertures are properly aligned during said laser welding.

35. The method of embodiment 32, further comprising:
dividing the continuous webs into multiple biosensor test strips.

36. The method of embodiment 27, wherein:
said laser welding includes laser welding around a perimeter of the sample-receiving chamber.

37. The method of embodiment 27, wherein:
said laser welding includes welding areas around the sample-receiving chamber.

CLAIMS

1. A biosensor, comprising:
a base substrate,
at least one cover layer overlying the base substrate, wherein the base substrate and the cover layer cooperate to define a sample-receiving chamber;
one of the base substrate and the cover layer being more transmissive than the other;
a reagent positioned within the sample-receiving chamber;
the base substrate and the cover layer providing an opening for the sample-receiving chamber along an edge therebetween; and
at least one laser weld joining the base substrate to the cover layer to form the sample-receiving chamber.

2. The biosensor according to claim 1, further comprising an electrode formed on the base substrate.

3. The biosensor according to claim 1, further comprising a spacing layer laser welded between the base substrate and the cover layer to define the sample receiving chamber.

4. The biosensor according to claim 3, further comprising:
a body cover attached to the spacing layer; and
the body cover being spaced apart from the cover layer to define a vent slot for venting air from the sample receiving chamber.

5. The biosensor according to claim 4, wherein the body cover is laser welded to the spacing layer.

6. The biosensor according to claim 1, wherein at least the cover layer has a channel indentation to form the sample-receiving chamber.

7. The biosensor according to claim 1, wherein the base substrate and the cover layer being laser welded around at least a portion of the periphery of the sample-receiving chamber

8. The biosensor according to claim 1, wherein the sample-receiving chamber has a volume of between about 20 and about 200 nL.

9. The biosensor of claims 1 to 8, , wherein the sample receiving chamber is a micro-capillary chamber sized to reduce hematocrit interference in a blood sample; and comprising a reagent disposed within the micro-capillary chamber to analyze the blood sample.

10. The biosensor of claim 9, wherein one of the base substrate and the cover layer is more absorptive of laser energy than the other at the one or more laser welds.

11. A method, comprising:
depositing a reagent on a base substrate; and
laser welding together the base substrate and a cover layer to form a sample-receiving chamber of a biosensor that contains the reagent.

12. The method of claim 11, wherein:
one of the base substrate and the cover layer is more transparent than the other; and
said forming the sample-receiving chamber includes laser welding through the one that is more transparent by directing a laser beam through the one that is more transparent.

13. The method of claim 11, further comprising:
providing continuous webs of the base substrate and the cover layer;
wherein said laser welding includes laser welding together the continuous webs of the base substrate and the cover layer to form a laminate, wherein the laminate includes multiple sample-receiving chambers containing the reagent; and
forming an opening for each sample-receiving chamber along an edge of at least one of the base substrate and cover layer.

14. The method of claim 13, wherein said laser welding includes:
rotating a rotary-type mask as the continuous webs of the base substrate and the cover layer move thereby, wherein the rotary-type mask includes a plurality of mask apertures; and
shining a laser beam through at least one of the mask apertures to form a laser weld between the continuous webs.

15. The method of claim 11, wherein:
said laser welding includes laser welding around a perimeter of the sample-receiving chamber or welding areas around the sample-receiving chamber.

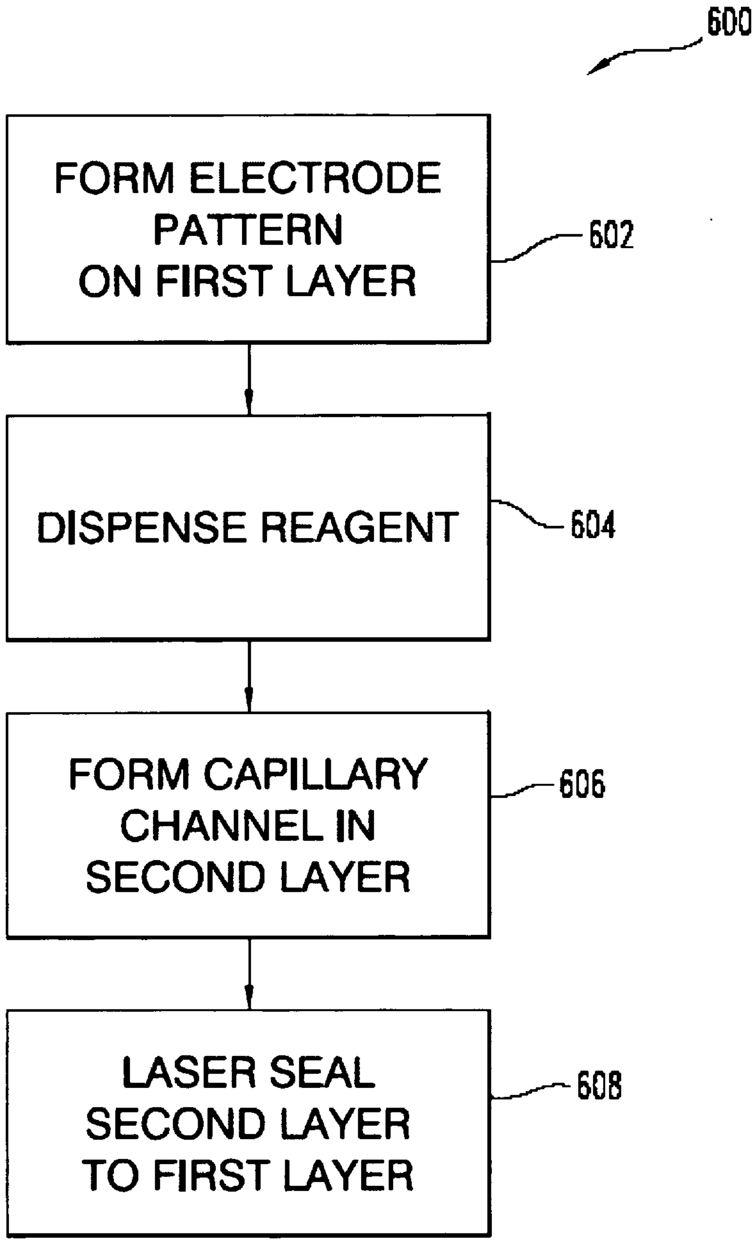
600
FORM ELECTRODE PATTERN ON FIRST LAYER
602
DISPENSE REAGENT
604
FORM CAPILLARY CHANNEL IN SECOND LAYER
606
LASER SEAL SECOND LAYER TO FIRST LAYER
608

Fig. 1

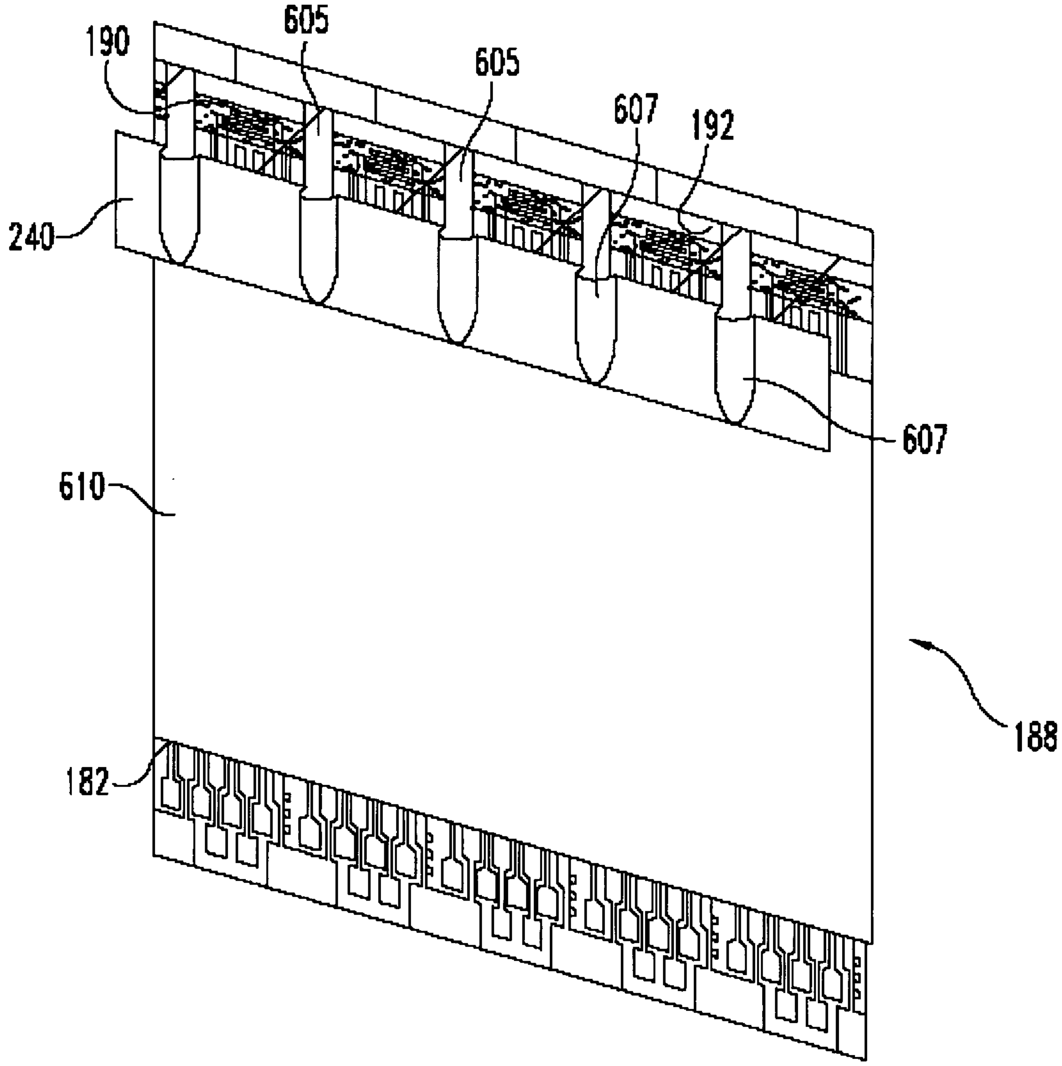

Fig. 2

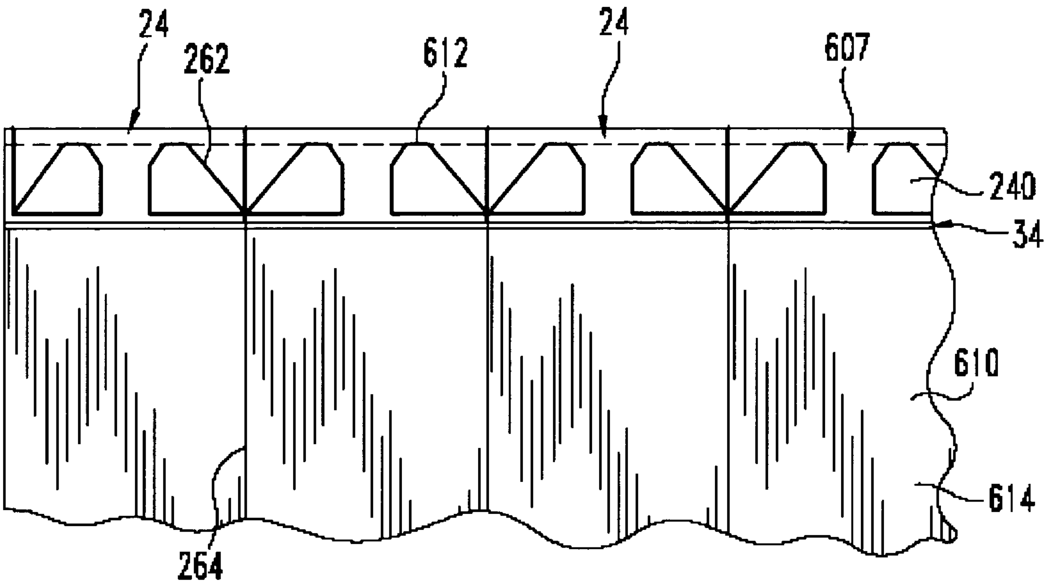
24
262
612
24
607
240
34
610
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Fig. 3

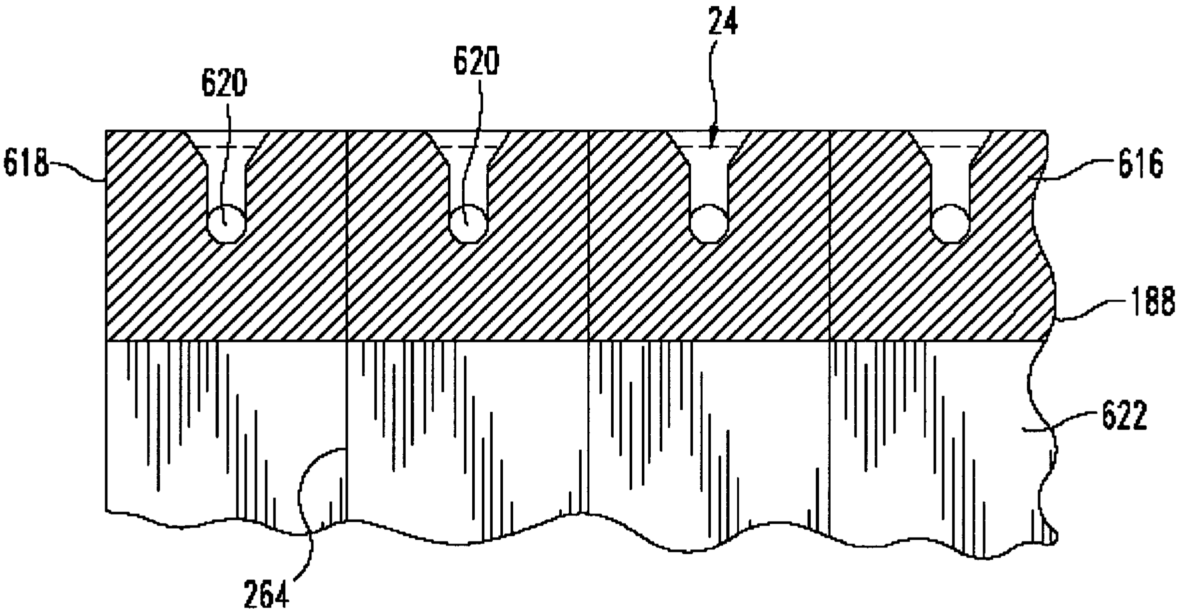
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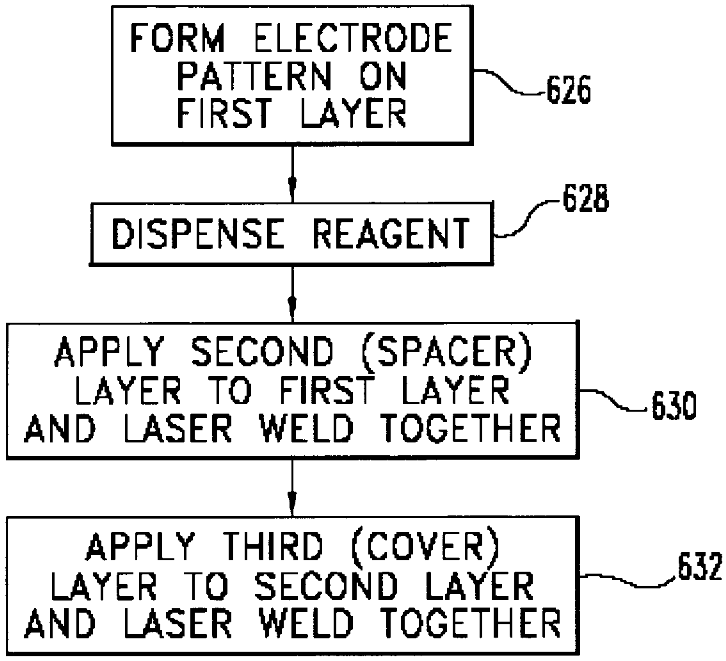
Fig. 4


FORM ELECTRODE PATTERN ON FIRST LAYER
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DISPENSE REAGENT
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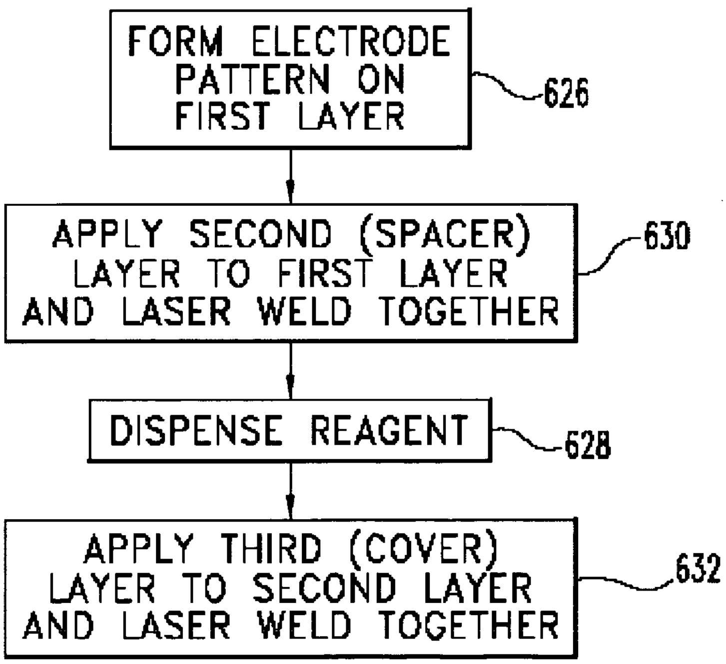
APPLY SECOND (SPACER) LAYER TO FIRST LAYER AND LASER WELD TOGETHER
630
APPLY THIRD (COVER) LAYER TO SECOND LAYER AND LASER WELD TOGETHER
632

Fig. 5A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APPLY SECOND (SPACER) LAYER TO FIRST LAYER AND LASER WELD TOGETHER
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DISPENSE REAGENT
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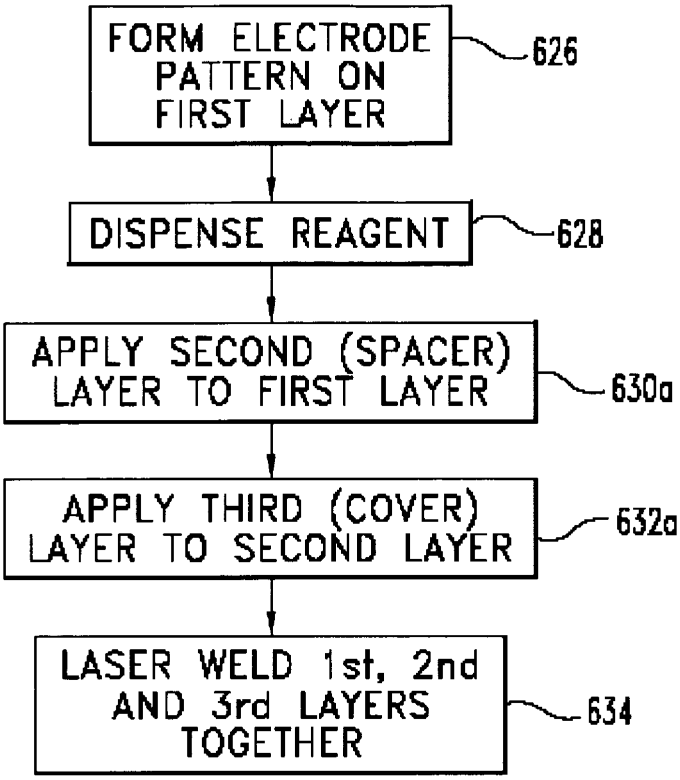
APPLY THIRD (COVER) LAYER TO SECOND LAYER AND LASER WELD TOGETHER
632

Fig. 5B


FORM ELECTRODE PATTERN ON FIRST LAYER
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DISPENSE REAGENT
628
APPLY SECOND (SPACER) LAYER TO FIRST LAYER
630a
APPLY THIRD (COVER) LAYER TO SECOND LAYER
632a
LASER WELD 1st, 2nd AND 3rd LAYERS TOGETHER
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Fig. 5C

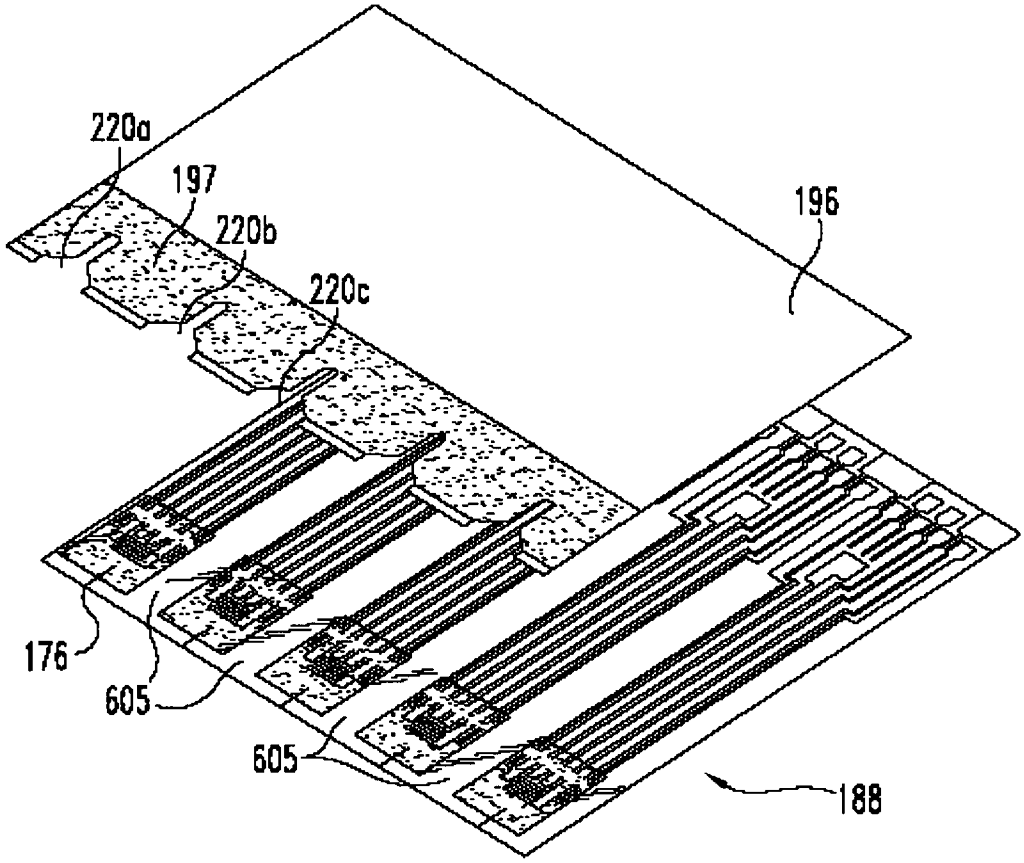

Fig. 6

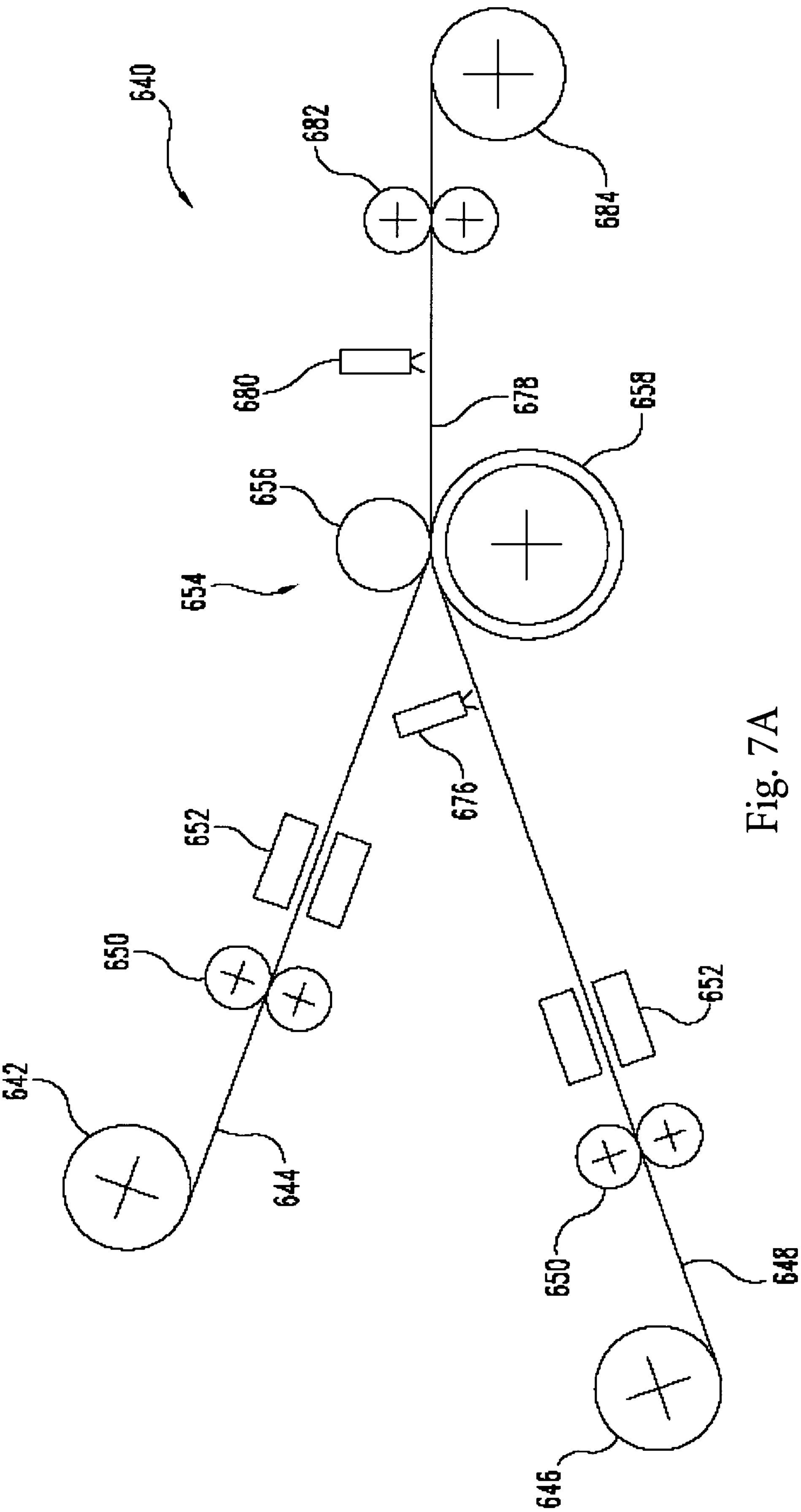
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Fig. 7A

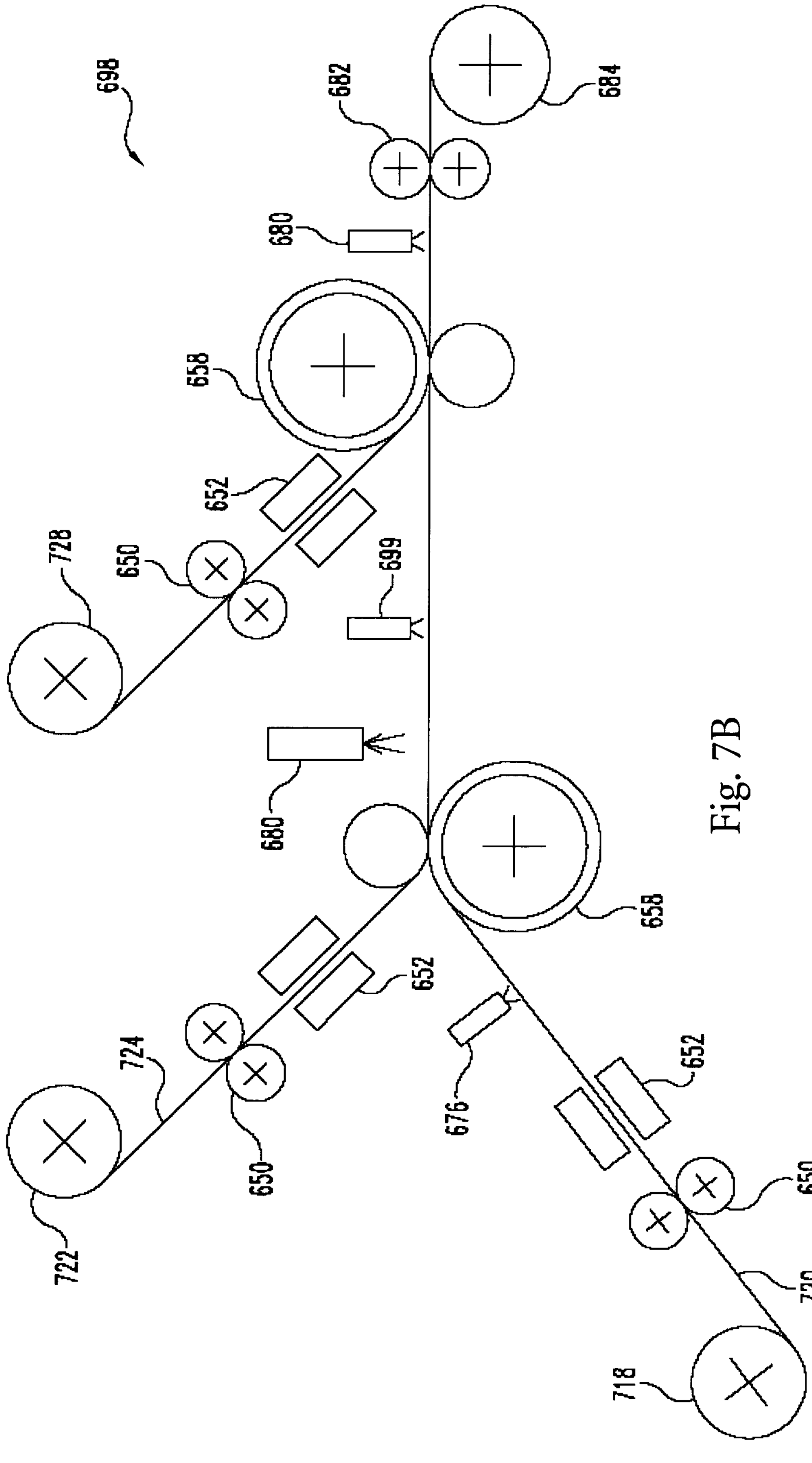
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Fig. 7B

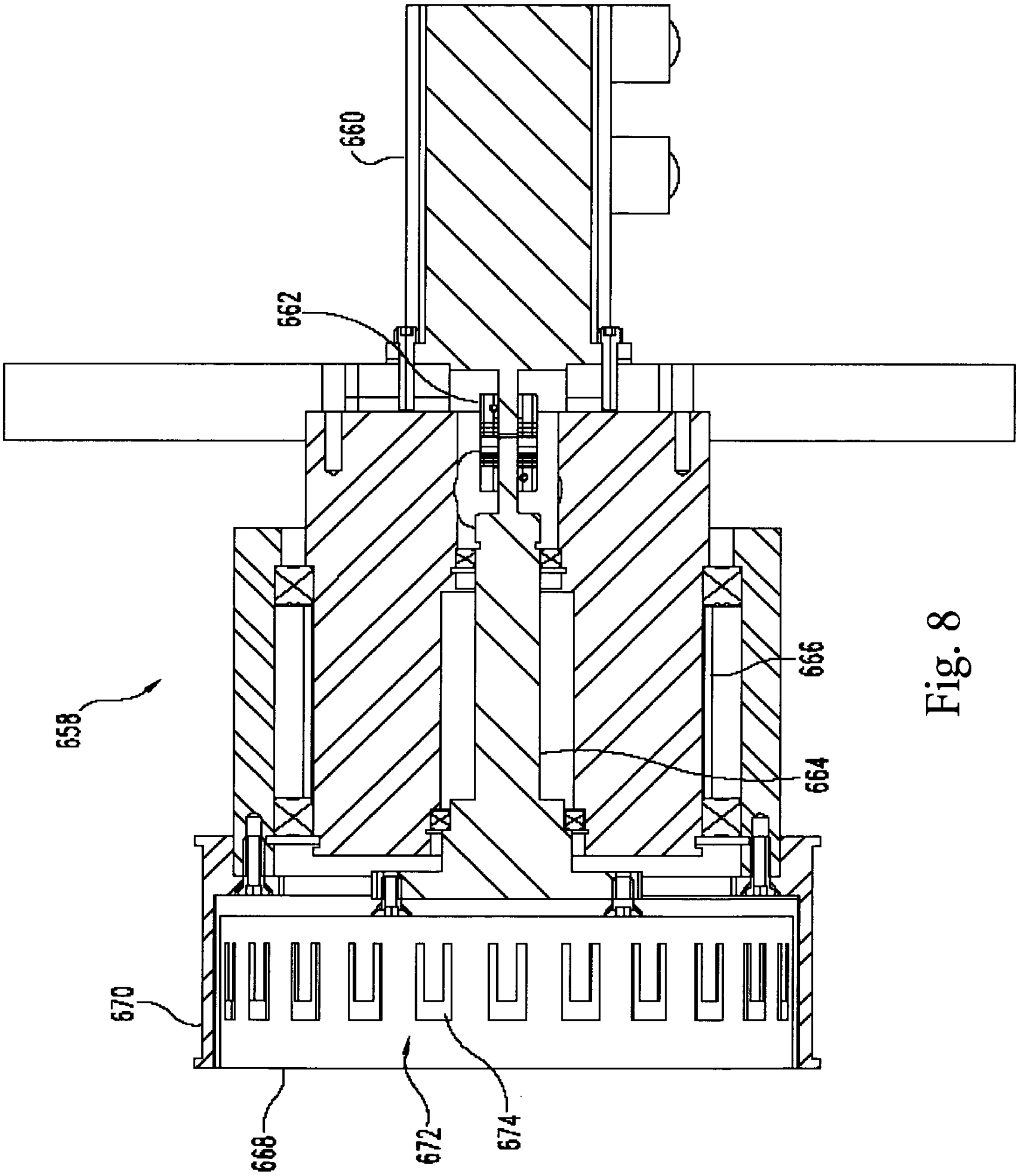


Fig. 8

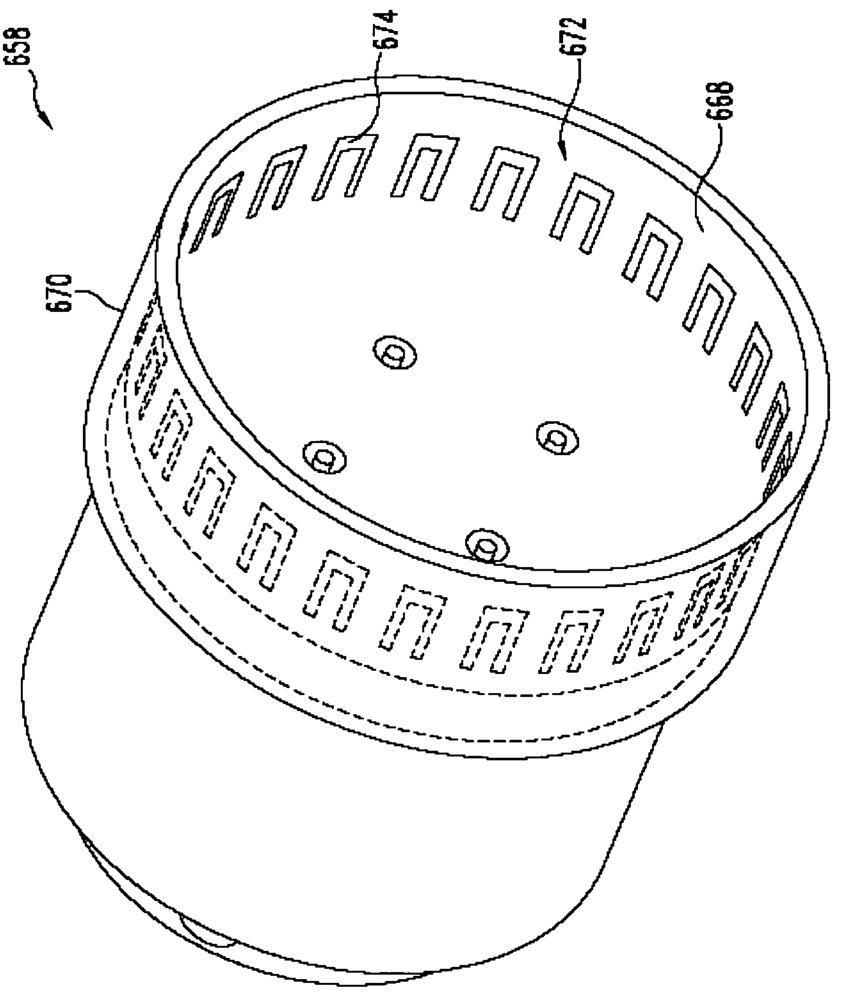
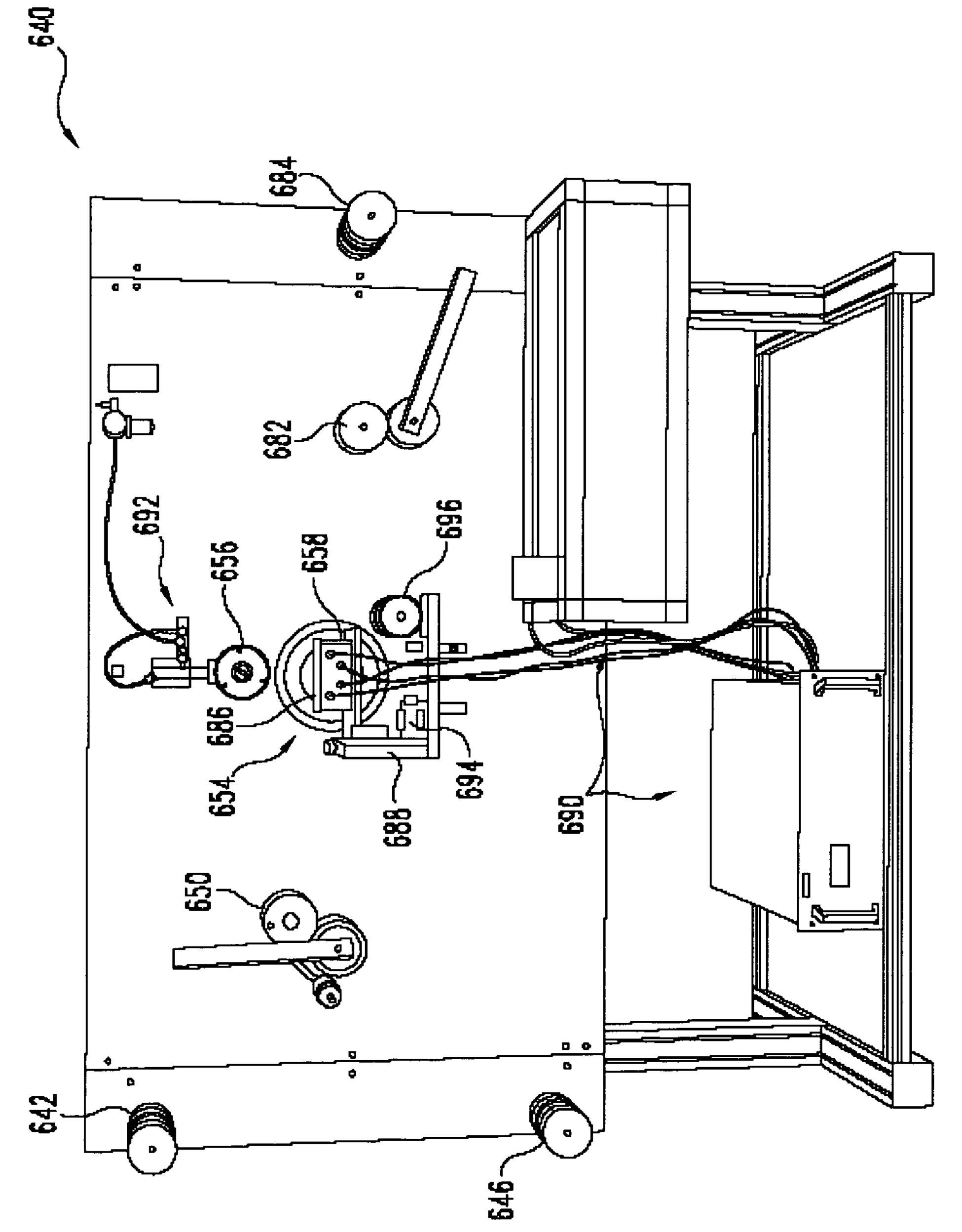


Fig. 9



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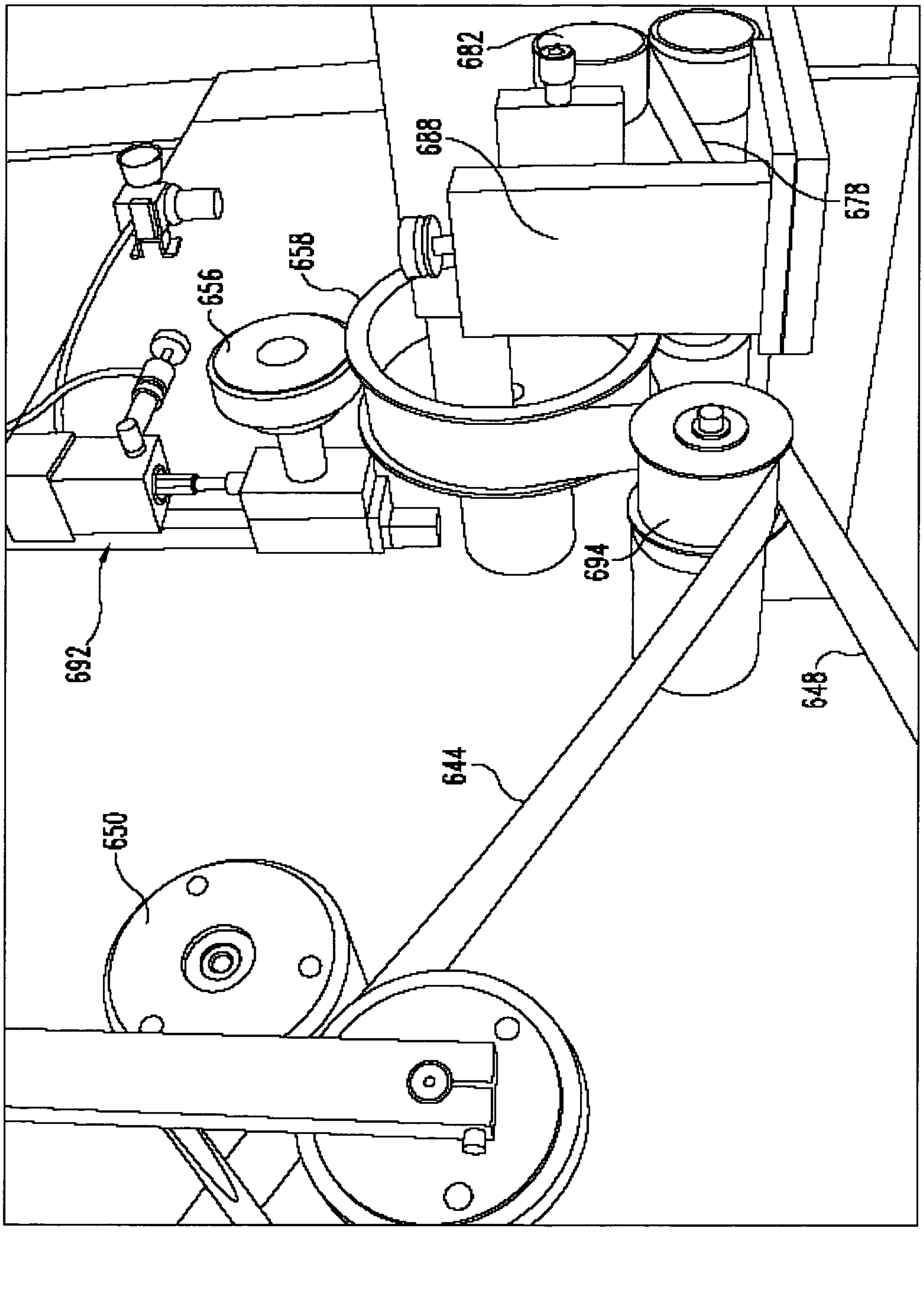
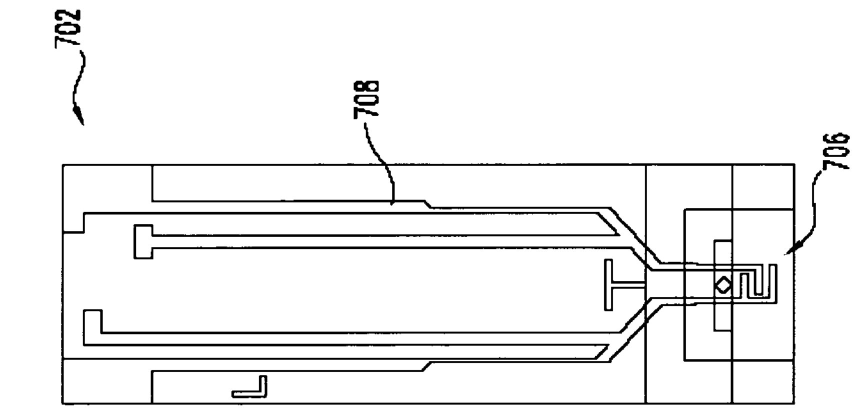


Fig. 11



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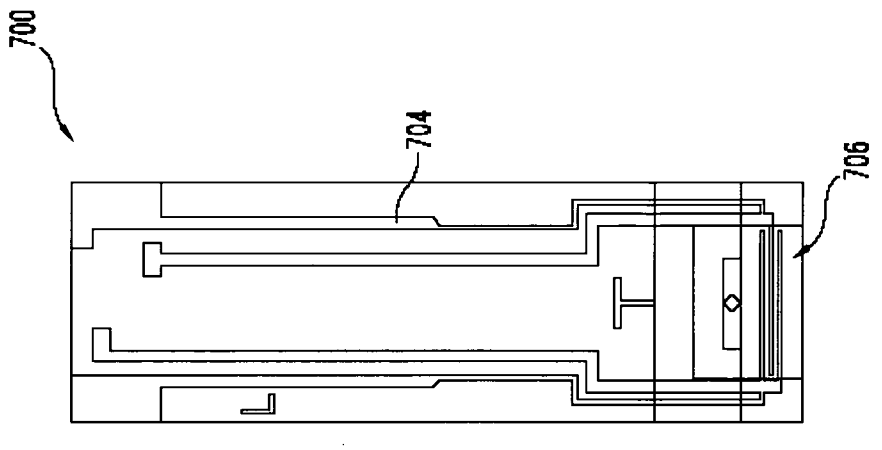

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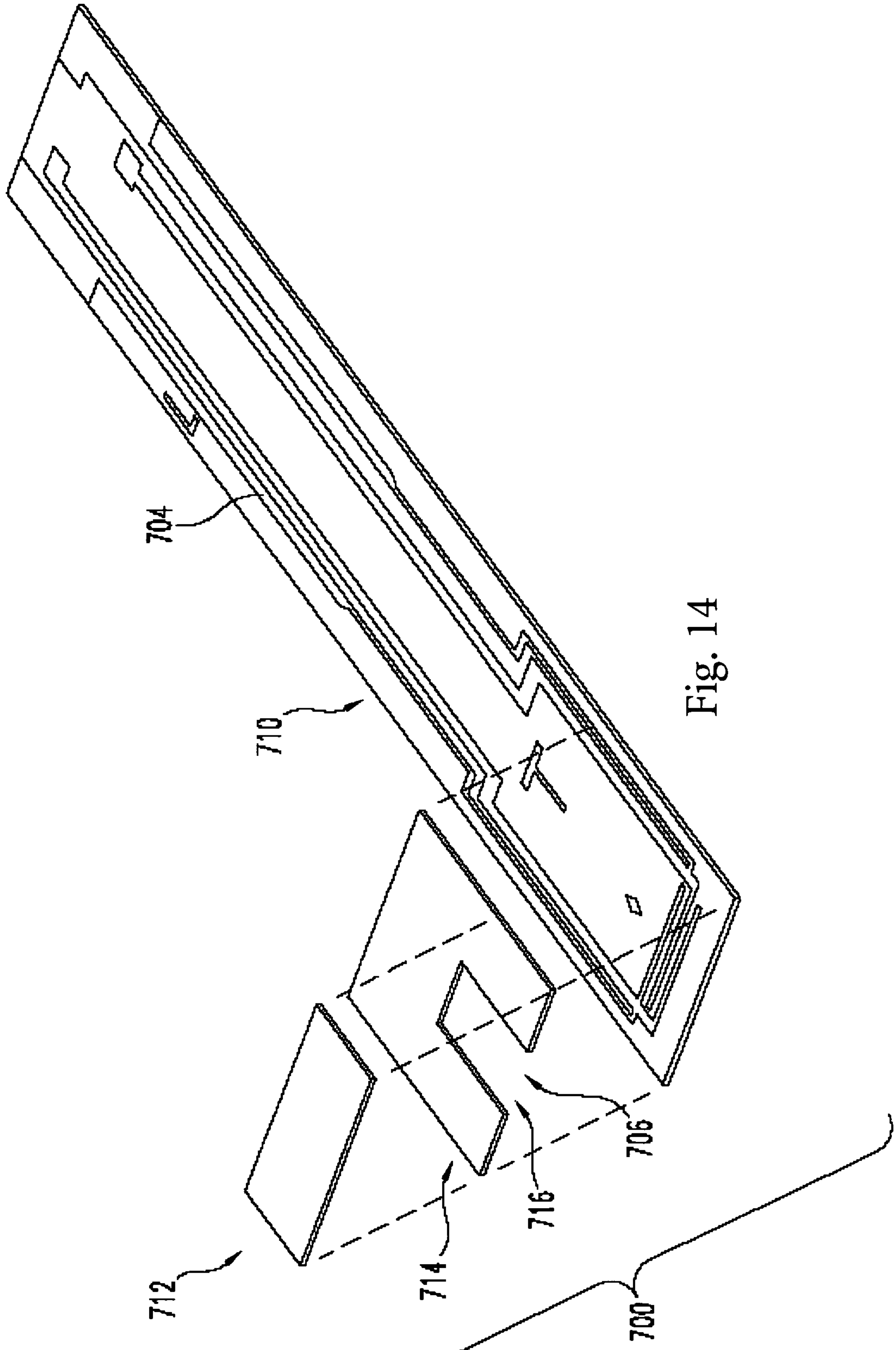

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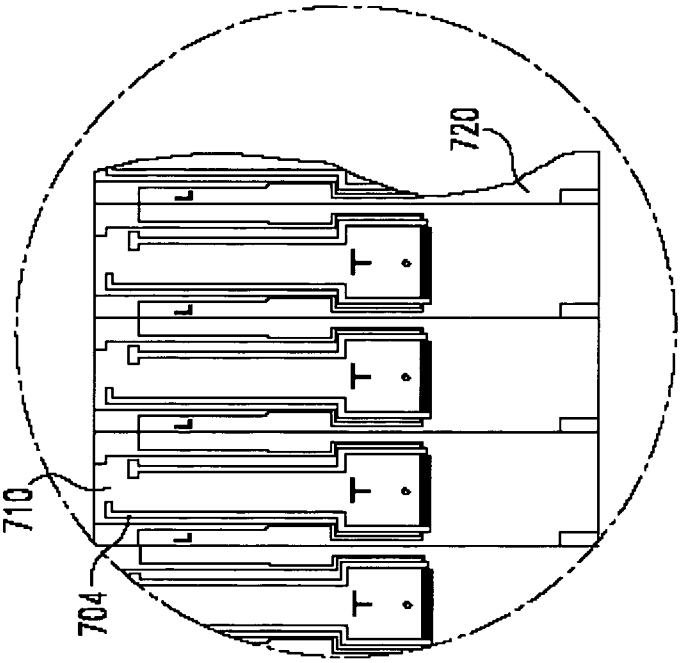


Fig. 16

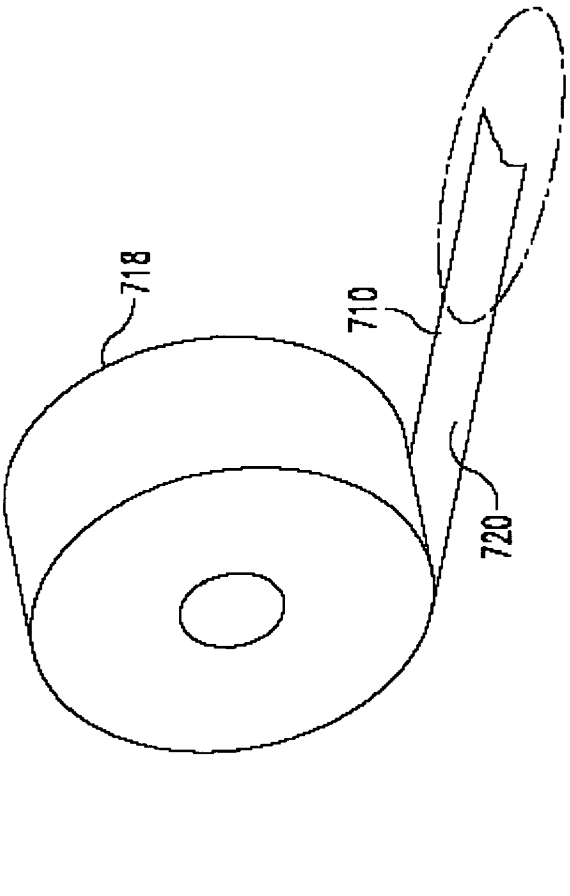
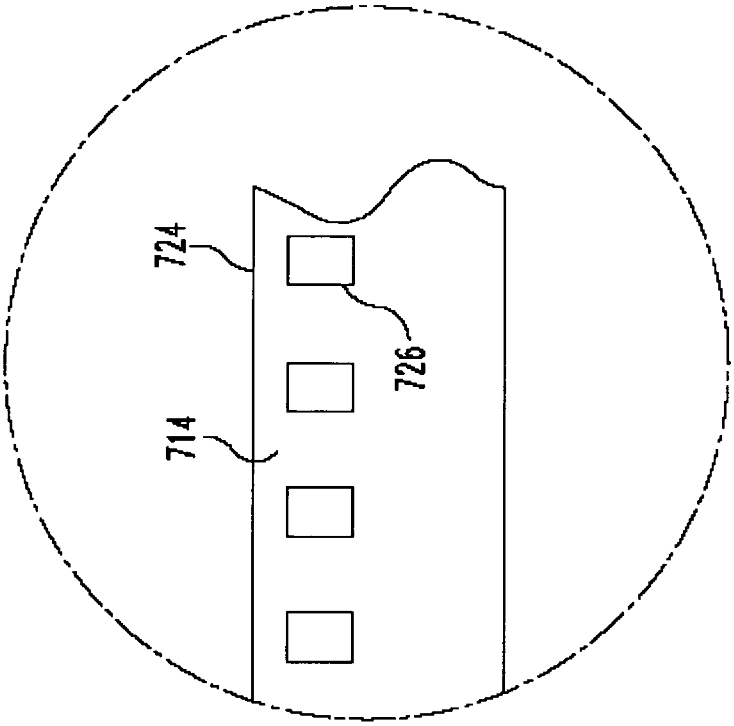


Fig. 15



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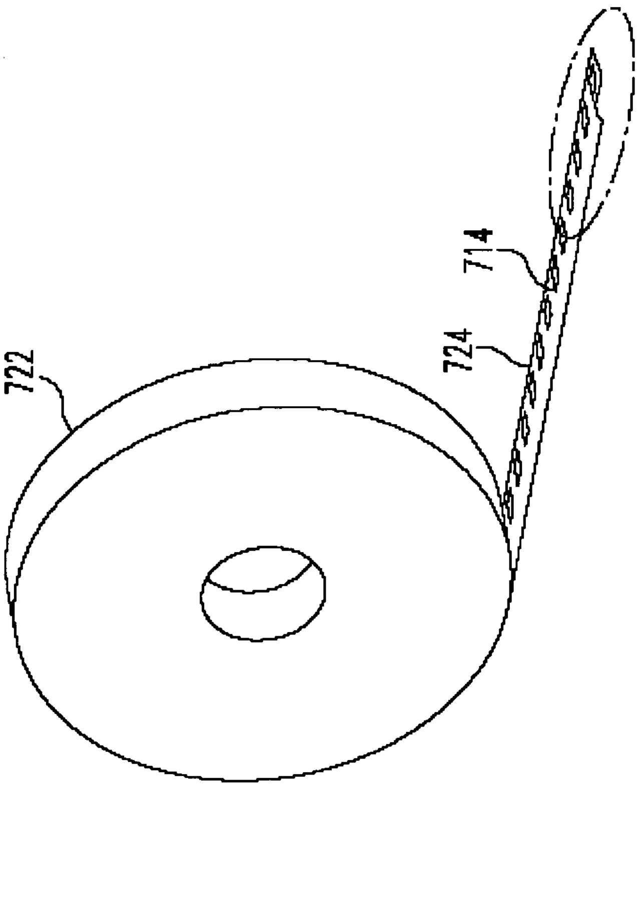


Fig. 17

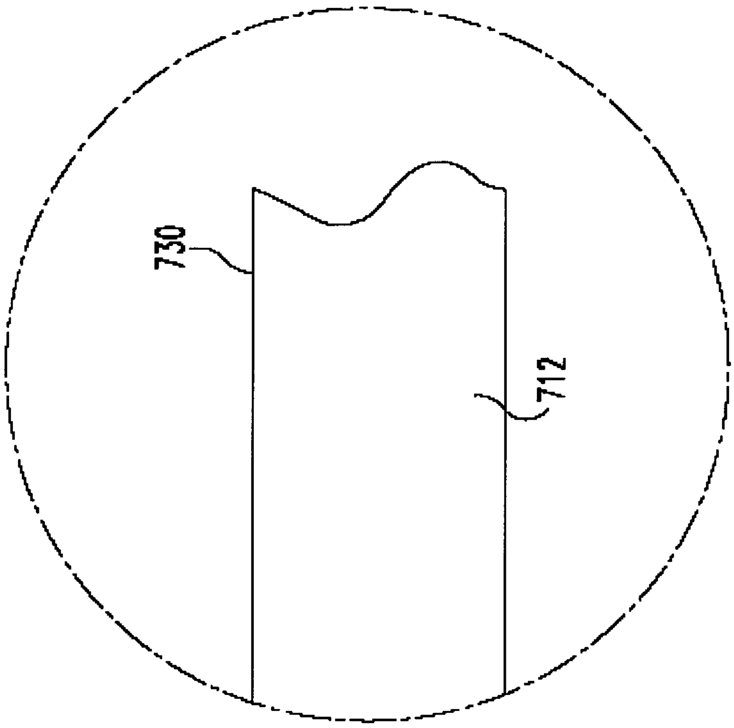


Fig. 20

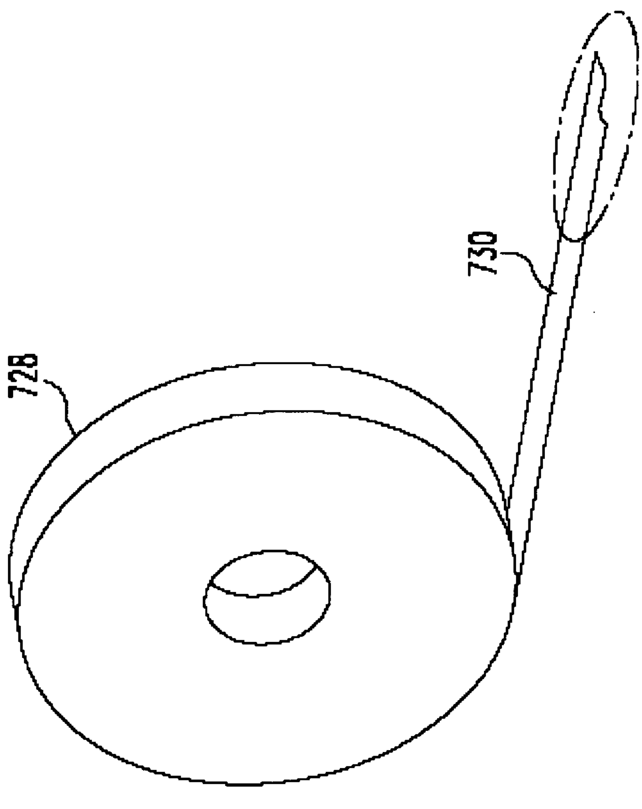
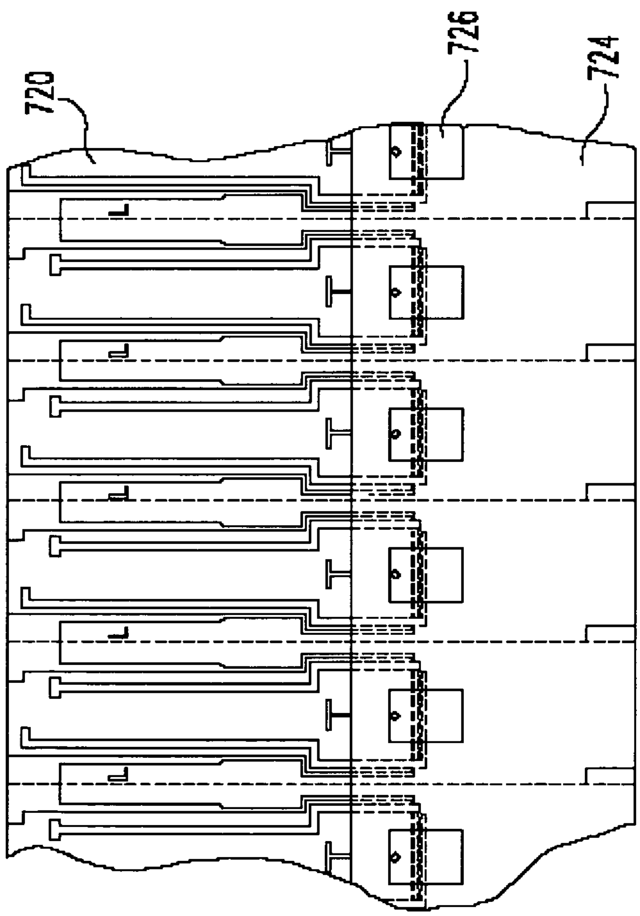


Fig. 19



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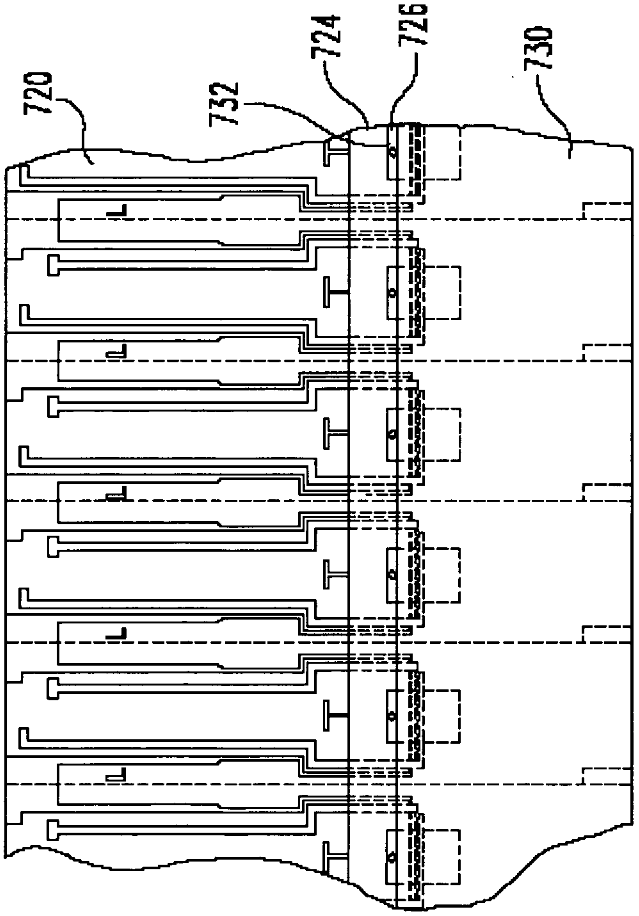

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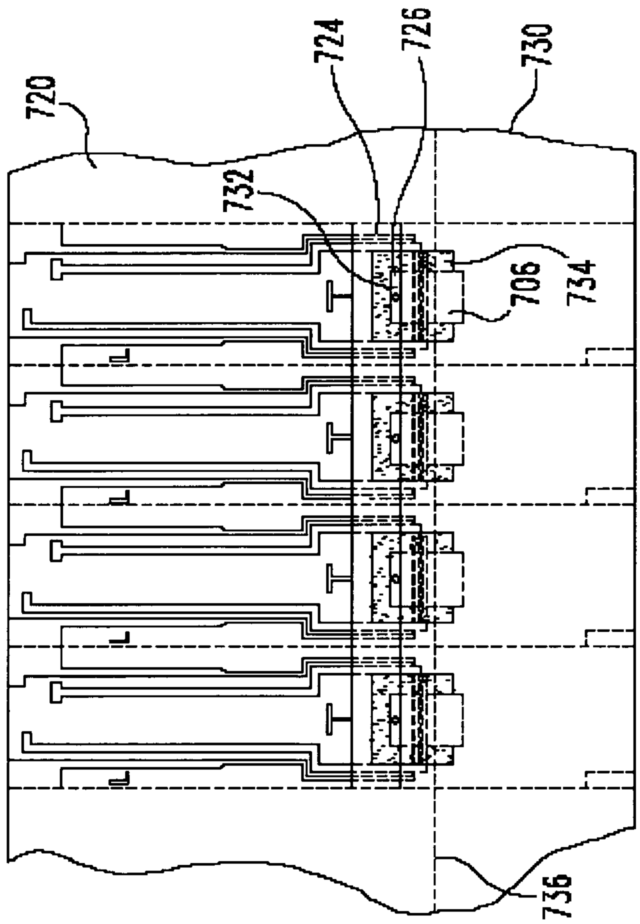

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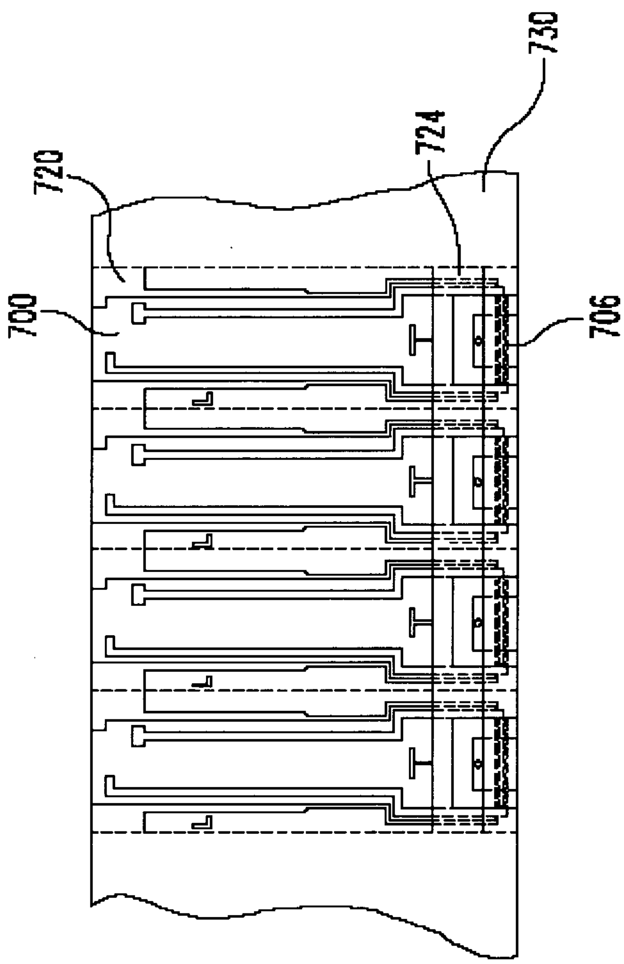

Fig. 24

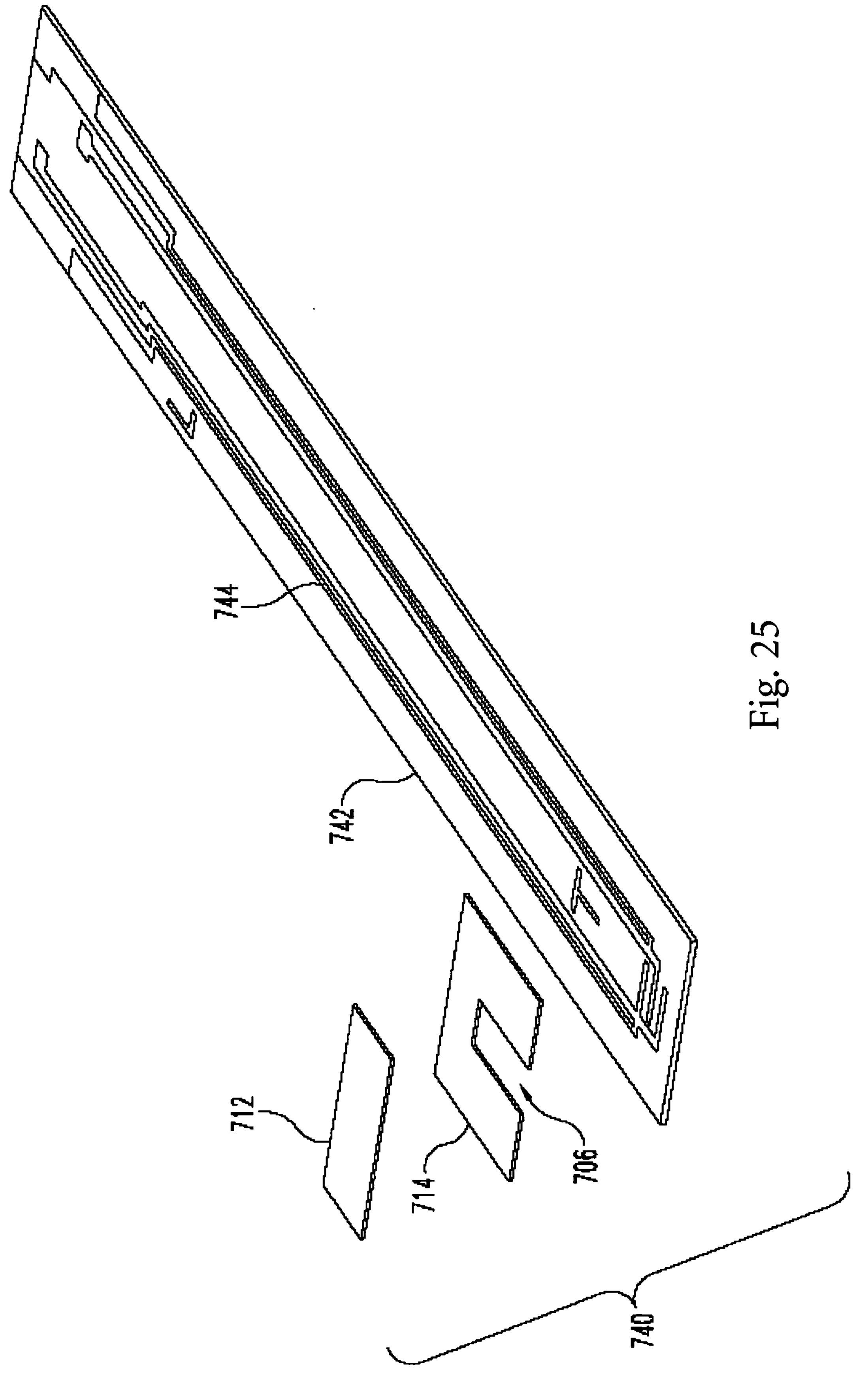

Fig. 25

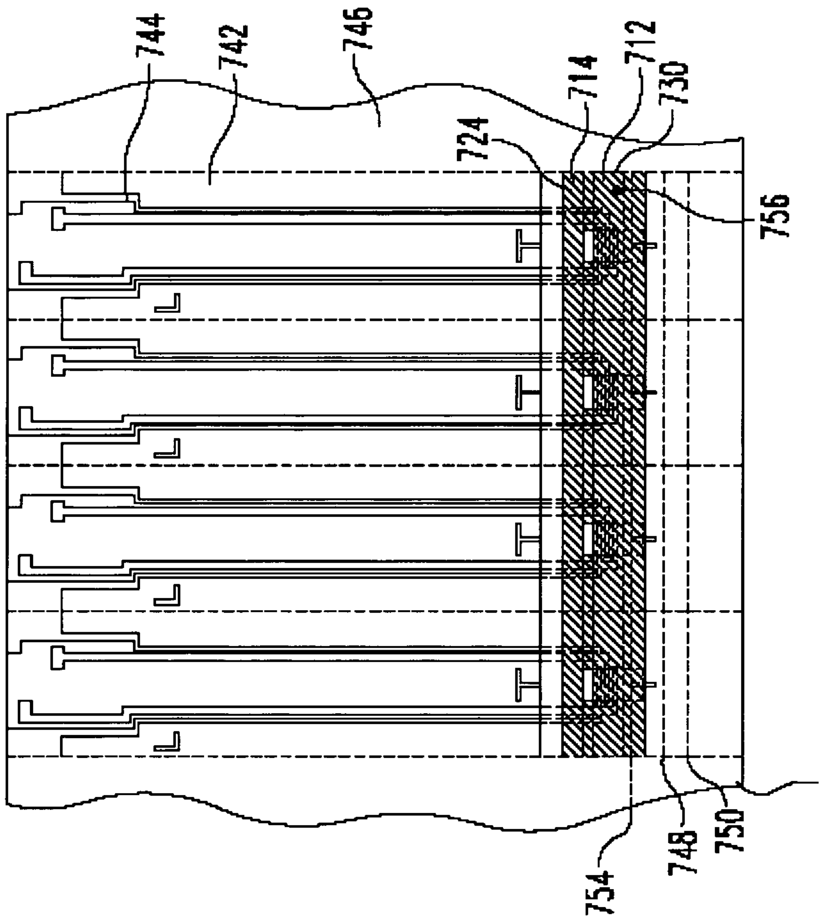

Fig. 26

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2008/005389

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N33/543

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)
G01N

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 practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PFLEGING ET AL: "Laser patterning and welding of transparent polymers for microfluidic device fabrication" PROC OF SPIE, no. 6107, 2006, XP002499485 the whole document -----	1-15
X	"RP shifts into gear" INDUSTRIAL LASER SOLUTIONS MAGAZINE, August 2006 (2006-08), XP002499486 Retrieved from the Internet: URL:http://www.industrial-lasers.com/display_article/262103/39/none/none/Deprt/RP-shifts-into-gear> [retrieved on 2008-10-13] the whole document -----	1-15

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"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

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 October 2008	29/10/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Pinheiro Vieira, E

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EBERHARDT ET AL: "Low cost fabrication technology for microfluidic devices based on micro injection moulding" PROC. M. TEC., 14 October 2003 (2003-10-14), - 15 October 2003 (2003-10-15) pages 129-134, XP002499487 the whole document -----	1-15
X	US 2006/057707 A1 (CUNNINGHAM BRIAN T [US] ET AL) 16 March 2006 (2006-03-16) paragraph [0164] - paragraph [0165]; claim 21; figure 10 -----	1-15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2008/005389

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2006057707 A1	16-03-2006	US 2003027327 A1	06-02-2003