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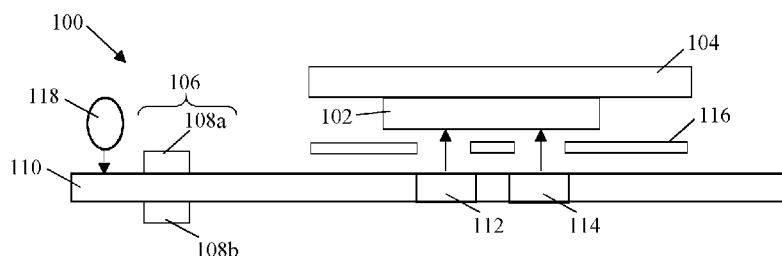


Figure 1

(57) Abstract: A lateral flow test device is disclosed comprising an optical detector configured to receive light from a test region of an assay test strip and to generate an electrical output based on the received light. An electrical signal processor is provided for analysing the electrical output and a flow sensor is configured to detect flow from a sample provided on the assay test strip at least prior to the flow reaching the test region. A method of operating a lateral flow test device is also disclosed.



Lateral Flow Test Device

Technical Field of the Disclosure

- 5 The disclosure relates to a lateral flow test device such as may be useful in biological applications, for example, in the areas of medical, environmental and veterinary diagnostics.

Background of the Disclosure

- 10 Diagnostic tests are commonly used for identifying diseases. A diagnostic test may be carried out in a central laboratory, whereby a sample, for example blood, is taken from a patient and sent to the central laboratory where the sample is analysed. A different setting for processing samples is at the point where care for the patient is delivered, which is referred to as point-of-care (POC) tests. POC tests allow for a faster diagnosis. Within the POC tests, different technology platforms can be used. A first class of POC tests are high end, microfluidic-based POC tests. These POC tests are mainly used in a professional environment such as hospitals or emergency rooms. A different technology platform is provided by lateral flow test technology. Lateral flow tests tend to be used in the consumer area, such as for pregnancy tests, but are also used across the whole diagnostic field as they are easy to produce and very cost-effective.

- 25 Lateral flow tests are very well known as such, but are briefly described by way of background. A lateral flow assay includes a series of capillary beds, such as pieces of porous paper, nitrocellulose membranes, microstructured polymer, or sintered polymer for transporting fluid across a series of pads by capillary forces. A sample pad acts as a sponge and is arranged to receive a sample fluid, and further holds an excess of the sample fluid. After the sample pad is saturated with sample fluid, the sample fluid migrates to a conjugate pad in which the manufacturer has stored the so-called conjugate. The conjugate is a dried format of bio-active particles in a salt-sugar matrix intended to create a chemical reaction between the target molecule (e.g., an antigen) and its chemical partner (e.g. antibody or receptor). While the sample fluid dissolves the salt-sugar matrix, it also mobilizes the bio-active particles and in one combined transport action the sample and conjugate mix with each other while flowing through the capillary beds. The analyte binds to the bio-active particles while migrating further through the
- 30
- 35

third capillary bed. This material has one or more areas, which are called stripes, where a third type of molecule has been immobilized by the manufacturer, in most cases an antibody or receptor addressed against another part of the antigen. By the time the sample-conjugate mix reaches these stripes, analyte has been bound on the bio-active particle and the third type of molecule binds the complex. When more fluid has passed the stripes, particles accumulate on the stripes and the stripes become visible, appear or are generated in a particular colour or with a fluorescent wavelength capability. In this way the stripe is optically detectable by colour or by fluorescent emission detection, respectively.

Typically, there are at least two stripes: a control stripe/line that captures the conjugate and thereby shows that reaction conditions and technology work, and a second stripe, the test stripe/line, that contains a specific capture molecule and only captures those particles onto which an analyte or antigen molecule has been immobilized. This makes the diagnostic result of the test visible for the patient. Some test results rely on the presence of fluorescent particles, which may not be visible to the user but can instead be detected by optical detectors when the stripes are illuminated. After passing the different reaction zones, the fluid enters the final porous material, which is a wick that acts as a waste container. In other examples, the stripes may be replaced with a series of dots on a test strip (e.g. in a matrix of 3x3 or 4x4 or 5x5 dots), with each dot potentially providing a different test.

In summary, lateral flow tests as such are well known and have four key elements: the antibody, the antigen, the conjugate and the complex. Despite these key elements being well established, the terminology used by the skilled person is not always consistent and different terms may refer to the same element. The antibody is also referred to as a receptor, chemical partner, or capture molecule. The antigen is also referred to as an analyte, target molecule, antigen molecule, target analyte or biomarkers. The sample typically contains the analyte, although that is not always the case. The conjugate is also referred to as (analyte) tags, tagging particles, chemical partner, (sample) conjugate mix, bioactive particles or conjugate receptors. Examples of conjugates are fluorescent particles, red particles or dyes. The complex is the combination of the antigen and conjugate. The complex is also referred to as a tagged analyte, or particles onto which the analyte molecule has been immobilised.

Typically, users of lateral flow tests wait for a reaction to be completed and then measure the outcome. However, this does not allow for dynamic measurements or any analysis of how a test is progressing.

- 5 It is therefore an aim of the present disclosure to provide a lateral flow test device that address one or more of the problems above or at least provides a useful alternative.

Summary

- 10 In most known lateral flow tests, sample progress along test strip is only detected and concluded from evolution of the test signal itself (i.e. due to the optical signal measured in the test window). However, this can result in initial response data and/or important kinetic data being missed (i.e. not observed).
- 15 In general, this disclosure proposes to overcome the above problems by including a sensor to act as a switch to detect the start of fluid transport along the test strip.

- Advantageously, this arrangement allows for dynamic measurements and data analysis. For example, the speed of sample flow along the test strip can be determined, which in
- 20 turn can provide information on the viscosity and thereby nature or species in the sample (e.g. urine, blood, saliva, amount of enzymes etc.). Activity and transport kinetics can also be determined, for example, based on a speed of reaction (e.g. measured from when the fluid reaches the test region as opposed to when an optical change is observed). In addition, knowledge that a test has begun and/or is in progress can be
- 25 useful for a user and can enable information to be gathered on how well tests are performing in practice. In some embodiments, detection of the start of fluid movement can be useful in saving energy (e.g. battery power), for example, by only powering on the optical detector and/or other functions like data analysis or data transfer, in time to start observing a reaction in the test region, when the fluid is actually expected to reach
- 30 the test region.

According to one aspect of the present disclosure, there is provided a lateral flow test device comprising:

- an optical detector configured to receive light from a test region of an assay test
- 35 strip and to generate an electrical output based on the received light;

an electrical signal processor for analysing the electrical output; and
a flow sensor configured to detect flow from a sample provided on the assay test strip prior to the flow reaching the test region.

5 Thus, embodiments of this disclosure provide an additional sensor arranged to detect the 'real' start of the test (e.g. when the test paper is wetted and the fluid flow begins). As mentioned above, this can be advantageous for dynamic lateral flow tests (e.g. where multiple measurements are taken over time) by allowing kinetic data to be gathered to provide additional information on the test activity and progress. Even for static lateral
10 flow tests (e.g. where a measurement is only taken at a single point in time), it can be beneficial to know that the test strip is moist with a sample and that the test measurement can start in a specified time window.

In some instances, disposable lateral flow tests may be provided which may be switched
15 on, for example, by removing a plastic insulating strip from a battery contact, and, in normal circumstances, it may take some time for a sample to be deposited on a test strip and the actual test to begin. In the prior art, the optical detector would be powered on, draining battery power by sensing light signals from the test region long before a sample actually reaches the test region. In embodiments of the present disclosure the flow
20 sensor may be configured to provide a signal indicating that a sample has actually been deposited (e.g. the test paper is moist and flow has begun) and therefore the optical detector can be switched on only when it is likely that the sample will reach the test region, thereby saving battery power.

25 The flow sensor may be configured to relay a message to the electrical signal processor in response to flow detection. The message may signify that sample flow has begun (i.e. a test is in progress).

The message may comprise an instruction to begin a timer or counter. This information
30 can be used together with information from the optical detector to determine a speed of flow of the sample and/or a speed of reaction.

The message may comprise an instruction to begin analysing the electrical output from the optical detector. The analysis may be instructed immediately or after a pre-

determined period (e.g. to allow for the flow to reach the test region and/or to allow for a reaction to take place).

5 The message may comprise an instruction to wake or power on the optical detector and/or another component. Thus, the device may be in a power-saving mode prior to detection of the start of fluid flow.

10 The message may comprise an instruction to notify a user that a test is in progress and/or relay information about a quality of a test. In some embodiments, a user may be provided with further instructions for carrying out the test and/or obtaining the results of the test (i.e. when to read a test output).

15 The electrical signal processor may be configured to perform kinetic analysis of the electrical output. The kinetic analysis may comprise dynamic measurement of the output from the optical detector (based on measurement in the test region), with respect to early fluid flow detection by the flow sensor. For example, a speed of fluid flow and/or a speed of reaction may be determined based on a time of detection by the flow sensor and a time of detection by the optical detector. In some embodiments, the kinetic analysis may be used to determine fluid characteristics (e.g. viscosity or a type of fluid – blood, urine, saliva etc.).

20

The flow sensor may comprise a droplet detector, for example, at or near an entry aperture of the device.

25 The flow sensor may comprise a capacitive sensor configured to sense a change in capacitance due to sample flow.

30 The capacitive sensor may comprise a first electrode and a second electrode, wherein the first electrode and the second electrode are arranged to be in a spaced relationship in a plane parallel and in proximity to a first side of the assay test strip, when the assay test strip is inserted into the device. The first electrode and the second electrode may be generally aligned with a direction of sample flow. However, it will be understood that the first electrode and the second electrode may be arranged at an angle (e.g. diagonally) across the direction of sample flow or they may be arranged transversely to

35 the direction of sample flow.

5 In some embodiments, the first electrode and the second electrode may be arranged to be in a spaced relationship such that the first electrode is adjacent a first side of the assay test strip and the second electrode is adjacent a second side of the assay test strip, when the assay test strip is inserted into the device. The first electrode and the second electrode may be in a plane orthogonal to a direction of sample flow along the assay test strip. In some embodiments, the first electrode and the second electrode may be spaced along a direction of sample flow. The first electrode and the second electrode may be arranged at an angle (e.g. diagonally) across the direction of sample flow.

10

The first and second electrodes may be arranged to be in non-contact proximity with the assay test strip (i.e. test paper) when inserted into the device. For example, an insulator may be provided between each of the first and second electrodes and the assay test strip (i.e. test paper). The first and second electrodes may be arranged to monitor dielectric permittivity, which will change when the test paper goes from dry to wet (e.g. when a fluid such as a water-based sample is deposited on the assay test strip). Notably, water has a high dielectric constant of approximately 80, which will result in a notable change in the dielectric permittivity sensed by the capacitive sensor.

15

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The capacitive sensor may comprise at least a third electrode, wherein the third electrode is arranged to be in a spaced relationship with the first and second electrodes in the plane parallel and in proximity to the first side of the assay test strip, when the assay test strip is inserted into the device.

25

The first electrode, the second electrode and the third electrode may be arranged such that one of the first electrode, the second electrode and the third electrode is arranged to form a capacitive coupling with each remaining electrode (i.e. there may be one common electrode in a two capacitor series).

30

The flow sensor may comprise a resistive sensor configured to sense a change in resistance due to sample flow.

35

The resistive sensor may comprise a first electrode and a second electrode, wherein the first electrode and the second electrode are arranged to be in a spaced relationship such that the first electrode is adjacent a first side of the assay test strip and the second

electrode is adjacent a second side of the assay test strip, when the assay test strip is inserted into the device. The first electrode and the second electrode may be in a plane orthogonal to a direction of sample flow along the assay test strip. In some embodiments, the first electrode and the second electrode may be spaced along a direction of sample flow. The first electrode and the second electrode may be arranged at an angle (e.g. diagonally) across the direction of sample flow.

In some embodiments, the first electrode and the second electrode are arranged to be in a spaced relationship in a plane parallel and in proximity to a first side of the assay test strip, when the assay test strip is inserted into the device. The first electrode and the second electrode may be generally aligned with a direction of sample flow. However, it will be understood that the first electrode and the second electrode may be arranged at an angle (e.g. diagonally) across the direction of sample flow or they may be arranged transversely to the direction of sample flow.

The first and second electrodes may be arranged to be in contact with the assay test strip (i.e. test paper) when inserted into the device. The first and second electrodes may be arranged to monitor current flow through the assay test strip and to detect when resistance is reduced (conductance increased) due to the presence of moisture from a sample flow through the assay test strip. It will be noted that the current flow through the assay test strip will be small such that it not interfere with the sample flow and/or any chemical reactions in the sample flow and/or any carrier materials on or in the test paper.

In either the capacitive sensor or the resistive sensor, any number of electrodes (e.g. 10 or so) can be provided. The electrodes may be provided on the same side of the assay test strip or they may be provided on opposite sides of the assay test strip or any combination of these options is possible. The main difference is that, for the resistive sensor the electrodes are arranged to be in contact with the assay test strip (i.e. test paper) when inserted into the device and for the capacitive sensor the electrodes are arranged not to be in direct contact with the assay test strip (i.e. test paper) when inserted into the device.

The flow sensor may comprise an optical sensor configured to sense a change in an optical property due to sample flow. The optical sensor may be in addition to the optical detector arranged to receive light from the test region or an optical path may be provided

such that a single optical detector may be configured to detect light from either or both of the test region and a start region.

5 The optical property may be reflectance, transmission, chemiluminescence or fluorescence, which may change when a sample is present.

10 The optical detector and/or optical sensor may be configured to detect light generated in the assay test strip (e.g. due to fluorescence of a target molecule) or to detect light reflected from or transmitted through the assay test strip. For example, the device may comprise one or more illuminators for generating light to be reflected from or transmitted through the assay test strip such that a change in reflectance or transmission may be observed by the optical detector and/or optical sensor based on a condition of the assay test strip (e.g. based on a presence of a sample flow or analyte).

15 The optical detector may be configured to receive light from a control region of an assay test strip and to generate a control electrical output based on the received light for analysis by the electrical signal processor.

20 Two or more flow sensors may be provided along a flow path of the assay test strip to allow for detection of flow at two or more regions of the flow path.

25 The electrical signal processor may be configured to receive input from each flow sensor and to determine a speed of flow based on a time of the detection of flow at each of the two or more regions. Thus, a double set of flow sensors allows for an initial speed determination of the sample before it reaches the test region.

The lateral flow test device may be configured as a point-of-care device. In some embodiments, the lateral flow test device may be a disposable device.

30 The lateral flow test device may be configured to detect one or more of: coronavirus; coronavirus antibodies. Many other applications are also possible within the areas of biological, medical, environmental and veterinary diagnostics.

35 According to a second aspect of this disclosure, there is provided a method of operating a lateral flow test device comprising:

detecting, using a flow sensor, flow from a sample provided on an assay test strip prior to the flow reaching a test region of the assay test strip;
receiving light, at an optical detector, from the test region;
generating, at the optical detector, an electrical output based on the received
5 light; and
analysing the electrical output at an electrical signal processor.

The method may comprise the flow sensor relaying a message to the electrical signal processor in response to flow detection. The message may signify that sample flow has
10 begun (i.e. a test is in progress).

The message may comprise an instruction to begin a timer or counter. Thus, the method may comprise beginning a timer or counter in response to flow detection.

15 The method may comprise the electrical signal processor measuring a time from an initial flow detection by the flow sensor to one or more of: a start of detection of light, a predefined change in detection of light, a threshold value of detection of light, a peak value of detection of light or an end of detection of light, by the optical detector 102.

20 The method may comprise determining kinetic information such as a speed of flow of the sample or a speed of reaction.

The method may comprise analysing the electrical output from the optical detector in response to flow detection. The analysis may be commenced immediately following flow
25 detection or after a pre-determined period (e.g. to allow for the flow to reach the test region and/or to allow for a reaction to take place).

The method may comprise waking or powering on the optical detector in response to flow detection. Thus, the device may be in a power-saving mode prior to detection of
30 the start of fluid flow.

The method may comprise notifying a user that a test is in progress. In some embodiments, the method may comprise providing a user with further instructions for carrying out the test and/or obtaining the results of the test (i.e. when to read a test
35 output).

The method may comprise performing kinetic analysis of the electrical output. This may comprise, for example, measuring a change in received light over a test period. The kinetic analysis may comprise dynamic measurement of the output from the optical detector (based on measurement in the test region and/or control region), with respect to early fluid flow detection by the flow sensor. For example, a speed of fluid flow and/or a speed of reaction may be determined based on a time of detection by the flow sensor and a time of detection by the optical detector. In some embodiments, the kinetic analysis may be used to determine fluid characteristics (e.g. viscosity or a type of fluid – blood, urine, saliva etc.). This improves the quality of the analysis.

The method may comprise receiving input from two or more flow sensors and determining a speed of flow based on a time of the detection of flow by at least two of the two or more flow sensors.

It is noted that although in prior art lateral flow devices it may be possible to follow the development of the test line and/or control line in time; without knowing when the flow has reached the test region/control region it is not clear when the test has actually started. However, in embodiments of this disclosure, it is possible to detect the beginning of the sample flow, before the fluid reaches the test region/control region, and therefore purer/cleaner, more quantitative dynamic measurements can be taken, with an more accurate and reproducible $t=0$ time stamp, which may be easier to interpret for individual components in the fluid.

Lateral flow test devices according to the present disclosure advantageously are more user-friendly because the device is able to detect when a test is being carried out (e.g. when a sample has been deposited) and so the device can offer analysis and/or guidance to a user during the measurement process, which increases the quality of the test. Furthermore, kinetic information can in some cases be used to determine whether an expected sample has been deposited or not (e.g. blood vs. urine) as a difference in viscosity may be deduced and this information can be used to ensure that accurate and reliable results are provided.

Brief Description of the Preferred Embodiments

Some embodiments of the disclosure will now be described by way of example only and with reference to the accompanying drawings, in which:

5 Figure 1 shows a lateral flow test device including a sensor in accordance with the present disclosure;

Figure 2 shows a lateral flow test device including a sensor in accordance with the present disclosure;

Figure 3 shows a lateral flow test device including an optical sensor in accordance with the present disclosure;

10 Figure 4 shows a lateral flow test device including two sensors in accordance with the present disclosure;

Figure 5 shows a lateral flow test device including two sensors, with a middle electrode in common, in accordance with the present disclosure;

15 Figure 6 shows a lateral flow test device including two separate sensors in accordance with the present disclosure;

Figure 7 shows a method of operating a lateral flow test device in accordance with the present disclosure; and

Figure 8 shows a graph illustrating optical measurements from a test region over time.

20 Detailed Description of the Preferred Embodiments

Generally speaking, the disclosure provides a lateral flow test device including a sensor configured to detect the start of fluid transport along a test strip.

25 Some examples of the solution are given in the accompanying figures.

Figure 1 shows a first lateral flow test device 100 including a first flow sensor 106 in the form of a resistive sensor in accordance with the present disclosure.

30 The first lateral flow test device 100 comprises an optical detector 102, and illumination sources (not shown), configured to receive light (which may be reflected or from fluorescence of the test material) from a test region 112 of an assay test strip 110 and to generate an electrical output based on the received light. In the present embodiment, the optical detector 102 is also configured to receive light from a control region 114 of
35 the assay test strip 110 and to generate an electrical output based on the light received

from the control region 114. However, the inclusion of a control region 114 is optional, but generally used to indicate that the fluid has been transported correctly over the assay test strip 110 (e.g. paper). As shown in Figure 1, light from the test region 112 and control region 114 is arranged to pass through a respective window or gap in a baffle substrate 116 defining an optical path to the optical detector 102. This ensures that only light from a respective one of the test region 112 and control region 114 is received in a respective region (which may be different or the same) of the optical detector 102. In some embodiments, the baffle substrate 116 may take a different form or may not be required.

The optical detector 102 may take the form of any known optical detector. In some embodiments, the optical detector 102 may be provided in an optical module such as that described in patent application no. GB2004488.9, which is incorporated herein by reference. The optical module may include a first light source (not shown) for illuminating the test region 112 of the assay and a second light source (not show) for illuminating the control region 114 of the assay. In other embodiments, for example, those relying on chemi-luminescence of a tagged analyte, no light sources may be required.

The electrical output from the optical detector 102 is input to an electrical signal processor 104 for analysis. The electrical signal processor 104 may take the form of any known electrical signal processor. In particular, the electrical signal processor 104 may be configured to measure the light detected by the optical detector 102 and to correlate said measurement with an expected measurement dependent on an amount of analyte present in the test region 112 at least. In particular, the electrical signal processor 104 and the optical detector 102 may be integrated in one application specific integrated circuit (ASIC). Furthermore, the optical detector 102 may contain spectral analysing capabilities, where multiple diodes are provided with different optical filters passing different optical wavelengths of light to the diodes.

The first flow sensor 106 is in the form of a resistive sensor configured to detect flow from a sample 118 provided on the assay test strip 110 prior to the flow reaching the test region 112. The first flow sensor 106 is configured to sense a change in resistance due to sample fluid flow. The first flow sensor 106 comprises a first electrode 108a and a second electrode 108b. The first electrode 108a and the second electrode 108b are arranged to be in a spaced relationship in a plane orthogonal to a direction of sample

flow along the assay test strip 110 such that the first electrode 108a is adjacent a first side of the assay test strip 110 and the second electrode 108b is adjacent a second side of the assay test strip 110, when the assay test strip 110 is inserted into the device 100.

5 Notably, for a resistive sensor, the first and second electrodes 108a, 108b are arranged to be in contact with the assay test strip 110 (i.e. test paper) when inserted into the device 100. The first and second electrodes 108a, 108b are arranged to monitor current flow through the assay test strip 110 and to detect when resistance is reduced (conductance increased) due to the presence of moisture from the sample flow along the assay test
10 strip 110.

In some embodiments, the first flow sensor 106 can be used in a capacitive (as opposed to resistive) mode. In such a configuration, both electrodes 108a, 108b would not be in direct contact with the assay test strip 110 (i.e. test paper), but they would be in close
15 proximity to assay test strip 110 (i.e. test paper), for example, with an insulator there-between. At a certain frequency of operation of the electrodes 108a, 108b, the wetting of the test paper by the sample 118 would be observed as a change in the dielectric constant of the test paper between the electrodes 108a, 108b and hence detected as a change in capacity value of the two electrodes 108a, 108b.

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The first flow sensor 106 is provided between the test region 112 and a region where the sample 118 is deposited on the assay test strip 110. Ideally the first flow sensor 106 is provided closer to the region where the sample 118 is deposited than the test region 112.

25 In operation, the assay test strip 110 is provided in the first lateral flow test device 100 and a sample 118 is deposited. The sample 118 may be, for example, blood, urine, saliva or any other liquid-based material on which the test is to be performed (e.g. derivatives of blood, urine, saliva or pre-treated liquids). Due to capillary action, the sample 118 will travel along the assay test strip 110 towards the test region 112 and
30 control region 114. When the fluid front of the sample 118 enters a region monitored by the first flow sensor 106 (e.g. the region between the first and second electrodes 108a, 108b) the resistivity (or capacitance) between the electrodes is altered due to the presence of the fluid and the sample flow is detected.

- In the present embodiment, the first flow sensor 106 is coupled to the electrical signal processor 104 such that the detected change in resistivity (or capacitance) is communicated via a wired (or wireless) connection to the electrical signal processor 104. The electrical signal processor 104 then begins a timer such that the detection of the start of fluid flow is $t=0$. At this point, the electrical signal processor 104 knows that a test is in progress and may communicate this to a user via a display (not shown). The device may then offer guidance to a user during the measurement process (e.g. to inform them that the result is being processed and/or when a result will be communicated).
- 10 The electrical signal processor 104 may dynamically or statically monitor the electrical output from the optical detector 102. For example, in a dynamic situation the electrical signal processor 104 may continually monitor the electrical output to determine the optical response (e.g. amount or spectrum of light) from the test region 112 as the flow reaches the test region 112 and the assay is performed to tag the analyte if present in the sample 118. In a static situation, the electrical signal processor 104 may be configured to take a single measurement at one or more points in time (e.g. at a predetermined time after $t=0$) to assess the optical response after the sample 118 has reached the test region 112 and/or after the assay is complete.
- 20 In some embodiments, kinetic information (e.g. such as the speed of flow along the assay test strip 110) may be calculated and may be used to determine whether an expected sample has been deposited or not (e.g. blood vs. urine). This may be possible because a difference in viscosity may result in a different speed of flow and this information can be used to ensure that accurate and reliable results are provided, based on the sample deposited. A speed of fluid flow and/or a speed of reaction may be determined based on a time of detection by the flow sensor 106 and a time of detection by the optical detector 102, since the distance between the two regions on the assay test strip 110 will be known.
- 30 In some instances, disposable lateral flow tests may be provided which may be switched on, for example, by removing a plastic insulating strip from a battery contact, and, in normal circumstances, it may take some time for the sample 118 to be deposited on the assay test strip 110 and the actual test to begin. In embodiments of the present disclosure the flow sensor 106 may be configured to provide a signal indicating that the sample 118 has actually been deposited (e.g. the test paper of the assay test strip 110

is moist and flow has begun) and therefore the optical detector 102 and/or any other parts/components of the device 100 can be switched on only when it is likely that the sample 118 will reach the test region 112, thereby saving battery power.

5 Figure 2 shows a second lateral flow test device 200 including a second flow sensor 206 in the form of a single-sided sensor configured to sense a change in capacitance or resistance due to sample flow, in accordance with the present disclosure. The second lateral flow test device 200 is similar to that described above for the first lateral flow test device 100 and so like reference numerals have been included. The only difference
10 between the first lateral flow test device 100 and the second lateral flow test device 200 is the configuration of the second flow sensor 206.

The second flow sensor 206 comprises a first electrode 208a and a second electrode 208b. The first electrode 208a and the second electrode 208b are arranged to be in a
15 spaced relationship in a plane parallel and in proximity to a first side of the assay test strip 110, when the assay test strip 110 is inserted into the device 200.

When the second flow sensor 206 is configured for operation as a capacitive sensor, the first and second electrodes 208a, 208b are arranged to be in non-contact proximity with
20 the assay test strip 110 (i.e. test paper) when inserted into the device 200, for example, with an insulator such as air or plastic in-between. The first and second electrodes 208a, 208b are arranged to monitor dielectric permittivity, which will change when the test paper goes from dry to wet (e.g. when a fluid such as a water-based sample 118 is deposited on the assay test strip 110). Notably, water has a high dielectric constant of
25 approximately 80, which will result in a notable change in the dielectric permittivity sensed by the second flow sensor 206.

In some embodiments, the second flow sensor 206 may be configured for operation as a resistive sensor and, in which case, the electrodes 208a, 208b will be in direct contact
30 with the assay test strip 110 (e.g. test paper).

As above, the second flow sensor 206 is coupled to the electrical signal processor 104 such that the detected change in capacitance (or resistance) is communicated via a wired (or wireless) connection to the electrical signal processor 104. The electrical signal
35 processor 104 then begins a timer such that the detection of the start of fluid flow is $t=0$.

At this point, the electrical signal processor 104 knows that a test is in progress and further analysis of the test may be carried in the same ways as described above.

Figure 3 shows a third lateral flow test device 300 including a third flow sensor 306 in the form of an optical sensor in accordance with the present disclosure. The third lateral flow test device 300 is similar to that described above for the first lateral flow test device 100 and so like reference numerals have been included. The only difference between the first lateral flow test device 100 and the third lateral flow test device 300 is the configuration of the third flow sensor 306 which is an optical sensor configured to sense a change in an optical property due to sample flow.

Notably, in the present embodiment, the optical sensor of the third flow sensor 306 is in addition to the optical detector 102 arranged to receive light from the test region 112 and control region 114. In other embodiments, an optical path may be provided such that a single optical detector 102 may be configured to detect light from either or both of the test region 112 and a start region (e.g. near where the sample 118 is deposited).

The optical property in the present embodiment is transmission as measured through the assay test strip 110. In this case, the third flow sensor 306 comprises an optical emitter 302 provided on a first side of the assay test strip 110 and an optical detector 304 provided on a second side of the assay test strip 110. The optical emitter 302 is configured to emit light through the assay test strip 110 (which may be provided with a suitably positioned optical window there-through) such that light transmitted through the assay test strip 110 is detected by the optical detector 304. It will be understood that presence of a sample fluid in the optical path of light emitted from the optical emitter 302 will result in a change in the light detected by the optical detector 304 (e.g. due to optical absorption and/or scattering by the fluid). Accordingly, the third flow sensor 306 will detect a change in optical transmission, which will indicate the start of fluid flow along the assay test strip 110.

As above, the third flow sensor 306 is coupled to the electrical signal processor 104 such that a detected change in transmission is communicated via a wired (or wireless) connection to the electrical signal processor 104. The electrical signal processor 104 then begins a timer such that the detection of the start of fluid flow is $t=0$. At this point,

the electrical signal processor 104 knows that a test is in progress and further analysis of the test may be carried in the same ways as described above.

5 In other embodiments, the third flow sensor 306 may be configured to measure reflectance or fluorescence or chemi-luminescence from the assay test strip 110 to determine when a sample fluid is present (e.g. by locating an emitter and detector on a same side of the assay test strip 110).

10 Figure 4 shows a fourth lateral flow test device 400 including two flow sensors 106, 406 in accordance with the present disclosure. The first of the two flow sensors is a sensor identical to the first flow sensor 106 described above in relation to Figure 1. The second of the two flow sensors is an additional flow sensor 406, which is configured to detect flow from a sample 118 provided on the assay test strip 110 after it has passed through a region monitored by the first flow sensor 106 and prior to the flow reaching the test
15 region 112. The additional flow sensor 406 is configured to sense a change in resistance (or capacitance) due to sample flow in a similar manner that of the first flow sensor 106. Thus, the additional flow sensor 406 comprises a first electrode 408a and a second electrode 408b. The first electrode 408a and the second electrode 408b are arranged to be in a spaced relationship in a plane orthogonal to a direction of sample flow along
20 the assay test strip 110 such that the first electrode 408a is adjacent a first side of the assay test strip 110 and the second electrode 408b is adjacent a second side of the assay test strip 110, when the assay test strip 110 is inserted into the device 100.

25 Notably, for resistive measurements the first and second electrodes 408a, 408b are arranged to be in contact with the assay test strip 110 (i.e. test paper) when inserted into the device 100. The first and second electrodes 408a, 408b are arranged to monitor current flow through the assay test strip 110 and to detect when resistance is reduced (conductance increased) due to the presence of moisture from the sample flow along the assay test strip 110.

30 When the two flow sensors 106, 406 are configured for operation as two capacitive sensors, the electrodes 108a, 108b, 408a, 408b will not be in direct contact with the assay test strip 110 (e.g. test paper). Instead, a thin insulator may be provided. The insulator may be, for example, air and/or plastic.

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The provision of two (or more) flow sensors 106, 406 along the flow path of the assay test strip 110 allows for detection of flow at two (or more) regions of the flow path.

As above, the additional flow sensor 406 is coupled to the electrical signal processor 104 such that the detected change in resistance (or capacitance) is communicated via a wired (or wireless) connection to the electrical signal processor 104. As the electrical signal processor 104 is configured to receive input from each of the two flow sensors 106, 406, the electrical signal processor 104 may be configured to determine a speed of flow based on a time of the detection of flow at each of the two regions monitored by the two flow sensors 106, 406. Thus, a double set of flow sensors 106, 406 allows for an initial speed determination of the sample before it reaches the test region 118. As above, further analysis of the test may be carried in the same ways as described above.

It should be noted that embodiments where multiple electrodes or flow sensors are provided are advantageous in that the flow speed of the sample fluid can be determined at the start of the assay test strip 110 and this can enable a prediction of when the sample fluid will arrive at the test region and/or control region. This allows for a more complete and quantitative analysis of the test results and cleaner dynamic measurements with clearer timing information.

Figure 5 shows a fifth lateral flow test device 500 including a double flow sensor 506 forming two sensors, with a middle electrode in common, in accordance with the present disclosure. The double flow sensor 506 is similar to that described above in Figure 2 and so like reference numerals will be used. The double flow sensor 506 comprises a first electrode 208a, a second electrode 208b and a third electrode 208c. The third electrode 208c is arranged to be in a spaced relationship with the first and second electrodes 208a, 208b in the plane parallel and in proximity to the first side of the assay test strip 110, when the assay test strip 110 is inserted into the device 500. The first electrode 208a and the second electrode 208b form a first coupling 502 and the second electrode 208b and the third electrode 208c form a second coupling 504. In other words, the second electrode 208b is a common electrode in a two sensor series.

When the double flow sensor 506 is configured for operation as two capacitive sensors, the electrodes 208a, 208b, 208c will not be in direct contact with the assay test strip 110

(e.g. test paper). Instead, a thin insulator may be provided. The insulator may be, for example, air and/or plastic.

5 In some embodiments, the double flow sensor 506 may be configured for operation as two resistive sensors and, in which case, the electrodes 208a, 208b, 508c will be in direct contact with the assay test strip 110 (e.g. test paper).

10 In operation, the first coupling 502 effectively serves to detect a change in capacitance (or resistance) in a first region of the assay test strip 110 and the second coupling 504 effectively serves to detect a change in capacitance (or resistance) in a second region of the assay test strip 110. Thus, the double flow sensor 506 functions in a similar manner to the two flow sensors 106, 406 of Figure 4 in allowing for detection of flow at two regions of the flow path, prior to the fluid flow reaching the test region 112.

15 As above, the double flow sensor 506 is coupled to the electrical signal processor 104 such that the detected change in capacitance (or resistance) for each of the first and second couplings 502, 504 is communicated via a wired (or wireless) connection to the electrical signal processor 104. Thus, the electrical signal processor 104 may be configured to determine a speed of flow based on a time of the detection of flow at each
20 of the two regions monitored by the first and second couplings 502, 504. As above, further analysis of the test may be carried in the same ways as described above.

25 When the double flow sensor 506 is configured for operation using resistive electrodes, the first coupling 502 is a resistive path effectively serving to detect a change in resistance in a first region of the assay test strip 110 and the second coupling 504 is a resistive path effectively serving to detect a change in resistance in a second region of the assay test strip 110. Thus, the double flow sensor 506 functions in a similar manner to the two flow sensors 106, 406 of Figure 4 in allowing for detection of flow at two regions of the flow path, prior to the fluid flow reaching the test region 112.

30

Figure 6 shows a lateral flow test device 600 including two separate sensors 206, 606 in accordance with the present disclosure.

35 The first of the two separate sensors is a sensor identical to the second flow sensor 206 described above in relation to Figure 2. The second of the two separate sensors is an

additional flow sensor 606, which is configured to detect flow from a sample 118 provided on the assay test strip 110 after it has passed through a region monitored by the second flow sensor 206 and prior to the flow reaching the test region 112. The additional flow sensor 606 may be configured to sense a change in capacitance or resistance due to sample flow in a similar manner to that of the second flow sensor 206. The additional flow sensor 606 comprises a third electrode 608a and a fourth electrode 608b. The first electrode 608a and the second electrode 608b are arranged to be in a spaced relationship in a plane parallel and in proximity to a first side of the assay test strip 110, when the assay test strip 110 is inserted into the device 600. Thus, the second flow sensor 206 forms a first coupling 602 and the additional flow sensor 606 forms a second coupling 604. In this case, there is no common electrode as there was in the embodiment of Figure 5.

When the two separate sensors 206, 606 are configured for operation as capacitive sensors, the electrodes 208a, 208b, 608a, 608b will not be in direct contact with the assay test strip 110 (e.g. test paper). Instead, a thin insulator may be provided. The insulator may be, for example, air and/or plastic.

In some embodiments, the two separate sensors 206, 606 may be configured for operation as resistive sensors and, in which case, the electrodes 208a, 208b, 608a, 608b will be in direct contact with the assay test strip 110 (e.g. test paper).

It will be noted that the use of capacitive flow sensors and resistive flow sensors may be mixed on one assay test strip.

In operation, the first coupling 602 effectively serves to detect a change in capacitance (or resistance) in a first region of the assay test strip 110 and the second coupling 604 effectively serves to detect a change in capacitance (or resistance) in a second region of the assay test strip 110. Thus, the two separate sensors 206, 606 function in a similar manner to the two flow sensors 106, 406 of Figure 4 in allowing for detection of flow at two regions of the flow path, prior to the fluid flow reaching the test region 112.

As above, the two separate sensors 206, 606 are coupled to the electrical signal processor 104 such that the detected change in capacitance (or resistance) for each of the first and second couplings 602, 604 is communicated via a wired (or wireless)

connection to the electrical signal processor 104. Thus, the electrical signal processor 104 may be configured to determine a speed of flow based on a time of the detection of flow at each of the two regions monitored by the first and second couplings 602, 604. As above, further analysis of the test may be carried in the same ways as described above.

5

In each of the above embodiments, the electrodes may comprise narrow metal or conductive polymer strips deposited on the assay test strip 110 (e.g. test paper), which are arranged for electrical connection to corresponding electrodes in the device.

10

In each of the above embodiments, the optical detector 102 may be configured to detect light generated in the assay test strip 110 (e.g. due to fluorescence of a target molecule) or to detect emitted light after it has been reflected from or transmitted through the assay test strip 110. For example, the device may comprise one or more illuminators for generating light to be reflected from or transmitted through the assay test strip 110 such that a change in reflectance or transmission may be observed by the optical detector 102 based on a condition of the assay test strip 110 (e.g. based on a presence of a sample flow or analyte) in the test region 112.

15

The optical detector 102 may be further configured to receive light from the control region 114 of the assay test strip 110 and to generate a control electrical output based on the received light for analysis by the electrical signal processor 104.

20

Figure 7 shows a method 700 of operating a lateral flow test device in accordance with the present disclosure. The method 700 comprises a first step 702 of detecting, using a flow sensor 106, flow from a sample 118 provided on an assay test strip 110 prior to the flow reaching a test region 112 of the assay test strip 110. A second step 704 comprises receiving light, at an optical detector 102, from the test region 112 and a third step 706 comprises generating, at the optical detector 102, an electrical output based on the received light. A fourth step 708 comprises analysing the electrical output at an electrical signal processor 104. The electrical output may be analysed in any of the ways described above.

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30

In more detail, the lateral flow test device may be configured as a disposable item, which may be in storage for a long period, before being bought or provided to a user. When the user wishes to use the device for a test they begin by either inserting a battery into

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the device or by removing a plastic insulating strip to activate the battery powered electronics of the device. At this moment, the electronic circuitry in the device begins to monitor the flow sensor for any change indicative of the assay test strip changing from dry to wet (e.g. by monitoring the capacitive/resistive/optical properties of the flow sensor as described above). The user then deposits the sample fluid as a droplet on the assay test strip and the flow sensor detects the droplet induced wetting of the assay test strip (e.g. paper). The flow sensor notifies the electrical signal processor that fluid has been detected and the device is primed for optical detection from the test region (i.e. test line) such that measurements can be taken and recorded to monitor the dynamic response as the fluid reaches the test region. Subsequently, the same process happens at the control region (i.e. control line). As such, the electrical signal processor is able to analyse the dynamic response from signals detected by the optical detector from the start of fluid flow detection by the flow sensor until a pre-determined time after the fluid has reached the test region and/or control region. The analysis may then be presented to the user, for example, via communication to a mobile phone application or any other display method.

Figure 8 shows a graph 800 illustrating example optical measurements from the test region 112 over time. The graph 800 shows a first optical response 802 with an initial peak and long tail of reducing signal intensity and a second optical response 804 having a delayed start when compared with the first optical response 802 and a slower, gradual increase in signal intensity up to a plateau. As illustrated by the graph 800, a static measurement taken at time A would indicate a higher signal intensity for the first optical response 802 and a lower signal intensity for the second optical response 804. By contrast, a static measurement taken at time B would indicate a higher signal intensity for the second optical response 804 and a lower signal intensity for the first optical response 802. Thus, the output from a given test may be highly dependent on the time when a static measurement is taken during the test. Embodiments of the present disclosure allow for consistent results to be taken by detecting a start time (e.g. $t=0$) when the sample 118 passes the flow sensor such that a measurement time can be determined based on a common starting point during the course of a given test. As such, results may be directly comparable across different tests as they will always be taken at the same point in time with respect to the optical response curve (i.e. at time A).

In other embodiments, it may be desirable to measure the dynamic shape of the optical response, for example, and this can be achieved by knowing the $t=0$ time (from detection of flow at the flow sensor) such that the optical response over a defined response window can be measured and analysed.

5

The lateral flow test devices described in this disclosure may be configured as point-of-care devices, which may optionally be disposable and which may be configured to detect one or more of: coronavirus; coronavirus antibodies; or many other things.

10

Embodiments of the present disclosure can be employed in many different applications, in particular, in the areas of biological, medical, environmental and veterinary diagnostics.

List of reference numerals:

15

100 first lateral flow test device

102 optical detector

104 electrical signal processor

106 first flow sensor

108a first electrode

20

108b second electrode

110 assay test strip

112 test region

114 control region

116 baffle

25

118 sample droplet

200 second lateral flow test device

206 second flow sensor

208a first electrode

30

208b second electrode

300 third lateral flow test device

302 optical emitter

304 optical detector

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306 third flow sensor

	400	fourth lateral flow test device
	406	additional flow sensor
	408a	first electrode
5	408b	second electrode
	500	fifth lateral flow test device
	502	first coupling
	504	second coupling
10	506	double flow sensor
	508c	third electrode
	600	sixth lateral flow test device
	602	first coupling
15	604	second coupling
	606	additional flow sensor
	608a	third electrode
	608b	fourth electrode
20	700	method of operating a lateral flow test device
	702	first step
	704	second step
	706	third step
	708	fourth step
25	800	graph
	802	first optical response
	804	second optical response
30	The skilled person will understand that in the preceding description and appended claims, positional terms such as 'above', 'along', 'side', etc. are made with reference to conceptual illustrations, such as those shown in the appended drawings. These terms are used for ease of reference but are not intended to be of limiting nature. These terms are therefore to be understood as referring to an object when in an orientation as shown	
35	in the accompanying drawings.	

Although the disclosure has been described in terms of preferred embodiments as set forth above, it should be understood that these embodiments are illustrative only and that the claims are not limited to those embodiments. Those skilled in the art will be able to make modifications and alternatives in view of the disclosure, which are contemplated as falling within the scope of the appended claims. Each feature disclosed or illustrated in the present specification may be incorporated in any embodiments, whether alone or in any appropriate combination with any other feature disclosed or illustrated herein.

CLAIMS:

1. A lateral flow test device comprising:
an optical detector configured to receive light from a test region of an
assay test strip and to generate an electrical output based on the received
light;
an electrical signal processor for analysing the electrical output; and
a flow sensor configured to detect flow from a sample provided on the
assay test strip prior to the flow reaching the test region.
2. The lateral flow test device of claim 1 wherein the flow sensor is configured
to relay a message to the electrical signal processor in response to flow
detection.
3. The lateral flow test device of claim 2 wherein the message comprises an
instruction to begin a timer or counter.
4. The lateral flow test device of claim 2 or 3 wherein the message comprises
an instruction to begin analysing the electrical output from the optical
detector.
5. The lateral flow test device of any of claims 2 to 4 wherein the message
comprises an instruction to wake or power on the optical detector and/or
another component.
6. The lateral flow test device of any of claims 2 to 5 wherein the message
comprises an instruction to notify a user that a test is in progress and/or relay
information about a quality of a test.
7. The lateral flow test device of any of claims 2 to 6 wherein the electrical signal
processor is configured to perform kinetic analysis of the electrical output.
8. The lateral flow test device of any preceding claim wherein the flow sensor
comprises a droplet detector.

9. The lateral flow test device of any preceding claim wherein the flow sensor comprises a capacitive sensor configured to sense a change in capacitance due to sample flow.
- 5 10. The lateral flow test device of any of claims 1 to 8 wherein the flow sensor comprises a resistive sensor configured to sense a change in resistance due to sample flow.
- 10 11. The lateral flow test device of claim 9 or 10 comprising a first electrode and a second electrode, wherein the first electrode and the second electrode are arranged to be in a spaced relationship in a plane parallel and in proximity to a first side of the assay test strip, when the assay test strip is inserted into the device.
- 15 12. The lateral flow test device of claim 9 or 10 comprising a first electrode and a second electrode, wherein the first electrode and the second electrode are arranged to be in a spaced relationship such that the first electrode is adjacent a first side of the assay test strip and the second electrode is adjacent a second side of the assay test strip, when the assay test strip is inserted into the device.
- 20 13. The lateral flow test device of claim 11 or 12 wherein the flow sensor comprises at least a third electrode, wherein the third electrode is arranged to be in a spaced relationship with the first and second electrodes.
- 25 14. The lateral flow test device of claim 13 wherein the first electrode, the second electrode and the third electrode are arranged such that one of the first electrode, the second electrode and the third electrode is arranged to form a coupling with each remaining electrode.
- 30 15. The lateral flow test device of any preceding claim wherein the flow sensor comprises multiple electrodes.

16. The lateral flow test device of any preceding claim wherein the flow sensor comprises an optical sensor configured to sense a change in an optical property due to sample flow.
- 5 17. The lateral flow test device of claim 16 wherein the optical property is one or more of: reflectance; transmission; fluorescence or chemi-luminescence.
- 10 18. The lateral flow test device of any preceding claim wherein two or more flow sensors are provided along a flow path of the assay test strip to allow for detection of flow at two or more regions of the flow path.
- 15 19. The lateral flow test device of claim 18 wherein the electrical signal processor is configured to receive input from each flow sensor and to determine a speed of flow based on a time of the detection of flow at each of the two or more regions.
- 20 20. The lateral flow test device of any preceding claim configured as a point-of-care device.
- 20 21. The lateral flow test device of any preceding claim configured to detect one or more of: coronavirus; coronavirus antibodies.
- 25 22. A method of operating a lateral flow test device comprising:
detecting, using a flow sensor, flow from a sample provided on an assay test strip prior to the flow reaching a test region of the assay test strip;
receiving light, at an optical detector, from the test region;
generating, at the optical detector, an electrical output based on the received light; and
30 analysing the electrical output at an electrical signal processor.

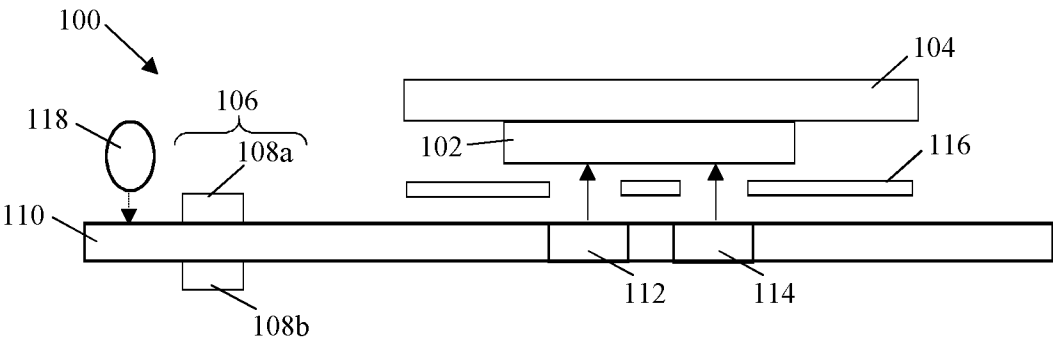


Figure 1

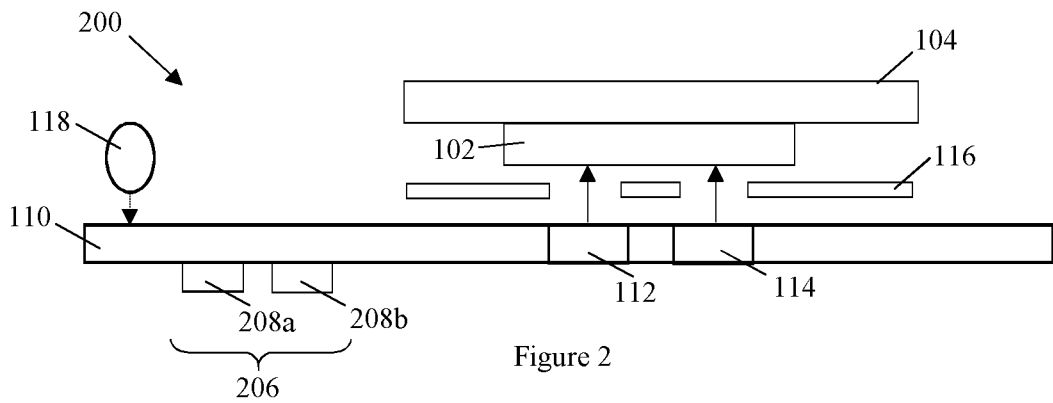


Figure 2

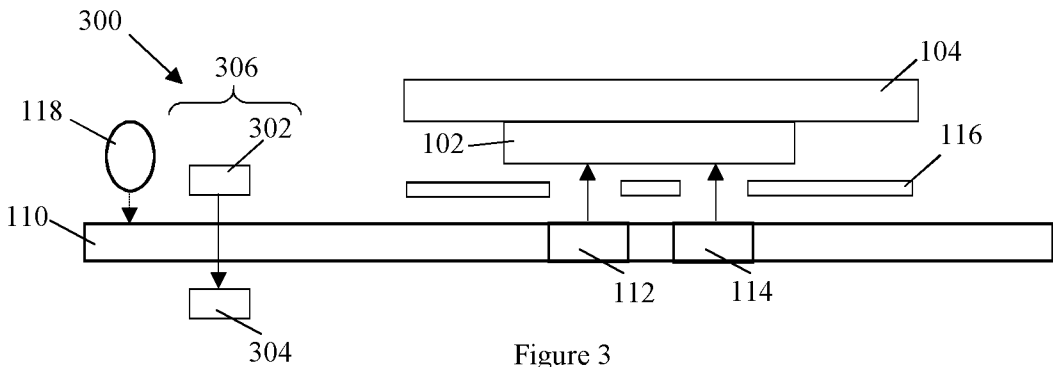


Figure 3

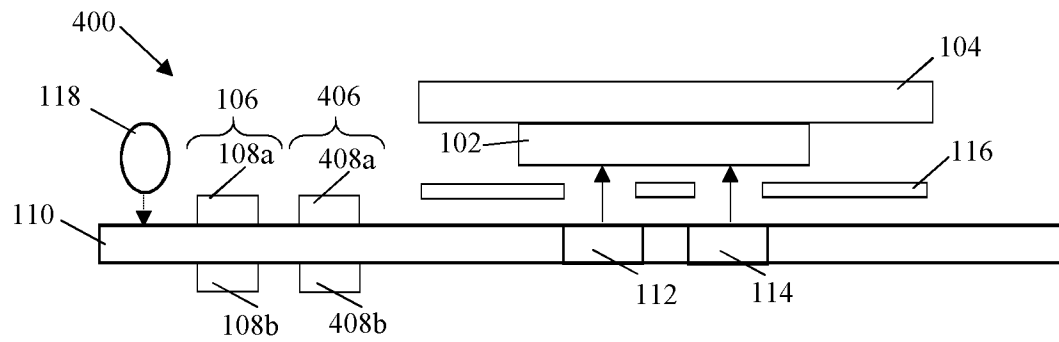


Figure 4

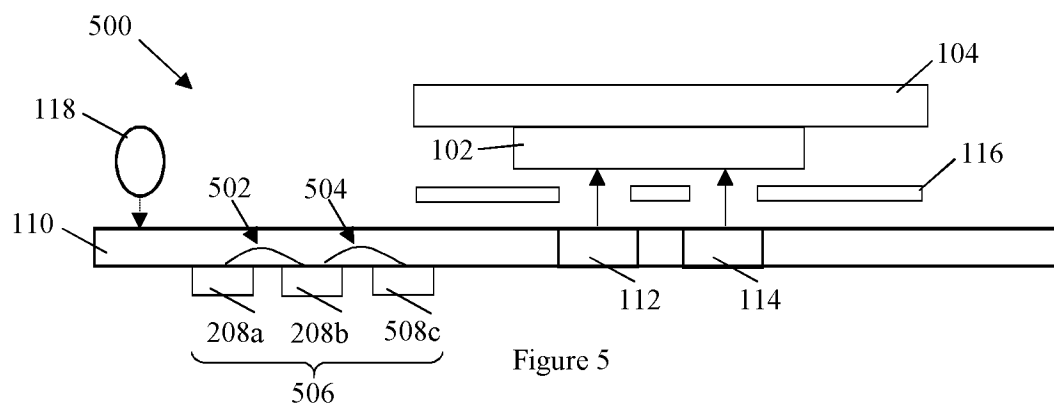


Figure 5

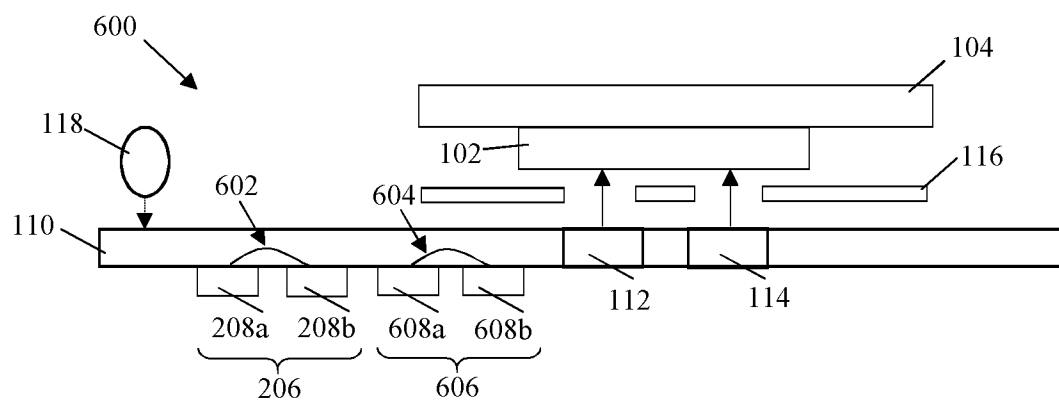


Figure 6

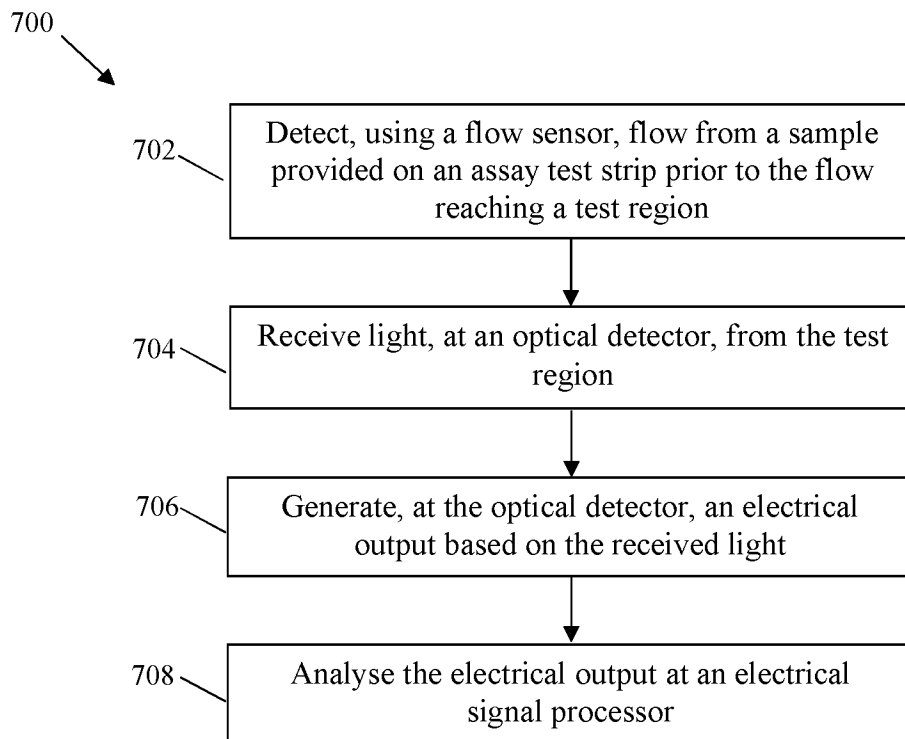


Figure 7

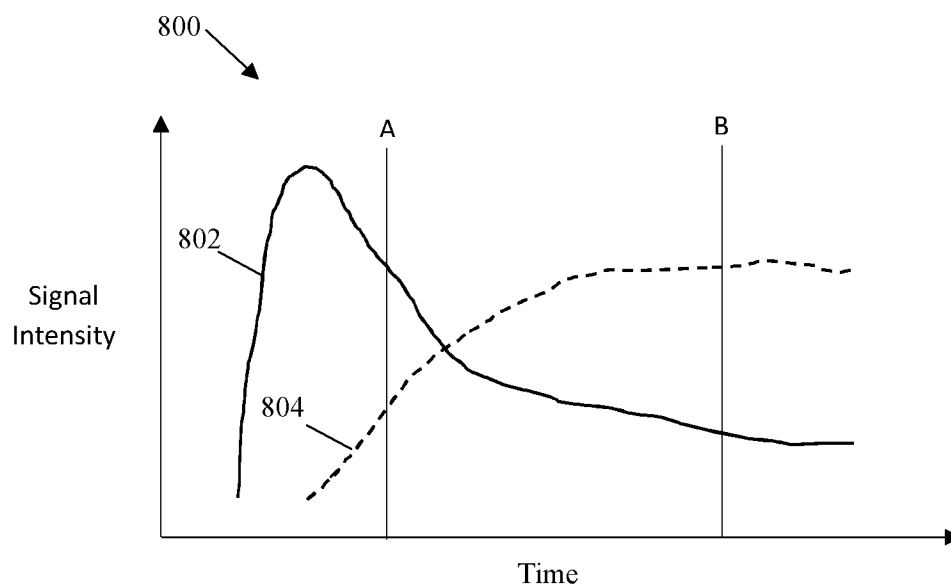


Figure 8

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2021/085617

A. CLASSIFICATION OF SUBJECT MATTER INV. G01N21/84 G01N21/77 G01N21/76 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		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "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 "Y" document of particular relevance;; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 17 March 2022		Date of mailing of the international search report 04/04/2022
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Koll, Hermann

INTERNATIONAL SEARCH REPORT

International application No

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X	US 2020/217799 A1 (MARKOVSKY ROBERT J [US] ET AL) 9 July 2020 (2020-07-09) paragraph [0092]; figure 1 -----	1, 20-22
X	US 2016/252441 A1 (ABBOTT TIMOTHY JOHN [GB] ET AL) 1 September 2016 (2016-09-01) paragraphs [0009], [0026]; claim 1 -----	1, 20-22

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