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(54) **MICROFLUIDIC CATRIDGE**

(57) The present invention relates to a cartridge (1) that is configured to perform an assay, when it is in use, to evaluate at least a parameter of a fluid sample, the cartridge (1) being electrically connected to a reader when it is in use, comprising: a planar substrate (2) with a top substrate surface (3) comprising at least substrate electrical contacts (6) and a bottom substrate surface (4) that is disposed opposite to the top substrate surface (3), at least a microfluidic channel (5, 5a, 20a, 21a) that is configured to receive the fluid sample to be evaluated, a biochip (7) comprising: a top biochip surface (8) and a bottom biochip surface (9) disposed opposite to the top biochip surface (8), biochip electrical contacts (12), biochip electrical connectors (12a) that are electrically coupled to at least some of the biochip electrical contacts (12) and formed on at least one of the top and the bottom biochip surfaces (8, 9), and a sensing aspect (10) comprising at least a biosensor (11) that is disposed relative to the microfluidic channel (5, 5a, 20a, 21a) to receive the fluid sample, and a sealing layer (13, 20, 2127) that forms a substantially fluid-tight sealant relative to at least one of the biochip (7) and the substrate (2) when the cartridge is in use, wherein the biochip (7) and the substrate (2) are in one of: an alignment configuration, in which the biochip electrical connectors (12a) and substrate electrical contacts (6) are in geometrical alignment with each other, and a compression configuration, when the cartridge (1) is in use, in which the aligned biochip electrical connectors (12a) and the substrate electrical contacts (6) are compressed together and are electrically connected.

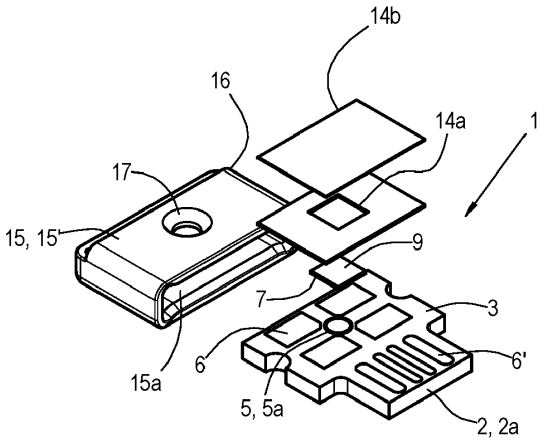


FIG. 1A1

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## Description

### Technical Field

**[0001]** The present invention relates to a cartridge that is configured to perform an assay to evaluate a fluid sample.

### Background

**[0002]** The importance of being able to evaluate specific parameters of fluid samples, by performing assays on them, in a portable, reliable and "no-lab" environment continues to be recognized. In this context, i-STAT® cartridges and corresponding hand-held readers, which have been developed by Abbott Laboratories, for single use, point of care measurement of fluid parameters, are known. The evaluated fluid samples are typically of a biological nature, such as, for example, blood. Such cartridges comprise biochips with biosensors that are configured for the measurement of specific parameters of a fluid sample that is under evaluation. To perform an assay on the fluid sample, electrical connection between the biochip and the reader is established via electrical contact pads on the biochip that are aligned and in electrical connection with reader electrical contact pads, which are also referred to as reader pins.

**[0003]** There are some issues associated with electrically connecting the biochip and the reader. Because of their disproportionate dimensions, it is challenging to align the microscopic biochip to the macroscopic reader to electrically connect them. So, macroscopic electrical contact pads are provided directly on the biochip that can be located with relative ease and aligned with increased accuracy with the similarly dimensioned, macroscopic electrical contact pads of the reader. An advantage associated with forming the macroscopic electrical contact pads directly on the biochip is that the biosensing/biomolecular material coated on the biosensors is not subjected to and/or adversely affected by further processing steps such as manipulation, (ultrasonic) agitation and/or high temperature that may result from mounting the biochip onto an intermediate substrate for electrically connecting the biochip to the reader.

**[0004]** An increased biochip dimensional size is linked to the electrical contact pads being provided directly on the biochip because: the contact pads are relatively large, and they are ideally spaced further away from the biosensors that are also provided on the biochip. Regarding the spacing consideration, it accounts for a reduced interaction and/or interference of the contact pads with the sensitive biomolecular material(s) coated onto the biosensors as described above. The spacing consideration also accounts for a fluidic connection of the biochip to microfluidic channels of the cartridge that deliver fluid samples to the biosensors and isolation of this fluidic aspect from an electrical aspect of the biochip through which electrical connection is established with the reader as described above.

**[0005]** Taking the example of a previously proposed cartridge, for a biochip area of approximately 35mm$^2$, approximately half of this area, >15mm$^2$, is allocated for: electrical connection to the reader, fluidic connection of the microfluidic channels to the biosensors on the biochip for fluid sample delivery, and isolation between these electrical and fluidic aspects. As discussed above, the relatively large electrical contact pads that are formed on the biochip to recover any alignment inaccuracy with the reader pins, may each be approximately 3-4mm$^2$. Accordingly, the burden of requiring such a large spatial overhead makes this a solution of increased cost and inefficient space usage in respect of the biochip.

**[0006]** It is known to apply flip-chip technology for the electrical connection of microscopic electrical contact pads of a chip to macroscopic electrical contact pads of a substrate. Regarding the electrical contact pads, they constitute a part of the layer composition of the chip. They are fabricated by wafer processing, which involves depositing metal layers using Physical Vapour Deposition (PVD), for example, and then plasma etching to pattern the layers. Metal bumps are formed on the electrical contact pads of the chip, thereby to facilitate any desired external electrical connection of the chip. For the metal bumps, different metals and their alloys may be used such as, for example, gold (Au), tin (Sn), silver (Ag), copper (Cu), nickel (Ni), and lead (Pb).

**[0007]** Flip-chip technology involves flipping a surface of the chip comprising its active circuitry facing down to the substrate and with correspondent electrical connectors/metal bumps on the chip and metallized electrical contact pads of the substrate in contact with each other from the outset. An underfill glue is applied to fill any gap between the chip and the substrate. The glue is cured by heating to a relatively high temperature. A subsequent shrinkage of the glue causes the metal bumps on the chip to become permanently pressed into the metallized contact pads of the substrate. In this way, the chip is electrically connected to the substrate. For this process of establishing electrical contact between the chip and the substrate to be economical as well as to be applicable to scale and to be usable in mass fabrication, "snap curing" gluing processes are used in which the glue is cured at high temperatures, typically well over >>50°C, in a matter of seconds or a few minutes.

**[0008]** In the present context of performing an assay, electrically connecting a biochip to a substrate using flip-chip technology would be incompatible with the biosensors, which comprise relatively sensitive biomolecular material(s) that are unable to sustain temperatures above >40°C and/or any of the standard packaging steps that would have to be performed for establishing the fluidic and electrical connection of the biochip with the substrate as described above.

**[0009]** Accordingly, it is a challenge to use a smaller biochip in a cartridge and to electrically connect it to a reader with minimal and/or less abrasive processing

steps in the context of performing assays with the cartridge.

**Summary of the invention**

**[0010]** According to an embodiment of the present invention, there is provided a cartridge that is configured to perform an assay, when it is in use, to evaluate at least a parameter of a fluid sample, the cartridge being electrically connected to a reader when it is in use, comprising: a planar substrate with a top substrate surface comprising at least substrate electrical contacts and a bottom substrate surface that is disposed opposite to the top substrate surface, at least a microfluidic channel that is configured to receive the fluid sample to be evaluated, a biochip comprising: a top biochip surface and a bottom biochip surface disposed opposite to the top biochip surface, biochip electrical contacts, biochip electrical connectors that are electrically coupled to at least some of the biochip electrical contacts and formed on at least one of the top and the bottom biochip surfaces, and a sensing aspect comprising at least a biosensor that is disposed relative to the microfluidic channel to receive the fluid sample, and a sealing layer that forms a substantially fluid-tight sealant relative to at least one of the biochip and the substrate when the cartridge is in use, wherein the biochip and the substrate are in one of: an alignment configuration, in which the biochip electrical connectors and substrate electrical contacts are in geometrical alignment with each other, and a compression configuration, when the cartridge is in use, in which the aligned biochip electrical connectors and the substrate electrical contacts are compressed together and are electrically connected.

**[0011]** Compatibility with sensitive biolayer material is ensured because high temperatures are not used for the assembly nor the application of an embodiment of the present invention. Instead, electrical connection between the biochip and the substrate is established by mechanically compressing the biochip into electrical contact with the substrate. Accordingly, and because of the reduced biochip size, especially compared to previously proposed assay devices, this translates into reduced sample volumes, reduced cost of production and savings in area overhead.

**[0012]** Preferably, the sealing layer comprises a compressibility characteristic at least such that the compression configuration can be activated.

**[0013]** Because the sealing layer is also compressed, like the biochip and the substrate, in the compression configuration, and it is not stiff, it poses no hinderance/resistance to the compression configuration and/or its activation. This feature therefore extends the advantage of increased reliability to an embodiment of the present invention.

**[0014]** Desirably, the sealing layer comprises at least one of: a pressure-sensitive adhesive layer, a silicon grease, a viscous oil, and a partially cured resist.

**[0015]** The sealing layer need not be restricted to a specific material but rather it can be implemented with a variety of different materials that may be chosen on account of cost and/or suitability.

**[0016]** Preferably, an embodiment of the present invention comprises an alignment feature that aligns and accommodates the biochip relative to the substrate in the alignment configuration.

**[0017]** This feature provides the advantages of increased ease, simplicity, and accuracy with which alignment of the biochip and the substrate is performed.

**[0018]** Desirably, an embodiment of the present invention comprises an adhesion layer that is configured to at least secure the biochip relative to the substrate in the alignment configuration. Preferably, the adhesion layer is also the sealing layer.

**[0019]** These features extend the advantages of increased reliability with which the biochip is aligned and secured positionally relative to the substrate in the alignment configuration, and increased versatility because the adhesion layer may additionally also perform a sealant function of the sealing layer, or it may be provided separately from the sealing layer.

**[0020]** Preferably, an embodiment of the present invention comprises a receptacle that is configured to receive the arrangement of the biochip and the substrate in the alignment configuration and to effectuate its alteration to the contact configuration.

**[0021]** This feature extends the advantages of ease of operation and implementation because by simply inserting the aligned biochip and substrate into a receptacle, an electrical connection between them is established.

**[0022]** Desirably, the receptacle comprises a bracket. This feature provides improved versatility and flexibility to an embodiment of the present invention.

**[0023]** Preferably, in the compression configuration, at least the biochip is in a mechanically compressed state in a direction normal to the substrate.

**[0024]** This feature provides ease of establishing electrical contact between the biochip and the substrate and is reliable enough given that the cartridge is single-use, and the assay runs for a relatively short period of time encompassing minutes to a few hours at the most.

**[0025]** Desirably, the sensing aspect and the biochip electrical connectors are respectively formed on the same surface or different surfaces of the biochip. An associated advantage is a further reduction in spatial overhead particularly in respect of the biochip.

**[0026]** Preferably, the biochip electrical connectors comprise metal bumps. This feature makes use of known technology and/or fabrication methods to facilitate electrical connection of the biochip.

**[0027]** Desirably, the substrate comprises at least one of a printed circuit board, a polymer material, flex circuit, printed electronics substrate, flat panel, and a glass substrate.

**[0028]** Some of the advantages associated with this feature include ease of fabrication, reduced cost of im-

plementation, and the increased versatility provided by the different choice in how the substrate can be implemented.

**[0029]** Preferably, the substrate electrical contacts are connected with electrical contacts of the reader. The biochip is electrically connected to the reader via the substrate and assay performance is initiated/triggered via an electrical signal that is received from the reader.

**[0030]** Preferably, the cartridge comprises a stacked configuration of sheets, wherein each sheet comprises a customized layer.

**[0031]** Advantages that are associated with this feature include: providing an alternative implementation of an embodiment of the present invention, the customized layers can be fabricated separately from each other, and ease of implementation and associated space economy since the sheets of customized layers are stacked onto each other.

**[0032]** Desirably, in the stacked configuration, the sealing layer is interspersed between the sheets.

**[0033]** The sealing layer is incorporated with ease into the stacked layer configuration to isolate the fluidic and electrical aspects in an embodiment of the present invention.

## Brief description of the drawings

**[0034]** Reference will now be made to the accompanying drawings in which:

Figures 1A1 and 1A2 schematically illustrate a respective top and bottom view of an embodiment of the present invention comprising a printed circuit board substrate.

Figures 1B1 and 1B2 schematically illustrate respective top and bottom views, corresponding with Figures 1A1 and 1A2, of a receptacle feature of an embodiment of the present invention.

Figures 2A1 and 2A2 schematically illustrate a respective top and bottom view of an embodiment of the present invention comprising a polymer substrate.

Figures 2B1 and 2B2 schematically illustrate respective top and bottom views, corresponding with Figures 2A1 and 2A2, of the receptacle feature.

Figures 3A1, 3A2 and 3A3 respectively give a top-view perspective of a progressively assembled embodiment of the present invention comprising a pressure sensitive adhesive layer.

Figures 4A1 and 4A2 respectively give a top-view perspective of a progressively assembled embodiment of the present invention in which biosensors and biochip electrical contacts are formed on different surfaces of the biochip.

Figures 5 shows an exploded view of an embodiment of the present invention comprising a stacked configuration.

## Description of the preferred embodiments

**[0035]** Within the description, the same reference numerals or signs have been used to denote the same parts or the like.

**[0036]** An embodiment of the present invention is used in conjunction with, and electrically connected to, a reader to perform an assay on a fluid sample for evaluating a specific parameter thereof.

**[0037]** Different structural and/or implementational configurations of an embodiment of the present invention are described here below.

**[0038]** In the drawings, a top and bottom view is referenced with a top/bottom surface of a substrate or receptacle, as applicable.

**[0039]** Also, to aid clarity, common structural/technical features with the embodiments of Figures 1 and 2 may not be marked in the drawings of subsequently described embodiments as shown in Figure 3 and 4, this having only been done for distinguishing and/or different features.

### Printed Circuit Board (PCB) Substrate + biosensors and biochip electrical contacts on the same biochip surface

**[0040]** Referring to Figure 1A1, an embodiment of the present invention pertains to a cartridge 1 comprising a planar substrate 2 having a top substrate surface 3 and an oppositely disposed bottom substrate surface 4. The fluid sample is received by the cartridge 1 at/in a microfluidic channel 5, which is realized in the present example as a circular port 5a formed in the substrate 2 with, for example, a 10 μl fluid/sample capacity. The top substrate surface 3 comprises active circuitry such as substrate electrical contacts 6. In the present embodiment, the cartridge 1 comprises a PCB substrate 2a.

**[0041]** The cartridge 1 also comprises a biochip 7 having a top biochip surface 8 and a bottom biochip surface 9. As most clearly seen from Figure 1A2, the top biochip surface 8 has a sensing aspect 10 comprising one or more of a biosensor 11, which is arranged relative to the microfluidic channel 5, 5a to be in contact with the fluid sample when an assay is performed. The biosensor 11 is coated with a biomolecular material that interacts with the specific parameter of the fluid sample that is to be interrogated. The top biochip surface 8 also comprises biochip electrical connectors 12a that are formed correspondently with biochip electrical contacts 12 within/on the biochip wafer 7. The biochip electrical connectors 12a comprise metal bumps that may be peripherally formed on the top biochip surface 8 as depicted in Figure

1A2. The biochip electrical connectors 12a may be formed from metals and their alloys, including gold, tin, silver, copper, nickel, and lead, for example. The metal bumps 12a comprise gold in an embodiment of the present invention.

**[0042]** In the present embodiment, and viewing Figure 1A1 in conjunction with Figure 1A2, in an initial alignment configuration, the biochip 7 is arranged relative to the underlying substrate 2 such that the biochip electrical connectors, 12a on the top biochip surface 8 are geometrically aligned with correspondent substrate electrical contacts 6 on the top substrate surface 3. In the alignment configuration, the biochip 7 and the substrate 2 are in physical contact with each other, as are/may be their respective electrical contacts 6, 12, 12a. To perform the alignment, high accuracy, active alignment machinery like die bonders, which are available during manufacturing of the cartridge 1, are used.

**[0043]** To initiate an assay being performed on a fluid sample, the biochip 7 and the substrate 2 arranged in the alignment configuration are inserted into a receptacle 15 at an opening 15a as shown in Figure 1B1. A resultant physical constriction that is effective in a direction that is substantially normal to the top substrate surface 3 causes the biochip 7 and the substrate 2 to be physically compressed together. The compression encompasses the biochip 7 and the substrate 2 being compressed relative to each other. Accordingly, the alignment configuration is altered to a compression configuration in which the aligned biochip electrical connectors/gold bumps 12, 12a and the substrate electrical contacts 6 are pressed into physical contact and electrical connection with each other. Accordingly, a reliable electrical connection is established between the biochip 7 and the substrate 2.

**[0044]** In a preferred embodiment, the receptacle 15 comprises a bracket 15' as shown in Figure 1B1 and 1B2. Referring to Figure 1B1, a readout feature 17 that is formed on a top surface 16 of the bracket 15' is aligned with the sensing aspect 10, 11 when the cartridge 1 is in use - it is configured to interact with the biochip 7 by shining infrared light onto it and to report on a target analyte concentration corresponding to the parameter evaluation of the fluid sample. Figure 1B2 depicts a bottom surface 18 of the bracket 15' comprising a liquid port 19 from where the fluid sample is delivered to the microfluidic channel 5, 5a once the compression configuration is established and an electrical aspect comprising the electrical connection of the biochip electrical connectors 12a and the substrate electrical contacts 6 is isolated from a fluidic aspect comprising the microfluidic channels 5, 5a and/or fluid sample delivery to the biosensors 11.

**[0045]** In an embodiment of the present invention, and when the cartridge 1 is in use, isolation between the fluidic aspect and the electrical aspect is achieved by a sealing layer 13 that is coated onto the top biochip surface 8 or the top substrate surface 3 (not shown), or it may be provided as a separate layer disposed between the biochip 7 and the substrate 2.

**[0046]** In an embodiment of the present invention, the sealing layer 13 has adequate compressibility such that, in response to the compression configuration being activated, it is also compressed relative to one or both of the biochip 7 and the substrate 2, to the extent that the electrical and fluidic aspects of an embodiment of the present invention are isolated from each other, it is not deformed/damaged, and it can sustain treatment/processing such as curing.

**[0047]** In Figures 1A1 and 1A2, a tape 14 with a pocket 14a is shown, which is dimensionally sized in proportion to, and such as to accommodate, the biochip 7. To secure the biochip 7 within the pocket 14a and so that it does not fall out when it is inserted into the bracket 15', a tape cover 14b is disposed overlying the tape 14 to provide a security measure. The pocket 14a within the tape 14 is an alignment window through which the biochip electrical connectors 12a and the substrate electrical contacts 6 are substantially aligned relative to each other in the alignment configuration as described above.

**[0048]** Returning to Figure 1B1, the bracket 15' loaded with the biochip 7 and the substrate 2 in the compression configuration, and isolation of the electrical and fluidic aspects having been established, is then conjoined with the reader (not shown) in the format that electrodes 6' of the substrate 2 are in electrical connection with the reader pins. In this way, the biochip 7 and the reader are electrically connected via the substrate 2.

**Polymer Substrate + biosensors and biochip electrical contacts on the same biochip surface**

**[0049]** Reference is made to Figures 2A1 and 2A2, which schematically illustrate a respective top and bottom view of an embodiment of the present invention, which differs from any one of the versions of Figure 1 described above in that it comprises a polymer substrate 2b. The polymer material may, for example be, PMMA, PC, PET, Polyester, COC, polyimide foils and sheets. Correspondent Figures 2B1 and 2B2 show the biochip 7 and the substrate 2 engaged in the compression configuration within the bracket 15'.

**[0050]** Figure 2A1 shows a further structural differentiation in that electrical connectors/lines 6" are formed on the top substrate surface 3 rather than being embedded within the substrate 2. They are configured to electrically couple the substrate electrical contacts 6 to the electrodes 6' for electrical connection to the reader.

**Pressure sensitive adhesive layer + sealant function**

**[0051]** Referring now to Figures 3A1, 3A2 and 3A3 which respectively show a top-view perspective of a progressively assembled embodiment of the present invention comprising a PSA layer 20 disposed between the biochip 7 and the substrate 2.

**[0052]** Via a cutout feature 20a in the PSA layer 20, the biochip electrical contacts 12a on the top biochip sur-

face 8 are aligned with the substrate electrical contacts 6 on the top substrate surface 3 for the alignment configuration. The biochip 7 is secured positionally by sticking it to the underlying adhesive surface of PSA layer 20 as shown in Figure 3A2.

**[0053]** In an embodiment of the present invention, the PSA layer 20 may be configured to have adhesive properties over the whole extent of its surface facing the biochip 7, which is the case in Figure 3A1 and Figure 3A2. In this case, the PSA layer 20 performs the role of: the adhesion layer 20 to which the biochip 7 is secured relative to the substrate 2 in the alignment configuration and the sealing layer 20 for isolating the fluidic and electrical aspects in response to activation of the compression configuration. So, the adhesion layer 20 and the sealing layer 13 are the same and embodied by the PSA layer 20.

**[0054]** Alternatively, the adhesion layer 20 and the sealing layer may be separate. In this case, and in one example, the PSA layer 20 may be configured to be adhesive only in some spots on its surface facing the biochip 7 (not shown) and an additional sealant underfill is inserted between the biochip 7 and the PSA layer 20.

**[0055]** The PSA layer 20 is preferably adhesive on both of its surfaces, and is a pressure sensitive, double-sided adhesive tape.

**[0056]** As per the previous embodiments, insertion of the cartridge 1 into a reader, or in the receptacle 15/bracket 15', which is depicted in Figure 3A3, activates the compression configuration that electrically connects the biochip 7 and the substrate 2. In the present embodiment, where the adhesive properties of the PSA layer 20 extend over its whole surface facing the biochip 7, the mechanical compression that ensues causes the biochip electrical connectors/gold bumps 12a to pierce through the PSA layer 20 and to be pressed relative to/into contact with the correspondent substrate electrical contacts 6. Where the PSA layer 20 is intact, and especially around the gold bumps 12a, it forms a fluid-tight sealant that provides isolation from the fluidic aspect, namely, the fluid sample delivered to the biosensors 11. In an alternative configuration, the PSA layer 20 comprises holes/spaces correspondent with the gold bumps 12a so that it need not be pierced as described above.

**[0057]** Delivery of the fluid sample to the biosensors 11 is done via the microfluidic channel 20a in the PSA layer 20, which is aligned with the liquid port 19 of the bracket 15', and the circular liquid port 5a on the top substrate surface 3.

**[0058]** The PSA layer 20 comprises a laminated, screen-printed, inkjet-printed, dispensed or if required, an ultraviolet cured layer.

**[0059]** In an embodiment of the present invention, the PSA layer 20 comprises a compressibility, which is able to sustain treatment/processing such as curing, for example, and also such that the compression configuration can be activated by insertion into the reader or receptacle 15, 15'.

**Biosensors and biochip electrical contacts on different surfaces of the biochip and through silicon vias**

**[0060]** Figures 4A1 and 4A2 give a top-view perspective of a progressively assembled embodiment of the present invention in which, and in contrast to the previously described embodiments, the biosensors 11 and biochip electrical connectors 12/gold bumps 12a are formed on different surfaces 8, 9, of the biochip.

**[0061]** From Figure 4A1, it can be seen that the biochip 7 is oriented so that the bottom biochip surface 9 comprising the gold bumps 12a faces the top substrate surface 3. Like the embodiment described with reference to Figures 1A1 and 1A2, a tape 14 with a tape pocket 14a is disposed above the top biochip surface 8. It is designed to accommodate the biochip 7 within the pocket 14a and so that the gold bumps 12a of the biochip 7 and the substrate electrical contacts 6 are aligned in the alignment configuration.

**[0062]** A sealing layer 21 is disposed above the tape 14 in the present embodiment. It comprises a liquid port 21a which delivers the fluid sample to the biosensors 11 of the biochip 7 when the cartridge 1 is in use. The sealing layer 21 may comprise adhesive surfaces, such as an adhesive underside so as to be securely positioned relative to the underlying tape 14. However, it is not restricted thereto and need not have any adhesive properties and/or surfaces.

**[0063]** In the compression configuration, the sealing layer 21 is mechanically compressed relative to the biochip 7 to form a leak proof seal/fluid-tight sealant that prohibits the fluid sample from flowing into the pocket 14a without interfering with its delivery through the liquid port 21a to the biosensor 11. In this way, the fluid sample introduced onto the top biochip surface 8, specifically to the biosensor 11, is isolated from and cannot leak down to the electrical connection between the substrate 2 and the biochip 7, which is established through their respective electrical contacts 12a, 6, being mechanically compressed into contact with each other in response to the activation of the compression configuration.

**[0064]** In the present embodiment, because the biochip 7 comprises through silicon vias (TSVs) in its body, the electrical contacts 6, 12a and the sensitive biosensors 10, 11 are conveniently disposed on opposite sides 8, 9, of the biochip 7.

**Stacked substrate configuration interspersed with PSA layers**

**[0065]** Figure 5 shows an exploded view of an embodiment of the present invention comprising a stacked cartridge 22 of sheets/foils 23, 24, 25, 26, 27 that are interspersed and joined together with PSA layers (not shown). Each PSA layer has a layout that is the intersection of the layouts of the layers in contact with it so not to obstruct openings. The sheets/foils 23, 24, 25, 26 are already bonded together during manufacturing. The joints be-

tween them are established by mechanical compression from insertion of the stacked cartridge 22 into the receptacle 15, 15' to establish electrical connection between the biochip 7 and substrate 2 and sealing of the microfluidic structures as described above with respect to the compression configuration.

**[0066]** Different sheets 23, 24, 25, 26 in the stack 22 carry different components with different functions and are analogous in structure and function with some aspects of the different embodiments of the present invention described above.

**[0067]** Turning to Figure 5, the topmost sheet/cover layer 23 comprises a liquid port 23a' where the fluid sample is received at/by the stacked cartridge 22.

**[0068]** Working down the stack 22 and interspersed between the topmost sheet 23 and a substrate sheet 25, is a spacer sheet 24 with a cutout feature 24a, which are analogous in function and properties to the tape 14 and tape pocket 14a described with reference to Figures 1 and 2. The cutout feature 24a accommodates the biochip 7 in a flipped configuration, that is, whereby the top biochip surface 8 comprising biosensors 11 and biochip electrical connectors/gold bumps 12a faces the substrate sheet 25. The spacer sheet 24 also comprises a through-hole 24a' that is aligned with the liquid port 23a' of the topmost sheet 23.

**[0069]** The substrate sheet 25 is metallized and comprises a top substrate surface layer 25' and a bottom substrate surface layer 25". The top substrate surface layer 25' comprises active components such as the substrate electrical contacts 6, which are coupled via electrical connector lines 6" to electrodes 6'. The substrate sheet 25 is arranged relative to the spacer sheet 24 in that the substrate electrical contacts 6 are substantially aligned to correspondent gold bumps 12a in the alignment configuration. The substrate sheet 25 may also comprise a filter 25a' aligned with at least the through hole 24a' in the spacer sheet 24 and is configured to remove particulates/impurities from the fluid sample that is to be subjected to an assay.

**[0070]** Arranged below the substrate sheet 25 is a fluidic aspect sheet 26 comprising at least a microfluidic channel 5. In the compression configuration, the microfluidic channel 5 transports the fluid sample from the filter 25a' to the biosensors 11 of the biochip 7 in an isolated mode from the electrical connection between the gold bumps 12a and the substrate electrical contacts 6 on the substrate sheet 25. Such isolation is due to the sealant function of the PSA sheet interspersed between any two sheets (not shown), which is activated in response to the mechanical compression driven by the compression configuration of the cartridge 1. The sealant function of the PSA sheet between the spacer sheet 24 and the substrate sheet 25 is also activated in the compression configuration, as described with reference to Figure 3, to thereby supplement the isolation of the fluidic and electrical aspects of the stacked cartridge 22.

**[0071]** A bottom sheet 27 arranged below the fluidic aspect sheet 23 completes the stack 22.

**[0072]** In an embodiment of the present invention the sealing layer 13, 20, 21 comprises a combination of: PSA material, a silicon grease, a viscous oil, and a partially cured resist. The silicon grease and viscous oil are in a dispensed form, and examples of the partially cured resist include photo-structured epoxies and appropriate polymers.

**[0073]** An embodiment of the present invention is not limited to the biochip electrical connectors/gold bumps 12, 12a being on one surface 8, 9, of the biochip 7 but may in fact be provided on both surfaces 8, 9, of the biochip 7. In this way, the number of electrical contacts 12, 12a that are incorporated on the biochip 7 may be increased without a need to compromise and increase the biochip area.

**[0074]** In order to simplify the bracket 15', at least one or both of the readout hole 17 and the liquid port 19 can be omitted - the readout may be done electrically and/or the sample feed channel may be integrated in the substrate 2 so the liquid port in the bracket 15' is not needed for feeding the fluid sample to the biosensors 11.

**[0075]** As described above, the microfluidic channel 5, 5a, 20a, 21a is formed in at least one of: the substrate 2, the sealing layer 13, 20, 21, and a customized channel layer 26. In this way, the microfluidic channel can be fabricated to suit any structural variation(s) and is a versatile feature of an embodiment of the present invention.

**List of reference numerals**

**[0076]**

| | |
|---|---|
| 1 | Cartridge |
| 2 | Substrate |
| 2a | PCB substrate |
| 2b | Polymer substrate |
| 3 | Top substrate surface |
| 4 | Bottom substrate surface |
| 5 | Microfluidic channel |
| 5a | Circular port |
| 6 | Substrate electrical contacts |
| 6' | Electrodes |
| 6" | Electrical connectors/lines |
| 7 | Biochip |
| 8 | Top biochip surface |
| 9 | Bottom biochip surface |
| 10 | Sensing aspect |
| 11 | Biosensor |
| 12 | Biochip electrical contacts |
| 12a | Biochip electrical connectors/Gold bumps |
| 13 | Sealing layer |
| 14 | Tape |
| 14a | Tape pocket |
| 14b | Tape cover |
| 15 | Receptacle |
| 15' | Bracket |
| 15a | Bracket opening |

| | |
|---|---|
| 16 | Top surface of bracket |
| 17 | Readout feature |
| 18 | Bottom surface of bracket |
| 19 | Liquid port of the bracket |
| 20 | PSA sealing layer |
| 20a | Microfluidic channel/cutout feature in PSA sealing layer 20 |
| 21 | Sealing layer |
| 21a | Microfluidic channel/liquid port formed in the sealing layer 21 |
| 22 | Stacked cartridge |
| 23 | Top sheet/cover layer |
| 23a' | Liquid port |
| 24 | Spacer sheet |
| 24a | Cutout feature for biochip |
| 24a' | Through-hole |
| 25 | Substrate sheet |
| 25' | Top substrate surface layer |
| 25" | Bottom substrate surface layer |
| 25a' | Filter |
| 26 | Fluidic aspect sheet |
| 27 | Bottom sheet |

## Claims

**1.** A cartridge (1) that is configured to perform an assay, when it is in use, to evaluate at least a parameter of a fluid sample, the cartridge (1) being electrically connected to a reader when it is in use, comprising:

a planar substrate (2) with a top substrate surface (3) comprising at least substrate electrical contacts (6) and a bottom substrate surface (4) that is disposed opposite to the top substrate surface (3),
at least a microfluidic channel (5, 5a, 20a, 21a) that is configured to receive the fluid sample to be evaluated,
a biochip (7) comprising: a top biochip surface (8) and a bottom biochip surface (9) disposed opposite to the top biochip surface (8), biochip electrical contacts (12), biochip electrical connectors (12a) that are electrically coupled to at least some of the biochip electrical contacts (12) and formed on at least one of the top and the bottom biochip surfaces (8, 9), and a sensing aspect (10) comprising at least a biosensor (11) that is disposed relative to the microfluidic channel (5, 5a, 20a, 21a) to receive the fluid sample, and
a sealing layer (13, 20, 21) that forms a substantially fluid-tight sealant relative to at least one of the biochip (7) and the substrate (2) when the cartridge is in use,
wherein the biochip (7) and the substrate (2) are in one of:

an alignment configuration, in which the biochip electrical connectors (12a) and substrate electrical contacts (6) are in geometrical alignment with each other, and
a compression configuration, when the cartridge (1) is in use, in which the aligned biochip electrical connectors (12a) and the substrate electrical contacts (6) are compressed together and are electrically connected.

**2.** The cartridge (1) as claimed in claim 1 wherein the sealing layer (13, 14, 20, 21) comprises at least one of: a pressure-sensitive adhesive layer (20), a silicon grease, a viscous oil, and a partially cured resist.

**3.** The cartridge (1) as claimed in claim 1 or 2 comprising an alignment feature (14, 14a) that aligns and accommodates the biochip (7) relative to the substrate (2) in the alignment configuration.

**4.** The cartridge (1) as claimed in any preceding claim comprising an adhesion layer (20) that is configured to at least secure the biochip (7) relative to the substrate (2) in the alignment configuration.

**5.** The cartridge (1) as claimed in claim 4 wherein the adhesion layer (20) is also the sealing layer (13).

**6.** The cartridge (1) as claimed in any preceding claim comprising a receptacle (15, 15') that is configured to receive the arrangement of the biochip (7) and the substrate (2) in the alignment configuration and to effectuate its alteration to the compression configuration.

**7.** The cartridge (1) as claimed in claim 6 wherein the receptacle (15, 15') comprises a bracket (15').

**8.** The cartridge (1) as claimed in any preceding claim wherein, in the compression configuration, at least the biochip (7) is in a mechanically compressed state in a direction normal to the substrate (2).

**9.** The cartridge (1) as claimed in any preceding claim wherein the sensing aspect (10, 11) and the biochip electrical connectors (12a) are respectively formed on the same surface (8, 9) or different surfaces (8, 9) of the biochip (7).

**10.** The cartridge (1) as claimed in any preceding claim wherein the biochip electrical connectors (12a) comprise metal bumps.

**11.** The cartridge (1) as claimed in any preceding claim wherein the substrate (2) comprises at least one of a printed circuit board (2a), a polymer material (2b), flex circuit, printed electronics substrate, flat panel,

and a glass substrate.

**12.** The cartridge (1) as claimed in any preceding claim wherein the substrate electrical contacts (6, 6', 6") are connected with electrical contacts of the reader.

**13.** The cartridge (1) as claimed in any preceding claim comprising a stacked configuration of sheets (22, 23, 24, 25, 26, 27), wherein each sheet (23, 24, 25, 26, 27) comprises a customized layer.

**14.** The cartridge (1) as claimed in claim 11 wherein the sealing layer (13) is interspersed between the sheets (23, 25, 26, 27).

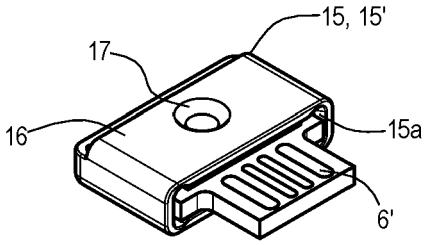


FIG. 1B1

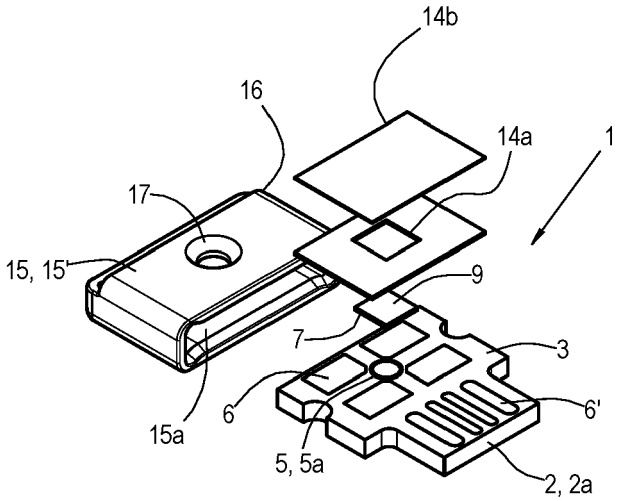


FIG. 1A1

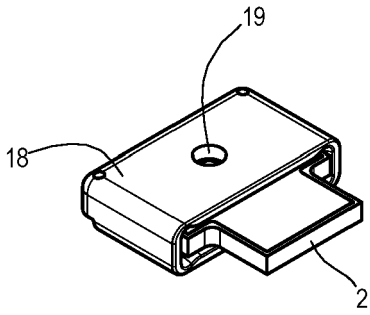


FIG. 1B2

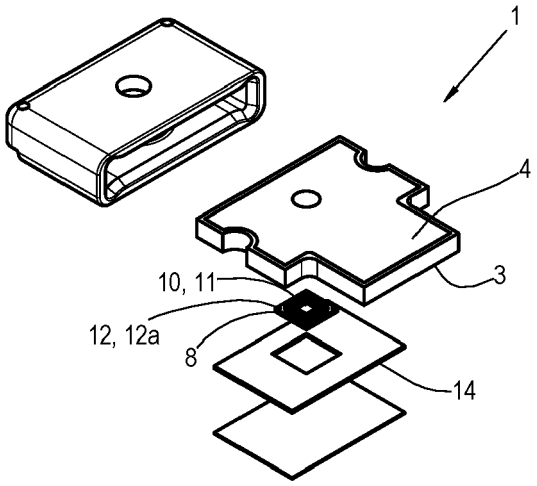


FIG. 1A2

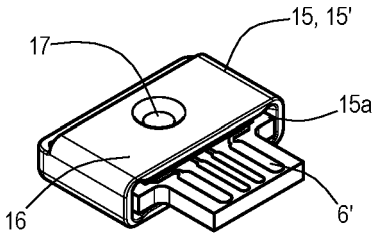


FIG. 2B1

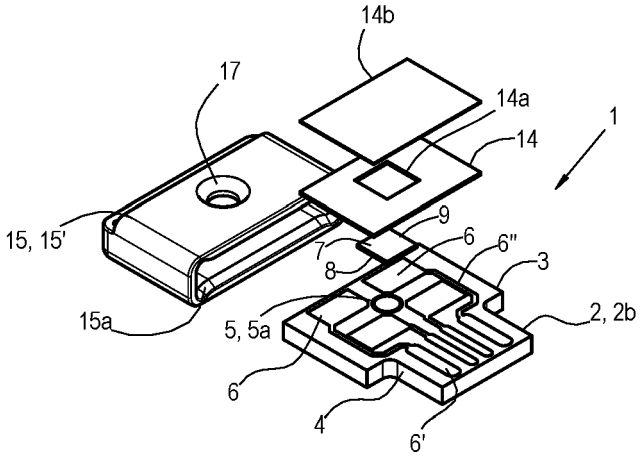


FIG. 2A1

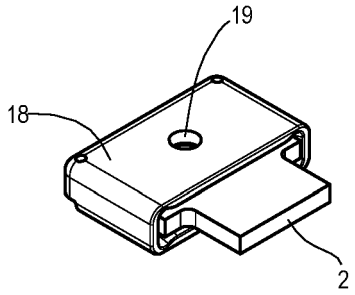


FIG. 2B2

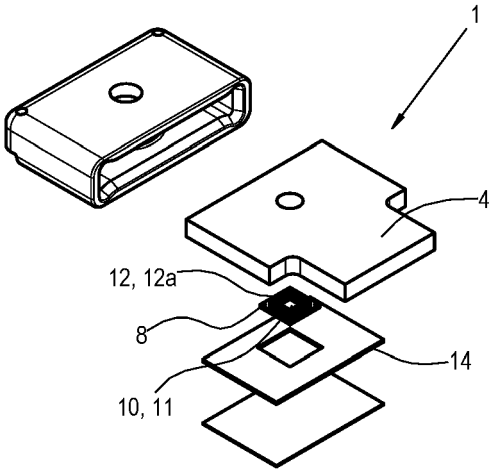


FIG. 2A2

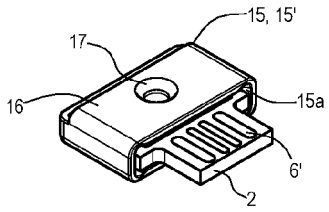


FIG. 3A3

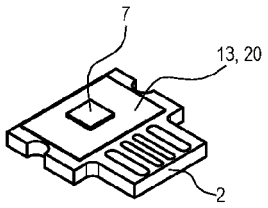


FIG. 3A2

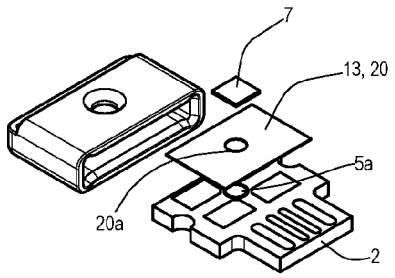


FIG. 3A1

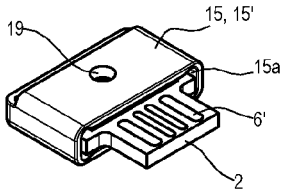


FIG. 4A2

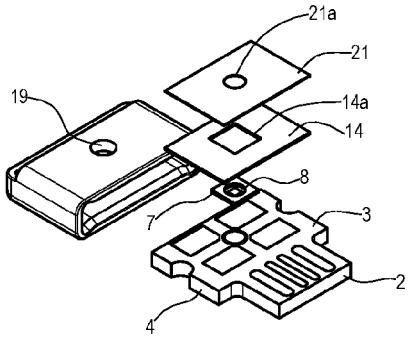


FIG. 4A1

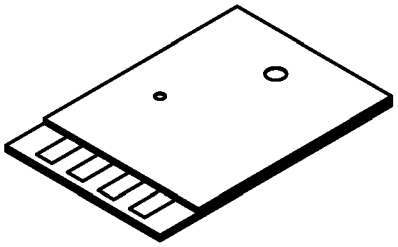

FIG. 5A

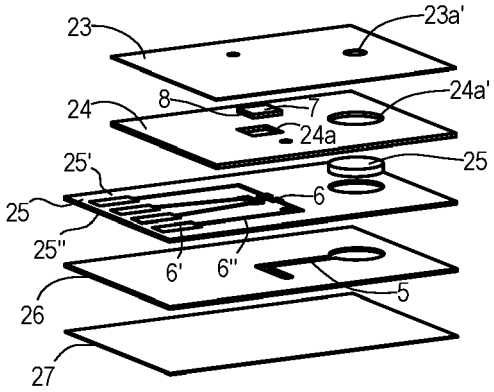


FIG. 5B

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# EUROPEAN SEARCH REPORT

Application Number
EP 23 15 0066

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| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | CLASSIFICATION OF THE APPLICATION (IPC) |
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| | | | B01L |

The present search report has been drawn up for all claims

| Place of search | Date of completion of the search | Examiner |
|---|---|---|
| The Hague | 14 June 2023 | Sinn, Cornelia |

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EPO FORM 1503 03.82 (P04C01)

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