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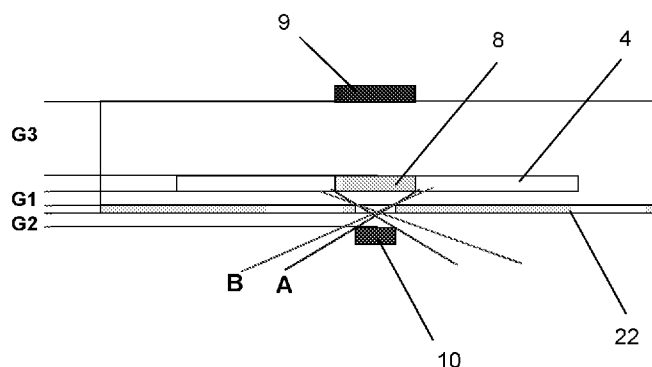


FIG. 2

(57) Abstract: An assay device for the quantitative determination of the concentration of at least one analyte in a liquid sample comprises a planar emitter (2), a planar detector (3) and a lateral flow membrane interposed between the emitter and the detector. The lateral flow membrane comprises at least one test region (8) for retaining tagging particles in the test region in dependence on the concentration of the analyte in the liquid sample. The emitter comprises an emission layer (9) of an organic electroluminescent material and the emission layer is arranged to illuminate the test region. The detector comprises an absorption layer (10) of an organic photovoltaic material and the absorption layer is arranged to detect light from the test region. The device further comprises a mask layer (22) interposed between the lateral flow membrane and the absorption layer, the mask layer having defined therein an aperture (30) configured to direct light from the test region onto the absorption layer.

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ASSAY DEVICE

This invention relates to an assay device for the quantitative determination of the concentration of at least one analyte in a liquid sample. The liquid sample may be a biological sample, e.g. plasma, serum or urine. The sample may alternatively be a sample reduced to a liquid, such as a plant or tissue extract.

BACKGROUND

Our patent application WO2015/121672 discloses assay devices for the quantitative determination of the concentration of at least one analyte in a liquid sample. The present invention, at least in its preferred embodiments aims to provide an alternative to devices of the prior art. In particular, embodiments of the invention improve the signal to noise ratio of the output from the assay device by optimising the optical configuration of the device components.

BRIEF SUMMARY OF THE DISCLOSURE

In accordance with the present invention there is provided an assay device for the quantitative determination of the concentration of at least one analyte in a liquid sample, the device comprising:

- a planar emitter;
- a planar detector;
- a lateral flow membrane interposed between the emitter and the detector;
- wherein the lateral flow membrane comprises at least one test region for retaining tagging particles in the test region in dependence on the concentration of the analyte in the liquid sample,
- wherein the emitter comprises an emission layer of an organic electroluminescent material and the emission layer is arranged to illuminate the test region, and
- wherein the detector comprises an absorption layer of an organic photovoltaic material and the absorption layer is arranged to detect light from the test region,
- wherein the device further comprises a mask layer interposed between the lateral flow membrane and the absorption layer, the mask layer having defined therein an aperture configured to direct light from the test region onto the absorption layer.

Thus, in embodiments of the present invention, the mask layer may act to provide, in effect, a pinhole camera to image the test region onto the absorption layer. This provides a very simple and effective optical configuration, which is relatively simple to manufacture.

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The device may further comprise at least one spacer layer. A spacer layer may be interposed between the absorption layer and the mask layer, between the lateral flow membrane and the mask layer and/or between the emission layer and the lateral flow membrane.

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In some embodiments, a spacer layer is interposed between the absorption layer and the mask layer. The spacer layer may have a thickness selected to maintain a required spacing between the mask layer and the absorption layer. In some embodiments the spacer layer between the absorption layer and the mask layer has a thickness of 10 to 1000 μm , from 50 to 500 μm or from 100 to 300 μm .

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In some embodiments, a spacer layer is interposed between the lateral flow membrane and the mask layer. The spacer layer may have a thickness selected to maintain a required spacing between the mask layer and the lateral flow membrane. In some embodiments the spacer layer between the lateral flow membrane and the mask layer has a thickness of from 10 to 1000 μm , from 50 to 500 μm or from 100 to 300 μm .

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In some embodiments a spacer layer is interposed between the emission layer and the lateral flow membrane, the spacer layer having a thickness selected to maintain a required spacing between the emission layer and the lateral flow membrane. In some embodiments the spacer layer between the emission layer and the lateral flow membrane has a thickness of from 100 μm to 5 mm, from 0.5 mm to 3 mm or from 1 mm to 2 mm (e.g. 1.3 mm).

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In some embodiments, a first spacer layer is interposed between the lateral flow membrane and the mask layer and a second spacer layer is interposed between the absorption layer and the mask layer, wherein the thickness of the first spacer layer and the second spacer layer are selected relative to the size of the aperture so that only light from the emitter which passes through the test region impinges on the detector.

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In some embodiments, a first spacer layer is interposed between the lateral flow membrane and the mask layer, a second spacer layer is interposed between the absorption layer and the mask layer, and a third spacer layer is interposed between the emission layer and the lateral flow membrane.

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In some embodiments the planar emitter, planar detector, lateral flow membrane, mask layer and, optionally, the spacer layer(s) are arranged as a stack (of layers). Each layer of the stack may be in direct contact with the adjacent layer(s). There may be substantially no air gap between the layers in the stack.

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In some embodiments, the device further comprises a housing. The housing may be formed of any suitable material, such as plastic.

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The stack of the planar emitter, the planar detector, the lateral flow membrane, the mask layer and, optionally the spacer layer(s) may be received within the housing. In some embodiments a portion of the stack (e.g. an end of the stack comprising at least the mask layer and, optionally the spacer layer(s)) extends outside of the housing. This portion may form a connector, thereby enabling a connection to be established with an external device.

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In some embodiments, the portion of the stack which forms the connector further comprises electrical conductors which extend from each of the emitter and detector layers, thereby enabling an electrical connection to be formed with, for example, a reader, a data collector, a communications module and/or a power supply. This enables the device to be powered without requiring a battery.

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In some embodiments, the electrical conductors are formed by printed tracks.

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The assay device may be configured for connecting to a communications module which is capable of communicating readings from the assay device to a user.

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In some embodiments, the mask layer and/or one or more of the spacer layer(s) comprises one or more holes and/or one or more recesses for locating the layer(s) on corresponding projections formed in the housing. This facilitates the correct alignment of the layers with each other and with the detector, emitter and lateral flow membrane.

In some embodiments, each of the mask layer and the spacer layers comprises one or more locating holes and one or more locating recesses.

5 In some embodiments, the first spacer layer (interposed between the lateral flow membrane and the mask layer) and/or second spacer layer (interposed between the absorption layer and the mask layer) comprise a central space which allows the passage of light therethrough. When arranged in a stack with the other layers, the central space(s) are aligned with the aperture(s) of the mask layer such that light can pass from the emitter to the detector, through the test region of the lateral flow
10 membrane.

In some embodiments, the third spacer layer (interposed between the lateral flow membrane and the mask layer) comprises a central space for receiving at least a part of the lateral flow membrane therein.

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The mask layer and/or the spacer layer(s) may be formed of paper, in particular black paper. Alternatively, the mask layer may be formed of optically opaque plastics sheet material or metal foil.

20 The absorption layer may define at least one pixel of organic photovoltaic material and the aperture may be configured to direct light from the test region onto an area of the absorption layer corresponding substantially to the pixel.

The pixel, the aperture, the test region and the emission layer may be aligned along a
25 common optical axis.

In some embodiments, the mask layer comprises a plurality of apertures. In some embodiments, the plurality of apertures are arranged in an array. For example, an array may comprise from 2 to 10 rows of apertures, each row comprising from 1 to 10
30 apertures. Each aperture may be aligned with a respective pixel of the detector.

The layer(s) between the lateral flow membrane and the absorption layer may comprise alignment holes through which markings on the lateral flow membrane and/or the absorption layer can be viewed to align the lateral flow membrane and/or the
35 absorption layer during assembly of the assay device.

In some embodiments, the mask layer comprises one or more alignment holes for aligning the mask layer with the absorption layer and/or the lateral flow membrane. The alignment holes may be located such that when the mask layer is assembled in a stack with the other layers of the device, alignment marks provided on the absorption layer and/or the lateral flow membrane can be viewed through the alignment holes, and through the central space of any spacer layers therebetween.

In broad terms, the invention provides an assay device for the quantitative determination of the concentration of at least one analyte in a liquid sample. The device comprises a planar emitter, a planar detector, a lateral flow membrane interposed between the emitter and the detector, a conjugate pad in fluid communication with a proximal end of the lateral flow membrane, the conjugate pad comprising optically detectable tagging particles bound to a first assay component, and a wicking pad in fluid communication with a distal end of the lateral flow membrane. The lateral flow membrane is formed from a light transmissive material and is capable of transporting fluid from the conjugate pad to the wicking pad by capillary action. The lateral flow membrane comprises at least one test region comprising an immobilised second assay component for retaining the tagging particles in the test region in dependence on the binding between the analyte, the first assay component and the second assay component in order to generate a concentration of tagging particles in the test region that is indicative of the concentration of the analyte in the liquid sample. The emitter comprises an emission layer of an organic electroluminescent material and the emission layer is aligned with the test region of the lateral flow membrane, whereby the emitter is capable of illuminating the test region. The detector comprises an absorption layer of an organic photovoltaic material and the absorption layer is aligned with the test region of the lateral flow membrane, whereby the detector is capable of detecting light from the test region.

Thus, the assay device provides a relatively simple construction that is capable of determining the result of an assay by optical measurement of the test region. Embodiments of the invention are capable of accurately determining the concentration of an analyte in a sample. However, it is not necessary in every embodiment of the invention for the device to determine the exact concentration of the analyte. For example, in some embodiments only a qualitative indication of the analyte

concentration may be determined. Typically, however, embodiments of the invention provide more than a simple yes/no indication of the presence of the analyte. The device improves upon the prior art by the ability to provide a quantitative indication of the concentration in a device that can be configured for single-use.

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At least one of the test regions may be in the shape of a substantially rectangular line. Alternatively, at least one of the test regions may be a circle, square or dot. It will be appreciated that the test regions may be supplied in any conceivable shape fitting within the boundary of the lateral flow membrane.

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In an embodiment of the invention, the tagging particles absorb light at a wavelength emitted by the emitter, and the detector is arranged to detect light from the emitter passing through the lateral flow membrane, whereby the attenuation of the light intensity detected by the detector due to absorption by the immobilised tagging particles is indicative of the concentration of the analyte in the liquid sample. For example, the tagging particles may be gold nanoparticles which appear red when concentrated and may be illuminated by green light from the emitter. As a further example, the tagging particles may be blue polystyrene particles and may be illuminated by red light from the emitter. The light from the emitter may be in the visible spectrum, but could also be in the ultraviolet or infra red wavelength ranges.

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In an embodiment of the invention, the tagging particles fluoresce under illumination at a wavelength emitted by the emitter, and the detector is arranged to detect such fluorescence through the lateral flow membrane, whereby the light intensity detected by the detector due to fluorescence of the immobilised tagging particles is indicative of the concentration of the analyte in the liquid sample. For example, the tagging particles may be fluorescein or fluorescein isothiocyanate (FITC) particles illuminated with blue light.

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The light transmissive material may become light transmissive when wetted by the liquid sample. The light transmissive material may be nitrocellulose. This material has been found to be particularly suitable. When dry, nitrocellulose is substantially opaque. However, when wet, the nitrocellulose may become light transmissive. In this way, the nitrocellulose is particularly suitable for use in head-on detection geometry, since light can be transmitted through the lateral flow membrane when wet. The lateral flow

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membrane may have a thickness of less than 200 microns, preferably less than 150 microns, more preferably less than 100 microns.

5 Close spacing of the emission layer and the absorption layer maximises the amount of captured light and therefore maximises the signal to noise ratio of the device.

10 The spacing between the facing surfaces of the emission layer and the lateral flow membrane may be in the range 1.3mm to 2mm, but can be in the range 1mm to 3mm or even in the range 100 microns to 5mm. Close spacing of the emission layer and the lateral flow membrane maximises the intensity of the emitted light at the membrane and therefore maximises the signal to noise ratio of the device.

15 The spacing between the facing surfaces of the absorption layer and the mask layer may be in the range 200 microns to 400 microns, but can be in the range 100 microns to 700 microns or even in the range 10 microns to 1,000 microns.. The spacing between the facing surfaces of the lateral flow membrane and the mask layer may be in the range 200 microns to 400 microns, but can be in the range 100 microns to 700 microns or even in the range 10 microns to 1,000 microns. Close spacing of the absorption layer and the lateral flow membrane maximises the intensity of the incident
20 light at the detector and therefore maximises the signal to noise ratio of the device.

The emitter may comprise an electrode layer interposed between the emission layer and the lateral flow membrane. The electrode layer of the emitter may comprise indium tin oxide. Typically, the emitter may be made up of a plurality of layers, including anode
25 and cathode layers. The emitter may comprise a barrier layer interposed between the electrode layer and the lateral flow membrane. The barrier layer may be provided by a substrate on which the emitter is formed. The barrier layer can protect the emission layer during construction of the device. The barrier layer may be the only layer between the electrode layer and the lateral flow membrane. In embodiments of the invention
30 there is no air gap between the emitter and the lateral flow membrane. This minimises the distance the light must travel from the emission layer to the lateral flow membrane. The detector may comprise an electrode layer interposed between the absorption layer and the lateral flow membrane. The electrode layer of the detector may comprise indium tin oxide. Typically, the detector may be made up of a plurality of layers,
35 including anode and cathode layers. The detector may comprise a barrier layer

interposed between the electrode layer and the lateral flow membrane. The barrier layer may be provided by a substrate on which the detector is formed. The barrier layer can protect the absorption layer during construction of the device. The barrier layer may be the only layer between the electrode layer and the lateral flow membrane. In
5 embodiments of the invention there is no air gap between the detector and the lateral flow membrane. This minimises the distance the light must travel from the lateral flow membrane to the absorption layer.

The emitter and/or the detector may be formed by deposition, in particular printing, of
10 layers on a substrate. In one embodiment, the emitter and the detector are each provided on separate substrates. The substrate may be flexible, for example PET, or may be rigid, for example glass. In a particularly advantageous embodiment the emitter and the detector are formed on a common substrate. The substrate may be folded about the lateral flow membrane. By depositing both the emitter and the detector on the
15 same substrate correct relative alignment of the emitter and the detector can be ensured.

Thus, there may be provided an electro-optical device comprising an emitter comprising an organic electroluminescent material and a detector comprising an
20 organic photovoltaic material, wherein the electroluminescent material and the photovoltaic material are deposited on a common substrate.

Typically, the emission layer comprises an organic electroluminescent material, such as polymers including poly(p-phenylene vinylene) or polyfluorene, or small molecules
25 including organometallic chelates, fluorescent or phosphorescent dyes, and conjugated dendrimers. The organometallic chelate may be Alq₃. The absorption layer typically comprises an organic photovoltaic material, such as the small molecules PCBM₆₀ or PCBM₇₀, or polymers such as polythiophenes. The absorption layer may comprise a blend of organic photovoltaic polymers such as polythiophenes and organic
30 photovoltaic small molecules such as PCBM₆₀ or PCBM₇₀. The polythiophene may be Poly(3-hexylthiophene) (P3HT).

The assay device may further comprise a sample pad in fluid communication with the conjugate pad and arranged to receive the liquid sample. The conjugate pad may
35 perform the role of a sample pad, where no distinct sample pad is provided.

In an embodiment of the invention, the lateral flow membrane comprises a plurality of discrete test regions and the emission layer comprises a plurality of discrete emission regions each aligned with a respective test region. Similarly, the lateral flow membrane may comprise a plurality of discrete test regions and the absorption layer may comprise a plurality of discrete absorption regions each aligned with a respective test region. In this way each test region may be provided with a respective emission region and/or a respective detection region. By providing discrete emission or absorption regions, respective test regions can be analysed independently and the risk of cross talk is minimised.

The lateral flow membrane may comprise a control region. The control region may be positioned between the test region(s) and the distal end of the lateral flow membrane, the control region may comprise an immobilised control component for retaining tagging particles in the control region and the emission layer and/or the absorption layer may comprise a discrete emission/absorption region aligned with the control region.

The first assay component may comprise a molecule which binds the analyte to the tagging particles and the second assay component may comprise a receptor for the analyte. This combination of components is useful in a sandwich assay.

The first assay component may comprise the analyte or an analogue thereof and the second assay component may comprise a receptor for the analyte. This combination of components is useful in a competitive assay. Alternatively, the first assay component comprises a receptor for the analyte and the second assay component comprises the analyte or an analogue thereof. The assay may be an immunoassay. The receptor may be an antibody which binds to the analyte or an analogue thereof.

The lateral flow membrane is provided on a transparent substrate. The substrate may provide mechanical stability to the lateral flow membrane.

The assay device may comprise a controller arranged to receive detection signals from the detector and to process the detection signals whereby to generate data indicative of the concentration of the analyte in the sample. The controller may be provided as

part of the assay device, for example within the same housing. The controller may also be arranged to control the emission of light from the emitter. The device may comprise a battery for powering the detector and the emitter. The device may be disposable.

5 Unlike some prior art devices for the quantitative determination of analyte concentration, the present invention provides the features of a lateral flow assay, an emitter and a detector in a single, stand-alone device. Since the device contains both the emitter and detector functions, this enables an external reader (if required) to be smaller, simpler and cheaper.

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However, it will be appreciated that in some embodiments (for example those in which a controller is provided), an external reader for reading the signal detected by the planar detector is not required, since 'reading' may be carried out by the device itself.

15 The device may be in the form of a cartridge.

The device may comprise an electrical interface for connection to an external device, such as a reader or a data collection device, wherein the electrical interface is configured to connect the detector and the emitter to the external device. In this way,
20 the device can be provided as a disposable cartridge.

In some embodiments, the device comprises components for wireless connectivity to an external device, e.g. via Bluetooth, a wireless network, 3G or 4G. This enables the signal received by the detector, or the data generated by the controller, to be
25 transmitted to a user.

The assay device may comprise at least a second lateral flow membrane arranged in parallel with the first lateral flow membrane between the emitter and the detector. In some embodiments, two, three, four or more lateral flow membranes are arranged in
30 parallel. Each strip of membrane material may be aligned with a row of apertures in the mask layer.

Thus, in accordance with an embodiment of the invention, a second lateral flow membrane allows multiple assay tests to be performed in parallel. In some

embodiments, the multiple assay tests may be testing for the same analyte in the same way.

5 Alternatively, the multiple assay tests may be testing for different analytes. Performing assay tests in parallel prevents the mechanism of one assay test interfering with the mechanism of a second assay test.

10 The second lateral flow membrane may be provided on the same sheet as the first lateral flow membrane. The second lateral flow membrane may be joined to the first lateral flow membrane. Alternatively, the second lateral flow membrane may be provided separately to the first lateral flow membrane.

15 The wicking pad may be in fluid communication with a distal end of the first lateral flow membrane and a distal end of the second lateral flow membrane. Thus, the first lateral flow membrane and the second lateral flow membrane both connect to the same wicking pad.

20 The conjugate pad may be in fluid communication with a proximal end of the first lateral flow membrane and a proximal end of the second lateral flow membrane. Thus, the first lateral flow membrane and the second lateral flow membrane both connect to the same conjugate pad.

25 The conjugate pad may comprise optically detectable tagging particles bound to a third assay component.

30 The optically detectable tagging particles bound to the third assay component may be optically different to the optically detectable tagging particles bound to the first assay component. Thus, the different colours of the optically detectable tagging particles allow two tests to be run in close proximity without the spectrum-matched light required to test the result of one test interfering with the spectrum-matched detector required to test the result of the second, neighbouring test.

35 The assay device may comprise a second conjugate pad in fluid communication with a proximal end of the second lateral flow membrane.

The second conjugate pad may comprise optically detectable tagging particles bound to a third assay component. The second conjugate pad may comprise optically detectable tagging particles bound to the first assay component.

5 The optically detectable tagging particles in the second conjugate pad may be optically different to the said optically detectable tagging particles in the first conjugate pad. Thus, the different colours of the optically detectable tagging particles allow two tests to be run in close proximity without the spectrum-matched light required to test the result of one test interfering with the spectrum-matched detector required to test the result of
10 the second, neighbouring test.

In some embodiments, the second lateral flow membrane may comprise at least a second test region comprising an immobilised fourth assay component for retaining the tagging particles in the second test region in dependence on the binding between the
15 analyte, the third assay component and the fourth assay component.

In some embodiments, the second lateral flow membrane may comprise at least a second test region comprising the immobilised first assay component for retaining the tagging particles in the second test region in dependence on the binding between the
20 analyte, the first assay component and the second assay component.

The (first) lateral flow membrane may comprise at least a second test region comprising an immobilised fourth assay component for retaining the tagging particles in the second test region in dependence on the binding between the analyte, a (said) third
25 assay component and the fourth assay component.

The emission layer may comprise a plurality of emitter pixels and a first emitter pixel may be aligned with the (first) test region of the first lateral flow membrane and a second emitter pixel may be aligned with the second test region.
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The absorption layer may comprise a plurality of detector pixels and a first detector pixel may be aligned with the (first) test region of the first lateral flow membrane and a second detector pixel may be aligned with the second test region. The second test region may be provided on the first lateral flow membrane or the second lateral flow
35 membrane.

The first emitter pixel and the second emitter pixel may be mutually spaced in the direction from the distal end to the proximal end of the lateral flow membrane.

- 5 The first detector pixel and the second detector pixel may be mutually spaced in the direction from the distal end to the proximal end of the lateral flow membrane.

The first detector pixel may be aligned with the first emitter pixel and the second detector pixel may be aligned with the second emitter pixel.

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Thus, the mutual spacing of the emitter and/or detector pixels minimises the amount of light from the first emitter pixel detectable in the second detector pixel or vice versa.

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The pixels may be defined as discrete regions of the emission layer or the absorption layer. Alternatively, the emission layer or the absorption layer may be masked to define the pixels.

According to a second aspect of the present invention there is provided an assay system comprising an assay device according to the first aspect of the invention, and a communications module.

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The communications module may comprise an electrical connection circuit board for connecting to the electrical connector of the assay device. The communications module may further comprise a data communication circuit board for communicating readings from the assay device to a user. Readings may be communicated directly to the user, i.e. via a user interface, or indirectly, e.g. via a computer or smart phone.

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According to a third aspect of the present invention there is provided a method of manufacturing an assay device, the method comprising:

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providing a planar emitter comprising an emission layer, a planar detector comprising an absorption layer, a lateral flow membrane and a mask layer having an aperture therein; and

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assembling the planar emitter, the planar detector, the lateral flow membrane and the mask layer to form a stack in which the lateral flow membrane is interposed between the emitter and the detector, and the mask layer is interposed between the lateral flow membrane and the absorption layer.

The assay device may be in accordance with the first aspect of the invention.

5 In some embodiments, assembling the stack comprises aligning an alignment hole, slot or recess provided in the mask layer (and any other layers interposed between the lateral flow membrane and the absorption layer) with a corresponding alignment mark on the absorption layer and/or the lateral flow membrane.

10 In some embodiments, the method further comprises providing one or more spacer layer(s) and assembling the spacer layer(s) with the other components of the assay device to form the stack. A central space formed in the spacer layer(s) may be aligned with the alignment hole, slot or recess of the mask layer, and with the central space of other spacer layer(s) if present.

15 In some embodiments, the mask layer is assembled with the spacer layer(s) prior to addition of the detector, the lateral flow membrane and the emitter.

20 The method may further comprise inserting the stack into a housing. In some embodiments the housing comprises one or more projections therein, and the stack is positioned in the housing such that the projections are received within locating holes and/or recesses provided in the mask and/or spacer layers of the stack.

BRIEF DESCRIPTION OF THE DRAWINGS

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Embodiments of the invention are further described hereinafter with reference to the accompanying drawings, in which:

Figure 1 is an illustration of an assay device;

30 Figure 2 is an illustration of an assay device according to an embodiment of the present invention;

Figure 3 is a stack of layers of the embodiment of Figure 2;

Figure 4 is an illustration of a third spacer layer of the stack of Figure 3;

35 Figure 5 is an illustration of a first or second spacer layer of the stack of Figure 3;

Figure 6A and 6B are an illustration of a mask layer of the stack of Figure 3;

Figure 7 is an illustration of an assay device according to an embodiment of the present invention;

Figure 8 shows a communications module for an assay device according to an embodiment of the present invention.

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DETAILED DESCRIPTION

Our patent application WO2015/121672 discloses assay devices of the general configuration shown in Figure 1. The assay device 20 takes the form of a cartridge for insertion into a cartridge reader and comprises a sample pad 6, in fluid communication with a conjugate pad 5. The conjugate pad 5 contains particle tags which are capable of binding to an assay component. A lateral flow membrane 4 is connected between the conjugate pad 5 and a wicking pad 7. When a sample is deposited on the sample pad 6, a reservoir of excess sample is formed. The excess sample migrates to the conjugate pad 5. This migration is first caused by the conjugate pad 5, then the wicking action of the lateral flow membrane 4 and then additionally the wicking pad 7. In the example shown, the lateral flow membrane 4 is formed from nitrocellulose. The conjugate pad 5 contains analyte tags. The analyte tags bind to the corresponding available analyte. Capillary action causes the liquid sample, containing any tagged analyte, to flow down the lateral flow membrane 4 from the conjugate pad 5 into the testing area 19 towards the wicking pad 7. Before the sample reaches the wicking pad 7, it encounters a reaction line 8 containing fixed receptors for the analyte. When the tagged analyte reaches this point, the receptors bind to the analyte, holding the analyte and the tags in place. The presence of the coloured analyte tag will cause the reaction line 8 to change colour as the concentration of the tags increases. In the presently described example, the concentration of the coloured tags is a direct indicator of the concentration of analyte at the reaction line which provides an indication of the concentration of the analyte in the liquid sample.

The above is an example of a sandwich assay technique. A competitive assay is also possible in which the intensity of the response from the reaction line 12 (usually a colour) is inversely proportional to the amount of analyte present in the sample. In one example of this technique, the conjugate pad 5 additionally contains a pre-tagged second analyte or analyte analogue. The analyte from the sample passes unchanged through the conjugate pad 5, and will bind to the receptors on a further reaction line 12, occupying receptor sites to which the pre-tagged analytes or analyte analogues would

otherwise bind. The less analyte there is in the sample, the more pre-tagged analyte or analyte analogue is able to bind to the receptors, resulting in a stronger colouring of the line. In a further example of this technique, the conjugate pad 5 could also or instead contain a tagged receptor. In this case fixed analyte or analyte analogue is immobilised on a reaction line. The more analyte present in the sample, the more of the tagged receptor that will bind to the analyte from the sample, and so not be available to bind to the fixed analyte or analyte analogue. The competitive assay technique may be used to qualitatively test for the absence of a particular analyte, though is not a purely binary test, and a very small amount of analyte in the sample is still likely to result in binding of the pre-tagged molecule (be that analyte, analyte analogue or receptor) at the position of the line. The competitive assay technique may instead be used to quantitatively indicate the concentration of a particular analyte in the liquid sample.

There is also a further line 13 of control receptors on the lateral flow membrane 4 which react with the tagged component itself. The control line 13 contains immobilised receptors which bind to the tagged component. The control line 13 should become coloured whenever the test is carried out, regardless of whether the sample contains any analyte. This helps confirm the test is performing correctly. In the presently described example, the reaction line 8 only changes colour when the analyte is present in the sample. In embodiments with multiple assays, there may be multiple control lines. In this way, the control lines can be used to determine whether each test to be performed by the lateral flow device has been performed. The control line 13 in the current example is provided downstream of the earlier reaction lines. By providing the control line 13 downstream of the reaction lines, the analyte tag must flow through the other reaction lines before they can bind to the control line indicating that a test has been carried out.

In the present case, the lateral flow membrane 4 is approximately 100µm thick and the reaction lines 8, 12 and control line 13 are each 1.0mm x 3.0mm with a 2.0mm gap between them. The lateral flow membrane is formed from nitrocellulose. The sample pad 6, conjugate pad 5, lateral flow membrane 4 and wicking pad 7 are provided on a transparent substrate 11.

A reference line 14 is provided on the lateral flow membrane 4 and is used for alignment during construction of the testing area 19. The reference line 14 is typically thinner than the reaction lines 8, 12 or control line 13. The reference line in the current example is 0.5mm x 5.0mm with a 1.5mm gap between the control line 13.

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A range of different tags and receptor lines can be used to determine the presence, absence, or concentration of multiple different analytes. The presence of some analytes may be tested in combination with the absence of different, or the same, analytes. Tests for example assays are described in WO2015/121672. Example labelling particles include gold nano-particles, coloured latex particles, or fluorescent labels.

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Whilst common household assay tests, such as some pregnancy tests, have an apparently binary result and require a user to manually interpret the results, the present device uses an Organic Light Emitting Diode (OLED) and opposed Organic Photo Diode (OPD) to measure the light absorption as a result of the analyte test. Whilst the presently described example uses the absorption of light by a substance to indicate the concentration of an analyte in a test sample, embodiments can equally be envisaged where the tag on the analyte is luminescent and emits light itself, either as a result of fluorescence, phosphorescence, or as a result of a chemical or electrochemical reaction.

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The OLED illuminates the sample with light having known characteristics (intensity, wavelength, etc). When light is received by the OPD, a current is generated. By measuring this current, the light absorbed by the immobilised labels at the reaction line, 8, 12 and surrounding membrane can be determined. This gives an indication of the concentration of tagged analyte present in the sample.

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The OLED is a layered structure sitting on a plastic substrate (PET). The OLED is formed from a layer of patterned ITO (indium tin oxide, which is conductive and transparent), a layer of hole injection material, a layer of active material, and a cathode. It is possible to maximize the forward emission of the device by tuning the thicknesses of the ITO and more importantly the active material and cathode. With such modifications in the stack geometry the amount of light being emitted perpendicular to the device can be maximised. This will mean that a larger proportion of light emitted by

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the OLED passes through the membrane, and impinges onto the OPD. In the present example, the OLED 2 contains emission regions 9, 16, 18, provided opposite the organic photovoltaic cell (OPD) 3, containing detection regions 10, 15, 17. The emission light colour of all three regions in the present example is green, as they are formed from a layer of the same material. Similarly, in the present example, the material of the OPD regions 10, 15, 17 is optimised to detect green light.

The OLED emission regions 9, 16, 18 and OPD detection regions 10, 15, 17 are sized to sit within the footprint of the reaction lines 8, 13, 14 containing bound receptors set up to catch and bind the tagged analyte (be that pre-tagged or otherwise). In the present case, this results in pixels 0.5mm x 2.0mm. Another factor which improves the proportion of the emitted light that can interact with the membrane and tagged analyte is the proximity of both the OLED and the OPD to the lateral flow membrane 4.

Figure 2 shows schematically a configuration of a OLED 9, lateral flow membrane 4 and OPD 10 in an assay device according to an embodiment of the present invention. In accordance with this embodiment, the OLED 9, reaction line 8 of the lateral flow membrane 4 and the OPD 10 are aligned along an optical axis. A mask layer 22 is interposed between the lateral flow membrane 4 and the OPD 10. The mask layer 22 is opaque to light, but has defined therein an aperture which is aligned with the optical axis of the OLED 9, reaction line 8 and OPD 10. As shown in Figure 2, the lateral flow membrane 4 is spaced from the mask layer 22 by a first spacing G1. The OPD 10 is spaced from the mask layer 22 by a second spacing G2 and the OLED is spaced from the lateral flow membrane 4 by a third spacing G3. The first spacing G1 and the second spacing G2 are selected relative to the size of the aperture so that only light from the OLED 9 passing through the reaction line 8 impinges on the OPD 10 (as indicated by rays A in Figure 2), whereas light from outside the region of the reaction line 8 (stray light) is directed outside of area of the OPD 10 (as indicated by rays B in Figure 2). In effect, the aperture acts as a pinhole camera to image the reaction line 8 onto the OPD 10. In this way, the amount of light transmitted through the reaction line 8 that reaches the OPD 10 can be maximised, while avoiding the OPD 10 being illuminated by stray light from outside the reaction line 8.

In the embodiment of Figure 2, the reaction line 8 has a width of 1mm and a length of 3mm, the aperture in the mask layer 22 has a width of 0.5mm and a length of 1.5mm

and the OPD pixel 10 has a width of 0.5mm and a length of 1.5mm. The first spacing G1 is in the range 100 microns to 300 microns, but can be in the range 50 microns to 500 microns or even in the range 10 microns to 1,000 microns. The second spacing G2 is in the range 100 microns to 300 microns, but can be in the range 50 microns to 500 microns or even in the range 10 microns to 1,000 microns. The third spacing G3 is in the range 1.3mm to 2mm, but can be in the range 1mm to 3mm or even in the range 100 microns to 5mm. The spacings G1, G2 and G3 and the aperture size may be optimised to maximise the signal level and minimise the stray light level at the OPD 10 for a given OPD pixel size and size of reaction line 8.

Figure 3 shows schematically a layer structure of an assay device according to an embodiment of the invention. The layer structure shown in Figure 3 enables the spacings G1, G2 and G3 described in relation to Figure 2 to be achieved accurately and consistently. The layers shown in Figure 2 form a stack comprising an OPD layer 3, a second spacer layer 21, a mask layer 22 as described above in relation to Figure 2, a first spacer layer 23, the lateral flow membrane 4, a third spacer layer 24 and the OLED layer 2.

Figure 4 shows in plan view the configuration of the third spacer layer 24. The third spacer layer defines a central space 25 which accommodates and locates the lateral flow membrane 4. The third spacer layer 24 has defined therein two locating holes 26, which locate the third spacer layer 24 on projecting bosses in a plastics housing for the assay device (not shown). At the edge of the third spacer layer 24 are defined four locating recesses 27 which further locate the third spacer layer 24 on corresponding projections in the plastics housing.

Figure 5 shows in plan view the configuration of the first and second spacer layers 23, 21, which each have the same configuration. The first and second spacer layers define a central frame 28 which allows the passage of light through the middle of the first and second spacer layers 23, 21. The first and second spacer layers 23, 21 have defined therein two locating holes 26, which locate the first and second spacer layers 23, 21 on projecting bosses in a plastics housing for the assay device (not shown), in the same manner as the third spacer layer 24. At the edge of the first and second spacer layers 23, 21 are defined four locating recesses 27 which further locate the first and second spacer layers 23, 21 on corresponding projections in the plastics housing.

Figures 6A and 6B show in plan view the configuration of the mask layer 22. Figure 6B is an enlarged view of a portion of the mask layer 22. Like the first and second spacer layers 23, 21 and the third spacer layer 24, the mask layer 22 has defined therein two locating holes 26, which locate the mask layer 22 on projecting bosses in a plastics housing for the assay device (not shown). At the edge of the mask layer 22 are defined four locating recesses 27 which further locate the mask layer 22 on corresponding projections in the plastics housing. In addition, the mask layer 22 has defined therein a 3 X 7 array of 21 apertures 30, each of which corresponds to the aperture described in relation to Figure 2 and is aligned with a respective OPD pixel 10 of the OPD layer 3 in the assembled stack. At the corners of the array of apertures 30, there are defined in the mask layer 22 four square alignment holes 31. The alignment holes 31 are located on the mask layer 22 within the rectangle defined by the central frame 28 of the first and second spacer layers 23, 21 and the corresponding central rectangular space 25 of the third spacer layer 24. The location of the alignment holes 31 relative to the central frame 28 of the first and second spacer layers 23, 21 and the central space 25 of the third spacer layer 24 allows a portion of the underlying OPD layer 3 defined by the alignment holes 31 to be viewed through the first and second spacer layers 23, 21, third spacer layer 24 and mask layer 22 in a partially assembled stack. The OPD layer 3 is provided with alignment marks printed on its surface in the same process as the printing of the active layers of the OPD layer 3. The OPD layer 3 is aligned with the mask layer 22 during assembly of the stack by aligning the alignment marks on the OPD layer 3 with the alignment holes 31 in the mask layer 22. When the alignment marks are aligned with the alignment holes 31, the alignment of OPD pixels 10 of the OPD layer 3 with the array of apertures 30 in the mask layer is ensured.

At one end of the array of apertures 30, there is defined in the mask layer 22 an alignment slot 32. The alignment slot 32 is located on the mask layer 22 within the rectangle defined by the central frame 28 of the first and second spacer layers 23, 21. The location of the alignment slot 32 relative to the central frame 28 of the first and second spacer layers 23, 21 allows a portion of the underlying lateral flow membrane 4 defined by the alignment slot 32 to be viewed through the first and second spacer layers 23, 21 and the mask layer 22 in a partially assembled stack. The lateral flow membrane 4 is provided with an alignment line printed on its surface in the same process as the application of the test regions 8 to the lateral flow membrane 4. The

mask layer 22 is aligned with the lateral flow membrane 4 during assembly of the stack by aligning the alignment line on the lateral flow membrane 4 with the alignment slot 32 in the mask layer 22. When the alignment line is aligned with the alignment slot 32, the alignment of the test regions 8 of the lateral flow membrane 4 with the array of apertures 30 in the mask layer is ensured.

With the described layer structure, the lateral flow membrane 4 may take the form of three parallel strips of membrane material, each strip aligned with one of the three rows of seven apertures 30 in the mask layer 22. In this way, three distinct assays can be carried out in parallel by the assay device, with each of the three strips having receptors for the respective assay.

The mask layer 22, first and second spacer layers 23, 21 and third spacer layer 24 are each formed of paper, in particular black paper, with the thickness of the layer determined by the weight of the paper. Thus, in this embodiment, the material of the mask layer 22 has a weight of 100 gsm and a nominal thickness of 120 microns, the material of the first and second spacer layers 23, 21 has a weight of 130 gsm and a nominal thickness of 180 microns and the material of the third spacer layer 24 has a weight of 540 gsm and a nominal thickness of 600 microns. The selection of the respective weights and thicknesses for the paper layers provides the required optical geometry described in relation to Figure 2. The black paper blocks any stray light to maximise the separation between the signals detected at each OPD pixel 10. The required shape of each of the mask layer 22, first and second spacer layers 23, 21 and third spacer layer 24 is achieved by laser cutting or die cutting the shape from a supply of paper of the appropriate weight and thickness. The mask layer 22, first and second spacer layers 23, 21 and third spacer layer 24 can alternatively be formed of opaque plastics material or metal foil.

Figure 7 shows an assay device according to an embodiment of the invention. The assay device comprises a plastics housing 40, which houses the OLED layer 2, the OPD layer 3 and the stack of the mask layer 22, first and second spacer layers 23, 21 and the third spacer layer 24. At one end of the housing the stack of the stack of the mask layer 22, first and second spacer layers 23, 21 and the third spacer layer 24 extends beyond the end of the housing 40 to form an electrical connector 42. Electrical conductors 44 extend from each of the OLED layer 2 and the OPD layer 3 to form the

electrical connector 42. The electrical connector 42 allows the assay device to be connected to a communications module 50 (described below) which supplies electrical power to the OLED layer 2 and the OPD layer 3 via the electrical conductors 44. In this way, the OLED layer 2 and the OPD layer 3 can be powered without requiring a battery within the housing 40. This significantly improves the disposability of the assay device. The electrical conductors 44 may take the form of printed tracks or the like.

Figure 8 shows the communications module 50 for connection to the assay device with the assay device 40 inserted in communications module 50. The communications module 50 comprises an electrical connection circuit board 52 which connects to the electrical connector 42 of the assay device when the assay device is inserted in the communications module. The communications module 50 also includes a data communication circuit board 54 which is in data communication with the electrical connection circuit board 52 and is configured to communicate readings from the assay device to a remote computer or smartphone, for example by Bluetooth® communication. Also shown clearly in Figure 8 is the analyte hole 46 in the housing 40, through which the analyte is applied to the lateral flow membrane 4.

In summary, an assay device for the quantitative determination of the concentration of at least one analyte in a liquid sample comprises a planar emitter 2, a planar detector 3 and a lateral flow membrane interposed between the emitter and the detector. The lateral flow membrane comprises at least one test region 8 for retaining tagging particles in the test region in dependence on the concentration of the analyte in the material and the emission layer is arranged to illuminate the test region. The detector comprises an absorption layer 10 of an organic photovoltaic material and the absorption layer is arranged to detect light from the test region. The device further comprises a mask layer 22 interposed between the lateral flow membrane and the absorption layer, the mask layer 22 having defined therein an aperture 30 configured to direct light from the test region onto the absorption layer.

Throughout the description and claims of this specification, the words “comprise” and “contain” and variations of them mean “including but not limited to”, and they are not intended to (and do not) exclude other moieties, additives, components, integers or steps. Throughout the description and claims of this specification, the singular encompasses the plural unless the context otherwise requires. In particular, where the

indefinite article is used, the specification is to be understood as contemplating plurality as well as singularity, unless the context requires otherwise.

5 Features, integers, characteristics, compounds, chemical moieties or groups described
in conjunction with a particular aspect, embodiment or example of the invention are to
be understood to be applicable to any other aspect, embodiment or example described
herein unless incompatible therewith. All of the features disclosed in this specification
(including any accompanying claims, abstract and drawings), and/or all of the steps of
any method or process so disclosed, may be combined in any combination, except
10 combinations where at least some of such features and/or steps are mutually
exclusive.

CLAIMS

1. An assay device for the quantitative determination of the concentration of at least one analyte in a liquid sample, the device comprising:
- 5 a planar emitter;
a planar detector;
a lateral flow membrane interposed between the emitter and the detector;
wherein the lateral flow membrane comprises at least one test region for retaining tagging particles in the test region in dependence on the concentration of the
- 10 analyte in the liquid sample,
wherein the emitter comprises an emission layer of an organic electroluminescent material and the emission layer is arranged to illuminate the test region, and
wherein the detector comprises an absorption layer of an organic photovoltaic
- 15 material and the absorption layer is arranged to detect light from the test region,
wherein the device further comprises a mask layer interposed between the lateral flow membrane and the absorption layer, the mask layer having defined therein an aperture configured to direct light from the test region onto the absorption layer.
- 20 2. An assay device as claimed in claim 1 further comprising at least one spacer layer interposed between the absorption layer and the mask layer, between the lateral flow membrane and the mask layer and/or between the emission layer and the lateral flow membrane.
- 25 3. An assay device as claimed claim 2, wherein the spacer layer is interposed between the lateral flow membrane and the mask layer, the spacer layer having a thickness selected to maintain a required spacing between the mask layer and the lateral flow membrane.
- 30 4. An assay device as claimed in claim 2 or claim 3, wherein a spacer layer is interposed between the emission layer and the lateral flow membrane, the spacer layer having a thickness selected to maintain a required spacing between the emission layer and the lateral flow membrane.

5. An assay device as claimed in any one of claims 2 to 4, wherein a spacer layer is interposed between the absorption layer and the mask layer, the spacer layer having a thickness selected to maintain a required spacing between the absorption layer and the mask layer.

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6. An assay device as claimed in any preceding claim, wherein the layer(s) between the lateral flow membrane and the absorption layer comprise alignment holes through which markings on the lateral flow membrane and/or the absorption layer can be viewed to align the lateral flow membrane and/or the absorption layer during assembly of the assay device.

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7. An assay device as claimed in any preceding claim, wherein the mask layer and/or the spacer layer(s) is formed of paper, in particular black paper, opaque plastics material or metal foil.

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8. An assay device as claimed in any preceding claim, wherein the aperture is configured to direct light from the test region onto an area of the absorption layer corresponding substantially to the pixel.

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9. An assay device as claimed in claim 7, wherein the pixel, the aperture, the test region and the emission layer are aligned along a common optical axis.

10. An assay device as claimed in any preceding claim, wherein the planar emitter, planar detector, lateral flow membrane, mask layer and, optionally, the spacer layer(s) are arranged as a stack.

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11. An assay device as claimed in claim 10, wherein each layer of the stack is in direct contact with the adjacent layer(s).

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12. An assay device as claimed in claim 10 or 11, further comprising a housing, wherein the stack is received within the housing and a portion of the stack extends outside of the housing, said portion forming a connector for connection to an external device.

13. An assay device as claimed in claim 12, wherein the mask layer and/or one or more of the spacer layer(s) comprises one or more holes, slots or recesses which locate the layer(s) on corresponding projections formed in the housing.

5 14. An assay device as claimed in any preceding claim, wherein the mask layer comprises a plurality of apertures arranged in an array.

10 15. An assay device as claimed in claim 14, wherein the assay devices comprises two or more lateral flow membranes arranged in parallel, and each membrane is aligned with a row of apertures in the mask layer.

16. An assay system comprising an assay device according to any one of claims 1 to 15 and a communications module.

15 17. A method of manufacturing an assay device, the method comprising:
providing a planar emitter comprising an emission layer, a planar detector comprising an absorption layer, a lateral flow membrane and a mask layer having an aperture therein; and
assembling the planar emitter, the planar detector, the lateral flow membrane
20 and the mask layer to form a stack in which the lateral flow membrane is interposed between the emitter and the detector, and the mask layer is interposed between the lateral flow membrane and the absorption layer.

25 18. The method according to claim 17, wherein assembling the stack comprises aligning an alignment hole, slot or recess provided in the mask layer, and in any other layers interposed between the lateral flow membrane and the absorption layer, with a corresponding alignment mark on the absorption layer and/or the lateral flow membrane.

30 19. The method according to claim 17 or 18, further comprising providing one or more spacer layer(s) and assembling the spacer layer(s) with the other components of the assay device to form the stack.

35 20. The method according to any one of claims 17 to 19, the method further comprising inserting the stack into a housing, wherein the housing comprises one or

more projections therein, and the method comprises positioning the stack in the housing such that the projections are received within locating holes and/or recesses provided in the mask and/or spacer layers of the stack.

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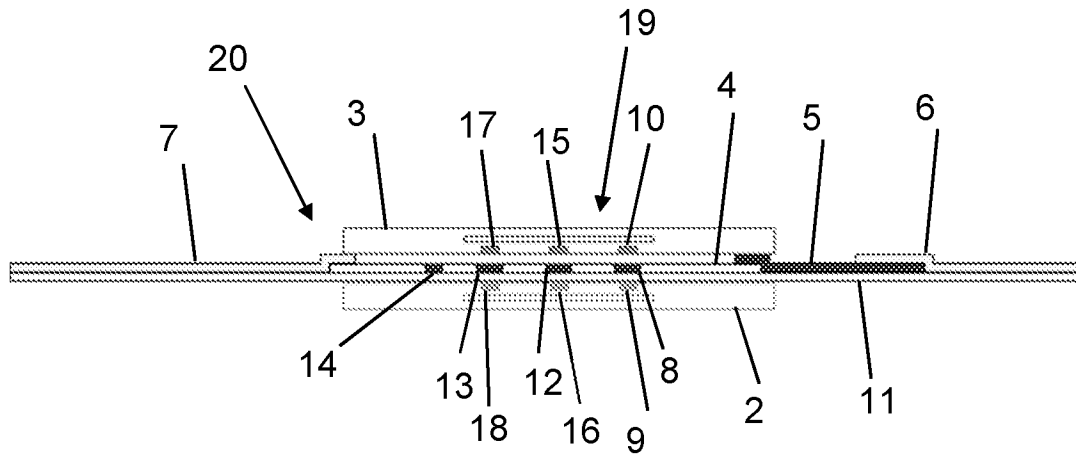


FIG. 1

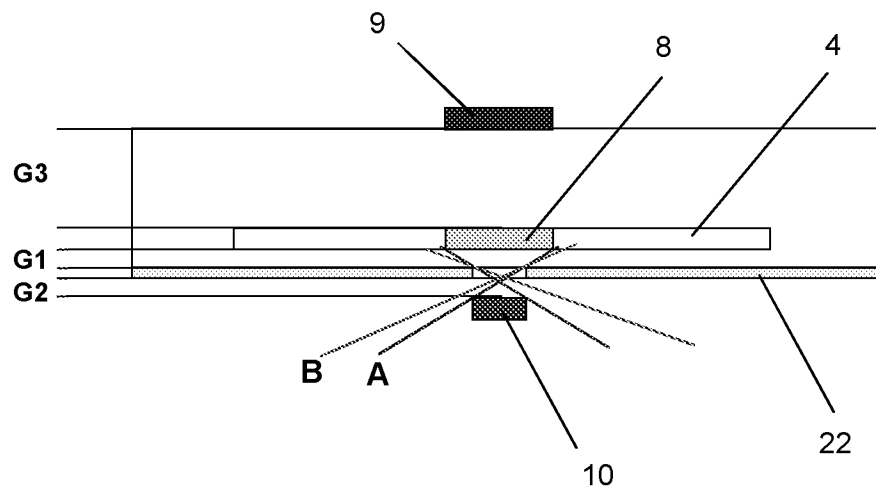


FIG. 2

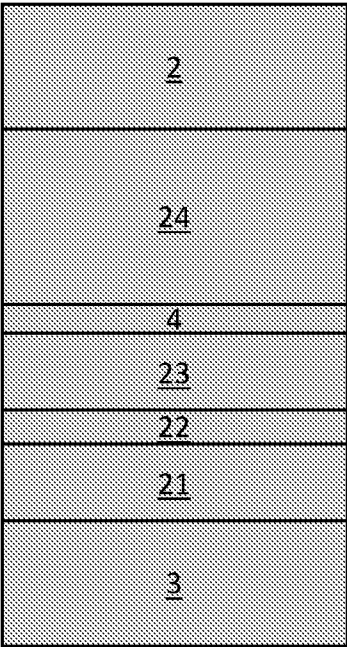


FIG. 3

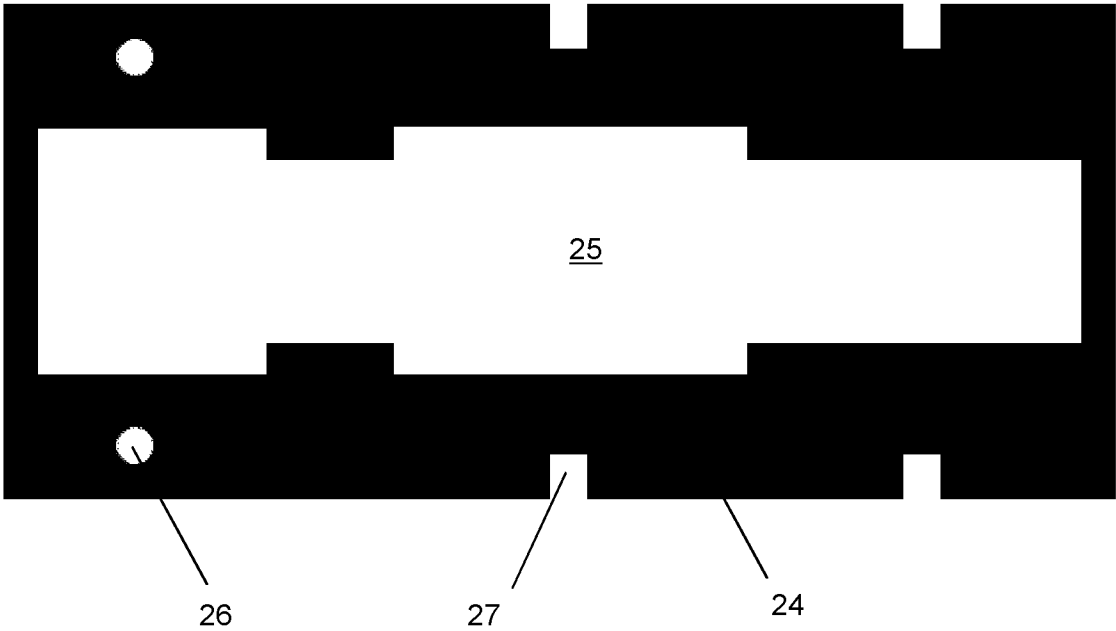


FIG. 4

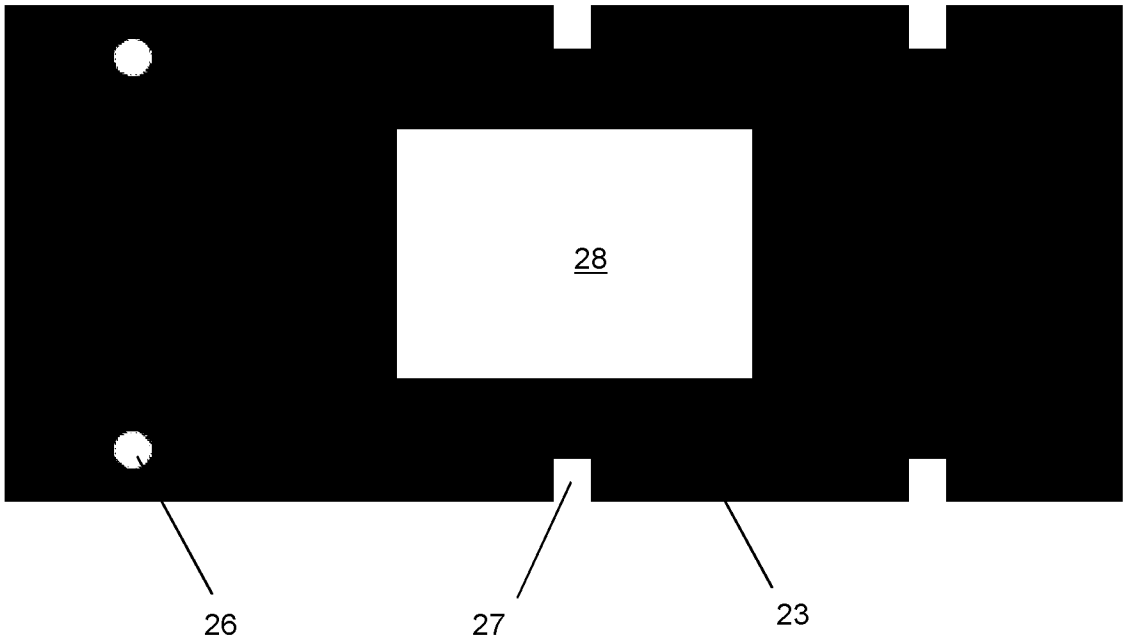


FIG. 5

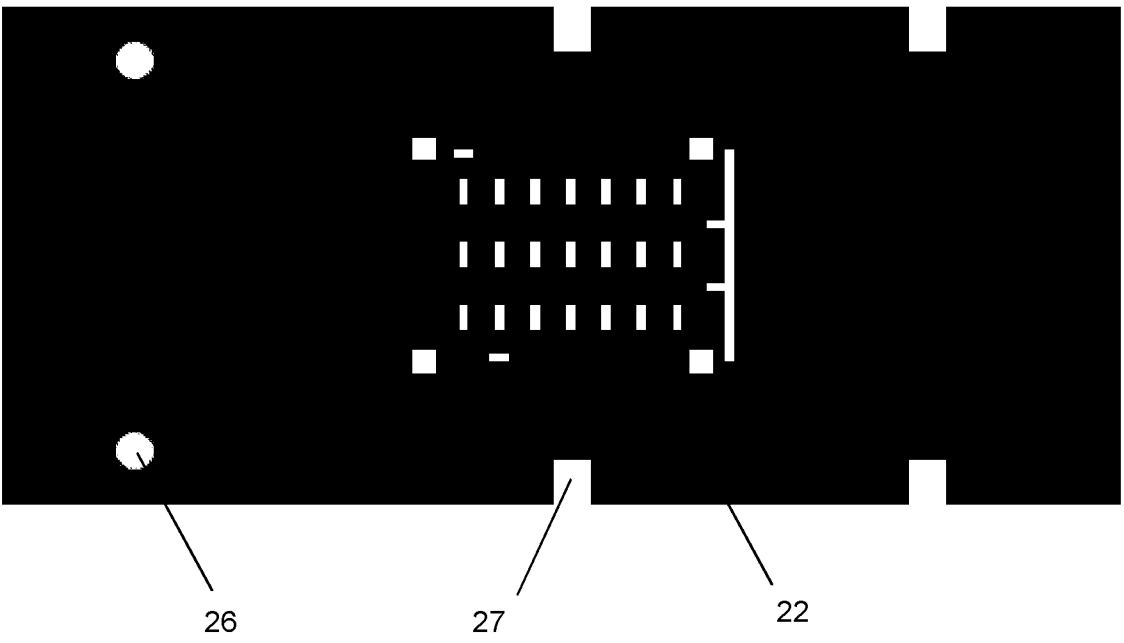


FIG. 6A

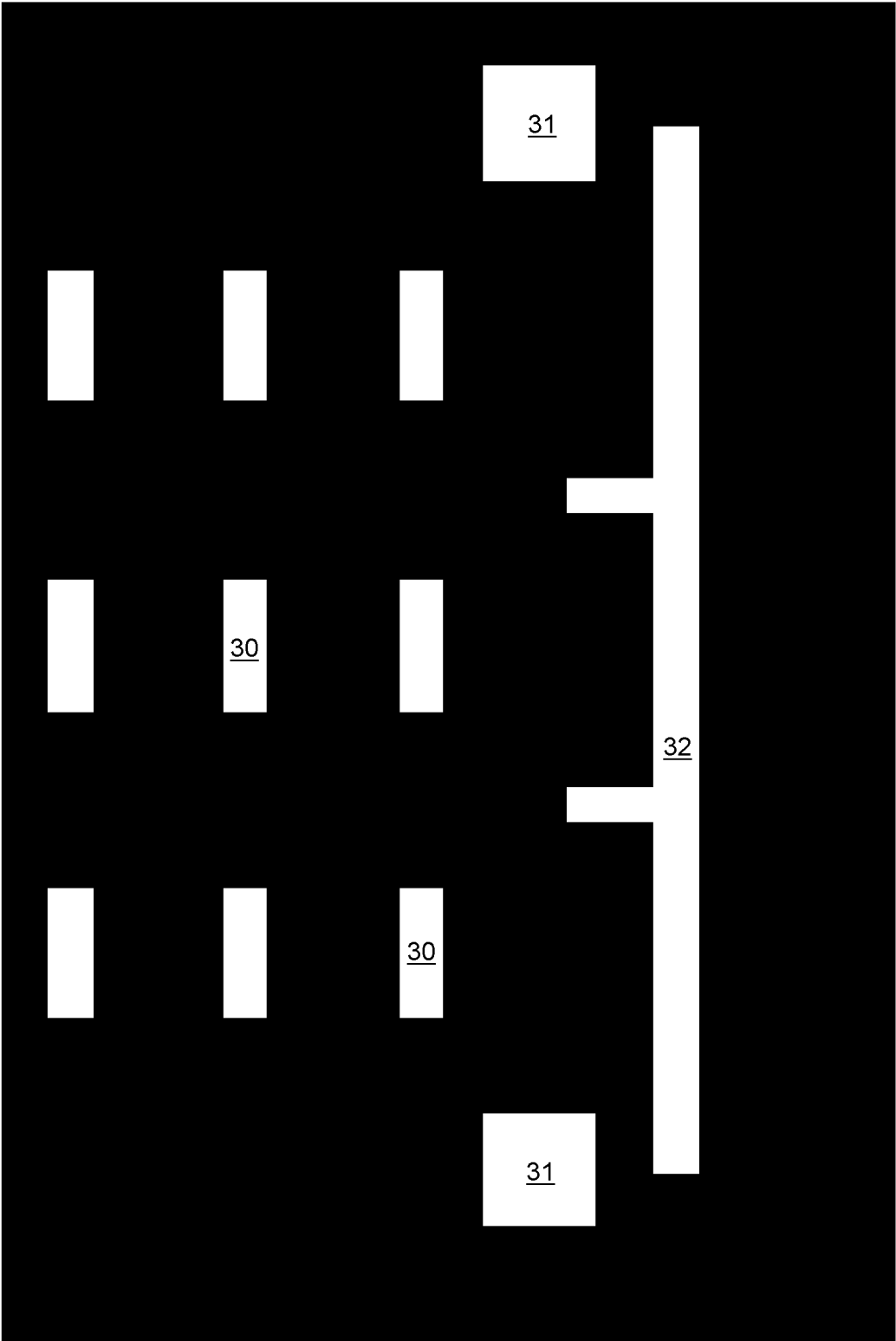


FIG. 6B

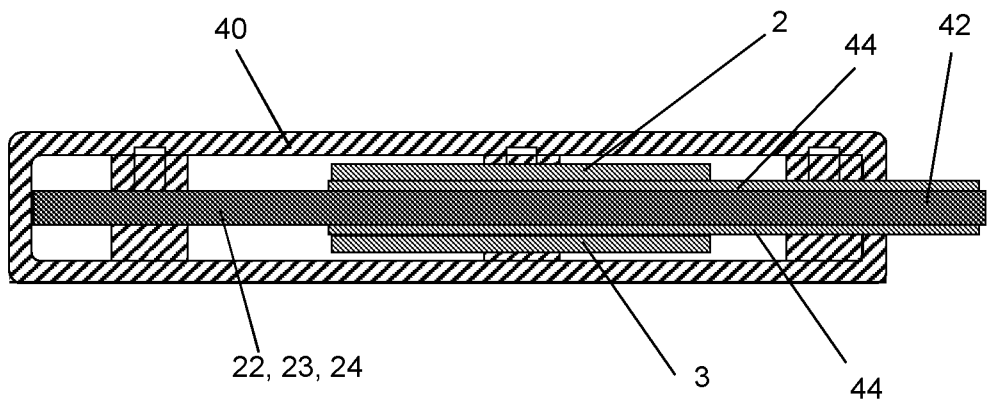


FIG. 7

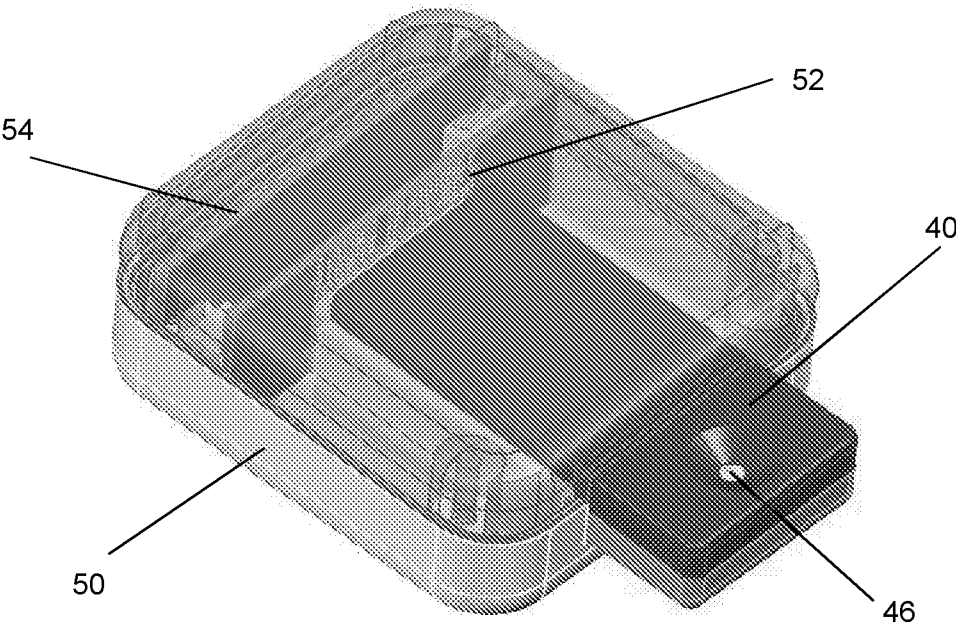


FIG. 8

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2017/051447

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N33/543
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, BIOSIS

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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X,P	WO 2017/029523 A1 (MOLECULAR VISION LTD [GB]; CAMBRIDGE DISPLAY TECH [GB]) 23 February 2017 (2017-02-23) paragraphs [0071], [0082], [0083]; figure 5; example 1	1-20
Y,P	WO 2017/029524 A1 (MOLECULAR VISION LTD [GB]; CAMBRIDGE DISPLAY TECH [GB]) 23 February 2017 (2017-02-23) claims	1-20
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	-/--	



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

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"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

18 August 2017

Date of mailing of the international search report

04/09/2017

Name and mailing address of the ISA/

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Authorized officer

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INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2017/051447

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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Information on patent family members

International application No

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