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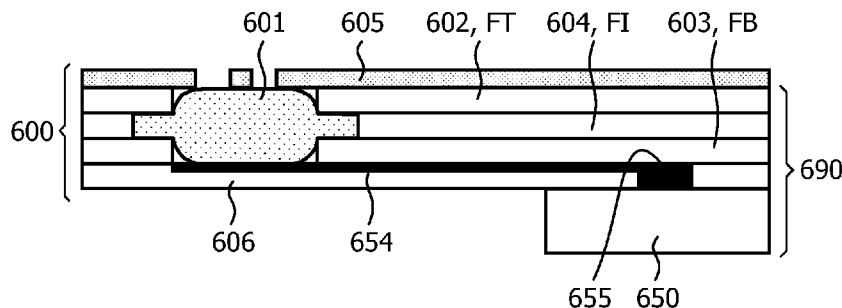
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(54) Title: FILTER UNIT FOR A CARTRIDGE



**FIG. 10**

(57) Abstract: The invention relates to a filter unit (600), a method for manufacturing such a filter unit, and a cartridge (690) comprising such a filter unit. The filter unit (600) is characterized in that it comprises a filter material (601) which is integrated into the aperture of at least one foil (602, 603, 604). In a preferred embodiment, the filter material (601) may be located in the aperture of an intermediate foil (604) which is embedded between a top foil (602) and a bottom foil (603). Such a filter unit (600) can readily be produced in cost-effective processes like roll-to-roll manufacturing technologies.



Filter unit for a cartridge

## FIELD OF THE INVENTION

The invention relates to a filter material and a filter unit for filtering a fluid, for example a biological sample like blood. Moreover, it relates to a cartridge comprising a filter unit and a method for manufacturing a filter unit.

## BACKGROUND OF THE INVENTION

The US 2011/0005341 A1 discloses a filtering apparatus comprising a filter material that is attached to an adhesive capillary structure made of a double-sided tape. A sample deposited on the filter material passes said material and enters the capillary structure for further investigation.

Moreover, the US 2010/0089815 A1 discloses a planar lateral flow filter that can be used for filtering whole blood. The filter is enclosed in a cartridge comprising ports for sample application and filtrate egress. Crush lines can optionally be generated in the filter in which the pores are compressed to direct fluid flow.

## SUMMARY OF THE INVENTION

It is an object of the invention to provide means that allow for a cost-effective production of filtering devices, particularly devices that can be used in biosensors for preparing small sample volumes.

This object is achieved by a filter unit according to claim 1, a cartridge according to claim 2, a method according to claim 3, and a filter material according to claim 4. Preferred embodiments are disclosed in the dependent claims.

Accordingly, the invention comprises a filter unit for filtering a fluid, for example a liquid of biological origin like blood, saliva, or urine. As usual, the process of "filtering" shall comprise that certain target components of the fluid are retained by the filter unit due to their specific physical and/or chemical properties (e.g. their size). The filter unit comprises the following components:

a) At least one foil that is impermeable to the fluid to be filtered and that comprises at least one aperture or opening.

In this context, the term "foil" shall denote as usual a sheet or layer of some (solid) material, wherein said material is preferably distributed homogeneously in said layer.

Moreover, the layer will typically have a uniform thickness and will be flat in the sense that its thickness is much smaller than its dimensions in the directions orthogonal to the thickness (i.e. width and length). Typically, the thickness will be in the range of 10  $\mu\text{m}$  to 1000  $\mu\text{m}$ , while length and width of the foil are in the range of several millimeters up to several centimeters. Furthermore, a foil is typically a self-supporting structure and flexible to a certain degree such that it is for example possible to bend it into a desired three-dimensional configuration or to coil it up.

b) A filter material that is permeable to at least a part of the fluid and that is integrated into the aforementioned aperture of the foil.

The integration of the filter material into the aperture of a foil means that filter material is (at least partially) located in the same layer as the foil, replacing foil material that has been removed to provide the aperture. Attachment of the filter material to the foil can be achieved in different ways, for example by gluing it to the borders of the aperture. Typically the aperture is completely filled by the filter material, implying that any fluid which passes through the aperture has to flow through the filter material. When the fluid permeates the filter material, an intimate interaction between filter material and fluid can take place by which the intended retention of target components from the fluid can be achieved. Target components like biological cells can for example be retrained by a porous filter material having a pore size smaller than the cell diameter.

By the integration of a filter material into the aperture of a foil, a filter unit is achieved that can substantially be processed in the same way as a foil. Such a filter unit can for example be produced and/or attached to other components by cost-effective manufacturing procedures like roll-to-roll techniques.

The invention further comprises a cartridge for processing a fluid, said cartridge comprising a substantially rigid carrier and a filter unit of the kind described above, wherein the carrier and the filter unit are attached (bonded) to each other.

The rigid carrier provides mechanical stability to the cartridge. Moreover, it may provide additional functions or components like examination chambers for detection processes.

Moreover, the invention comprises a method for manufacturing a filter unit comprising a filter material, particularly a filter unit of the kind described above. The method comprises the following steps, which can be executed in the listed order, in reverse order, or simultaneously:

- Bonding of two foils to each other such that they embed a filter material between them.
- Providing at least one aperture in each foil at the position of the filter material.

If the aforementioned step is done first, i.e. before the bonding of the two foils, the apertures are provided at the position where the filter material shall be located during the bonding step.

By embedding a filter material between two foils, a sandwich structure is achieved in which said filter material is firmly integrated while being accessible through the apertures in the foils. Moreover, such a procedure is compatible with effective production processes like roll-to-roll manufacturing techniques.

According to a further and independent aspect, the invention relates to a filter material for filtering fluids, for example a liquid of biological origin like blood, saliva, or urine. The filter material may particularly be used in a filter unit, cartridge and/or method of the kind described above, but it may as well be used in other devices and applications, too. The filter material comprises the following components:

- A matrix material having pores through which the fluid to be filtered can flow (at least partially, i.e. with the exception of the target components to be retained).
- A filling material that is disposed in the pores of the aforementioned matrix material in a sub-portion of the matrix material. The chemical and/or physical composition of the filling material is usually different from that of the matrix material, i.e. both materials can be distinguished when the sub-portion is analyzed. The concentration of filling material outside the sub-portion is typically zero or at least below a given threshold.

The described filter material has the advantage that the whole volume of the matrix material is functionally split into at least two portions, namely the sub-portion comprising the filling material and the remainder. Because the average free pore size in the sub-portion is typically smaller than in the remainder (due to an additional presence of filling material) and/or because of the properties of the filling material, the passage of fluid can be impaired or completely prohibited in said sub-portion. This can be used to direct the fluid flow through the filter material and particularly to keep the fluid away from regions where it is not allowed or needed, for example because these regions are used for other purposes (like mounting). When small sample volumes shall be processed, for example volumes of about 5  $\mu\text{L}$  (5  $\text{mm}^3$ ) or less, the filter material has the advantage to minimize losses of sample by blocking dead volumes within the matrix material that might otherwise fill with (lost) sample.

As a complete volume of the matrix material can be blocked, the proposed filter material is more reliable and robust than e.g. filters with linear "crush lines" which have the inherent risk to be locally penetrated. Moreover, the blocked sub-portion can already be generated during the manufacturing of the filter material. It hence comes as an intrinsic property of the filter material and needs not be produced by additional features of a filter unit, cartridge or the like in which the filter material is used. It should be noted that a conventional filter material consists completely and solely of "matrix material", i.e. the two terms are synonymous in this case.

The filter material, the filter unit, the cartridge that comprises such a filter unit, and the method are different solutions to the same problem. Explanations and definitions provided for one of these solutions are therefore valid for the other solutions, too. In the following, various preferred embodiments of the invention will be described that are specific embodiments of this filter material, filter unit, cartridge, and method.

The foil or at least one of the foils of the filter unit may preferably comprise materials selected from the group consisting of polyethylene (PE), polymethyl methacrylate (PMMA), cyclopolyolefine (COP, COC), polycarbonate (PC), polypropylene (PP), polyethylene terephthalate (PET), polyethylene naphthalate (PEN), polyvinyl chloride (PVC), polyimides (PI), polystyrene and oriented polystyrene (PS, OPS), polyvinylidene chloride (PVDC), polyamides, nylon (e.g. cast, oriented or coex, PA, 6, 11, 12, amorphous, polyarylamide MXD6), polyvinyl butyral (PVB), liquid crystal polymers (LCP), and fluoropolymers (particularly PCTFE).

The kind of the filter material and/or matrix material will be chosen in view of the application at hand, i.e. with respect to the fluid to be processed and the target components to be retained. Typically, the filter/matrix material will be porous with an average pore size ranging between about 0.1  $\mu\text{m}$  and about 1000  $\mu\text{m}$ . Appropriate filter/matrix materials comprise for example asymmetric polysulphone membranes (e.g. Vivid™ Plasma Separation Membrane of Pall Corporation, Port Washington, NY, USA; VF blood separation filters of Whatman plc, Maidstone, UK).

As explained in connection with the manufacturing method, a preferred way to integrate filter material into an aperture of a foil is to arrange said filter material between two foils, which will in the following be called "top foil" and "bottom foil" for purposes of reference. The size (area) of the filter material is in this case preferably chosen larger than that of one aperture in one foil, preferably larger than that of both apertures in both foils. The

border of the filter material will then be firmly held (sandwiched) between the top and bottom foil.

In a further development of the aforementioned embodiment, the filter material is arranged in the aperture of a third foil, called "intermediate foil" in the following, wherein said intermediate foil is enclosed between the top foil and the bottom foil. The thickness of the intermediate foil is preferably the same as or less than the thickness of the filter material. Moreover, the aperture in the intermediate foil is preferably large enough to completely accommodate the filter material without overlap. As already mentioned, the apertures in the top and bottom foil, on the contrary, are preferably smaller than the area of the filter material. The provision of the intermediate foil has the advantage that the filter material can better be integrated into the stack of foils, particularly without the generation of undesirable dead volumes.

If the filter unit comprises a stack of two or more foils, all these foils may be identical in geometry and material. In an alternative embodiment, there are at least two foils of the stack that have different geometry and/or that consist of different materials. For example, the thickness, the total area, or the aperture size or shape of two foils may be different.

In a specific embodiment, peripheral zones or edge areas of the filter material are mounted / clamped between the top and bottom foils at the level of the intermediate foil.

This can prevent the sample fluid to flow through these peripheral zones or edge areas – that would lead to a loss of the sample quantity which would be a significant drawback for small volume samples.

Pores of said edge areas or peripheral zones may be filled with a filling material.

The one or more foils that are comprised by the filter unit may geometrically be layers of uniform thickness. In a preferred embodiment, at least one foil of the filter unit may however comprise one or more cavities, i.e. spaces where foil material is missing in comparison to the geometry of a uniform layer. Cavities in a foil may readily be produced for example by hot embossing. A cavity may for example be generated around the border of an aperture of a foil to create a space in which filter material can be accommodated. Moreover, cavities in a foil may constitute channels, chambers or the like through which fluid can flow for processing purposes.

In a related embodiment, a foil of the filter unit may optionally comprise protrusions that define regions of material additional to the geometry of a uniform layer. This embodiment is largely equivalent to the aforementioned one as a foil with a three-dimensional structure that deviates from a simple uniform layer geometry can be regarded as a foil with cavities (in a thick layer) or a foil with protrusions (from a thin layer). Generally, a structured foil may comprise both cavities and protrusions.

The filter material of the filter unit may preferably have on at least one side a dome shape, i.e. it bulges into one direction out of the plane of the filter unit or its foils, respectively. Such a dome shape is often advantageous during the processing of a fluid. For example, a droplet of a sample deposited onto the filter may more readily be absorbed if the filter material bulges towards the drop. Similarly, a dome shape of the filter material may be used to guarantee contact of the filter material to subsequent components of the filter unit or the cartridge. This minimizes dead volume and ensures that fluid which has passed the filter material is forwarded by capillary forces. It should be noted that the filter material may have a dome shape in one direction only or in two (opposite) directions. In the latter case, the cross section of the filter material within the foil aperture will typically be convex.

In a further embodiment, a holding element may be provided for pressing or biasing the filter material in one given direction. As a consequence of this pressing, the aforementioned dome shape (in one direction) may result. In general, the pressing by the holding element can be used to guarantee a certain geometry of the filter material and/or to guarantee contact between the filter material and subsequent components of the filter unit or the cartridge.

The aforementioned holding element may for example be realized by an additional layer, particularly an additional foil, of the filter unit that presses the filter material in one direction. This realization of the holding element may readily be produced, for instance by the same roll-to-roll processes by which the filter unit itself is manufactured.

In many applications, one side of the filter material will remain accessible during the intended use of the filter unit. Access may for example be necessary to deposit sample fluid onto the filter material. In a preferred embodiment, a side of the filter material that is accessible during use is designed to hold a quantity of a given fluid that ranges between a given minimum and a given maximum quantity, provided that the fluid completely covers the filter material and that it is held by (molecular) adhesion forces only. A design parameter that is relevant for this aim is the size and shape of the aperture in the outer foil which determines the area of the filter material that is directly accessible. Another important

design parameter is the surface chemistry at the respective filter side, particularly the chemistry of the associated foil and/or the filter material. The surface of the foil may for example be hydrophobic in order to repel an aqueous fluid like blood. With the described design it can be guaranteed that a desired quantity of blood is taken up by the filter material after the application of an undefined amount of blood to the accessible filter side. If less than the minimum amount of fluid is applied, at least a part of the filter material will not be covered by the fluid, which can readily be detected by visual inspection.

The one or more foils of the filter unit may have just a single aperture at which the filter material is located. In a more elaborate design, the filter material of the filter unit may be covered by a foil with at least two apertures providing access to the same element of filter material. This foil with the several apertures may particularly be arranged on the side of the filter material that remains accessible during use. Using a plurality of small apertures instead of a single large aperture above the filter material helps to prevent an undesired contact between the filter material and large objects, for example instruments or the finger of a user (e.g. during direct uptake of fingerprick blood). Direct touching can be prevented if the apertures are sufficiently small, for example having a diameter of less than about 5 mm.

The filter unit may optionally comprise electrical components, particularly electrical leads, electrodes, and/or an RF ID tag. These components are preferably generated in the same manufacturing procedure as the foil, using for example roll-to-roll techniques. Electrically conductive structures may for example be printed onto a foil comprised by the filter unit.

The carrier of the cartridge may optionally comprise some structure for supporting the filter material of the filter unit. This support may provide mechanical stability to the filter material and contact between the carrier and the filter material.

In general, the carrier may comprise any material or structure that is suited for the intended purpose. In a particular embodiment, the carrier may at least locally be transparent to allow for the optical examination or processing of the applied fluid.

The carrier of the cartridge may optionally comprise at least one cavity for the accommodation of a fluid, wherein said cavity is preferably connected to the filter material. In the latter case, fluid can be transported through the cavity towards the filter material, or fluid that has passed the filter material can be taken up by the cavity for further processing steps. The cavity in the carrier may for instance comprise one or more (elongated) channels for transporting fluid or one or more chambers for accommodating fluid during processing steps.



In a further development of the aforementioned embodiment, at least one cavity of the carrier is covered by a foil of the filter unit that is attached to the carrier. An elaborate structure of cavities (e.g. channels and/or chambers) in the carrier can thus readily be produced, for example by injection molding, as the cavities may initially be open at the side which is later covered by the foil of the filter unit.

According to another preferred embodiment of the invention, a first (micro-) fluidic system is located on a first side of the filter material, and a second (micro-) fluidic system is located on the opposite side of the filter material. For purposes of reference, the first fluidic system will in the following be called "pre-treatment fluidic system", and the second one "post-treatment fluidic system". The names indicate that the pre-treatment fluidic system typically transports raw (untreated) fluid, while the post-treatment fluidic system is only reached by filtered (treated) fluid. The provision of a pre-treatment and a post-treatment fluidic system on opposite sides of the filter material has the advantage that one and the same sample of a fluid can be processed in parallel with and without a filtering step, respectively. Thus it is for example possible to examine whole blood (in the pre-treatment fluidic system) as well as blood plasma (in the post-treatment fluidic system) from a single blood sample.

Depending on the intended application and processing, the aforementioned fluidic systems may individually be designed. In a preferred embodiment, the pre-treatment fluidic system may for example comprise an inlet for fluid, e.g. for a drop of blood. This fluid will then spread in the pre-treatment fluidic system, where certain investigations or processing steps can be done, and also pass through the filter material to the post-treatment fluidic system for the execution of other processing steps.

The pre-treatment fluidic system may for example comprise a processing chamber for the processing of a fluid that has NOT passed the filter material.

Similarly, the post-treatment fluidic system may comprise a processing chamber for the processing of a fluid that has passed the filter material.

According to another embodiment of the invention, the filter unit and/or the carrier comprises a processing chamber that is located adjacent to the filter material and in which fluid can be processed, for example be investigated with respect to the presence of certain target substances. Most preferably, said processed fluid is a fluid which has passed the filter material. Arrangement of a processing chamber directly adjacent to the filter material helps to minimize the required amount of fluid and the time for processing it because losses of material and time during a transport of the fluid (from the filter material to the processing chamber) are avoided.

In the following, various preferred embodiments of the invention will be discussed that relate particularly to the filter material in which a filling material is disposed in the pores of a sub-portion.

During the use of any filter material, a part of this material will typically be needed for mounting and sealing purposes and hence be lost for filtering. With the filter material of the present invention, such parts can be constituted by the sub-portion which comprises a filling material to reduce or completely prevent the loss of fluid in dead volumes.

The present invention also relates to a method for manufacturing a filter material which comprises the following steps:

- Providing a matrix material that has pores through which fluid can flow. This step can particularly comprise the production of said matrix material from given raw materials according to processes known in the art of filter manufacturing, and/or it may comprise the shaping of prefabricated matrix material in desired sizes and forms.

- Disposing and/or generating a filling material in the pores of the aforementioned matrix material within a sub-portion of the matrix material. This may for example be achieved by filling said pores with a separate filling material, or by transforming the original matrix material (chemically and/or physically) into a "filling material".

The filling material may particularly be repellent to the fluid to be filtered. For example, the filling material may be hydrophobic if the fluid to be filtered is an aqueous liquid like blood. Similarly, a hydrophilic filling material might be used if a hydrophobic fluid shall be filtered. Using a repellent filling material has the advantage that the entrance of fluid into the respective sub-portion of the matrix material can be prevented even if there are open pores. Hence some porous structure can be left in this portion of the matrix material, which allows for example to squeeze the sub-portion for mounting purposes or the like.

In a preferred embodiment of the invention, the sub-portion of the matrix material that contains the filling material comprises at least about 20 %, preferably at least about 50 %, most preferably at least about 75 % of the total volume of the filter material (in its non-compressed state). In this case a large or even the largest part of the filter material is constituted by the sub-portion, i.e. this portion has a non-negligible size. If only small amounts of the fluid to be filtered are available, it is therefore particularly favorable that this fluid is prevented from getting lost in the sub-portion.

It was already mentioned that a part of a filter material will usually be needed for mounting and/or sealing purposes. For the filter material of the invention, the sub-portion in which the pores comprise the filling material is therefore preferably at least partially used

for or intended for mounting of the filter material. Thus the necessary mounting structure can be provided without generation of dead volumes in which sample fluid would be lost.

The sub-portion of the matrix material in which the pores contain the filling material may optionally be or comprise a peripheral zone of the filter material, for example a ring of certain widths at the periphery of a disc shaped filter material. The peripheral zone is particularly suited for mounting the filter material in a sealed manner.

There are different ways how filling material can be transferred into the pores of a matrix material. According to a preferred embodiment, the filling material is filled into the pores of the sub-portion of the matrix material while being in a liquid state. Once being in the pores, the initially liquid filling material may solidify. This solidification may for example occur due to chemical reactions taking place in the filling material. A chemical and/or physical solidification of the filling material may occur spontaneously, or it may be initiated and/or supported by the application of a solidification-initiator like heat and/or radiation, for example UV radiation.

In general, care has to be taken during the manufacturing procedure that filling material is finally only present in the desired sub-portion of the matrix material and not in other regions. One approach to achieve this is by supplying the filling material in such a low quantity that it can only fill the intended sub-portion and not more than that. A thin layer of a wax-like material could for example be locally applied (e.g. only at the edge) and then reflowed by a (possibly local) heat pulse, wherein the amount of filling material is chosen such that it is just enough to locally saturate the rim of the matrix material. There is simply not enough material to fill more than the intended area.

Another approach would be to apply a (fast-) solidification-initiator at the border of the sub-portion to be filled (e.g. by applying it to the whole area outside this sub-portion) and then to supply the filling material to said sub-portion. When this filling material reaches the border of the sub-portion, it is affected by the solidification-initiator which shall be strong enough that immediate solidification of filling material occurs. This prevents further spread of the filling material into areas outside the intended sub-portion. For example, the central area of a matrix material could be illuminated with a high UV intensity at the moment the filling material is supplied, wherein a filling material is used that instantly solidifies at UV exposure. If the filling material is supplied from the edge of the matrix material and if the solidification is quick enough, the filling material will not be able to reach the central part of the filter. It solidifies at the edge of the UV illuminated central area of the filter.

Moreover, a localized application of a solidification-initiator like UV radiation further allows to solidify the filling material only in selected areas of the matrix material and to later remove non-solidified excess filling material.

According to another embodiment of the manufacturing method of filter material, the initial matrix material is brought into contact with a solid filling material, and said filling material is then molten such that it flows into the pores of the sub-portion of the matrix material. Next, it is preferably solidified there as described with respect to the aforementioned embodiment. The flow of molten filling material into the pores of the matrix material may preferably be driven by capillary forces, thus insuring that a complete filling takes place.

In general, the filling material may be any chemical substance that is suited for the desired purpose and that is compatible with the matrix material and its intended application. In a preferred embodiment, the filling material may comprise a glue or a wax. These materials can readily fill pores of a matrix material while being in a liquid state and then be fixed there by subsequent solidification.

Characteristic parameters of the matrix material like its (average) pore size will be chosen with respect to the application it is intended for. In a preferred embodiment of the invention, the matrix material is suited for separating plasma from whole blood. This may for example be achieved if the effective maximal pore size of the matrix material is smaller than about 2  $\mu\text{m}$  at the relevant locations in the filter.

According to another embodiment of the invention, the matrix material comprises at least two parts of different (average) pore sizes. Accordingly, different target components of the fluid to be filtered will be retained by these two parts. A part of the matrix material with a larger average pore size may preferably be arranged in front of a part with smaller average pores size (seen in flow direction of the fluid to be filtered). Large components of the filtered fluid will then be retrained first. The sub-portion of the matrix material that comprises a filling material is preferably located in a part with a smaller pore size in order to prevent the loss of already pre-filtered sample fluid.

It is to be understood that the terms “filter unit”, “cartridge”, “filter material” are used to identify different elements of a general filter device or filter system, the filter material being the core part of the filter device, the filter unit being the filter material with its holding members and the cartridge being the whole microfluidic device incorporating the filter unit and the filter material. Each one of the “filter unit”, “cartridge”, “filter material” defines different levels of the filter device and can therefore be protected as such. The filter

system may further comprise an analyzer arranged to receive the cartridge for analyzing purpose of the sample.

## BRIEF DESCRIPTION OF THE DRAWINGS

These and other aspects of the invention will be apparent from and elucidated with reference to the embodiments described hereinafter.

In the drawings:

Fig. 1 shows a schematic cross section through a first filter unit according to the invention;

Fig. 2 shows an exploded perspective view of the filter unit of Figure 1;

Fig. 3 shows a top view onto the filter unit of Figure 1 (top drawing) and top views onto the foils constituting said filter unit (bottom three drawings);

Fig. 4 shows a cross section through a cartridge comprising the filter unit of Figure 1 before the attachment of the filter unit to the carrier;

Fig. 5 shows a cross section through a cartridge with a second filter unit comprising foils of different thicknesses;

Fig. 6 shows a cross section through a cartridge comprising a third filter unit with an additional top foil for holding the filter material;

Fig. 7 shows views onto the bottom side of four embodiments of the additional top foil of the cartridge of Figure 6, said embodiments comprising apertures with radial slots, an aperture composed of three connected small circular openings, and an aperture composed of three unconnected small circular openings, respectively;

Fig. 8 shows a cross section through a cartridge comprising a fourth filter unit with a bottom foil that is larger to cover an associated carrier and with an additional top foil having several openings;

Fig. 9 shows a cross section through a cartridge comprising a fifth filter unit before the attachment of the filter unit to the carrier, wherein the bottom foil of the filter unit covers open cavities of the carrier;

Fig. 10 shows a cross section through a cartridge comprising a sixth filter unit with a post-treatment fluidic system;

Fig. 11 shows a top view onto a cartridge comprising a seventh filter unit and an associated carrier, wherein the filter unit has a pre-treatment and a post-treatment fluidic system;

Fig. 12 shows a cross section through the cartridge of Figure 11;

Fig. 13 shows a top view onto a cartridge comprising an eighth filter unit with a pre-treatment fluidic system, wherein processing chambers are located adjacent to the filter material;

Fig. 14 shows a cross section through the cartridge of Figure 13;

Fig. 15 shows a top view onto a cartridge similar to that of Figures 11 and 12 but with a pre-treatment fluidic system that splits into three parallel branches;

Fig. 16 shows a top view onto a cartridge similar to that of Figures 13 and 14 but with a pre-treatment fluidic system that splits into three parallel branches;

Fig. 17 shows a cross section through a cartridge comprising an eleventh filter unit that allows for the application of a sample liquid under visual control, showing the case in which a maximal amount of fluid is applied;

Fig. 18 shows the cartridge of Figure 17 when a minimal amount of fluid is applied;

Fig. 19 shows a cross section through a twelfth filter unit comprising a filter material with a sub-portion that is filled with filling material;

Fig. 20 shows a top view onto the filter material of Fig. 19 for two different diameters;

Fig. 21 shows a cross section through a thirteenth filter unit comprising a filter material with two parts of different pore size and a sub-portion filled with filling material.

Like reference numbers or numbers differing by integer multiples of 100 refer in the Figures to identical or similar components.

## DETAILED DESCRIPTION OF EMBODIMENTS

Biosensors are known for the detection of specific target molecules in body fluids like saliva, urine, and especially blood. A biosensor platform as it is for example known from the US 2010/0310423 A1 (also called Philips "Magnetech" platform) uses multi-chamber disposable cartridges. Separate detection chambers are used for the selective detection of different target proteins using immunoassays based on magnetic particles and optical detection methods (e.g. frustrated total internal reflection (FTIR), or single bead detection).

In order to reduce costs of the aforementioned biosensors, a more cost effective design of the disposable cartridge is desirable. Preferably the new design should allow for a production based on roll-to-roll manufacturing techniques (e.g. hot embossed

foils, lamination, etc.). Thus the easy combination of a number of functions (capillary fluid transport, RF-ID, filter mounting, electrochemistry etc.) in simple subunits can be achieved that can still be combined with injection molded cartridge parts (if necessary, e.g. for sensitive optical detection and/or evanescent field excitation). Another objective is to allow the detection of target molecules in both blood and plasma starting from a limited volume blood sample (fingerprick). Moreover, optimal exploitation of small sample volumes is desirable. According to one aspect, the proposed approach suggests a switch to roll-to-roll processing wherever possible. An advantage of this approach is that some functionalities are already made in roll-to-roll processes (e.g. RF tags), which enables a smooth integration.

An important aspect of the invention is hence a filter mounted in a foil, enabling the use of low-cost roll-to-roll (R2R) production technology. This subunit can be supplemented with other foil based functionalities (e.g. screen printed electrodes, RF-ID tag, capillary channels, hot-embossed structures). The foil based subunit may be combined with an injection molded part (if needed) to form a disposable cartridge. The injection molded part contains the critical functionalities that cannot be realized in R2R technology.

In the following, a number of examples of the combination of a roll-to-roll subunit ("filter unit") and an injection molded part ("carrier") that together form a cartridge for e.g. the Magnotech platform will be described. All examples include a blood separation filter that is mounted using lamination techniques. For some applications the injection molded part can be replaced by a foil based part as well, leading to a fully foil based cartridge.

Figure 1 shows a filter unit 100 (not to scale) according to a first embodiment of the invention. The coordinate device shown in this Figure applies similarly to Figures 4, 5, 8, 9, 10, 12, 14, 17, 18, 19, and 21 (i.e. to all Figures where no other coordinate device is shown). Figures 2 and 3 show an exploded view and a top view of the filter unit 100, respectively.

The filter unit 100 comprises a filter material 101 that is porous and therefore (partially) permeable to a fluid like a sample of blood. As can be seen from Figure 2, the filter material 101 is provided as an approximately circular disk. This disc of filter material 101 fits into an associated aperture A' of an "intermediate foil" 104/FI.

Moreover, the filter unit 100 comprises a top foil 102/FT and a bottom foil 103/FB, wherein the terms "top" and "bottom" refer to the position of these foils in the drawings. The top and bottom foils 102, 103 have holes or apertures A that are smaller than the disc of the filter material 101, and they are laminated to opposite sides of the

aforementioned intermediate foil 104. Accordingly, the top foil 102 and the bottom foil 103 enclose the intermediate foil 104 and the filter material 101. As can be seen from Figure 1, the filter material 101 is thicker than the intermediate foil 104. It is therefore compressed and bulges (in positive and negative z-direction) within the apertures A of the top and bottom foil.

It should be noted that in all drawings the foils that function as a "top foil", a "bottom foil", or an "intermediate foil" have additionally been tagged by the reference signs FT, FB, and FI, respectively, to highlight their unique roles.

An experimental blood separation test was performed with a filter unit like that of Figures 1–3, comprising a test filter material (Pall Vivid Plasma Separation membrane grade GX; diameter 10 mm) laminated between foils. The sample volume (about 40  $\mu$ L) used was deliberately chosen too large to provoke edge leakage. However, no leakage was observed (i.e. the outer border of the filter material, which is enclosed between the top and bottom foil, remains substantially dry). Clear plasma was observed at the outlet side of the filter material.

While the filter unit 100 of Figures 1–3 consists of three foils, it is clear that lamination of the filter material between just two foils or layers is possible as well. In this case one or both foils will preferably have an embossed structure around the aperture for the filter material.

Figure 4 shows a cartridge 190 consisting of the filter unit 100 of Figures 1–3 and a carrier 150, wherein these two components are shown immediately before they are attached to each other using lamination technology.

The carrier 150 consists of a body 151, which is for example made from transparent plastic by injection molding and which comprises a filter support 153, one or more processing/detection chambers 155, and a channel 154 connecting the support to said chamber(s). Moreover, the carrier 150 comprises a laminate 152 which covers and closes the processing chamber 155 and the associated channel 154.

The embodiment of the filter unit 100 is symmetric in the sense that the geometry of the apertures A and the thicknesses of the top and bottom foils 102, 103 are identical. In practice, it can be advantageous to choose an asymmetric structure (different aperture diameter, different foil thicknesses etc.). Figure 5 shows an exemplary cartridge 290 with a filter unit 200 having an asymmetric design: the bottom foil 203/FB is thicker than the top foil 202/FT (and the intermediate foil 204/FI). Asymmetry can be deliberately introduced by the order in which the lamination is executed or by the asymmetric nature of the filter material itself. Asymmetric situations will generally result in doming of the filter material,



upwards or downwards. This doming can be used to enhance the good contact that is normally required between the filter material and the filter support. Especially in the situation of a blood separation filter combined with a very limited sample volume it is advantageous to strictly reduce the dead volume between filter and filter support to a minimum.

The carrier 250 that is attached to the filter unit 200 creates a processing chamber 255 immediately adjacent to the exit side of the filter material 201. Hence no fluid is lost for a transport from the filter to the processing chamber. The carrier 250 may for example be a rigid component (e.g. an injection molded plastic part), or an additional foil.

Figures 6 and 7 illustrate another method to guarantee a good physical contact between the filter material 301 of a filter unit 300 and the filter support on a carrier 350. Here, an additional top layer or top foil 305 is added as a "holding element" with the function to press the filter material 301 down towards the filter support.

Four exemplary options for the design of the aperture A in the additional top foil 305 that can be used to guarantee good physical contact between the filter and the filter support are shown in Figure 7. In the upper two drawings, the aperture A in the additional top foil 305 is surrounded by radial slots or cuts that allow to bend the ring-shaped border of the aperture downwards (it should be noted that the drawings show the additional top foil upside down).

In the third drawing from the top of Figure 7, a single aperture A is composed of three separate small circular openings or holes that are connected by a central hole. This results in three fingers that can be deformed to press the filter material on the filter support in the centre of the filter.

In the lowermost drawing of Figure 7, the whole aperture A consists of three separate (unconnected) circular holes. Hence the additional top foil is flat by itself but prevents domed filters to take a domed shape in the wrong direction when pressed against the filter support. Moreover, such an additional top foil also helps to prevent touching of the filter material. A foil thickness of about 0.3 mm combined with holes of 3 mm diameter protects the filter quite adequately against touching with a finger.

Figure 8 shows a fourth embodiment of a filter unit 400 in which the bottom foil 403/FB has a larger area than the top foil 402/FT and the intermediate foil 404/FI above it. Such a large bottom foil 403 can be used to close open cavities (not shown) when it is attached to a carrier 450. Moreover, the filter unit 400 comprises an additional top foil 405 having several apertures A1, A2 above the filter material 401 to prevent touching of the filter material and to bend it downwards.

The filter unit 500 shown in Figure 9 is similar to that of the Figure 8 but with all four foils 502/FT, 503/FB, 504/FI, and 505 extending over the whole area of the associated carrier 550. It can be seen that the bottom foil 503 adopts the function of the standard laminate that closes the channels and the detection chambers of the injection molded carrier 550. Hence two functions are combined here in a single foil-based subunit. The carrier 550 still contains the plasma drain channel 554 and detection chambers 555 on the right hand side. Filter unit 500 and injection molded carrier 550 are attached to each other to constitute the final cartridge 590.

Figure 10 shows another embodiment of a cartridge 690 comprising a filter unit 600 and a carrier 650. Here, the filter unit 600 consists of the following components (from top to bottom):

- an additional top layer 605 for holding the filter material down;
- a top foil 602/FT with an aperture;
- an intermediate foil 604/FI with an aperture that contains the filter material 601, for example a blood separation filter;
- a bottom foil 603/FB with an aperture;
- an additional bottom foil 606.

The additional bottom foil 606 comprises a plasma drain channel 654 and a processing chamber 655 (realized as an aperture or hole in the foil). The drain channel 654 bridges the distance between the filter position and the processing chamber 655. A filter support structure and the plasma drain channel 654 may be embossed in the additional bottom foil 606 (and/or the bottom foil 603).

The injection molded carrier 650 serves as an optical detection part that is reduced in size to the detection zone. The reduced size allows a faster and more cost effective manufacturing. The use of high grade optical material for the injection molding of the carrier 650 is reduced in this way.

Figures 11 and 12 show a top view onto and a cross section through a cartridge 790 comprising a seventh embodiment of a filter unit 700 and an associated carrier 750, wherein the filter unit has a pre-treatment and a post-treatment fluidic system. The filter unit 700 comprises the (blood) filter material 701 that is arranged in an intermediate foil 704 and laminated between a top foil 702 and a bottom foil 703.

Moreover, an additional top foil 705 is provided on the top foil 702. This additional top foil 705 comprises a "pre-treatment fluidic system" with a blood deposition hole 710 and an integrated blood supply channel 711 that connects this hole 710 to the blood

separation filter 701. The blood supply channel 711 also serves to fill specific detection chambers 712 for blood (schematically represented by the rectangular structures in Figure 11).

Furthermore, an additional bottom layer 706 is provided that comprises a "post-treatment fluidic system" with a plasma drain channel 754 and a plasma detection chamber 755. The channel 754 supplies plasma to the detection chamber 755 on the right hand side. This part is similar to that of Figure 10.

The main objective of this embodiment is to use a single (fingerprick) blood sample with a limited total sample volume for both measurements in blood and plasma. Another advantage of such a structure is that the filter material 701 is brought closer to the plasma detection area 755, thus reducing the volume of plasma needed. This is because the distance between the sample deposition area 710 and the detection area 755 does not have to be bridged by a long plasma channel filled with plasma that is not used in a test.

An example of an application of the cartridge 790 is that one or several of the blood detection chambers 712 (or the channel 711 itself) is used for electrochemistry, while the plasma in the post-treatment fluidic system is used for detection of proteins. In order to realize electrochemical detection procedures, screen-printed electrodes as they are used in microscale electrochemistry can for example be realized on one of the foils (e.g. 705, 702) used in the lamination process.

The components used in the pretreatment of a blood separation filter can be incompatible with electrochemical measurements in blood. A way to cope with this kind of interferences is to fluidically separate the filter material 701 and the detection chambers 712, 755 for blood and plasma.

It should be noted that the provision of a pre-treatment fluidic system and a post-treatment fluidic system which are coupled by a fluid-treatment element is an independent aspect of the invention.

In this example the size of the injection molded carrier 750 for optical detection can also be reduced to a minimum as the majority of the functionality is transferred to the laminated structure of the filter unit 700.

Figures 13 and 14 show a cartridge 890 that is a modification of the cartridge of Figures 11 and 12. Again there is a combination of a laminated filter material 801 and a pre-treatment fluidic system, the latter comprising an integrated blood supply channel 811 between a blood deposition hole 810 and the filter material.

The components that are different relate to the post-treatment fluidic system behind the filter material 801. In particular, processing chambers 855 are formed in the carrier 850 which is attached at the aperture in the bottom foil 803. Hence the processing chambers 855 with the detection area for plasma are directly under the blood separation filter material 801.

One objective of the cartridge 890 is to allow detection of target molecules and/or electrochemical properties in both blood and plasma. Moreover, the proposed structure brings the filter material 801 closer to the plasma detection area 855 to reduce the volume of plasma needed. The distance between the sample deposition area 810 and the detection area 855 does not have to be bridged by a plasma channel filled with plasma that is not used in a test. Instead, optimal use of the plasma generated is made and the required sample volume is reduced to a minimum. Another important advantage is that the time between sample deposition and the arrival of plasma in the detection zone is reduced. As soon as the filter is wetted with blood, the first plasma arrives almost instantaneously at the bottom side of the filter. Moreover, a considerable fraction of the cartridge 890 can be made in a roll-to-roll technology which is meant to reduce the overall costs.

It should be noted that the arrangement of a processing chamber (e.g. 855) immediately adjacent to a fluid-treatment element (e.g. the filter material 801) is an independent aspect of the invention.

In principle it is also possible to distribute the fluid to be filtered (e.g. blood) over several separation filters. This can for instance be useful if the chemical pre-treatment components present in a blood separation filter for one test are incompatible with the components used in the filter or detection area for another test.

Figure 15 shows a top view onto a cartridge 990 that is an application of the aforementioned principle to the cartridge of Figures 11 and 12. The cartridge 990 comprises a pre-treatment fluidic system with an inlet 910 (blood deposition position) and an associated channel 911 that splits into three branches. One or more detection chambers 912 (for blood) can be coupled to the channel 911 before the branching point, and one or more detection chambers 913 (for blood) can be coupled to the branches of the channel 911 after the branching point.

Each branch of the channel 911 leads to another filter (sub-) unit with (different) filter materials 901. Moreover, a separate post-treatment fluidic system with channels 954 and detection chambers 955 (for plasma) is provided behind each filter

material 901. As exemplarily shown for one of these channels 954, branching can occur in these channels, too.

Figure 16 shows a top view onto a cartridge 1090 that is an application of the above mentioned principle to the cartridge of Figures 13 and 14. The cartridge 1090 comprises a pre-treatment fluidic system with an inlet 1010 (blood deposition position) and an associated channel 1011 that splits into three branches. One or more detection chambers 1012 (for blood) can be coupled to the channel 1011 before the branching point, and one or more detection chambers 1013 (for blood) can be coupled to the branches of the channel 1011 after the branching point. The cartridge 1090 allows the distribution of blood over several different blood separation filters. This can be useful if e.g. the chemical pre-treatment components present in the blood separation filter for one test are incompatible with the components used in the filter or detection area for another test. Detection areas 1055a, 1055b, 1055c for plasma directly under the filter materials 1001 are represented by rectangles in Figure 16. The detection may for example comprise the detection of target molecules and/or of electrochemical properties.

A key feature of the cartridges 790, 890, 990, and 1090 of Figures 11–16 is the simultaneous detection in blood and plasma originating from the same blood sample. The cartridge designs are simple and inexpensive as several functions (capillary fluid transport, filter mounting, separation of blood and plasma, simultaneous detection in blood and plasma) are combined using lamination technology. This allows cost-effective mass production of disposable cartridges on a roll-to-roll basis.

An additional key feature of the cartridges 990 and 1190 of Figures 13, 14, and 16 is a biosensor cartridge with a detection area for plasma directly under the blood separation filter.

For a reliable progress of the test procedure it is often important to deposit a specified sample volume between a minimum value and a maximum value. In practice, there is however often an uncertainty whether or not the right amount of sample has been deposited on a biosensor cartridge in case of sample deposition without the use of a sample volume measuring device. One important example is the direct blood deposition from a finger (after a fingerprick) on a cartridge. In this case only visual control is possible.

As a solution to the aforementioned problem, an additional top layer may be added on top of the filter material (or, more generally, on top of a sample deposition pad or structure) with one or several sample deposition holes. By a proper choice of e.g. the thickness of the additional top layer and the diameter of the sample deposition hole(s), the

difference in visual appearance between a minimal and maximum deposited sample volume can be pronounced. This allows visual control of deposited sample volume even for the difficult situation of direct blood deposition from a finger after a fingerprick.

Figures 17 and 18 illustrate the aforementioned approach, showing a cross section through a filter unit 1100 that comprises a filter material 1101 mounted using lamination technology such that it is encompassed by a top foil 1102/FT and a bottom foil 1103/FB. An additional top layer 1105 is provided to pronounce the difference between the situations when a maximum volume of a sample B (e.g. 30  $\mu$ L; Figure 17) and when a minimal sample volume (e.g. 20  $\mu$ L; Figure 18) has been added. The thickness of the additional top layer 1105 and the diameter of its deposition hole H are chosen such that the difference in maximum and minimum sample volume can easily be judged visually after blood separation. This allows visual control of deposited sample volume even for the difficult situation of direct blood deposition from a finger.

In particular, the recess H in the additional top layer 1105 should be large enough to accommodate the total sample volume range. By making the hole diameter smaller than the diameter of the filter material 1101, the visual difference between the extremes can be enlarged. The dashed line in Figure 17 indicates the difference in volume between minimum and maximum volume of sample B. The maximum volume is achieved if no further sample fluid can be held by molecular adhesion forces.

Whether or not enough blood has been deposited can hence be judged from the presence of at least a concave meniscus in the sample deposition hole. In case of maximum blood deposition, a strongly convex meniscus is formed. The total filter area should be wetted with blood, although the layer in the centre may be thin. If less than the minimal sample volume is added, the (e.g. white) filter material clearly becomes visible through the sample blood layer in the centre of the filter.

The additional top layer 1105 can best be hydrophobic to pronounce this effect. The visual evaluation can be based on the color of the central area of the filter and/or on the shape of the blood meniscus. The shape of the meniscus is seen best by observing it under an oblique angle. The convex blood meniscus that occurs in case of sufficient sample deposition even contributes to the capillary forces that drive the blood separation.

If needed, the total sample volume range that can be visually judged can be reduced by use of more than one deposition hole above the same filter material.

While the aforementioned embodiment has been described for a situation of fingerprick blood deposition on a blood separation filter, it is clear that similar issues play a

role for other systems without blood separation filter (e.g. direct detection of biomarkers in blood). There the blood separation filter will be replaced by another type of sample deposition pad or structure.

An additional advantage of the cover layer on top of the filter is protection of the filter against unintentional touching. Moreover, the cover layer can also be used to improve and guarantee the physical contact between the filter and the filter support under the filter.

It has repeatedly been mentioned that the present invention is especially concerned with the situation of very small filters and minimal sample volumes (e.g. of blood). Another, independent approach to this problem is illustrated in Figures 19-21. This approach comprises modifications of the filter material, wherein the modified filter material can be applied in any application at hand. Without loss of generality, the filter material will in the following be explained with reference to its integration into a filter unit of the kind described above (i.e. the modified filter material can be used as the filter material 101-1101 in any of the above embodiments).

Figure 19 schematically shows a cross section through a filter unit 1200 that may for example serve for the separation of plasma from whole blood. The filter unit comprises a filter material 1201 that is embedded between a top foil 1202/FT and a bottom foil 1203/FB at the level of an intermediate foil 1204/FI. The filter material 1201 comprises as essential component a "matrix material" 1201a that has pores through which the fluid to be filtered can pass.

In order to allow for the analysis of minimum blood sample volumes, the uptake of plasma by areas used for mounting should be minimized because this plasma would be lost for the intended detection purposes. It is therefore proposed to prevent the fluid to be filtered from saturating such portions of a filter material.

In the embodiment of Figure 19, the peripheral zones or edge areas of the filter material 1201 are used for mounting/clamping and should hence be kept free from sample fluid. It is therefore proposed to treat this sub-portion of the filter material such that the pores are clogged and/or that the capillary force that drives plasma into this area is removed. This can be realized by locally filling up the pores of the matrix material 1201a in this area with a fluid or solid filling material 1201b and/or by making that region very hydrophobic by the application or generation of a hydrophobic filling material 1201b to the pores of the matrix material.

There are several ways to achieve this, for example:

- Saturating the edge area with a minimal amount of glue/wax as filling material followed by curing (thermally or with UV radiation).
- Saturating the edge area with a minimal amount of hydrophobization fluid (as filling material), possibly followed by curing (thermally or with UV radiation). Suited hydrophobization fluids comprise for example: siloxanes (e.g. octadecyltrichlorosilane); oleaginous materials; (mineral) oil; Zonyl 8857A (DuPont, USA); DURALON UltraTec (COTEC GmbH, Karlstein, Germany); AF1600, AF2400 Fluoropolymers (DuPont); EGC-1700 (3M, USA); Halar® ECTFE (Solvay Solexis); Tefzel® ETFE (DuPont); or Teflon® FEP (DuPont) (wherein a selection has to be made in relation to assay interference of these chemicals).
- Bringing the filter edge in contact with a thin wax layer (as filling material) and applying local reflow by local heating or by laser induced reflow.

When whole blood shall be filtered with the filtering unit 1200, the lamination of the filter material results in edge clamping and hence reduced pore size, which already prevents the red blood cells from entering the edge region. Unfortunately this is not automatically true for the plasma. Especially the finest pores are therefore to be filled/treated first. Capillary forces that transport filling material into the matrix material work in the right direction in this case for the reflow like approaches, especially if they can be applied after or together with a lamination procedure.

Figure 20 shows a top view of two filter materials 1201 and 1201' of different size with the relevant sub-portion being a ring-shaped edge area that comprises the filling material 1201b and 1201b', respectively. It can be seen that the edge area of (constant) diameter  $d$  becomes increasingly important with decreasing filter diameter as a possible loss factor for plasma. If the objective is to reduce the blood sample volume to an absolute minimum, it is attractive to reduce the filter size and to position the detection zone directly under the filter. Moreover, the Figure suggests that it is also very attractive to pre-treat the edge of the filter, especially on the bottom (filtrate) side, such that plasma cannot enter the edge zone .

Figure 21 shows a cross section through another modified filter unit 1300 (wherein the intended flow direction is indicated by block arrows). The difference to the embodiment of Figure 19 is that the filter material 1301 now consists of two different parts of matrix material, namely a top part 1301c with larger average pore size and a bottom part 1301a with smaller average pore size. In this case it is preferred that a filling



material 1301b is applied to the part 1301a with the smaller pore size. This is because primarily this part will contain the valuable plasma.

As described above, an edge portion of the matrix material 1301a may be saturated with a glue or wax that prevents loss of plasma. A tiny amount of wax or glue can be applied in this area, just enough to fill the tiny pores in the outer edge. The material can be applied locally and can be reflowed or cured with local heat or UV input (i.e. using a laser).

It should be noted that only reagents which do not influence the final assay should be used as filling material. Moreover, it is important to leave the central area of the filter unchanged in order to maintain the normal blood separation function.

The above filter material enables a disposable cartridge, e.g. for a blood sensor system, in which the tiny pores in the clamping edge region of a blood separation filter are filled up with another, preferably solid and/or hydrophobic material (e.g. glue or wax). This prevents loss of plasma and thus increases the plasma yield. This is especially useful for tiny filters and sample volumes, where the filter edge area used for mounting is comparable or larger than the central area used for plasma generation. The filling material can be applied locally and can be reflowed or cured with local heat or UV input (i.e. using a laser). The blood separation filter can be mounted by lamination technology. Alternatively, the blood separation filter can first be placed on a base part after which the entire cartridge is closed with a foil, thereby fixing the filter.

Features of the embodiments described above with respect to the Figures can be combined and/or modified in various ways.

For example, the filling of the cartridges was assumed to be based on autonomous, capillary driven fluid flow. It is however also possible to stimulate fluid flow by applying over-pressure on the inlet side, under-pressure on the vent side of the cartridge, or by mechanical stimulation of fluid flow by cartridge manipulation (i.e. peristaltic flow generated by the user or the analyzer).

Another possible modification comprises the deposition of samples. In the above examples, capillary pick-up by an inlet port at a front side of the cartridge and by associated channels in a (top) foil has been described. Alternatively, capillary pick-up of a sample could take place at the side (like in a glucose strip). The filter material could for example be accessible at a side face of a filter unit, e.g. between the top and bottom foil, allowing to apply sample to it through this side.

Moreover, the examples given above were mostly explained with respect to blood samples (of biological or non-biological origin) and blood separation filters. It is however clear that the scope of the invention includes other samples and filters, too. Accordingly, the described devices and procedures can generally be used to treat (e.g. filter) a "raw fluid", wherein the "treated fluid" may then further be processed in the same device.

The advantages of the use of a (partly) foil based cartridge will steadily increase with the increasing number of technologies that become available on foil (e.g. conductive patterns, RF-IDs, screen printed electrodes for electrochemistry, advanced hot embossing patterns, etc.).

It should be noted that the part in front of the filter material of any shown embodiment can be combined with the part behind the filter material of any other shown embodiment of the invention. Similarly, any described filter unit 100, 200, ... 1300 can be combined with any described carrier 150, 250, ... 1150.

While the invention has been illustrated and described in detail in the drawings and foregoing description, such illustration and description are to be considered illustrative or exemplary and not restrictive; the invention is not limited to the disclosed embodiments. Other variations to the disclosed embodiments can be understood and effected by those skilled in the art in practicing the claimed invention, from a study of the drawings, the disclosure, and the appended claims. In the claims, the word "comprising" does not exclude other elements or steps, and the indefinite article "a" or "an" does not exclude a plurality. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures cannot be used to advantage. Any reference signs in the claims should not be construed as limiting the scope.

## CLAIMS:

1. A filter unit (100, 200, ... 1300) for filtering a fluid, comprising:
  - a) at least one foil (FT, FB, FI) that is impermeable to the fluid and that comprises at least one aperture (A, A');
  - b) a filter material (101, 201, ... 1301) permeable to at least a part of the fluid, said filter material being integrated into said aperture of the foil (FT, FB, FI).
2. A cartridge (190, 290, ... 1190) comprising a rigid carrier (150, 250, ... 1150) and a filter unit (100, 200, ... 1300) according to claim 1 that are attached to each other.
3. A method for manufacturing a filter unit (100, 200, ... 1300) with a filter material (101, 201, ... 1301), said method comprising the following steps:
  - attaching two foils (FT, FB) to each other such that they enclose the filter material (101, 201, ... 1301) between them;
  - providing at least one aperture (A) in each foil (FT, FB) at the position of the filter material (101, 201, ... 1301).
4. A filter material (1201, 1201', 1301) for filtering a fluid, particularly a filter material for a filter unit (1200, 1300) according to claim 1, comprising:
  - a matrix material (1201a, 1201a', 1301a, 1301c) with pores through which the fluid can pass;
  - a filling material (1201b, 1201b', 1301b) that is disposed in said pores in a sub-portion of the matrix material (1201a, 1201a', 1301a).
5. The filter unit (100, 200, ... 1300) according to claim 1, characterized in that the filter material (101, 201, ... 1301) is arranged in the aperture (A') of an intermediate foil (FI) that is embedded between a top foil (FT) and a bottom foil (FB).

6. The filter unit (400) according to claim 5, wherein peripheral zones or edge areas of the filter material (1201) are mounted/clamped between the top and bottom foils (1202/FT, 1202/FB) at the level of the intermediate foil (1204/FI), and wherein pores of said edge areas or peripheral zones are filled with a filling material (1201b, 1201b', 1301b).
7. The filter unit (600, 700, 800) according to claim 1, characterized in that at least one foil (606, 702, 705, 706, 802, 805) of the filter unit comprises at least one cavity (654, 655, 711, 754, 755, 811).
8. The filter unit (100, 200, ... 1100) according to claim 1, wherein the filter material (101, 201, ... 1101) has a dome shape.
9. The filter unit (300, 400, ... 1300) according to claim 1, comprising a holding element for pressing the filter material (301, 401, ... 1301) in one direction, said holding element preferably being an additional foil (305, 405, ... 1305).
10. The filter unit (1100) according to claim 1, wherein a side of the filter material (1101) that is accessible during use is designed to hold a quantity of fluid (B) ranging between a given minimum and a maximum when said quantity covers the complete filter material (1101) and is only held by adhesion forces.
11. The filter unit (400) according to claim 1, wherein the filter material (401) is covered by a foil (405) with at least two apertures (A1, A2) providing access to the filter material (401).
12. The cartridge (190, 590, 890, 1090) according to claim 2 or 12, wherein the carrier (150, 550, 850, 1150) comprises at least one cavity (153, 154, 155, 553, 554, 555, 855) for the accommodation of fluid, said cavity preferably being connected to the filter material (101, 601, 801, 1101).
13. The cartridge (590) according to claim 11, characterized in that at least one cavity (553, 554, 555) of the carrier (550) is covered by a foil (503) of the associated filter unit (500).
14. The cartridge (790, 890, 990, 1090) according to claim 2, wherein a pre-treatment fluidic system is located on a first side of the filter material (701, 801, 901,

1001) and a post-treatment fluidic system is located on the opposite side of the filter material., and wherein the pre-treatment fluidic system comprises an inlet (710, 810, 910, 1010) where a fluid can be introduced and/or a processing chamber (712, 812, 912, 913, 1012, 1013) for the processing of a fluid that has not passed the filter material (701, 801, 901, 1001).

15. The cartridge (290, 890, 1090) according to claim 2, comprising a processing chamber (255, 855, 1055a, 1055b, 1055c) that is located adjacent to the filter material (201, 801, 1001) and in which fluid can be processed.

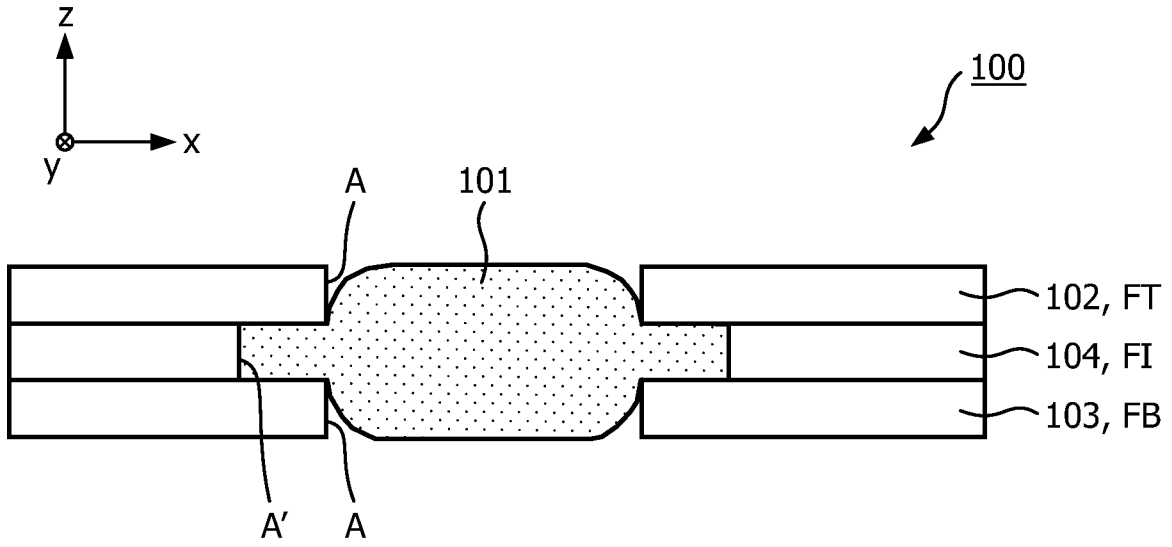


FIG. 1

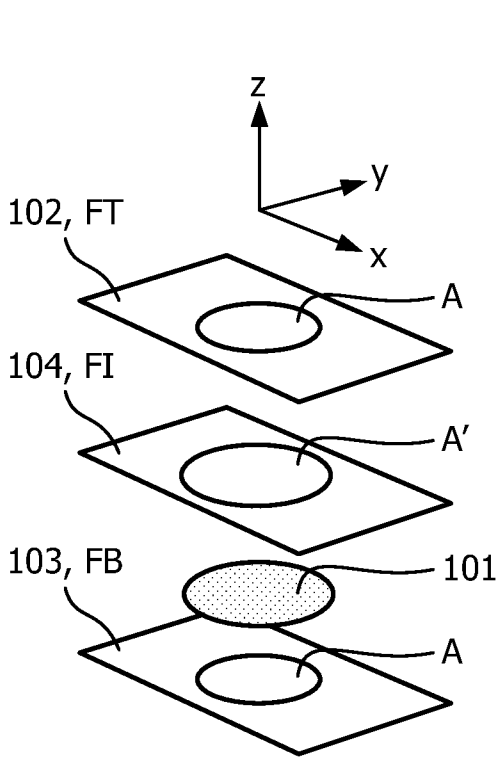


FIG. 2

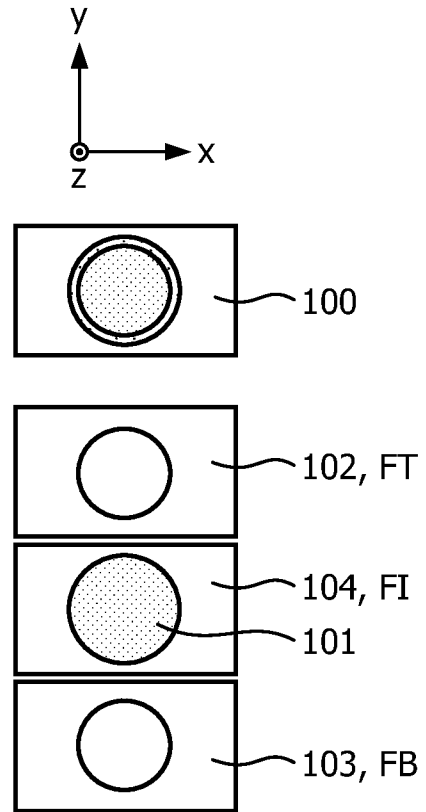


FIG. 3

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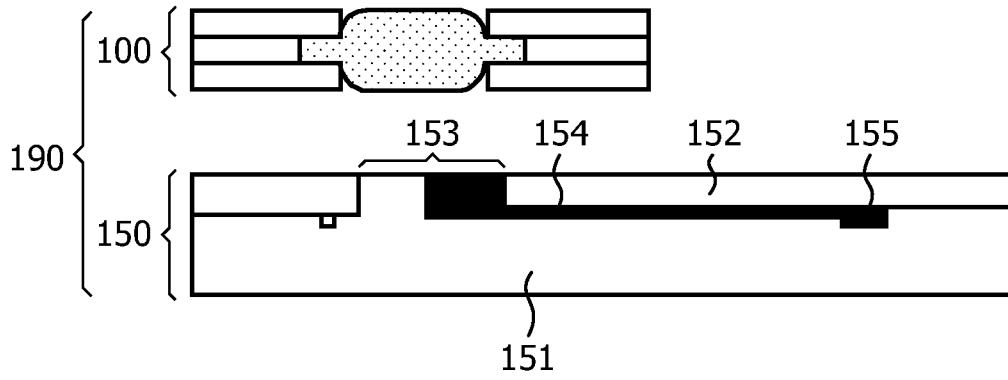


FIG. 4

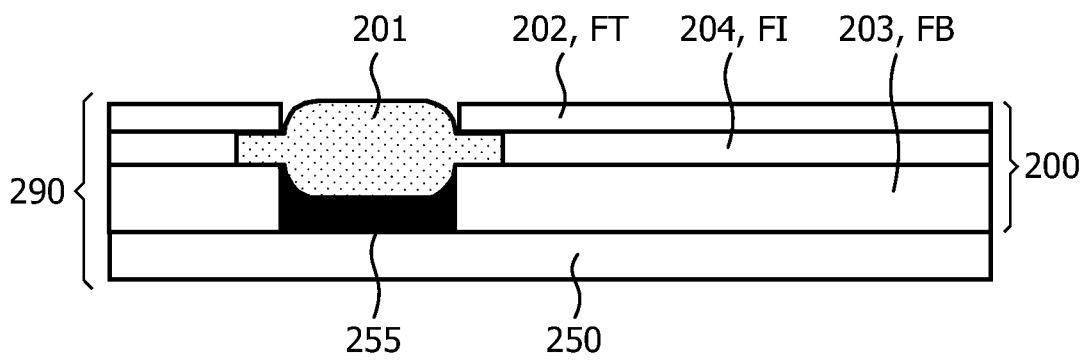


FIG. 5

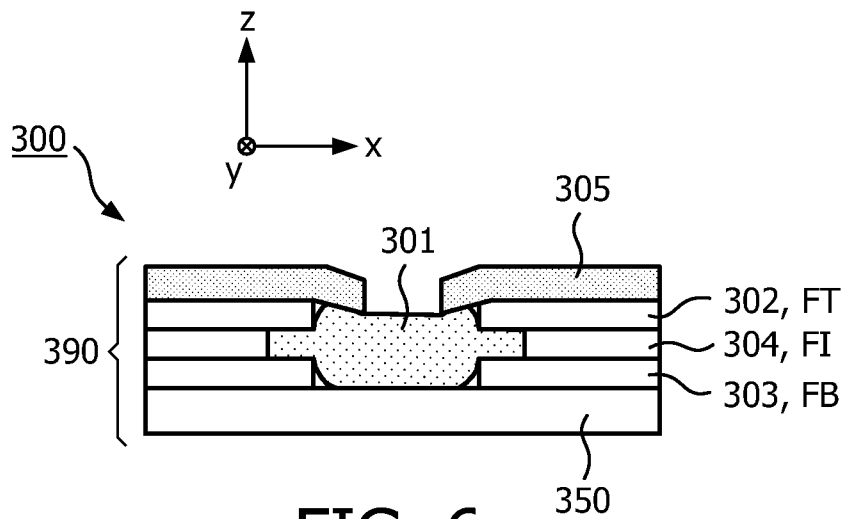


FIG. 6

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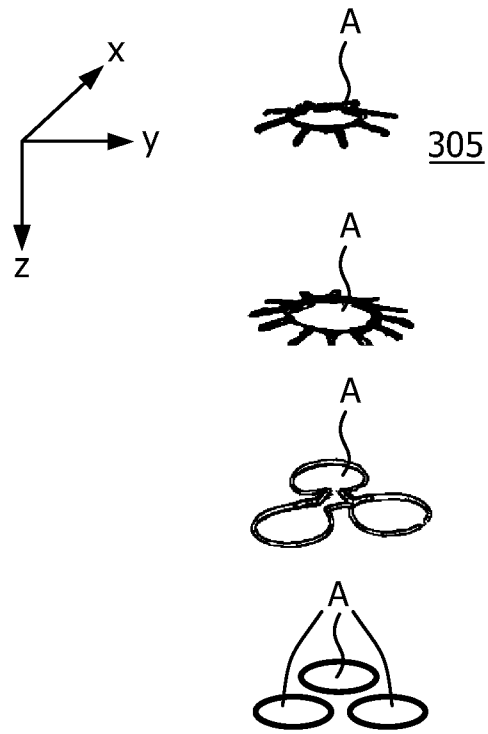


FIG. 7

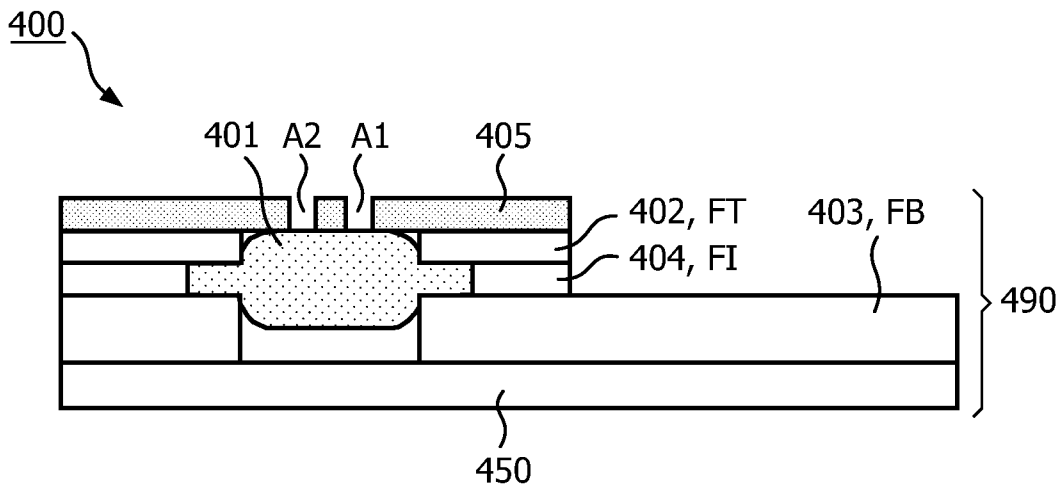


FIG. 8



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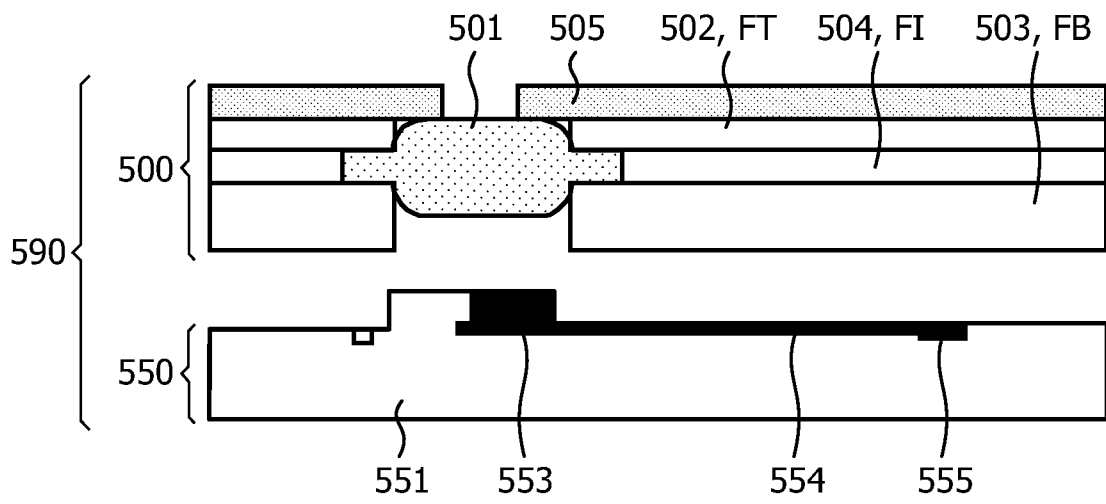


FIG. 9

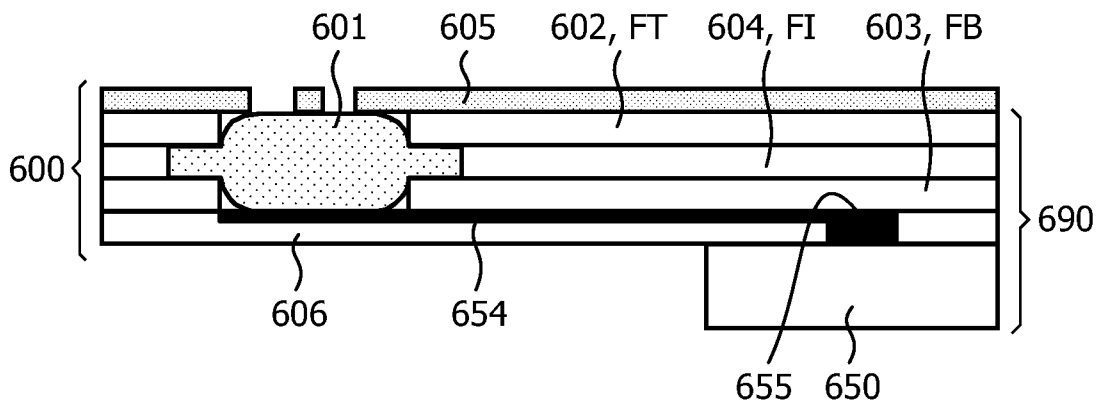


FIG. 10

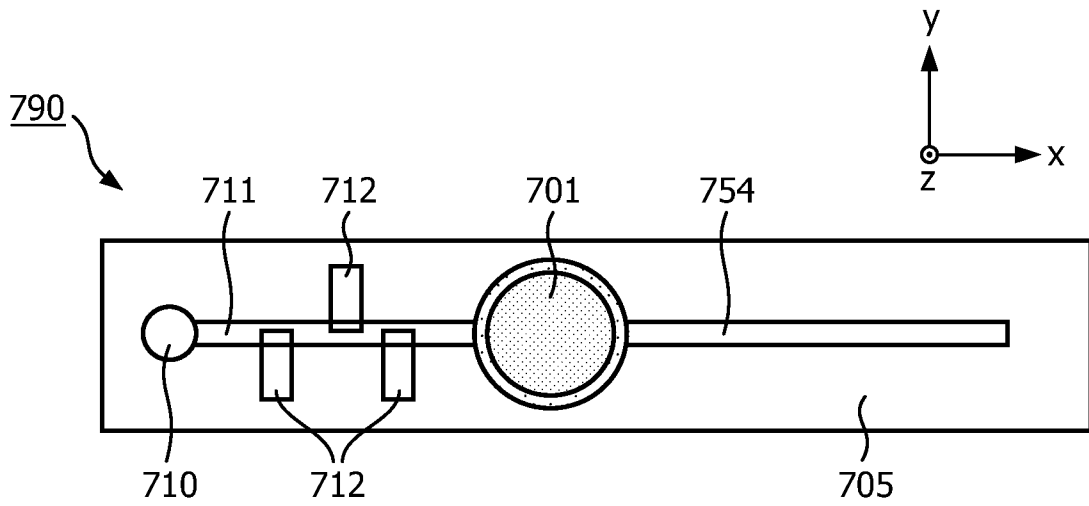


FIG. 11

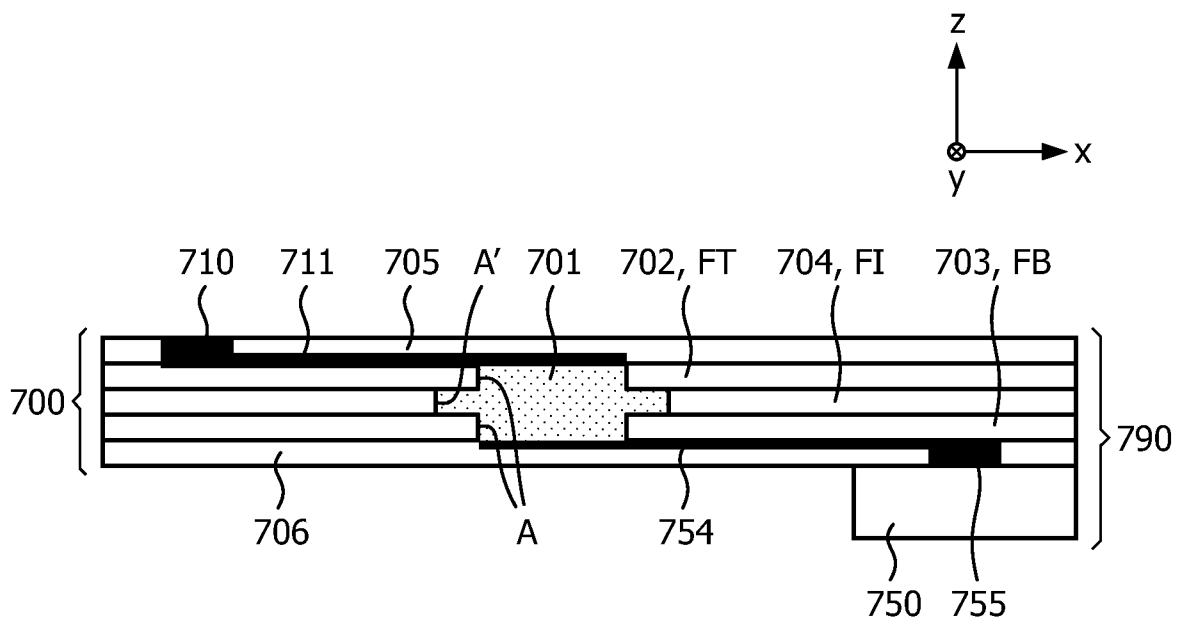


FIG. 12

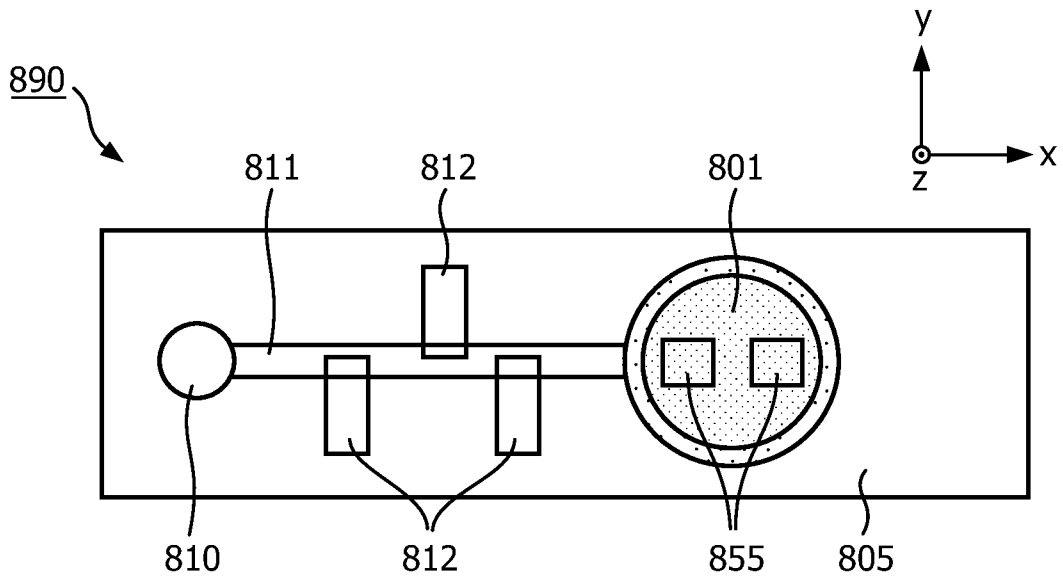


FIG. 13

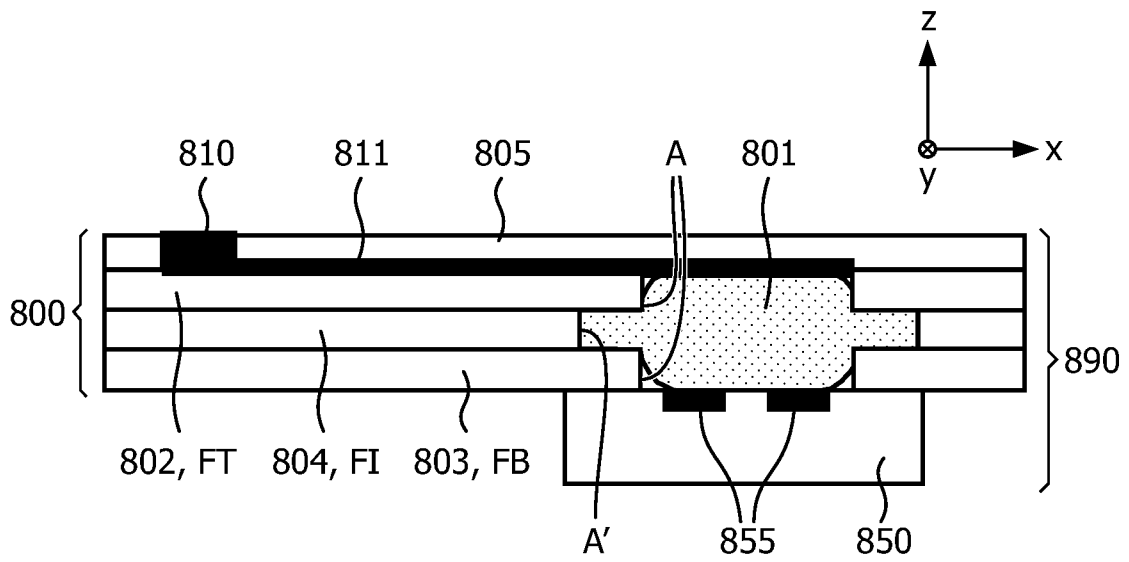


FIG. 14

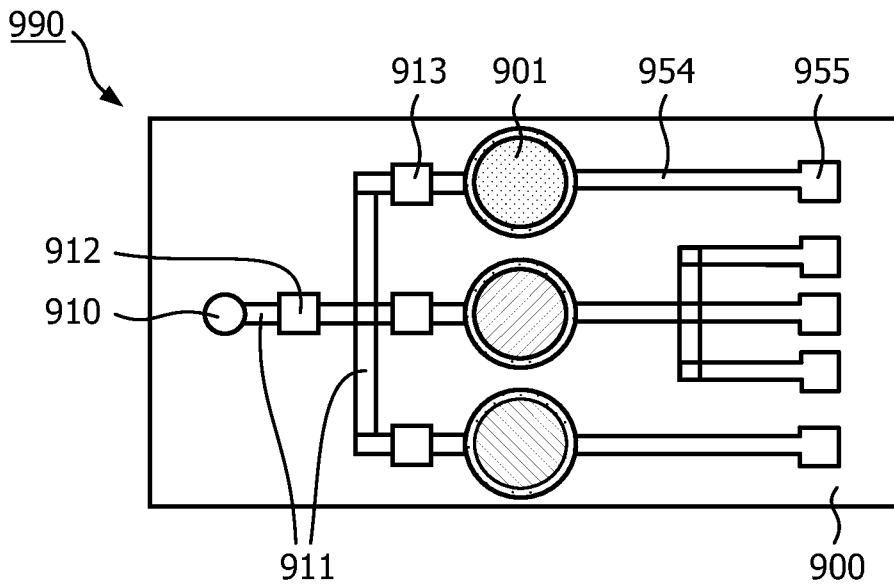


FIG. 15

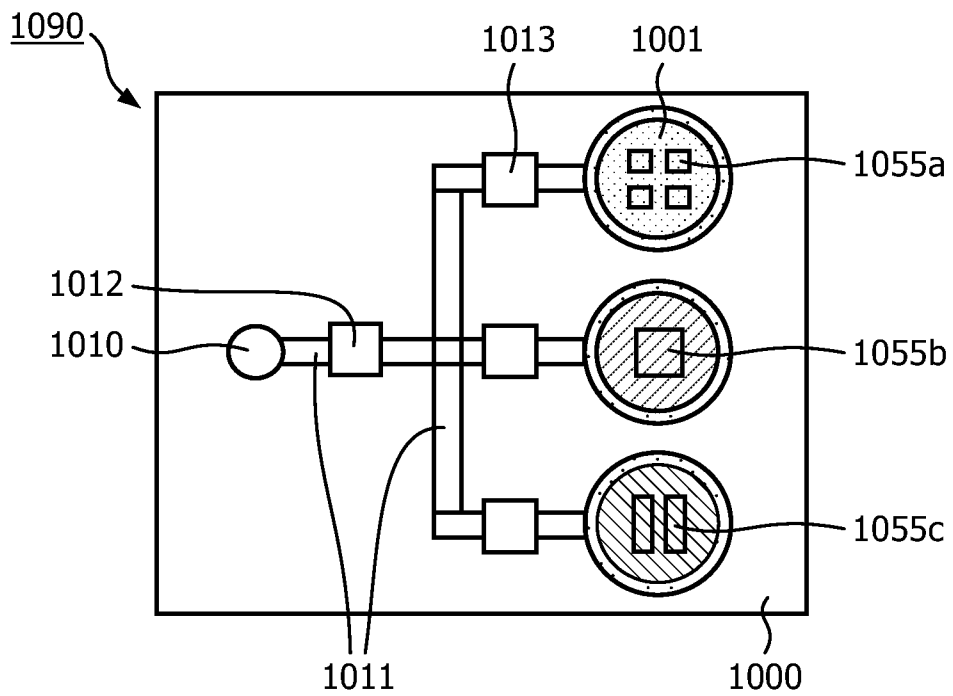


FIG. 16

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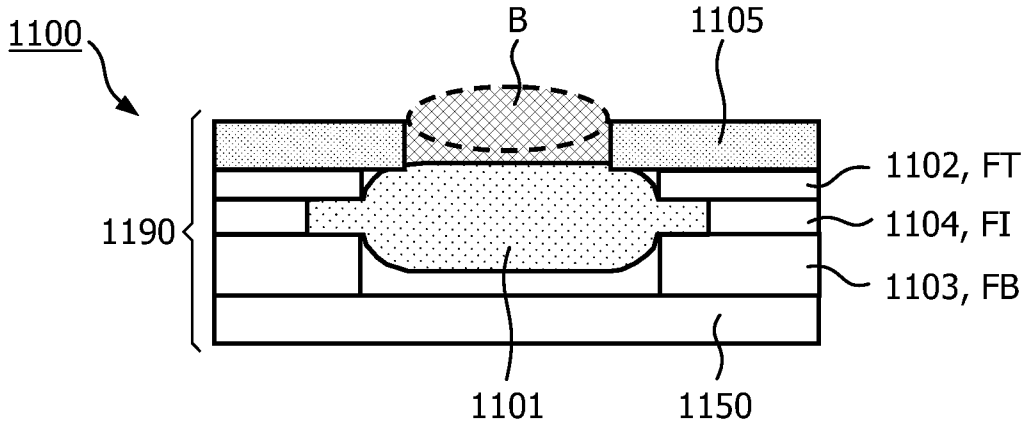


FIG. 17

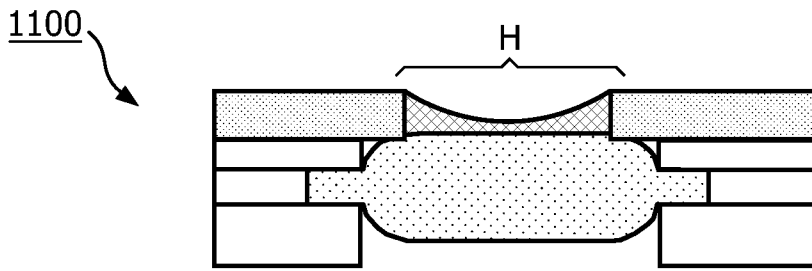


FIG. 18

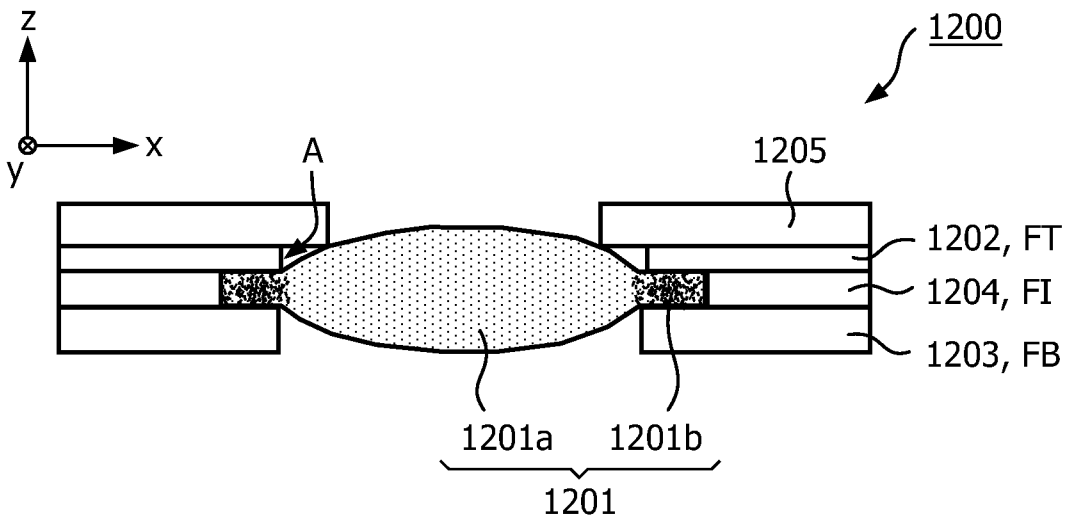


FIG. 19

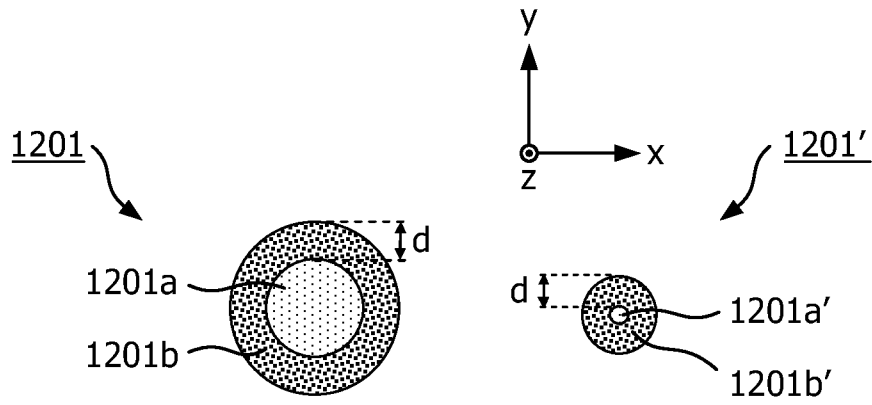


FIG. 20

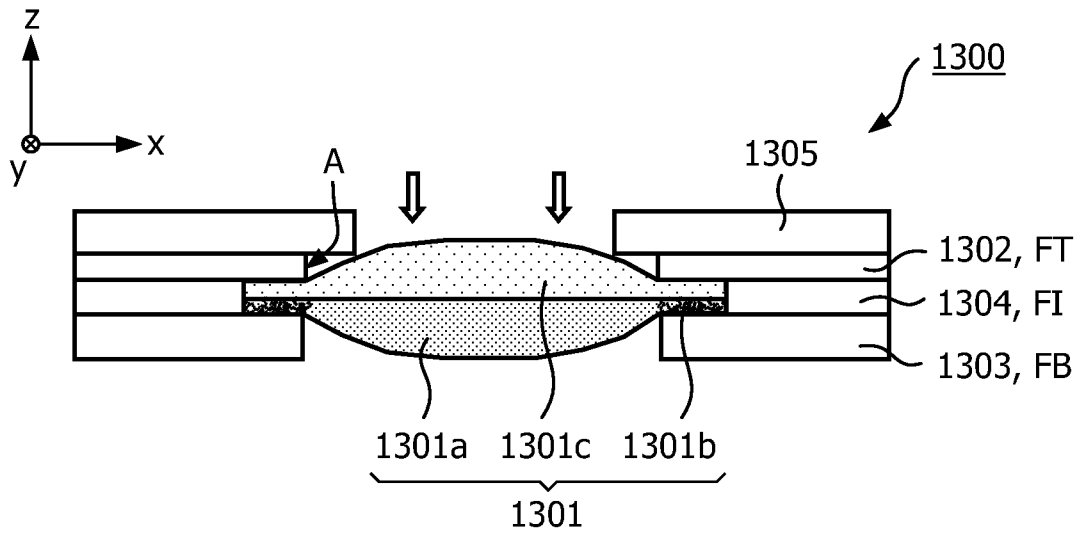


FIG. 21

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/IB2013/050563

**A. CLASSIFICATION OF SUBJECT MATTER**  
INV. B01L3/00  
ADD.

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)  
B01L

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
EPO-Internal, 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	WO 2011/131471 A1 (BOEHRINGER INGELHEIM MICROPART [DE]; BLANKENSTEIN GERT [DE]; HELLMICH-) 27 October 2011 (2011-10-27) page 5, line 32 - page 6, line 4; figures 1-9 page 10, line 34 - page 11, line 17 page 16, line 19 - page 18, line 11 -----	1-3,5, 7-15
X	WO 2011/038458 A1 (MYCROLAB DIAGNOSTICS PTY LTD [AU]; ATKIN MICAH [AU]) 7 April 2011 (2011-04-07) page 21, lines 4-8; figure 14 page 24, line 33 - page 25, line 4 -----	1,3,5-7, 10
X	US 2010/322824 A1 (NEIJZEN JACOBUS HERMANUS MARIA [NL]) 23 December 2010 (2010-12-23) the whole document -----	1-3,7, 9-15
	-/--	

Further documents are listed in the continuation of Box C.       See patent family annex.

\* Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"&amp;" document member of the same patent family</p>
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Date of the actual completion of the international search  <p style="text-align: center;">10 June 2013</p>	Date of mailing of the international search report  <p style="text-align: center;">25/06/2013</p>
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  <p style="text-align: center;">Viskanic, Martino</p>
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## INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2013/050563

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2004/253624 A1 (SMITH ROGER E [US] ET AL) 16 December 2004 (2004-12-16) paragraphs [0058], [0362] - [0365]; figures 18-21 -----	1,2,4



# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/IB2013/050563
---

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011131471 A1	27-10-2011	EP 2560756 A1	27-02-2013
		US 2013112612 A1	09-05-2013
		WO 2011131471 A1	27-10-2011
-----			
WO 2011038458 A1	07-04-2011	AU 2010302952 A1	10-05-2012
		CN 102844176 A	26-12-2012
		EP 2483075 A1	08-08-2012
		US 2012184046 A1	19-07-2012
		WO 2011038458 A1	07-04-2011
-----			
US 2010322824 A1	23-12-2010	EP 2208048 A1	21-07-2010
		US 2010322824 A1	23-12-2010
		WO 2009060357 A1	14-05-2009
-----			
US 2004253624 A1	16-12-2004	EP 1766084 A2	28-03-2007
		US 2004253624 A1	16-12-2004
		US 2009011403 A1	08-01-2009
		US 2009142748 A1	04-06-2009
		WO 2005118863 A2	15-12-2005
-----			