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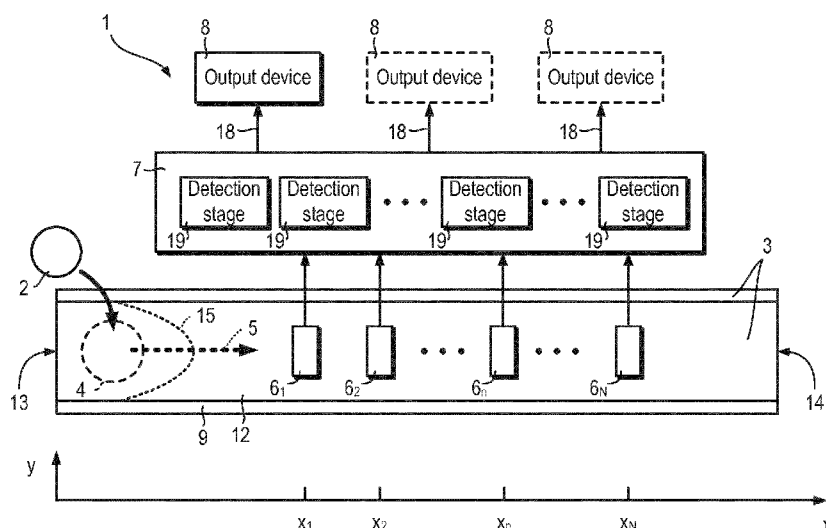


Fig. 1

(57) Abstract: An analytical test device (1) includes a lateral flow type strip (3). The lateral flow type strip includes a region (4) for receiving a liquid sample (2) and a path (5) for transporting the liquid sample (2) away from the sample receiving region (4). The analytical test device (1) also includes at least one moisture-sensitive resistor (6_n) disposed in the sample receiving region (4) and/or along the path (5), each respective resistor (6_n) arranged to be exposed to the liquid sample (2) when the liquid sample (2) reaches the resistor (6_n). The analytical test device (1) also includes a circuit (7) configured to signal (18) progress of the liquid sample through the strip (3) in dependence upon resistances of the moisture-sensitive resistor(s) (6_n).

LATERAL FLOW TEST STRIP COMPRISING MOISTURE-SENSITIVE RESISTORS

Field of the invention

5 The present invention relates to an analytical test device, in particular to a lateral flow-type test device.

Background

Biological testing kits may be used for a variety of reasons including, for instance, preliminary diagnosis, screening and management of long term health conditions. For
10 example, quantitative testing of blood samples using disposable test strips including electrodes treated with reagents sensitive to glucose is described in WO 2014/096407 A1, US 2014/0005492 A1 and WO 2008/059336 A2. US 2014/0001043 A1 describes a test sensor including a biosensor for measuring levels of, e.g. glucose, which includes fill electrodes which are sample sufficiency electrodes separated by a gap for sensing
15 the presence of a biological fluid.

Lateral flow devices (also known as “lateral flow immunoassays”) are a variety of biological testing kit. Lateral flow devices may be used to test a liquid sample, such as saliva, blood or urine, for the presence of an analyte. Examples of lateral flow devices
20 include home pregnancy tests, home ovulation tests, tests for other hormones, tests for specific pathogens and tests for specific drugs. For example, EP 0 291 194 A1 describes a lateral flow device for performing a pregnancy test.

In a typical lateral flow testing device, a liquid sample is introduced at one end of a
25 porous strip which is then drawn along the strip by capillary action (or “wicking”). A portion of the lateral flow strip is pre-treated with labelling particles which are activated with a reagent which binds to the analyte to form a complex, if the analyte is present in the sample. The bound complexes and also unreacted labelling particles continue to propagate along the strip before reaching a testing region which is pre-
30 treated with an immobilised binding reagent which binds bound complexes of analyte and labelling particles and does not bind unreacted labelling particles. The labelling particles have a distinctive colour, or other detectable optical or non-optical property, and the development of a concentration of labelling particles in the test regions provides an observable indication that the analyte has been detected.

A lateral flow device usually requires that an appropriate volume of liquid sample sample be provided. For example, there should not be too little liquid sample to perform the test correctly or too much liquid sample which can cause the liquid sample to propagate along the porous strip by “flooding” instead of wicking. This may lead to
5 false positive or negative results.

Some lateral flow devices test for elevated levels of an analyte which is expected to be normally present in background concentrations, for example some hormone tests. In such devices, the result should be checked within a certain duration during which the
10 test result is developed, but before background levels result in a false positive indication. One approach is to use light sources and photodetectors to monitor the progress or read the result of a lateral flow test. For example, US 2005/0037511 A1 describes an assay result reading device including at least one light source emitting light incident upon at least one of two or more spatially separated zones of a carrier,
15 and a photodetector capable of detecting light emanating from each of the two zones and generating signals representing the presence or absence of a fluid sample. A computation circuit calculates a flow rate for a fluid flowing along the carrier, compares the calculated flow rate to upper and lower limits, and rejects the assay result if the calculated flow rate is outside the upper and lower limits. However, using light sources
20 and detectors may cause a lateral flow device to be relatively bulky due to the need for providing optical paths. Additionally, optical reading and/or monitoring may be relatively expensive to implement for a disposable lateral flow test device.

Summary

According to a first aspect of the invention there is provided an analytical test device including a lateral flow type strip as specified in claim 1. The lateral flow type strip includes a region for receiving a liquid sample and a path for transporting the liquid sample away from the sample receiving region. The analytical test device also includes at least one moisture-sensitive resistor disposed in the sample receiving region and/or along the path, each respective resistor arranged to be exposed to the liquid sample when the liquid sample reaches the resistor. The analytical test device also includes a circuit configured to signal progress of the liquid sample through the strip in dependence upon resistances of the moisture-sensitive resistor(s).

Thus, moisture-sensitive resistors may be used for measuring and/or metering the progress of a liquid sample, which is suspected of containing an analyte, along the path.

The device may include at least two moisture-sensitive resistors disposed spaced apart in the sample receiving region and/or along the path. The at least two moisture sensitive resistors may be spaced apart by predetermined distances based on calibrations performed using liquid samples having known volumes.

Each moisture-sensitive resistor may include or consist of a region of conductive polymer. The conductive polymer is preferably deposited from solution, for example by printing. The conductive polymer may be poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS).

The path may be defined by a surface of a substrate and the region of conductive polymer may be disposed on the surface of the substrate. The path may include a strip of porous material overlying the surface of the substrate.

Each moisture-sensitive resistor may include a first electrode disposed on the surface of the substrate and a second electrode disposed on the surface of the substrate and spaced apart from the first electrode. Each moisture-sensitive resistor may include a region of solution processed conductive polymer having a resistivity which changes when exposed to water, the solution processed conductive polymer disposed onto the first surface and connecting between the first and second electrodes.

The device may include first and second test regions, wherein the at least two moisture-sensitive resistors may include first and second resistors and the first resistor is interposed between the first and second test regions. The first and second test regions may be regions treated with reagents for binding a complex of an analyte and a labelling particle. The first and second test regions may be regions upon which one or more light-emitting diodes (LEDs) are directed for making reflectance or transmittance measurements. The first and second test regions may be a working electrode and a counter-electrode respectively, for an electrochemical cell configured to determine an analyte concentration.

10

The circuit may include at least two detection stages, each detection stage may be configured to detect a change in value of resistance of one or more moisture sensitive resistors.

15 The device may further include at least one output device configured to receive output signal(s) from the circuit. The output device(s) may include indicators such as, for example, one or more light-emitting diodes (LEDs) or an array of light-emitting diodes. The output device may include one or more organic light-emitting diodes (OLEDs) or an array of organic light emitting diodes. The output device may include a buzzer. The output device may include a liquid crystal display.

20

The device may include at least two light-emitting diodes and at least two detection stages. Each detection stage may correspond to a moisture-sensitive resistor and to a light emitting diode, and each detection stage may configured to illuminate the corresponding light-emitting diode in response to detecting a change in the value of resistance of the corresponding moisture sensitive resistor. The light-emitting diodes may by organic light-emitting diodes.

25

The device may include one or more (organic) light-emitting diodes configured to illuminate the path and at least one photo-detector configured to receive light reflected or transmitted by the path. The detection circuit may be configured to illuminate the one or more (organic) light-emitting diodes in response to detecting a change in the value of resistance of a corresponding moisture sensitive resistor and may also be configured to determine a concentration of analyte in dependence upon an intensity of reflected or transmitted light detected by at least one photo-detector.

35

Each detection stage may include an amplifier or inverter having a gain configured to depend upon the value of resistance of one or more moisture sensitive resistors.

5 Each detection stage may include a two-step amplifier including first and second common source transconductance amplifiers, wherein a corresponding moisture sensitive resistor is connected to the drain of a transistor of the first transconductance amplifier and the output of the first transconductance amplifier provides the input to the second transconductance amplifier.

10 Each detection stage may include a reference resistor and a transistor. The reference resistor may be connected in series with a corresponding moisture-sensitive resistor and the output of the potential divider may be configured to switch the transistor. The transistor may be a field effect transistor or a thin-film transistor having a drain connected to a light-emitting diode or an organic light-emitting diode.

15 The circuit may be configured, in response to determining that the liquid sample has reached a predetermined position, to trigger a test. The circuit may be configured, in response to determining that the liquid sample has reached a predetermined position, to illuminate one or more light emitting diodes configured for performing reflectance or
20 transmittance measurements on the path.

The circuit may be configured, in response to determining that the liquid sample has reached a predetermined position, to activate an electrochemical cell configured to perform quantitative measurements of an analyte concentration in the liquid sample.

25 The path may include a substrate and an elongate porous strip supported on the substrate extending in a first direction between first and second ends. The sample receiving region may be disposed at the first end and may be configured to propagate the liquid sample through the porous strip towards the second end.

30 The device may further include a conjugate pad treated with at least one particulate labelled binding reagent for binding an analyte to form a labelled-particle-analyte complex when the analyte is contained in the liquid sample. The device may further include a test portion comprising at least one test region treated with an immobilised
35 binding reagent for binding the labelled-particle-analyte complex.

The test portion may further include a control region treated with a second immobilised binding reagent for binding the particulate labelled binding reagent. The porous strip may further include a wicking portion to absorb liquid sample after it has progressed through the test portion. The sample receiving region, conjugate portion, test portion
5 and wick portion may be provided as a single elongate porous strip, or may each be provided by separate porous strips which are connected end-to-end or partially overlapped.

The device may further include a number of first moisture-sensitive resistors which are
10 disposed in contact with the sample receiving region and spaced apart in the first direction.

The detection circuit may be configured to detect changes in values of resistance of each of the first moisture-sensitive resistors and, in response to detecting changes in values
15 of resistance to provide output signal(s) to cause one or more output devices to indicate to a user that a sufficient volume of liquid sample has been received. A sufficient volume is enough to enable testing of the liquid sample for the presence of an analyte, but not enough to cause overfilling, or “flood” filling of the porous strip.

The detection circuit may be configured to determine a flow-rate of the liquid sample through the sample receiving region based on the spacing of the first moisture-sensitive resistors and the corresponding times at which changes in values of resistance are detected. The detection circuit may be configured to determine that a sufficient volume of liquid sample has been received by comparing a flow rate determined from the first
20 moisture-sensitive resistors to predetermined minimum and maximum flow rates. The detection circuit may be configured, in response to determining that a sufficient volume of liquid sample has been received, to provide an output signal to cause an output device to indicate to a user that a sufficient volume of liquid sample has been received. The detection circuit may be configured, in response to determining that an insufficient
25 or excessive volume of liquid sample has been received, to provide an output signal to cause an output device to indicate to a user that the test results are not valid.
30

One or more second moisture-sensitive resistors may be disposed in contact with the test portion, spaced apart in the first direction between a test region and the second
35 end.

The detection circuit may be configured to detect changes in values of resistance of each of the second moisture-sensitive resistors and, in response to detecting changes in values of resistance, to provide output signal(s) to cause an output device to indicate to a user that a test has completed and the result can be read. The detection circuit may
5 be configured to start a timer in response to detecting changes in values of resistance of one or more of the second moisture-sensitive resistors and to provide the output signal when the timer has elapsed.

The detection circuit may be configured to determine a flow-rate of the liquid sample
10 through a part of the test portion based on the spacing of the second moisture-sensitive resistors and the corresponding times at which changes in values of resistance are detected. The detection circuit may be configured to determine whether the flow rate through the testing portion is sufficient for a valid test of the liquid sample by comparing a flow rate determined from the second moisture-sensitive resistors to
15 predetermined minimum and maximum flow rates. The detection circuit may be configured, in response to determining that there was a sufficient flow rate through the testing portion, to provide an output signal to cause an output device to indicate to a user that the results of testing a liquid sample for an analyte are valid. The detection circuit may be configured, in response to determining that there was an insufficient or
20 excessive flow rate through the testing portion, to provide an output signal to cause the output device(s) to indicate to a user that the test results are not valid.

One or more third moisture-sensitive resistors may be disposed in contact with the test portion spaced apart in the first direction between the test region and the conjugate
25 portion.

The detection circuit may be configured to determine a flow-rate of the liquid sample through the test portion based on the spacing of the third moisture-sensitive resistors and the corresponding times at which changes in values of resistance are detected. The
30 detection circuit may be configured to determine whether the flow rate into the testing portion is sufficient for a valid test of the liquid sample by comparing a flow rate determined from the third moisture-sensitive resistors to predetermined minimum and maximum flow rates. The detection circuit may be configured, in response to determining that there is a sufficient flow rate into the testing portion, to provide an
35 output signal to cause an output device to indicate to a user that the results of testing a liquid sample for an analyte are valid. The detection circuit may be configured, in

response to determining that there was an insufficient or excessive flow rate into the testing portion, to provide an output signal to cause an output device to indicate to a user that the test results are not valid.

- 5 The detection circuit may be configured to compare a difference between flow rates of liquid sample determined from the second and third moisture-sensitive resistors with predetermined minimum and maximum flow rate differences. The detection circuit may be configured, in response to determining that a difference between flow rates determined from the second and third moisture-sensitive resistors does not lie between
10 predetermined minimum and maximum flow rates, to provide an output signal to cause the output device(s) to indicate to a user that the test results are not valid.

The substrate may be a flexible substrate having first and second halves which is arranged to be folded along a fold line so that the first half provides a first surface of the
15 substrate and the second half provides a second surface opposite to the first surface. The moisture-sensitive resistors may be printed onto the first half. Some or all of the circuit elements of a detection stages corresponding to each moisture-sensitive resistor may be printed onto the second half. Some or all of the circuit elements forming each detection stage may be covered by a waterproof layer. Each detection stage may
20 include a reference resistor and a transistor printed onto the second half of the flexible substrate. Contact pads and conductive traces connecting to or between moisture-sensitive resistors, reference resistors and transistors may be printed on the first and second halves of the flexible substrate.

- 25 According to a second aspect of the invention there is provided a testing kit including the device.

According to a third aspect of the invention there is provided a method of using the device, the method including adding a liquid sample to the sample receiving region.

- 30 According to a fourth aspect of the invention there is provided a method of operating the device, the method including receiving a liquid sample on the sample receiving region. The method also includes determining that the liquid sample has reached a predetermined position. The method also includes in dependence upon the liquid
35 having reached the predetermined position, sending one or more output signals to at least one output device.

Brief Description of the Drawings

Certain embodiments of the present invention will now be described, by way of example, with reference to the accompanying drawings in which:

Figure 1 illustrates a test device which includes moisture-sensitive resistors;

5 Figure 2 illustrates a side view of part of a sensor shown in Figure 1;

Figure 3A is a plan view of a first example of moisture-sensitive resistor;

Figure 3B is a plan view of a second example of moisture-sensitive resistor;

Figure 3C is a plan view of a second example of moisture-sensitive resistor;

10 Figure 4 schematically illustrates resistances of moisture-sensitive resistors under wet and dry conditions;

Figure 5 illustrates an amplifier circuit for detecting a change in the resistance of a moisture-sensitive resistor;

Figure 6 illustrates a potential divider circuit suitable for detecting a change in the resistance of a moisture-sensitive resistor;

15 Figure 7 illustrates propagation of a liquid sample through a test device at different times;

Figure 8 schematically illustrates changing resistance values of moisture-sensitive resistors in response to the progress of a liquid sample through a test device;

Figure 9 illustrates a first lateral flow device including moisture-sensitive resistors;

20 Figure 10 illustrates a second lateral flow device including moisture-sensitive resistors;

Figures 11 to 13 illustrate printing moisture-sensitive resistors and reference resistors onto a flexible substrate; and

Figure 14 is a plan view of a moisture-sensitive resistor and a corresponding detections stage printed onto a flexible substrate.

25

Detailed Description of Certain Embodiments

Referring to Figures 1 and 2, a device 1 is shown for testing a liquid sample 2 and which is capable of monitoring and/or metering the liquid sample 2, for example determining whether sufficient liquid sample 2 has been introduced into the device 1, and triggering
30 testing of the liquid sample 2, such as on-device reflection or transmission spectroscopy.

The device 1 includes a lateral flow-type strip 3 which includes a region for receiving a sample 4 (sample receiving region) intended to receive the liquid sample 2, a path 5 for
35 transporting the liquid sample 2 away from the sample receiving region 4 and a set of N moisture-sensitive resistors $6_1, \dots, 6_N$ spaced apart along the path, and a detection circuit

7 (herein also referred to as a “module”) which is configured to meter liquid sample 2 volume, or to monitor progress of the liquid sample 2 along the path, in dependence upon resistances of the moisture-sensitive resistors 6. There may be one resistor or more than one resistor, i.e. $N \geq 1$. The device 1 also includes, at least one output device
5 8 in the form of light-emitting diodes (LEDs) or organic light-emitting diodes (OLEDs).

The lateral-flow type strip 3 includes a generally elongate substrate 9 having first and second opposite faces 10, 11 (or “surfaces”). The moisture-sensitive resistors 6 are disposed on the first surface 10 of the substrate 9. The substrate 9 may take the form
10 of, for example, a conventional printed circuit board (PCB) substrate or a foil-coated flexible polymer polyethylene terephthalate (PET), polyethylene naphthalate (PEN) or polyimide (PI). An elongate porous strip 12 overlies the first surface 10 of the substrate 9 and the moisture-sensitive resistors $6_1, \dots, 6_N$ and runs between first and second ends 13, 14. The porous strip 12 can hold and transport the liquid sample 2. The porous strip
15 12 may transport the liquid sample 2 by capillary action (also known as “wicking”). The porous strip 12 may be made from one or a combination of materials such as, for example, cellulose filter, nitrocellulose, polyvinylidene fluoride, polyethersulfone (PES), charge modified nylon, surface modified polyester or glass fiber.

20 As will be explained in more detail later, a liquid sample 2 suspected of including an analyte is introduced to a sample receiving region 4 (which may be a part of the lateral flow strip 3 or a separate region of material) proximate to the first end 13 of the lateral flow strip 3 and propagates through the porous strip 12 in a direction of flow (herein labelled as the x-axis) towards the second end 14. The liquid sample 2 propagates along
25 the porous strip 12 by a capillary action. A flow front 15 separates a substantially dry portion 16 of the porous strip 12 from a moistened portion 17 of the porous strip 17 which contains the liquid samples 2.

The elongate porous strip 12 is in contact with the moisture-sensitive resistors $6_1, \dots, 6_N$,
30 such that each resistor $6_1, \dots, 6_N$ is exposed to the liquid sample 2 when the liquid sample 2 reaches the resistor $6_1, \dots, 6_N$.

The detection circuit 7 is configured to provide output signals 18 to at least one output device 8 in dependence upon values of resistance of the moisture sensitive resistors 6_n .
35 The detection circuit 7 includes a number M of detection stages $19_1, \dots, 19_m, \dots, 19_M$. Each detection stage 19_m is configured to detect changes in the resistance of one or

more corresponding moisture-sensitive resistors 6_n . For example, each detection stage 19_m may detect that the resistance of one or more corresponding moisture-sensitive resistors 6_n has decreased (or increased as appropriate), indicating that liquid sample 2 is in contact with the respective moisture-sensitive resistor(s) 6_n . The detection circuit
5 7 includes at least one detection stage 19_m , and may include up to a number of detection stages 19_m equalling the number N of moisture-sensitive resistors 6_n , i.e. $1 \leq M \leq N$. The detection stages 19_m need not all correspond to the same number of moisture-sensitive resistors 6_n . For example, a first detection stage 19_1 may correspond to a single moisture-sensitive resistor 6_1 and a second detection stage 19_2 may correspond to a pair
10 of moisture-sensitive resistors $6_2, 6_3$. The detection circuit 7 may be implemented using conventional electronic components supported on a PCB substrate (not shown) provided separately to the substrate 9. In some examples, the detection circuit 7 may take the form of a microcontroller. The detection circuit 7 may be implemented using a mixture of conventional electronic components supported on a separate PCB substrate
15 (not shown) and printed electronic components supported on the first and/or second surfaces 10, 11 of the substrate 9. In some cases, the entire detection circuit 7 may be provided by printed components disposed on the first and/or second surfaces 10, 11 of the substrate 9.

20 Thus, one or more moisture-sensitive resistors 6_n may be used to detect the extent of propagation, the volume and/or flow rate of a liquid sample 2 transported through a porous strip 12, for example in a lateral flow-type device.

The at least one output device 8 may include a number of light-emitting diodes (LEDs),
25 for example, organic light-emitting diodes (OLEDs). The device 1 may include one output device 8 corresponding to each moisture-sensitive resistor 6_n , or the sensor may include output devices 8 corresponding to two or more moisture-sensitive resistors 6_n . Each output device 8 receives output signals 18 from the detection circuit 7 and provides an indication to a user in response to the output signals 18. For example, to
30 inform a user that a sufficient volume of liquid sample 2 has been introduced, to inform a user that a test is completed or to inform a user whether test results are valid or invalid. A sufficient volume of liquid sample 2 is enough to allow the liquid sample 2 to be tested for the presence or concentration of an analyte, but not so much as to cause overfilling, or "flood" filling of the porous strip 12. Output devices 8 need not be LEDs
35 or OLEDs and may alternatively include LED or OLED arrays, a buzzer (not shown) or a liquid crystal display (LCD) (not shown) for providing more detailed indications.

A battery (not shown), provides power to the detection circuit 7 and the output device(s) 8. The power to the detection circuit 7 and the output device(s) 8 may be controlled by a switch (not shown), or may be activated by a one-time switch (not shown) when a device 1 is first removed from its packaging.

The moisture-sensitive resistors 6_n may be spaced apart in the first direction x along the length of the substrate 9 between the first and second ends 13, 14. The moisture-sensitive resistors 6_n may be evenly or unevenly spaced at predetermined locations, for example at respective locations $x_1, x_2, \dots, x_n, \dots, x_N$. Alternatively, the moisture-sensitive resistors 6_n may be arranged as groups of two or more moisture-sensitive resistors 6_n , with smaller spacing within a group and larger spacing between groups. For example with $x_3 - x_2 \gg x_2 - x_1$. For example, each group of moisture-sensitive resistors $6_n, 6_{n+1}$ etc may correspond to one detection stage 19_m . The positions x_n of moisture-sensitive resistors 6_n in the first direction x may be predetermined using calibration measurements performed using liquid samples 2 of known volumes.

Referring also to Figure 3A, each moisture-sensitive resistor 6_n includes a first electrode 20 and a second electrode 21 disposed spaced apart on the first surface 10 of the substrate 9. A region of moisture-sensitive material 22 having a resistivity which changes when exposed to water is printed onto the first surface 10 to connect between the first and second electrodes 20, 21. The region of moisture-sensitive material 22 may be printed over the first and second electrodes 20, 21. The moisture-sensitive material 22 may be any conductive polymer known in the art and which exhibits moisture sensitive resistance such as, for example, Poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS). The polymer material may be printed on the substrate using ink-jet printing, screen printing, thermal printing, gravure printing, dispensing, micro-dispensing or other suitable methods. The substrate may be a flexible polymer substrate such as, for example, a polyethylene terephthalate (PET) substrate, polyethylene naphthalate (PEN) substrate or a polyimide (PI) substrate.

The first and second electrodes 20, 21 are connected by conductive traces 23 to contact pads 24 formed on the first surface 10 proximate or adjacent to a first edge 25 of the first surface 10 which is parallel to the first direction x . The first and second electrodes 20, 21 may take the form of substantially parallel, rectangular, electrodes, spaced apart by a distance L . For example, the first and second electrodes 20, 21 may simply be

extensions of the conducting traces 23 which are covered over by the region of moisture-sensitive material 22. The contact pads 24 are relatively wider than the conducting traces 23 to facilitate connecting the moisture-sensitive resistor 6_n to the detection circuit 7 where this is provided on a separate substrate. The first and second
5 electrodes 20, 21, the conductive traces 23 and the contact pads 24 may be formed by evaporation or sputtering of a conductive material such as, for example, gold. Alternatively, the first and second electrodes 20, 21, the conductive traces 23 and the contact pads 24 may be formed by printing conductive inks containing, for example, silver, carbon or other conductive particles. The first and second electrodes 20, 21, the
10 conductive traces 23 and the contact pads 24 may be formed by inkjet printing, screen printing, thermal printing, gravure printing, dispensing, micro-dispensing or any other suitable method.

Alternative arrangements of the first and second electrodes 20, 21 and the region of
15 moisture-sensitive material 22 can provide the moisture-sensitive resistor(s) 6_n.

For example, referring also to Figure 3B, a second moisture-sensitive resistor 6_b is the same as the moisture-sensitive resistor 6_n, except that the second electrode 21_b extends from a contact pad 24_b formed proximate or adjacent to a second edge 26 of the first
20 surface 10 parallel and opposite to the first edge 25.

Referring also to Figure 3C, a third moisture-sensitive resistor 6_c is the same as the moisture-sensitive resistor 6_n, except that interdigitated protrusions 27 extend perpendicularly from both the first and second electrodes 20_c, 21_c. The third moisture-
25 sensitive resistor 6_c may have a reduced the total resistance compared to the moisture-sensitive resistor 6_n.

To reduce or remove interference from a conductive liquid sample 2, a layer of waterproof or water resistant material (Figure 12) may optionally be applied over the
30 first surface 10 leaving only the region of moisture-sensitive material 22 exposed. Alternatively, a layer of waterproof or water resistant material may be selectively applied to the conducting traces 23, 23_b and contact pads 24, 24_b. When some or all of the detection circuit 7 is supported on the first and/or second surfaces 10, 11, the moisture-sensitive resistors 6_n may be connected to the detection circuit 7 using
35 additional conductive traces (Figures 11, 14) and/or vias (not shown) instead of contact pads 24, 24_b.

Figure 4 shows plots of dry resistance $R_{\text{dry}}(t)$ and wet resistance $R_{\text{wet}}(t)$ of an example moisture-sensitive resistor 6_{test} over time. The example resistor 6_{test} included first and second electrodes 20, 21 in the form of evaporated gold traces connected by a 2 mm by 2 mm region of PEDOT:PSS in the form of Clevios (RTM) AI4083 GSD. The resistance $R_{\text{dry}}(t)$ of the example resistor 6_{test} was measured without water over a period of time, and the resistance $R_{\text{wet}}(t)$ of the moisture-sensitive resistor 6_{test} when exposed to water was measured by covering the region of moisture-sensitive material 22 with approximately 2 μl of water.

10

As shown in Figure 4, the resistance of the example resistor 6_{test} was observed to be sufficiently sensitive to moisture that the resistance changed as a result of the humidity of exhaled breath. The dry resistance $R_{\text{dry}}(t)$ increases with time. The increase was reversible and is thought to be attributable to ambient moisture which is driven off during testing by the associated small current flow. For all tested values of initial resistance, the wet resistance $R_{\text{wet}}(t)$ showed a large decrease in resistance compared to the dry resistance $R_{\text{dry}}(t)$. Observed decreases in the wet resistance $R_{\text{wet}}(t)$ were all in excess of 500 k Ω . The wet resistance $R_{\text{wet}}(t)$ was not observed to vary with time. The decrease of resistance was reversible upon drying. Drying the PEDOT:PSS provided a larger initial value of resistance and consequently provided a greater response to the addition of moisture. The specific values of resistance can be controlled by selecting the size of the region of moisture-sensitive material 22 and the size, shape and separation of the first and second electrodes 20, 21.

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Referring also to Figure 5, a detection stage 19_m for detecting a change in resistance of a moisture-sensitive resistor 6_n may take the form of 2-step inverter based DC amplifier 28. The 2-step inverter based DC amplifier amplifies an input voltage V_{in} to an output voltage V_{out} with a gain dependent on the resistance of a moisture-sensitive resistor 6_n . A first step includes a first transistor T_1 in the form of a p-channel organic thin-film transistor (OTFT). The gate of the first transistor is connected to an input voltage V_{in} , the source is connected to ground and a moisture-sensitive resistor 6_n is connected in series between the drain of the first transistor T_1 and a bias voltage V_0 . The bias voltage V_0 is negative when p-channel transistors T_1 , T_2 are used. In this way, the first step provides a common source transconductance amplifier. The gate of a second transistor T_2 is connected between the moisture-sensitive resistor 6_n and the drain of the first transistor T_1 . The second transistor T_2 likewise takes the form of a p-channel OTFT.

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The source of the second transistor T_2 is connected to ground and a reference resistor 29, having resistance value R_{ref} is connected in series between the drain of the second transistor T_2 and the bias voltage V_o . In this way, the second step also provides a common source transconductance amplifier, taking the output of the first step as input.

5 The input voltage V_{in} and the initial dry resistance R_{dry} of the moisture-sensitive resistor 6_n may be selected so that the voltage at the gate of the second transistor T_2 is just above a gate threshold voltage for conduction in the (p-channel) second transistor T_2 .

10 In the dry initial state, the voltage at the gate of the second transistor T_2 is just above a gate threshold voltage for conduction, and consequently the current through the second transistor T_2 is low or negligible and the voltage at V_{out} is substantially equal to the bias voltage V_o . When moisture contacts the moisture-sensitive resistor 6_n , the resistance drops substantially to the wet resistance R_{wet} , whereas the transconductance of the first transistor T_1 remains the same as the input voltage V_{in} is constant. As a result, the
15 voltage at the gate of the second transistor T_2 is decreased towards the bias voltage V_o . Since in the dry initial state the gate voltage to the second transistor T_2 is set to be just above the conduction threshold, the decrease in the gate voltage in the wet state increases the transconductance of the second transistor by a substantially amount, i.e. so as to be much larger than $1/R_{ref}$, and the output voltage V_{out} becomes substantially
20 equal to ground.

Thus, detection of the change in resistance of the moisture-sensitive resistor 6_n may be performed using a relatively simple 2-step inverter based DC amplifier 28 which may be compact and inexpensive. Because the second transistor T_2 is switched by a
25 decrease in the resistance of the moisture-sensitive resistor 6_n , the 2-step inverter based DC amplifier 28 can be used even when the dry resistance $R_{dry}(t)$ of the moisture-sensitive resistor 6_n increases in the time before the flow front 15 arrives at the corresponding location x_n .

30 The first and second transistors T_1 , T_2 and the reference resistor 29 may be printed onto the upper surface 10 or lower surface 11 of the substrate 9 by printing of suitable conductive inks and semiconducting polymers. For example, conductive parts may be printed using conductive inks containing particles, of silver or carbon or conductive polymers. For example, semiconducting parts may be printed using organic
35 semiconductors derived from a range of material systems such as, for example, rubrene, tetracene, pentacene, and semiconducting polymers such as polythiophenes.

For example gate dielectrics may be printed using organic dielectrics such as, for example, polytetrafluoroethylene (PTFE), polyvinylidene fluoride (PVDF) poly vinylalcohol (PVA), or polymethylmethacrylate (PMMA). Parts may be printed using suitable methods such as inkjet printing, screen printing, thermal printing, gravure printing, dispensing or micro-dispensing methods.

The first and second transistors T_1 , T_2 and the reference resistor 29 may be protected from the liquid sample 2 by a waterproof or water resistant layer (Figure 12) formed by, for example, applying a lacquer or printing a water resistant ink or polymer.

10

Thus, using printed electronics methods the moisture-sensitive resistors 6_n may be provided on the same substrate as a corresponding detection stages 19_n , simplifying manufacture and reducing the size and cost of a disposable lateral flow device having liquid sample metering and/or monitoring functions.

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Although the 2-step inverter based DC amplifier 28 has been described with reference to first and second steps in the form of transconductance amplifiers, the 2-step inverter based DC amplifier 28 may alternatively include other types of common source voltage amplifiers with minimal modifications.

20

Referring also to Figure 6, a detection stage 19_m for detecting a change in resistance of a moisture-sensitive resistor 6_n may alternatively take the form of a potential divider circuit 30. A moisture-sensitive resistor 6_n is connected in series with a reference resistor 29 between a bias voltage V_o and ground. The gate of a third transistor T_3 is connected between the moisture-sensitive resistor 6_n and the reference resistor R_{ref} . The third transistor T_3 may take the form of an OTFT with either an n-channel or p-channel. The sign of the bias voltage V_o depends on whether the third transistor T_3 is n-channel or p-channel. The resistance value R_{ref} of the reference resistor 29 is chosen with reference to the dry resistance R_{dry} of the moisture-sensitive resistor 6_n , so that in the dry initial state the gate of the third transistor T_3 is biased to just below (for n-channel) or just above (for p-channel) the conduction threshold. Subsequently, when the flow front 15 reaches the moisture-sensitive resistor 6_n , the decrease in resistance to the wet resistance R_{wet} value shifts the gate voltage of the third transistor T_3 towards the bias source and switches on the channel of the third transistor T_3 . In the potential divider circuit 30, any increase in the dry resistance $R_{dry}(t)$ before arrival of the flow front 15 will shift the gate voltage of the third transistor T_3 away from the bias voltage

V_o , making the potential divider circuit 30 robust against the measurement time increases observed in the PEDOT:PSS based test resistor 6_{test} . The third transistor T_3 may be used directly to illuminate an LED driven by an LED power supply V_{LED} . For example, the LED may take the form of an OLED.

5

Thus, detection of the change in resistance of the moisture-sensitive resistor 6_n may be performed using a relatively simple potential divider circuit 30 which may be compact and inexpensive.

10 The third transistor T_3 and the reference resistor 29 may be printed onto the upper surface 10 or lower surface 11 of the substrate 9 using the same or similar materials and methods as the 2-step inverter amplifier 28. The third transistor T_3 and the reference resistor 29 may be protected from the liquid sample 2 by a waterproof or water resistant layer (Figure 12) formed by, for example, applying a lacquer or printing a
15 water resistant ink or polymer.

Thus, using printed electronics methods the moisture-sensitive resistors 6_n may be provided on the same substrate as a corresponding detection stage 19_n , simplifying manufacture and reducing the size and cost of a disposable lateral flow device.

20

Reference resistors 29 may optionally be formed in the same way and using the same materials as moisture-sensitive resistors 6_n , provided that they are prevented from contacting the liquid sample 2 by, for example, a waterproof or water resistant layer (Figure 12).

25

Detection stages 19_n are not limited to the 2-step inverter based DC amplifier 28 or the potential divider circuit 30 and any circuit for measuring resistance values, or which can be made sensitive to resistance values, may be used instead. Simpler detection stages 19_n using fewer electronic components are preferred for low cost, disposable
30 lateral flow devices. In particular, simpler detection stages 19_n may be applied directly to the substrate 9 using printed electronics methods. However, in some applications explained hereinafter, detection circuits 7 providing more complex functionality may alternatively be provided by a conventional microcontroller (not shown) provided separately from the substrate 9.

35

Using moisture-sensitive resistors to meter liquid sample volume

Referring to Figures 1, 2, and 7, a part of a second device 31 for metering a volume of liquid sample 2 including first, second and third moisture-sensitive resistors 6₁, 6₂, 6₃ is shown at three different times T₁, T₂, T₃ following the introduction of a liquid sample 2.

5 The second device 31 is the same as the device 1, except that the detection circuit 7b includes first, second and third detection stages 19₁, 19₂, 19₃ corresponding to each respective moisture-sensitive resistor 6₁, 6₂, 6₃ and that each detection stage 19_n is connected to a corresponding output device 8 in the form of first, second and third OLEDs 32₁, 32₂, 32₃. Each detection stage 19₁, 19₂, 19₃ detects a change in the
10 resistance value of the corresponding moisture-sensitive resistive element 6₁, 6₂, 6₃ and in response to the change in the resistance provides an output signal 18₁, 18₂, 18₃ to cause the corresponding OLED 32₁, 32₂, 32₃ to be illuminated. The output signals 18₁, 18₂, 18₃ may simply correspond to supplying power to the corresponding OLED 32₁, 32₂, 32₃.

15 The positions x₁, x₂, x₃ of the moisture-sensitive resistive elements 6₁, 6₂, 6₃ in the first direction x are determined so that the corresponding OLEDs 32₁, 32₂, 32₃ will be illuminated when a pre-calibrated volume of liquid sample 2 has been introduced into the porous strip 12. The positions x₁, x₂, x₃ of moisture-sensitive resistors 6₁, 6₂, 6₃ may
20 be determined by calibrations performed using known volumes of liquid sample 2. For example, using three moisture-sensitive resistive elements 6₁, 6₂, 6₃ are used, then the corresponding OLEDs 32₁, 32₂, 32₃ may be illuminated in response to detecting that 33%, 67% and 100% of the required volume of liquid sample 2 has been received.

25 Referring also to Figure 8, the resistance values of the first, second and third moisture-sensitive resistors 6₁, 6₂, 6₃ is shown as a function of time.

At time T₁, the flow front 15 has passed the first moisture-sensitive resistor 6₁ and the exposure to water has caused the corresponding resistance value to fall to R_{wet}. The
30 first detection stage 19₁ has sent an output signal 18₁ to illuminate the first OLED 32₁ indicator. However, the second and third moisture-sensitive resistors 6₂, 6₃ remain dry and have the corresponding dry resistance value R_{dry}. At time T₂, the flow front 15 has passed the second moisture-sensitive resistor 6₂ and decreased the resistance value to R_{wet}. In response, the second detection stage 19₂ sends an output signal 18₂ causing a
35 second OLED 32₂ to become illuminated. At time T₃, the flow front has passed the third moisture-sensitive resistor 6₃, and the third OLED 32₃ will be illuminated. The

flow front 15 continues propagating through the porous strip 12 towards the second end 14.

Referring also to Figures 5 and 6, the first, second and third detection stages 19₁, 19₂, 19₃ may be provided by, for example, the 2-step inverter based DC amplifier 28 or the potential divider circuit 30

Of course, the second device 31 may include more or fewer than three moisture sensitive resistors 6_n and corresponding detection stages 19_n and OLEDs 32_n. As the liquid sample 2 passes each moisture-sensitive resistor 6_n, the corresponding detection stage 19_n is triggered to illuminate an OLED 32_n. This indicates to a user of the second device 31 that a certain volume of liquid sample 2 has been delivered.

In this way, a user of the second device 31 can be provided with simple and easily understood feedback about the progress of introducing a liquid sample 2. A user will be able to see when a sufficient volume of liquid sample 2 has been added, for example saliva, and that further liquid sample 2 is not required for the test. This may be particularly useful for preventing under-filling in which there is an insufficient volume of liquid sample 2 to perform a test. This may also help prevent overfilling, in which an excessive volume of liquid sample 2 overflows the porous strip 12 and propagates towards the second end 14 by “flooding” instead of wicking. Under or overfilling may invalidate the results of a lateral flow device. The use of printed moisture-sensitive resistors 6_n provides a compact, low cost and scalable approach for providing this additional functionality to a lateral flow device. When detection stages 19_n are also printed onto the substrate, the size, cost and scalability may be further improved.

First lateral flow device

Referring to Figures 1 to 4 and 9, an example of a first lateral flow device 33 incorporating a device 1, 31 is shown. A brief summary of the operation of lateral flow devices may be helpful, in so far as it is relevant to understanding the herein described devices 1, 31. However, as the moisture-sensitive resistors 6_n are responsive to water, details of the specific chemistries used to test for particular analytes is not relevant to understanding of the devices 1, 31, and is omitted.

The first lateral flow device 33 includes a porous strip 12 divided into a sample receiving portion 34, a conjugate portion 35, a test portion 36 and a wick portion 37.

The porous strip 12 is in contact with the upper surface 10 of the substrate 9, and both are received into a base 38. The substrate 9 may be attached to the base 38. A lid 39 is attached to the base/tray 38 to secure the porous strip 12 and cover parts of the porous strip 12 which do not require exposure. The lid 39 includes a sample receiving window
5 40 which exposes part of the sample receiving portion 34 to define the sample receiving region 4. The lid 39 also includes a result viewing window 41 which exposes a part of the test portion 36. The lid and base 38, 39 are made from a polymer such as, for example, polycarbonate, polystyrene, polypropylene or similar materials.

10 A liquid sample 2 is introduced to the sample receiving portion 34 through the sample receiving window 40 using, for example, a dropper 42 or similar implement. The liquid sample 2 is transported along towards the second end 14 by a capillary, or wicking, action of the porosity of the porous strip 34, 35, 36 37. The sample receiving portion 34 of the porous strip 12 is typically made from fibrous cellulose filter material.

15 The conjugate portion 35 has been pre-treated with at least one particulate labelled binding reagent for binding an analyte which is being tested for to form a labelled-particle-analyte complex (not shown). A particulate labelled binding reagent is typically, for example, a nanometer or micrometer sized particle which has been
20 sensitised to specifically bind to the analyte. The particles provide a detectable response, which is usually a visible optical response such as a particular colour, but may take other forms. For example, particles may be used which are visible in infrared, which fluoresce under ultraviolet light, or which are magnetic. Typically, the conjugate portion 35 will be treated with one type of particulate labelled binding reagent to test
25 for the presence of one type of analyte in the liquid sample 2. However, lateral flow devices may be produced which test for two or more analytes using two or more particulate labelled binding reagents concurrently. The conjugate portion 35 is typically made from fibrous glass, cellulose or surface modified polyester materials.

30 As the flow front 15 moves into the test portion 36, labelled-particle-analyte complexes and unbound label particles are carried along towards the second end 14. The test portion 36 includes one or more test regions 43 and control regions 44 which are exposed by the result viewing window 41 of the lid 39. A test region 43 is pre-treated with an immobilised binding reagent which specifically binds the label particle-target
35 complex and which does not bind the unreacted label particles. As the labelled-particle-analyte complexes are bound in the test region 43, the concentration of the

- label particles in the test region increases. The concentration increase causes the colour or other indicator of the label particle to become observable. If the test region 43 changes colour (or changes colour within a prescribed period), then the test for the presence of the analyte is positive. If the analyte is not present in the liquid sample 2, then the test region does not change colour (or does not change colour within a prescribed duration) then the test is negative. Alternatively, if the label particles emit a detectable signal, for example by fluorescence, then the detected emission increases as the concentration of label particles bound in the test region 43 increases.
- 10 To provide distinction between a negative test and a test which has simply not functioned correctly, a control region 44 is often provided between the test region 43 and the second end 14. The control region 44 is pre-treated with a second immobilised binding reagent which specifically binds unbound label particles and which does not bind the labelled-particle-analyte complexes. In this way, if the test has functioned
- 15 correctly and the liquid sample has passed through the conjugate portion 35 and test portion 36, the control region 44 will change colour. The test portion 36 is typically made from fibrous nitrocellulose, polyvinylidene fluoride, polyethersulfone (PES) or charge modified nylon materials.
- 20 The wick portion 37 provided proximate to the second end 14 soaks up liquid sample 2 which has passed through the test portion 36 and helps to maintain through-flow of the liquid sample 2. The wick portion 37 is typically made from fibrous cellulose filter material.
- 25 The device 1, 31 may be incorporated into the first lateral flow device 33. A group of moisture-sensitive resistors 6₁, 6₂, 6₃, 6₄ are disposed on the substrate 9 in contact with the sample receiving portion 34 and spaced apart in the first direction x between the region 4 and the second end 14. The detection circuit 7 is housed in the base 38 or the lid 39 and connected to the moisture sensitive resistors 6₁, 6₂, 6₃, 6₄ using conductive
- 30 traces 23 and contact pads 24. Alternatively, the detection circuit 7 may be provided on the lower side 11 of the substrate 9, for example, by printing the detection circuit 7 onto the lower side 11 of the substrate 9. When the detection circuit 7 is provided on the lower side 11 of the substrate 9, connection to the moisture sensitive resistors 6₁, 6₂, 6₃, 6₄ may be provided by conductive traces 23 and vias (not shown) through the substrate
- 35 9. The output device(s) 8, 32 are housed in the lid 39 to provide information to a user of the lateral flow device 33.

Referring also to Figures 7 and 8, the detection circuit 7 may be the detection circuit 7b of the second device 31 and may include a detection stage 19₁, 19₂, 19₃, 19₄ and an OLED 32₁, 32₂, 32₃, 32₄ corresponding to each of the moisture sensitive resistors 6₁, 6₂, 6₃, 6₄.

5 As explained hereinbefore, each detection stages 19 detects a decrease in the resistance value of the corresponding moisture-sensitive resistor 6_n when flow front 15 of the liquid sample 2 is detected, and illuminates the corresponding OLED 32_n.

10 In this way, a user of a lateral flow device 33 can be informed when a sufficient volume of liquid sample 2 has been added, for example saliva, and that further liquid sample 2 is not required for the test. This may particularly useful for preventing under-filling and/or overfilling which may cause the test to fail or to be inaccurate.

15 Additional or alternative functionality may be provided using the moisture sensitive resistors 6₁, 6₂, 6₃, 6₄. For example, the detection circuit 7 may record a time at which each of the moisture sensitive resistors 6₁, 6₂, 6₃, 6₄ experiences a drop in resistance value due to passage of the flow front 15. The detection circuit 7 may then determine a flow rate for the liquid sample 2 based on the recorded times and known spacing of the moisture sensitive resistors 6₁, 6₂, 6₃, 6₄. The determined flow rate may be compared to
20 pre-calibrated minimum and maximum values corresponding to minimum and maximum volumes of liquid sample 2. If a sufficient volume has been received, i.e. if the determined flow rate is between the pre-calibrated minimum and maximum values, then the detection circuit 7 sends an output signal 18 to the output device 8. The output signal 18 causes the output device 8 to provide an indication to a user that the
25 test results are valid. If an insufficient or excessive volume has been received, i.e. if the determined flow rate is respectively below or above the pre-calibrated minimum and maximum values, then the output device 8 may instead be caused to provide an indication to a user that the test results are not valid. For example, by illuminating a green LED if the results are valid but illuminating a red LED if the results are not valid.

30 There are many varieties of lateral flow-type device for testing liquid samples for the presence of one or more analytes. Although one type of a lateral flow device 33 has been described, the device 1, 31 may be readily incorporated into any other type of lateral flow-type device in the same or similar way, in order to provide equivalent
35 functionality. For example, the device 1, 31 may be included in sandwich, competitive and quantitative lateral flow-type tests.

Second lateral flow device

Referring also to Figure 10, a second lateral flow device 45 may incorporate additional moisture-sensitive resistors 6_n disposed in contact with the test portion 36.

5

The second lateral flow device 45 is the same as the first lateral flow device 33, except that a second group of moisture-sensitive resistors 6₅, 6₆ are disposed in contact with the test portion 36 and spaced apart in the first direction x between the test region 43 and the second end 14, and a third group of moisture-sensitive resistors 6₇, 6₈ are
10 disposed in contact with the test portion 36 and spaced apart in the first direction x between the conjugate portion 35 and the test region 43.

The second group of moisture-sensitive resistors 6₅, 6₆ may be used to indicate to a user that the test result has been developed and may be validly read. Many lateral flow-type
15 devices will require at least a predetermined duration to elapse before the user can consult the test region 43 to read the result. When a lateral flow device is used to detect elevated levels of an analyte which is naturally present at a lower, background concentration, for example a hormone test, the test region 43 should be consulted during a certain period. For example, long enough for the test to have developed but
20 not so long that natural or background levels of the analyte in the liquid sample 2 give rise to a false positive result. Taking readings based on the time elapsed after a liquid sample 2 is introduced may be less accurate due to variability in the volume of liquid sample 2 introduced and in the materials providing the porous strip 12.

25 The detection circuit 7 may detect when the flow front 15 has reached the second group of moisture-sensitive resistors 6₅, 6₆ located past the test region. The detection circuit 7 may send an output signal 18 to cause the output device 8 to indicate to the user that the test is completed and may be read. The output signal 18 may be provided immediately upon detecting the change in resistance of the second group of moisture-sensitive resistors 6₅, 6₆. Alternatively, the detection of a change in resistance may
30 trigger a timer, and the output signal 18 may be sent once the timer has elapsed.

The detection circuit 7 may additionally or alternatively detect the times at which each moisture-sensitive resistors 6₅, 6₆ of the second group registers a change in resistance.
35 Using these recorded times and known spacing of the moisture-sensitive resistors 6₅, 6₆, the detection circuit 7 may determine a flow rate through the testing portion 36.

The determined flow rate through the testing portion 36 may be compared to pre-calibrated values obtained using known volumes of liquid sample 2 to determine a time that the output signal 18 should be sent to indicate that the test is completed.

- 5 The detection circuit 7 may also compare the determined flow rate using the second group of moisture-sensitive resistors 6₅, 6₆ to pre-calibrated minimum and maximum values corresponding to minimum and maximum volumes of liquid sample 2. If the determined flow rate is within the predetermined range, the detection circuit 7 sends an output signal 18 to cause the output device 8 to provide an indication that the test result
10 is valid. If the determined flow rate is not within the predetermined range, a different indication can be provided to the user so that they may repeat the test.

The validity of a test using a lateral flow device 45 may be assessed by testing the flow rate of the flow front 15 before it reaches the test region 43. The detection circuit 7 may
15 detect the times at which each moisture-sensitive resistor 6₇, 6₈ of the third group registers a change in resistance. Using these recorded times and known spacing of the moisture-sensitive resistors 6₇, 6₈, the detection circuit 7 may determine a flow rate into the testing portion 36. The detection circuit 7 may also compare the determined flow rate into the testing portion 36 to pre-calibrated minimum and maximum values
20 corresponding to minimum and maximum known volumes of liquid sample 2. If the determined flow rate into the testing portion 36 is within the predetermined range, then an indication may be provided that the test is valid. If the determined flow rate into the testing portion 36 is outside the predetermined range, then an indication may be provided that the test is not valid.

25

Sensor with integrated detection stages

In general, the detection circuit is provided on a separate circuit substrate (not shown) from the substrate 9. For example, the detection circuit 7 may be housed in the base 38 or lid 39 of a lateral flow device 33, 45. However, integrating some or all of the
30 elements of the detection stages 19 or a detection circuit 7 onto the same substrate 9 as the moisture-sensitive resistors 6_n may help to simplify manufacture, reduce costs and make the resulting devices 1, 31 more compact.

Referring to Figures 1 to 3, 6 and 11 to 13, a method of fabricating a substrate 9 having
35 moisture-sensitive resistors 6_n on an upper surface 10 and reference resistors 29 on the lower surface 11 is explained.

Referring in particular to Figure 12, the substrate 9 may be formed from a flexible substrate 46 in the form of a strip extending between a first end 13 and a second end 14 in the first direction x. The flexible substrate 46 is divided into a first half 47 and a second half 48 by a fold line 49. The flexible substrate 46 has a first edge 50 parallel to the first direction x and located in the first half 47 and a second edge 51 parallel to the first direction x and located in the second half 48. The flexible substrate may be, for example, a foil of polyethylene terephthalate (PET), polyethylene naphthalate (PEN) or poly(imide) (PI).

Moisture-sensitive resistors 6_n are disposed on the first half 47 and corresponding reference resistors 29_n are disposed on the second half 48. Each moisture-sensitive resistor 6_n includes first and second electrodes 52, 53. The first and second electrodes 52, 53 are rectangular, parallel and spaced apart. A region of moisture-sensitive material 22 is printed over the first and second electrodes 52, 53 to connect them. The first electrode 52 extends perpendicularly towards the first edge 50, and is connected to a contact pad 54 disposed proximate or adjacent to the first edge 50 by a conductive trace 55. The second electrode 53 extends perpendicularly away from the first edge 50 and is connected to a third electrode 56 of a corresponding reference resistor 29_n by a conductive trace 57.

Each reference resistor 29_n includes third and fourth electrodes 56, 58. The third and fourth electrodes 56, 58 are rectangular, parallel and spaced apart. A region of moisture-sensitive material 22 is printed over the third and fourth electrodes 56, 58 to connect them. The fourth electrode 58 extends perpendicularly towards the second edge 51, and is connected to a contact pad 59 disposed proximate or adjacent to the second edge 51 by a conductive trace 60. The third electrode 56 extends perpendicularly away from the second edge 51 and is connected to the second electrode 53 of the corresponding moisture-sensitive resistor 6_n by the conductive trace 57. A contact pad 61 disposed proximate or adjacent to the second edge 51 provides the output from the potential divider formed by the moisture-sensitive resistor 6_n and the reference resistor 29_n via a conductive trace 62. The conductive trace 62 forms a junction 63 with the conductive trace 57 connecting the second and third electrodes 53, 56.

Referring in particular to Figure 12, the reference resistor 29_n also includes a layer or waterproof material 64 which covers the corresponding region of moisture-sensitive material 22 connecting the third and fourth electrodes 56, 58.

5 Referring in particular to Figure 13, the flexible substrate 46 is folded in half around the fold line 49 so that the first half 47 forms the upper surface 10 of the substrate 9 with the moisture-sensitive resistor 6_n exposed and the second half 48 forms the lower surface 11 of the substrate 9 with the reference resistor 29_n protected by the waterproof layer 64. If the folding damages the connectivity of a conductive trace 57 connecting
10 respective second and third electrodes 53, 56, it may be repaired using a small amount of conductive ink or conductive glue in the folded state.

The contact pad 54 connected to the first electrode 52 is connected to a bias voltage V_o provided by a battery (not shown), the contact pad 59 connected to the fourth electrode
15 58 is connected to ground and the contact pad 61 connected to the junction 63 is connected to the gate of a third transistor T_3 housed elsewhere, for example on a separate substrate (not shown).

In this way, the reference resistors 29_n may be substantially the same as moisture-sensitive resistors 6_n , whilst being protected from exposure to the liquid sample 2.
20 Consequently, the behaviour of the reference resistors 29_n in response to ambient conditions other than moisture, for example temperature, may be substantially the same as that of the moisture-sensitive resistors 6_n . This may allow for a more reliable or more sensitive comparison.

25 The contact pads 54, 59, 61, conductive traces 55, 57, 60, 62 and electrodes 52, 53, 56, 58 may be printed on the flexible substrate 46 using conductive inks, for example, using inks containing conductive particles of silver, carbon or conductive polymers. The regions of moisture-sensitive material 22 are printed using a conductive polymer with
30 suitable moisture-sensitivity, for example PEDOT:PSS. The layer of waterproof material 64 may be printed using a waterproof or water resistant polymer. Elements may be printed using inkjet printing, screen printing, thermal printing or gravure printing.

In this way, a device 1, 31 for providing metering and/or monitoring of a liquid sample 2 in a single use disposable lateral flow testing device 33, 45 can be manufactured relatively cheaply and in large volumes.

5 Referring also to Figure 14, a third transistor T_3 may be printed onto a second flexible substrate 65 so that each detection stage 19_n of the detection circuit 7 may be provided by a potential divider circuit 30 provided integrally on the substrate 9.

10 The second flexible substrate 65 is similar to the flexible substrate 46, except that a third transistor T_3 is additionally printed onto the second half 48 of the second substrate 65. The transistor may be printed using the same or similar materials and methods described in relation to the 2-step inverter amplifier 28 and the potential divider circuit 30. The gate of the transistor T_3 is connected to the output from the potential divider formed by the moisture-sensitive resistor 6_n and the corresponding
15 reference resistor 29_n via a conductive trace 66 which forms a junction 67 with the conductive trace 57 connecting the second and third electrodes 53, 56. The source of the transistor T_3 is connected to the contact pad 59 common to the fourth electrode 58 by a conductive trace 68. A contact pad 69 disposed proximate or adjacent to the second edge 51 is connected to the drain of the transistor T_3 by a conductive trace 70.

20 The contact pad 54 connected to the first electrode 52 is connected to a bias voltage V_o provided by a power source (not shown). The contact pad 59 connected to the fourth electrode 58 and the source of the third transistor T_3 is connected to ground. The contact pad 69 connected to the drain of the transistor T_3 is connected to an LED, for
25 example an OLED 32_n , (Figure 7) housed separately. A waterproof layer (not shown) may be applied to substantially all of the second half 48 of the second flexible substrate 65.

In this way, a detection stage 19_n for detecting a change in the resistance of a
30 corresponding moisture-sensitive resistor 6_n and illuminating an LED indicator, e.g. OLED 32_n , can all be provided on a single substrate using printing of conductive inks, semiconducting polymers and moisture-sensitive polymers. This allows a device 1, 31 for metering or monitoring liquid sample 2 to be manufactured relatively cheaply, in large volumes and made more compact by removing the need for a separate circuit
35 substrate to support the detection circuit 7.

Modifications

It will be appreciated that many modifications may be made to the embodiments hereinbefore described. Such modifications may involve equivalent and other features which are already known in the design, manufacture and use of analytical test devices and which may be used instead of or in addition to features already described herein.
Features of one embodiment may be replaced or supplemented by features of another embodiment.

Lateral flow devices incorporating the device 1, 31, may be provided as components of a testing kit including accessories such as, for example, specimen containers, reagents for pre-treating specimens and tools for introducing a liquid sample which is suspected of containing an analyte to the lateral flow-type strip 3 such as, for example, pipette droppers 42.

It has been described the region of moisture sensitive material 22 is printed over the first and second electrodes. However, this need not be the case and alternatively the region of moisture-sensitive material 22 may be printed onto the first surface 10 and the first and second electrodes 20, 21 may be printed overlying the region of moisture-sensitive material 22.

Examples of lateral flow devices 33, 45 have been described in which multiple moisture sensitive resistors 6 are disposed in contact with the path 5. However, multiple moisture sensitive resistors 6 need not be used. For example, in some lateral flow-type devices a single moisture sensitive resistor 6 may be disposed in contact with the path 5. The single moisture sensitive resistor 6 may be used to switch on an output device 6. For example an LED indicator may communicate to a user that the liquid sample 2 has reached a predetermined reference point. For example, a single moisture sensitive resistor 6 may be disposed in contact with the conjugate portion 35 to indicate that the testing has started. This may provide a user with a more reliable starting point to begin timing the test when compared to the time of introducing the liquid sample to the sample receiving portion 35. Alternatively, in another example a single moisture sensitive resistor 6 may be disposed in contact with the distal end of the path 5, for example in contact with the wick pad 37. This may provide a user with re-assurance that the liquid sample 2 has propagated all the way through the device and the results may be relied upon. Alternatively, a single moisture sensitive resistor 6 contacting the wick pad 37 may trigger an indication that the test is completed.

Although lateral flow-type devices have been described in which the path 5 is provided by an elongate porous strip 12, 34, 35, 36, 37, a lateral flow-type device need not include porous media in order to provide the path 5. For example, the path 5 may be provided by an open channel which is narrow in at least one transverse direction, so as to draw a liquid sample 2 along the path 5 by capillary action. For example, moisture-sensitive resistors 6 may be applied to monitor volumes and/or flow rates in a microfluidics channel (now shown) or between a pair of closely spaced opposed surfaces (not shown).

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Although claims have been formulated in this application to particular combinations of features, it should be understood that the scope of the disclosure of the present invention also includes any novel features or any novel combination of features disclosed herein either explicitly or implicitly or any generalization thereof, whether or not it relates to the same invention as presently claimed in any claim and whether or not it mitigates any or all of the same technical problems as does the present invention. The applicant hereby gives notice that new claims may be formulated to such features and/or combinations of such features during the prosecution of the present application or of any further application derived therefrom.

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CLAIMS

1. An analytical test device comprising:
a lateral flow type strip which comprises:
5 a region for receiving a liquid sample;
a path for transporting the liquid sample away from the sample receiving region;
at least one moisture-sensitive resistor disposed in the sample receiving region and/or along the path, each respective resistor arranged to be exposed to the liquid
10 sample when the liquid sample reaches the resistor; and
a circuit configured to signal progress of the liquid sample through the strip in dependence upon resistances of the moisture-sensitive resistor(s).
2. A device according to claim 1, comprising at least two moisture-sensitive resistors
15 disposed spaced apart in the sample receiving region and/or along the path.
3. A device according to claims 1 or 2, wherein each moisture-sensitive resistor comprises a region including or consisting of a conductive polymer material.
- 20 4. A device according to claim 3, wherein the conductive polymer comprises PEDOT:PSS.
5. A device according to claims 3 or 4, wherein the path is defined by a surface of a substrate and the region of conductive polymer is disposed on the surface of the
25 substrate.
6. A device according to claim 5, wherein the path comprises a strip of porous material overlying the surface of the substrate.
- 30 7. A device according to any one of claims 1 to 6, comprising first and second test regions, wherein the at least two moisture-sensitive resistors comprise first and second resistors and the first resistor is interposed between the first and second test regions.
8. A device according to any one of claims 1 to 7, wherein the circuit comprises at
35 least two detection stages, each detection stage configured to detect a change in value of resistance of one or more moisture sensitive resistors.

9. A device according to any one of claims 1 to 7, further comprising:
at least two light-emitting diodes;
at least two detection stages;
- 5 wherein each detection stage corresponds to a moisture-sensitive resistor and to a light emitting diode, and wherein each detection stage is configured to illuminate the corresponding light-emitting diode in response to detecting a change in the value of resistance of the corresponding moisture sensitive resistor.
- 10 10. A device according to claims 8 or 9, wherein each detection stage comprises an amplifier or inverter having a gain configured to depend upon the value of resistance of one or more moisture sensitive resistors.
11. A device according to claims 8 or 9, wherein each detection stage comprises:
- 15 a reference resistor; and
a transistor;
wherein the reference resistor is connected in series with a corresponding moisture-sensitive resistor and the output of the potential divider is configured to switch the transistor.
- 20 12. A device according to any one of claims 1 to 11, wherein the circuit is configured, in response to determining that the liquid sample has reached a predetermined position, to trigger a test.
- 25 13. A device according to claim 12, wherein the circuit is configured, in response to determining that the liquid sample has reached a predetermined position, to illuminate one or more light emitting diodes configured for performing reflectance or transmittance measurements on the path.
- 30 14. A device according to claim 12, wherein the circuit is configured, in response to determining that the liquid sample has reached a predetermined position, to activate an electrochemical cell configured to perform quantitative measurements of an analyte concentration in the liquid sample.
- 35 15. A device according to any one of claims 1 to 14, wherein the path comprises a substrate and an elongate porous medium supported on the substrate extending in a

first direction between first and second ends, wherein the sample receiving region is disposed at the first end and is configured to propagate the liquid sample through the porous medium towards the second end.

5 16. A device according to claim 15, further comprising:

a conjugate pad treated with at least one particulate labelled binding reagent for binding an analyte to form a labelled-particle-analyte complex when the analyte is contained in the liquid sample; and

10 a test portion comprising at least one test region treated with an immobilised binding reagent for binding the labelled-particle-analyte complex.

17. A device according to claim 16, wherein a plurality of first moisture-sensitive resistors are disposed in contact with the sample receiving region and spaced apart in the first direction.

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18. A device according to claims 16 or 17, wherein one or more second moisture-sensitive resistors are disposed in contact with the test portion, spaced apart in the first direction between a test region and the second end.

20 19. A device according to any one of claims 16 to 18, wherein one or more third moisture-sensitive resistors are disposed in contact with the test portion spaced apart in the first direction between the test region and the conjugate portion.

20. A testing kit comprising a device according to any one of claims 1 to 19.

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21. A method of using a device according to any one of claims 1 to 19, the method comprising adding a liquid sample to the sample receiving region.

30 22. A method of operating a device according to any one of claims 1 to 19, the method comprising:

receiving a liquid sample on the sample receiving region;

determining that the liquid sample has reached a predetermined position; and

in dependence upon the liquid having reached the predetermined position,

sending one or more output signals to at least one output device.

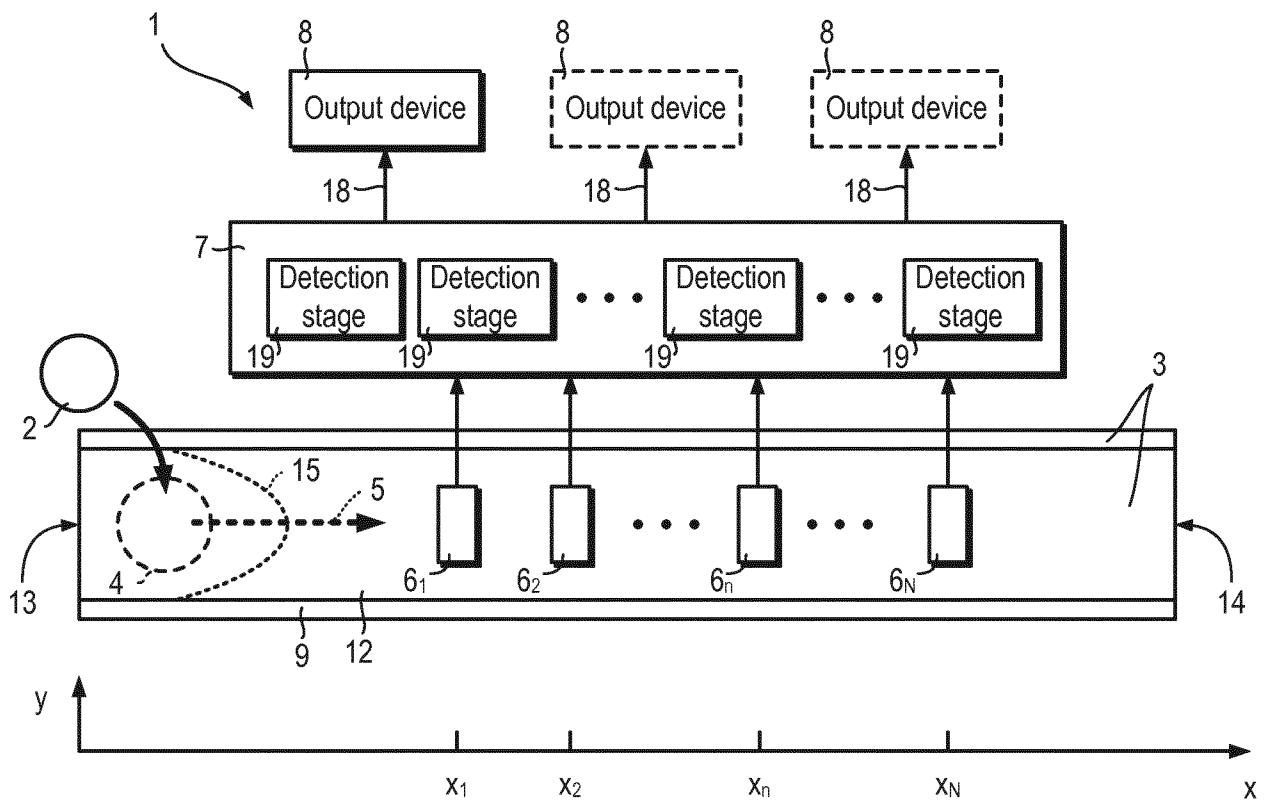


Fig. 1

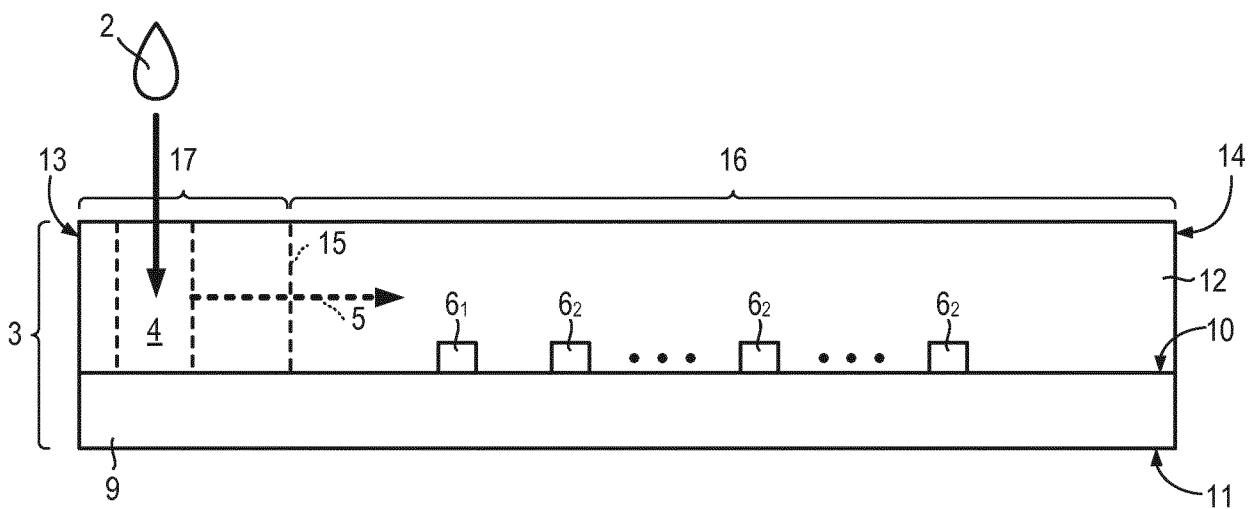


Fig. 2

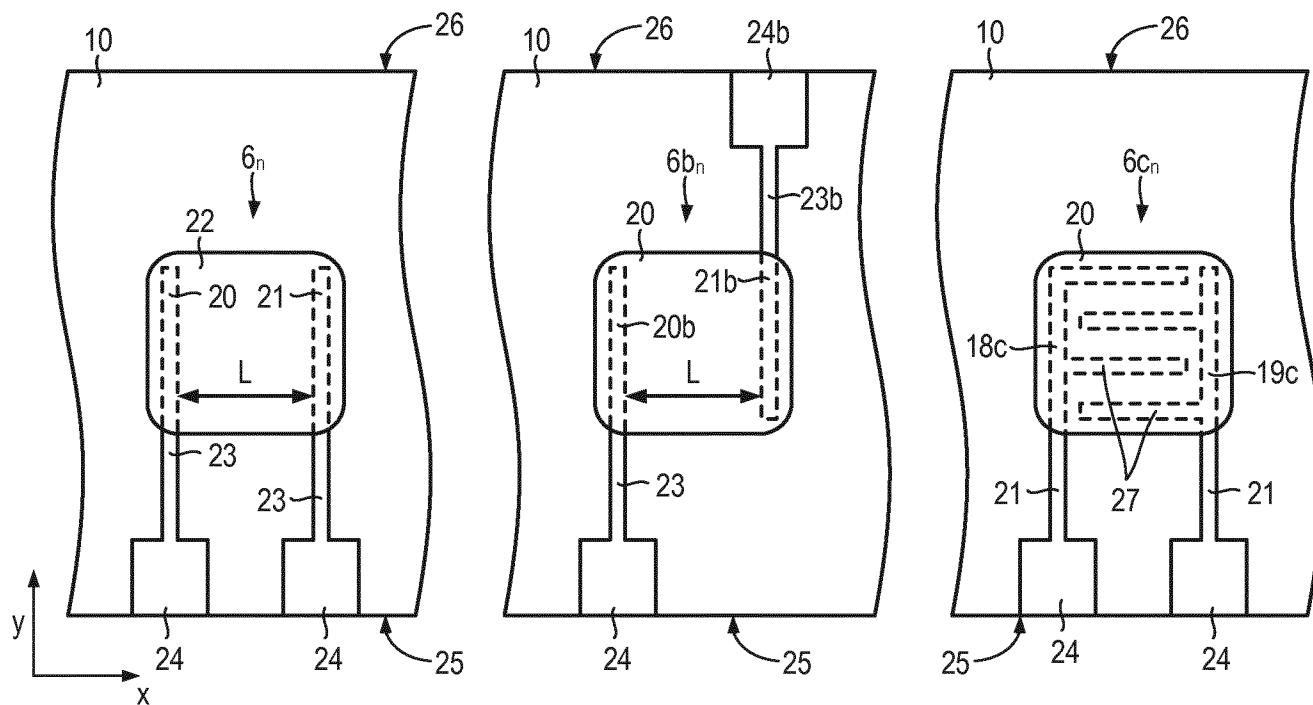


Fig. 3A

Fig. 3B

Fig. 3C

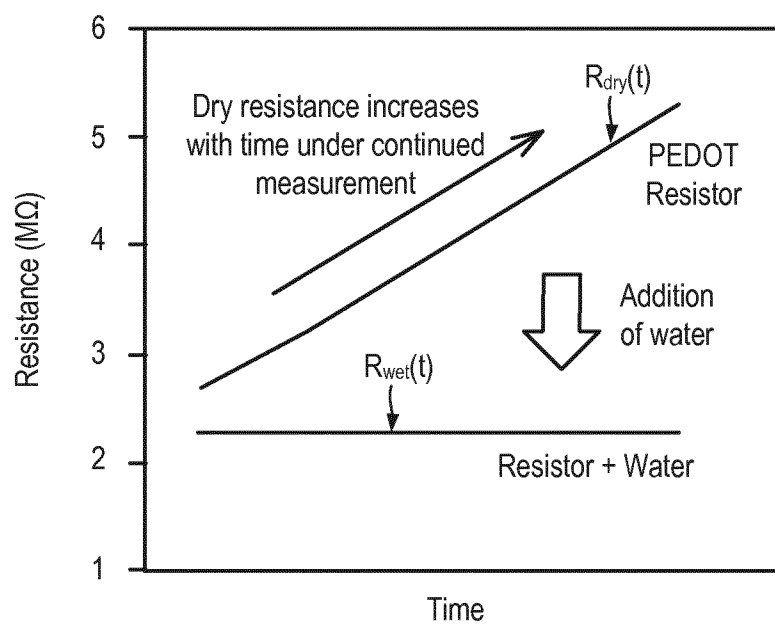


Fig. 4

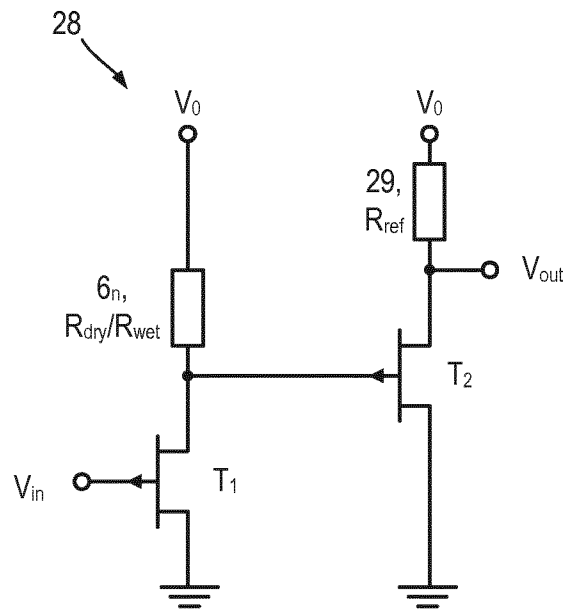


Fig.5

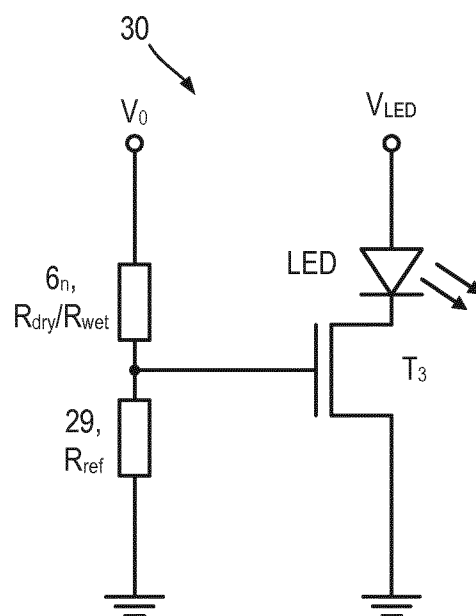


Fig. 6

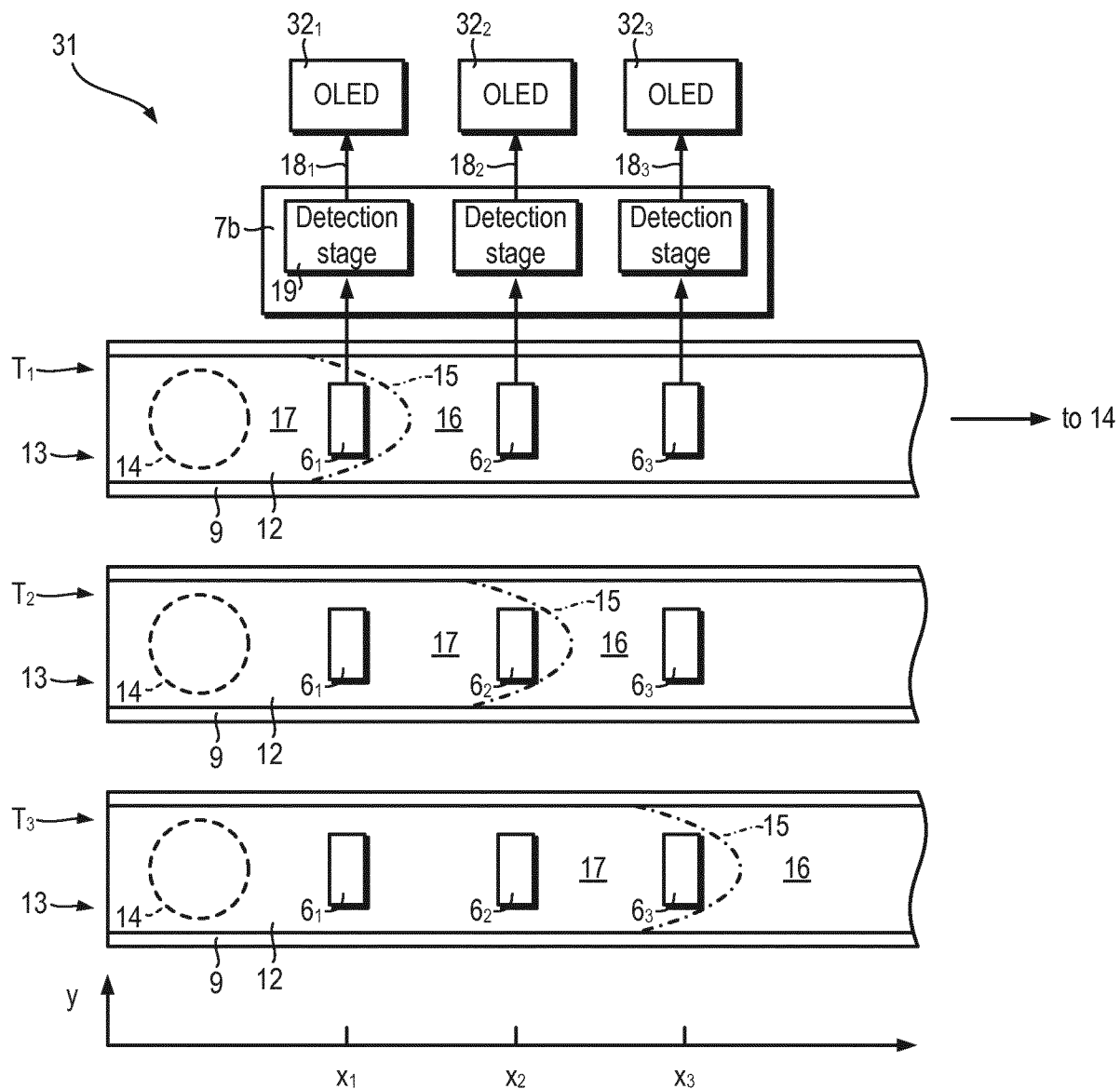


Fig. 7

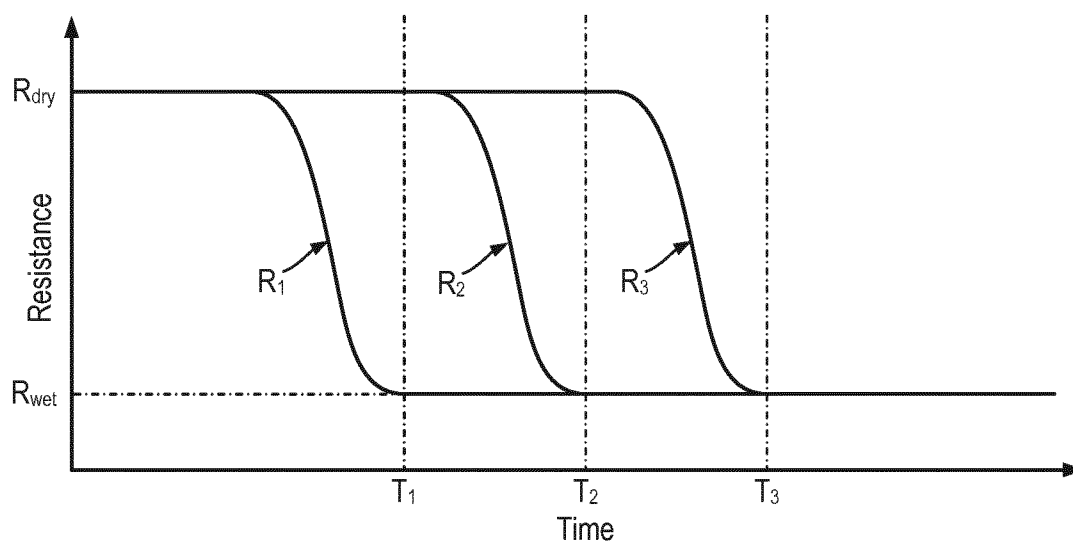
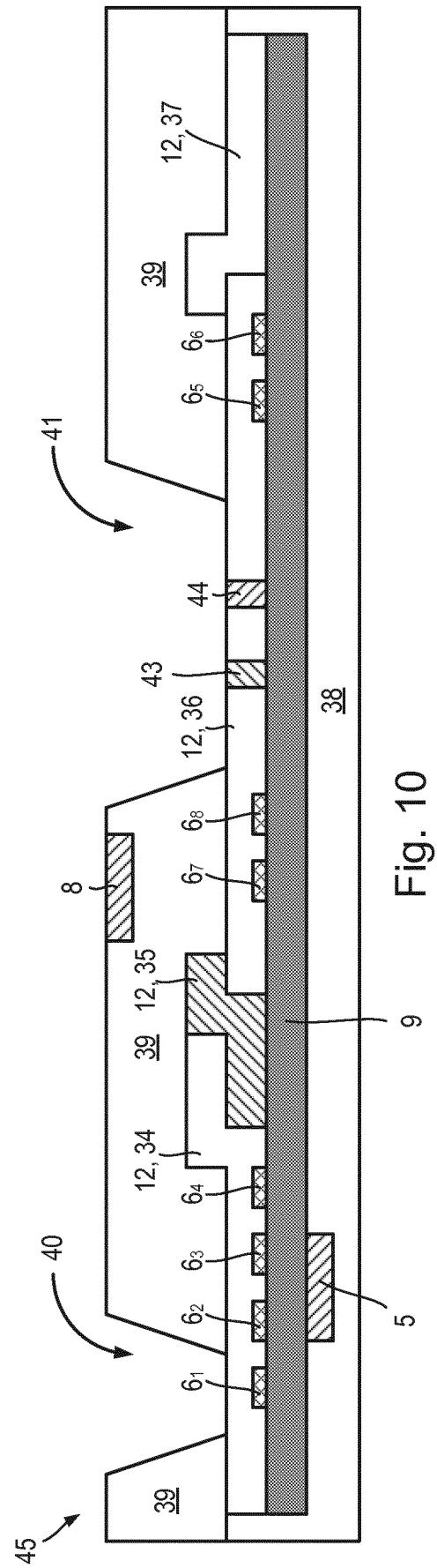
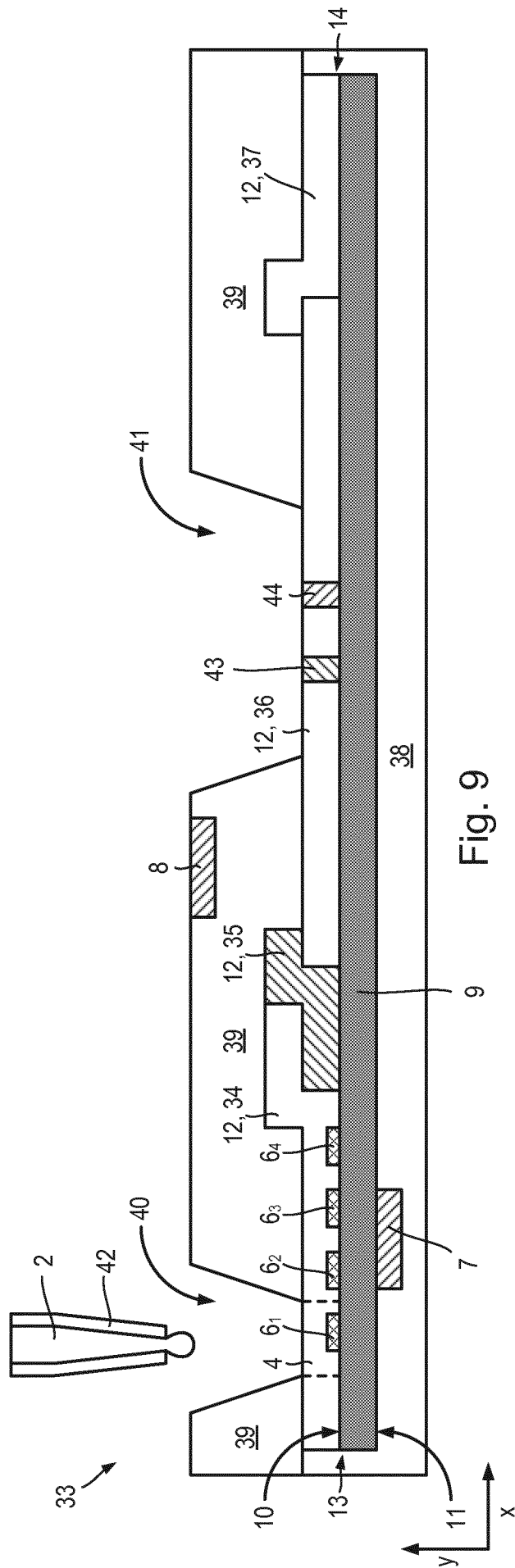


Fig. 8



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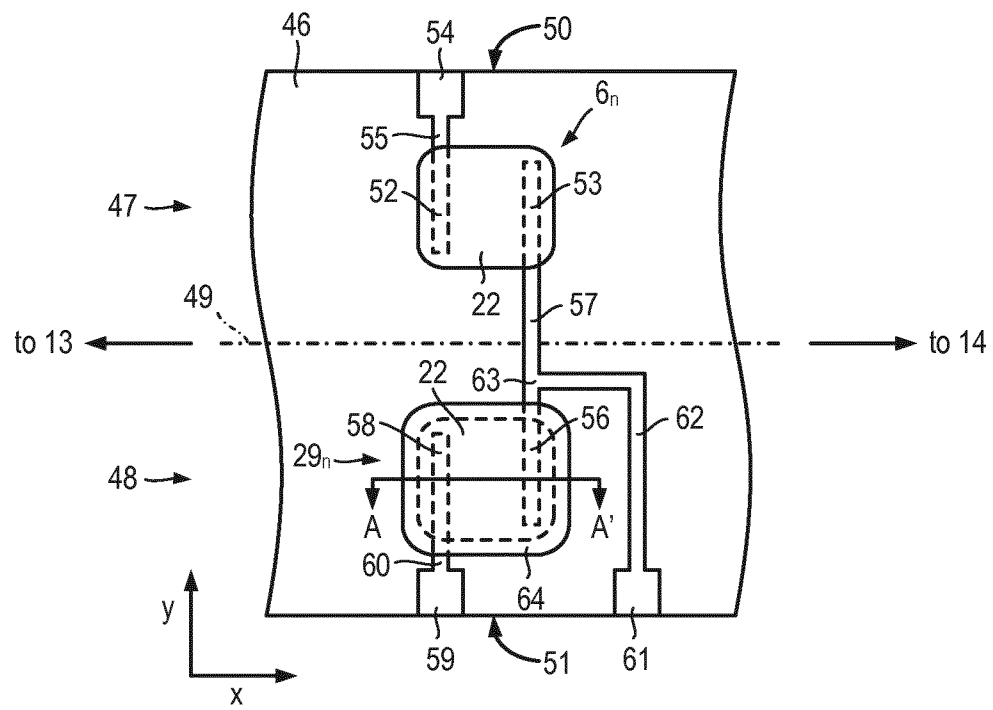


Fig. 11

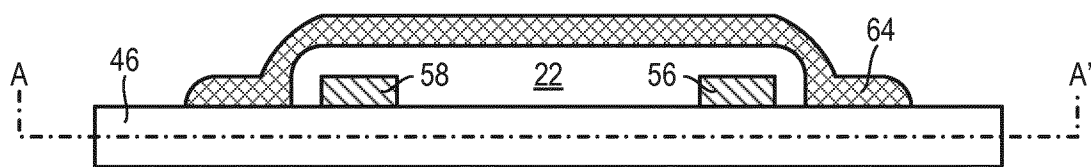


Fig. 12

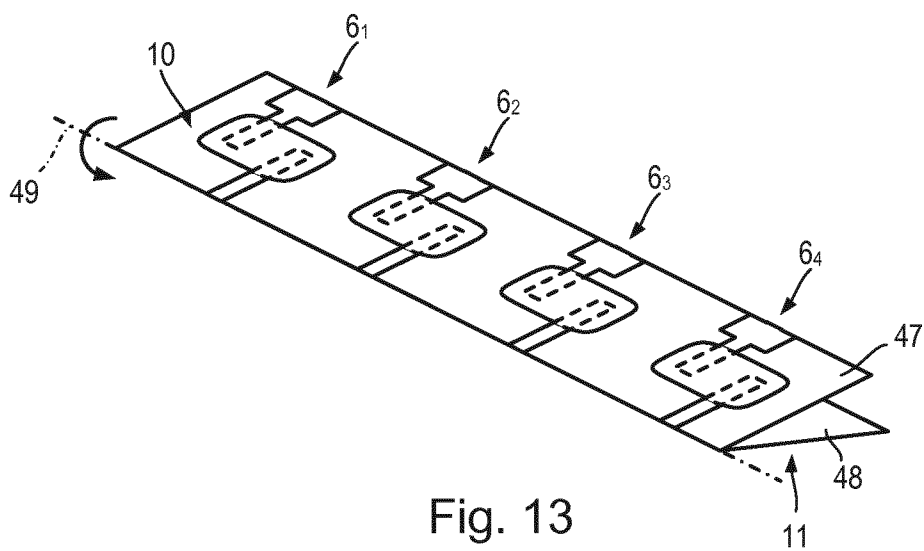


Fig. 13

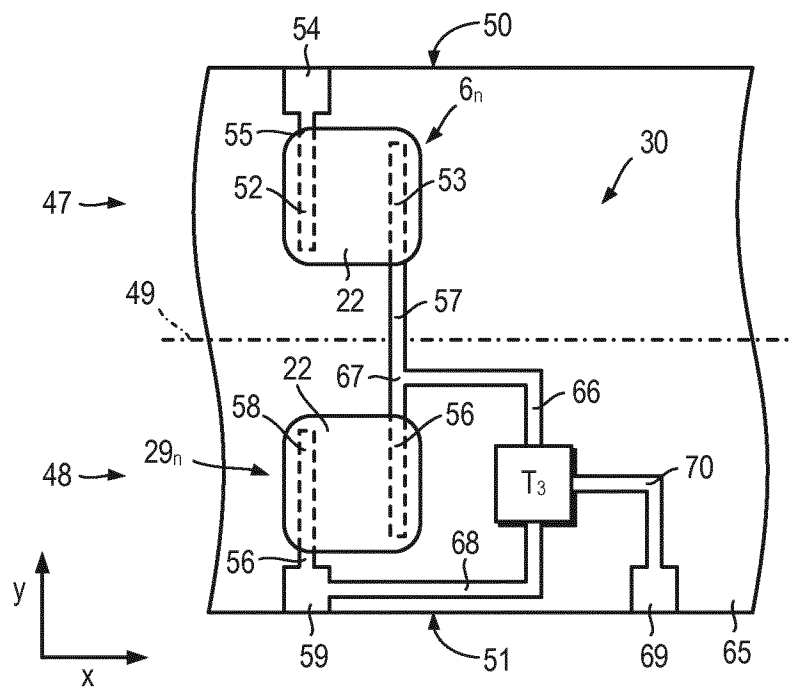


Fig. 14

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/055484

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N33/558
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)
G01N

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2006/010072 A2 (CHURCH & DWIGHT CO INC [US]; NAZARETH ALBERT R [US]; DELAHANTY FRANCIS) 26 January 2006 (2006-01-26) page 19, line 4 - line 9; claims 1, 10; figure 18	1-22
X	WO 2006/119203 A2 (BECKMAN COULTER [US]; ZWEIG STEPHEN ELIOT [US]) 9 November 2006 (2006-11-09) paragraph [0132] - paragraph [0134]; figures 2A-2C paragraph [0138] - paragraph [0139]; figure 4; example 6 paragraph [0166]	1-22
X	US 2008/267823 A1 (WANG YI [US] ET AL) 30 October 2008 (2008-10-30) paragraph [0145]; claims	1-22



Further documents are listed in the continuation of Box C.



See patent family annex.

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

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

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search

3 May 2017

Date of mailing of the international search report

17/05/2017

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No
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Information on patent family members

International application No

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