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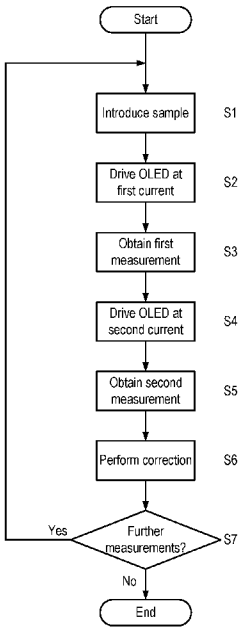

Fig.11

(57) Abstract: An assay device is described for determining the presence and/or concentration of a target analyte within a liquid transport path having a first end, a second end and a sample receiving portion proximate to the first end. The liquid transport path is configured to transport a liquid sample received in the sample receiving portion towards the second end. The assay device includes one or more organic light emitting diodes configured to illuminate a section of the liquid transport path located between the sample receiving portion and the second end. Each organic light emitting diode includes a first light emitting material which emits light centred around a first wavelength and a second light emitting material which emits light centred around a second wavelength. A ratio of emission intensity between the first and second light emitting materials varies in dependence upon a driving current supplied to the organic light emitting diode. The assay device also includes one or more photodetectors configured to receive light from the section of the liquid transport path illuminated by the organic light emitting diode. The assay device also includes a controller configured to drive the organic light emitting diode at a first driving current and obtain a first absorbance value based on the photodetector signal. The controller is also configured to drive the organic light emitting diode at a second driving current and obtain a second absorbance value based on the photodetector signal. The controller is also configured to determine the presence and/or concentration of a target analyte within the liquid transport path in dependence on a difference of the first and second absorbance values.

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BIOASSAY DEVICE WITH OLED LIGHT SOURCE

Field of the invention

The present invention relates to an assay device.

Background

Biological testing for the presence and/or concentration of an analyte may be conducted for a variety of reasons including, amongst other applications, preliminary diagnosis, screening samples for presence of controlled substances and management of long term health conditions.

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

In a typical lateral flow testing strip, a liquid sample is introduced at one end of a porous strip which is then drawn along the strip by capillary action (or "wicking"). A portion of the lateral flow strip is pre-treated with labelling particles which are activated with a reagent which binds to the analyte to form a complex, if the analyte is present in the sample. The bound complexes and also unreacted labelling particles continue to propagate along the strip before reaching a testing region which is pre-treated with an immobilised binding reagent which binds bound complexes of analyte and labelling particles and does not bind unreacted labelling particles. The labelling particles have a distinctive colour, or other detectable optical or non-optical property, and the development of a concentration of labelling particles in the test regions provides an observable indication that the analyte has been detected. Lateral flow test strips may be based on, for example, colorimetric labelling using gold or latex nanoparticles, fluorescent marker molecules or magnetic labelling particles.

Another variety of biological testing involves assays conducted in a microfluidic device, or one or more channels thereof. Liquid assays may be measured based on colorimetry or fluorescence. An advantage of some liquid based assays is that they may allow tests

to be conducted using very small (e.g. picolitre) volumes. Some immunoassays may be conducted in a microfluidic device.

Sometimes, merely determining the presence or absence of an analyte is desired, i.e. a qualitative test. In other applications, an accurate concentration of the analyte may be desired, i.e. a quantitative test. For example, WO 2008/101732 A1 describes an optical measuring instrument and measuring device. The optical measuring instrument includes at least one source for providing at least one electromagnetic beam to irradiate a sample and to interact with the specimen within the sample, at least one sensor for detecting an output of the interaction between the specimen and the electromagnetic beam, an integrally formed mechanical bench for the optical and electronic components and a sample holder for holding the sample. The at least one source, the at least one sensor, and the mechanical bench are integrated in one monolithic optoelectronic module and the sample holder can be connected to this module.

Quantitative detectors for biological testing methods may require optical components such as beamsplitters, lenses, monochromators, filters etc. Such components may be complex, expensive and/or bulky, and may have properties which vary considerably with the wavelength of light.

Summary

According to a first aspect of the invention there is provided an assay device for determining the presence and/or concentration of a target analyte within a liquid transport path having a first end, a second end and a sample receiving portion proximate to the first end. The liquid transport path is configured to transport a liquid sample received in the sample receiving portion towards the second end. The assay device includes one or more organic light emitting diodes configured to illuminate a section of the liquid transport path located between the sample receiving portion and the second end. Each organic light emitting diode includes a first light emitting material which emits light centred around a first wavelength and a second light emitting material which emits light centred around a second wavelength. A ratio of emission intensity between the first and second light emitting materials varies in dependence upon a driving current supplied to the organic light emitting diode. The assay device also includes one or more photodetectors configured to receive light from the section of the liquid transport path illuminated by the organic light emitting diode. The assay device also includes a controller configured to drive the organic light emitting diode at a first driving current and obtain a first absorbance value based on the photodetector signal. The controller is also configured to drive the organic light emitting diode at a second driving current and obtain a second absorbance value based on the photodetector signal. The controller is also configured to determine the presence and/or concentration of a target analyte within the liquid transport path in dependence on a difference of the first and second absorbance values.

The first wavelength may correspond to a peak emission wavelength of the first light emitting material. The second wavelength may correspond to a peak emission wavelength of the second light emitting material. Each of the first and/or second light emitting materials may emit light within a range having a full-width at half maximum of no more than 10 nm, no more than 25 nm, no more than 50 nm, no more than 100 nm, no more than 200 nm, or no more than 300 nm.

The difference of the first and second absorbance values may be a weighted difference.

An optical path between the one or more organic light emitting diodes and the one or more photodetectors may include no monochromator(s). The optical path may include no beamsplitter(s) between the one or more organic light emitting diodes and the one or more photodetectors. The optical path may include no fibre couplers and/or fibre

splitters between the one or more organic light emitting diodes and the one or more photodetectors.

The photodetector(s) may take the form of photodiodes, photoresistors, phototransistors, complementary metal-oxide semiconductor (CMOS) pixels, charge coupled device (CCD) pixels, photomultiplier tubes or any other suitable photodetector. The photodetector(s) may take the form of organic photodiodes. Organic photodiodes may be solution processed.

The assay device may include a plurality of photodetectors arranged in an array. The array may include more photodetectors in a first direction than in a second, perpendicular direction.

A slit or aperture may be included in the optical path between the one or more organic light emitting diodes and the illuminated section of the liquid transport path. A slit or aperture may be included in the optical path between the illuminated section of the liquid transport path and the one or more photodetectors. Each slit may have adjustable width. Each slit may have a width of greater than or equal to 1 mm. Each slit may have a width between 100 μm and 1 mm inclusive. Each slit may have a width between 300 μm and 500 μm inclusive.

A diffuser may be included in the optical path between the one or more organic light emitting diodes and the illuminated section of the liquid transport path. A diffuser may be included in the optical path between the illuminated section of the liquid transport path and the one or more photodetectors.

The first and second light emitting materials may be comprised within a single layer of each organic light emitting diode.

The first light emitting material and the second light emitting material may be comprised within different layers of each organic light emitting diode. The first or second light emitting material may be comprised within a light emitting layer and the other light emitting material may be comprised in a different layer of each organic light emitting diode.

The assay device may be configured to perform an immunoassay test.

The first wavelength may be absorbed by the target analyte or by a label substance bound to the target analyte, and the second wavelength may be substantially not absorbed by the target analyte or the label substance bound to the target analyte.

The label substance may include labelling particles, labelling dyes and so forth. The label substance may be gold nanoparticles. The first and second wavelengths may be selected in dependence upon the absorbance spectrum of the target analyte or labelling substance. The first and second wavelengths may be selected such that the target analyte or labelling substance has relatively higher absorbance at the first wavelength than at the second wavelength. The first and second wavelengths may be selected such that the target analyte or labelling substance has relatively higher absorbance at the second wavelength than at the first wavelength. The ratio of target analyte absorbance at the first and second wavelengths may be at least two, up to and including five, up to and including ten or more than ten.

The first and second wavelengths may lie in the range between 300 nm and 1500 nm inclusive. The first and second wavelengths may lie in the range between 400 nm and 800 nm inclusive.

The liquid transport path may comprise a porous strip. The porous strip may be a lateral flow test strip. The porous strip may include nitrocellulose or other fibrous materials capable of transporting an aqueous liquid by capillary action, whether inherently or following appropriate surface treatments.

The liquid transport path may comprise one or more microfluidic channels. The one or more microfluidic channels may form a part of a microfluidic device.

The photodetector may be configured to receive light transmitted through the liquid transport path. The photodetector may be configured to receive light reflected and/or scattered from the liquid transport path.

The one or more photodetectors may include a plurality of photodetectors arranged to form an image sensor, the image sensor configured to image all or a part of the section of the liquid transport path illuminated by the organic light emitting diode.

The assay device may further include an output device.

The output device may comprise one or more output light emitters. The controller may be configured to cause the one or more output light emitters to visually indicate the presence and/or concentration of the target analyte.

The output device may comprise a display. The controller may be configured to cause the display to visually indicate the presence and/or concentration of the target analyte.

The output device may comprise a wired or wireless communication interface. The controller may be configured to cause the communication interface to output an indication of the presence and/or concentration of the target analyte via the communication interface.

The assay device may include the liquid transport path.

The assay device may be configured to receive the liquid transport path.

According to a second aspect of the invention there is provided a method of using the assay device. The method includes applying a liquid sample to the sample receiving portion of the liquid transport path.

According to a third aspect of the invention there is provided a method of determining the presence and/or concentration of a target analyte within a liquid transport path having a first end, a second end and a sample receiving portion proximate to the first end. The liquid transport path is configured to transport a liquid sample received in the sample receiving portion towards the second end. The method includes driving one or more organic light emitting diodes at a first driving current. The one or more organic light emitting diodes being configured to illuminate a section of the liquid transport path located between the sample receiving portion and the second end. Each organic light emitting diode including a first light emitting material which emits light centred around a first wavelength and a second light emitting material which emits light centred around a second wavelength. A ratio of emission intensity between the first and second light emitting materials varies in dependence upon a driving current supplied to the organic light emitting diode. The method also includes obtaining a first absorbance value based on a photodetector signal received from one or more

photodetectors configured to receive light from the section of the liquid transport path illuminated by the one or more organic light emitting diodes. The method also includes driving the one or more organic light emitting diodes at a second driving current. The method also includes obtaining a second absorbance value based on the photodetector signal. The method also includes determining the presence and/or concentration of a target analyte within the liquid transport path in dependence on a difference of the first and second absorbance values.

The method may also include applying a liquid sample to a sample receiving portion of a liquid transport path.

Brief Description of the Drawings

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

Figure 1 illustrates an assay device;

Figure 2 illustrates schematic emission spectra of an organic light emitting diode at several different driving currents;

Figure 3 illustrates an example of an organic light emitting diode stack;

Figure 4 illustrates an example layer structure of an organic light emitting diode;

Figure 5 illustrates a lateral flow test strip;

Figure 6 illustrates the structure of a lateral flow test strip;

Figure 7 illustrates an absorbance spectrum of labelling particles used in a lateral flow test strip;

Figure 8 illustrates absorbance values corresponding to a first driving current;

Figure 9 illustrates absorbance values corresponding to a second driving current;

Figure 10 illustrates a difference of absorbance values corresponding to first and second driving currents;

Figure 11 is a process flow diagram of a method of using an assay device;

Figure 12 illustrates an assay device configured for measurements in a transmission geometry;

Figure 13 illustrates an assay device configured for measurements in a reflection geometry;

Figure 14 illustrates an assay device including an image sensor;

Figure 15 illustrates a self-contained lateral flow testing device;

Figures 16A and 16B illustrate a reading device for lateral flow test strips;

Figure 17 shows measured emission spectra from an exemplary organic light emitting diode at first and second driving currents;

Figure 18 shows the dependence of the ratio of emission intensities at first and second wavelengths as a function of drive current for the exemplary organic light emitting diode;

Figure 19 shows measured organic photodiode signals corresponding to different driving currents of an organic light emitting diode, as a function of position along a lateral flow test strip, and a difference between the organic photodiode signals.

Detailed Description of Certain Embodiments

If the number and complexity of optical components in a quantitative detector could be reduced, then the size and cost of the detector could be reduced. This would be of particular advantage for handheld or portable testing devices, and for single use home testing kits.

The minimum threshold for detecting an analyte may be improved if the signal to noise ratio of the measurement could be improved. Additionally, improvements in the signal to noise ratio may also allow for an analyte concentration to be determined with improved resolution.

Referring to Figure 1 an assay device 1 is shown.

The assay device 1 includes one or more organic light emitting diodes 3, one or more photodetectors 4, a controller 5 and one or more output devices 6. The assay device 1 may include an integrated liquid transport path 2. Alternatively, the assay device 1 may be configured to receive a separate liquid transport path 2 in the form of a lateral flow test strip 33 (Figure 5) or one or more channels of a microfluidic device (not shown). The liquid transport path 2 is configured to perform a colorimetric assay test such as, for example, an immunoassay test. The assay device 1 is configured to read the results of the colorimetric assay test using the pairing of one or more organic light emitting diodes 3 and one or more photodetectors 4.

The liquid transport path 2 has a first end 7, a second end 8 and a sample receiving portion 9 proximate to the first end 7. The liquid transport path 2 is configured to transport a liquid sample 10 received in the sample receiving portion 9 towards the second end 8. A flow front 11 separates a wet portion of the liquid transport path 2 from a dry portion. The flow front 11 moves towards the second end 8 in a flow direction 12.

The liquid transport path 2 transports the liquid sample 10 by wetting/capillary action. For example, the liquid transport path 2 may take the form of a porous medium such as, for example, a lateral flow test strip 33 (Figure 5). A porous medium forming the liquid transport path 2 may include nitrocellulose or other fibrous materials capable of transporting an aqueous liquid by capillary action, whether inherently or following appropriate surface treatments. Alternatively, the liquid transport path 2 may take the

form of one or more micro-fluidic channels of a micro-fluidic device. Micro-fluidic channels are sufficiently thin in at least one dimension that capillary forces may act to draw in the liquid sample 10.

The one or more organic light emitting diodes 3 (OLED), are configured to illuminate an illuminated section 13 of the liquid transport path 2 located between the sample receiving portion 9 and the second end 8. When the assay device 1 includes an integrated liquid transport path 2, the one or more organic light emitting diodes 3 are arranged relative to the illuminated section 13 during fabrication/assembly. When the assay device 1 is configured to receive a separate liquid transport path 2, either the assay device 1, the liquid transport path 2, or both, may be configured with features to enable accurate and reproducible alignment of one or more regions of interest of the liquid transport path 2 with the one or more organic light emitting diodes 3. For example, either or both of the assay device 1 and the liquid transport path 2 may include registration indicia. In other examples, the assay device 1 may include a channel 59 (Figure 16A) having a specific length such that a liquid transport path 2 may be positioned correctly by simply being placed with the first or second end 7, 8 abutting a closed end 60 (Figure 16B) of the channel 59 (Figure 16B).

Referring also to Figure 2, schematic emission spectra of an organic light emitting diode 3 are shown for a variety of different driving currents, I_d.

Each organic light emitting diode 3 includes a first light emitting material which emits light 14 centred around a first wavelength λ_1 and a second light emitting material which emits light 15 centred around a second wavelength λ_2. The one or more organic light emitting diodes 3 may be solution processed.

The colour of light emission by the organic light emitting diode 3 can be tuned through setting the driving current I_d when the organic light emitting diode 3 includes the first and second light emitting materials. As explained in further detail hereinafter, the first and second light emitting materials may be either mixed in a single light emitting layer. Alternatively the first and second light emitting materials may be disposed in two separate layers. For example, the organic light emitting diode 3 may include a light emitting layer 30 (Figure 4) including a first light emitting material which emits green light, and an interlayer (not shown) which includes a second light emitting material which emits near infrared (NIR) light. The recombination zone of the organic light

emitting diode 3 may be tuned to enhance the colour variations as a function of the driving current I_d.

A ratio of emission intensity between the first and second light emitting materials varies in dependence upon the driving current I_d supplied to the organic light emitting diode 3. Denoting the emitted intensity of first light 14 as $E(\lambda_1)$ and the emitted intensity of second light 15 as $E(\lambda_2)$, the ratio $E(\lambda_1)/E(\lambda_2)$ is a function of driving current I_d. For example, at a relatively high driving current I_d, the corresponding organic light emitting diode 3 emission spectrum 16 may display roughly equal emission intensities $E(\lambda_1)$ and $E(\lambda_1)$, in other words, the ratio $E(\lambda_1)/E(\lambda_2)$ is approximately equal to 1. At a relatively reduced driving current I_d, the corresponding organic light emitting diode 3 emission spectrum 17 may display reduced emission intensity $E(\lambda_1)$, $E(\lambda_2)$ at both the first and second wavelengths λ_1, λ_2. However, the emission intensity $E(\lambda_1)$ at the first wavelength λ_1 may be reduced by a larger amount that the emission intensity $E(\lambda_2)$ at the second wavelength λ_2. As a result, the ratio $E(\lambda_1)/E(\lambda_2)$ becomes less than one. As the driving current I_d is further reduced, the ratio $E(\lambda_1)/E(\lambda_2)$ in the corresponding emission spectrum 18 may be further reduced.

Alternatively, in some examples, the ratio $E(\lambda_1)/E(\lambda_2)$ may become larger than one when the driving current I_d is reduced.

The first wavelength λ_1 may correspond to a peak emission wavelength of the first light emitting material. The second wavelength λ_2 may correspond to a peak emission wavelength of the second light emitting material. The first and/or second light emitting materials may emit light within a range having a full-width at half maximum of no more than 10 nm, no more than 25 nm, no more than 50 nm, no more than 100 nm or no more than 200 nm. The first and second wavelengths λ_1, λ_2 may be selected in dependence upon the absorbance spectrum of a target analyte which is known or suspected to be present in the liquid sample 10. The first and second wavelengths λ_1, λ_2 may be selected such that a target analyte has relatively higher absorbance at the first wavelength λ_1 than at the second wavelength λ_2. The ratio of target analyte absorbance at the first and second wavelengths λ_1, λ_2 may be at least two, up to and including five, up to and including ten or more than ten. Alternatively, first and second wavelengths λ_1, λ_2 may be selected such that a target analyte has relatively higher absorbance at the second wavelength λ_2 than at the first wavelength λ_1. A target analyte may be any suitable labelling molecule or particle such as, for example, gold nanoparticles. The

first and second wavelengths λ_1, λ_2 may lie in the range between 300 nm and 1500 nm inclusive. The first and second wavelengths λ_1, λ_2 may lie in the range between 400 nm and 800 nm inclusive.

The one or more photodetectors 4 are arranged and configured to receive light 14, 15 from the section 13 of the liquid transport path 2 illuminated by the organic light emitting diode 3. The one or more photodetectors 4 may receive light 14, 15 transmitted through the illuminated section 13, reflected from within the illuminated section 13, re-emitted within the illuminated section, and so forth. The one or more photodetector(s) are sensitive across a broad wavelength range which includes at least the first and second wavelengths λ_1, λ_2. The one or more photodetectors 4 may take the form of photodiodes, photoresistors, phototransistors, complementary metal-oxide semiconductor (CMOS) pixels, charge coupled device (CCD) pixels, photomultiplier tubes or any other suitable photodetector. The one or more photodetectors may take the form of organic photodiodes. Organic photodiodes may be solution processed. The assay device 1 may include a plurality of photodetectors 4 arranged in an array. A photodetector array may include more photodetectors 4 in a first direction than in a second, perpendicular direction.

An optical path between the one or more organic light emitting diodes 3 and the one or more photodetectors 4 may include no monochromator(s). The optical path between the one or more organic light emitting diodes 3 and the one or more photodetectors 4 may include no beamsplitter(s) between the illuminated section 13 and the one or more photodetectors 4. The optical path between the one or more organic light emitting diodes 3 and the one or more photodetectors 4 may include no fibre couplers and/or fibre splitters between the illuminated section 13 and the one or more photodetectors 4.

The optical path between the one or more organic light emitting diodes 3 and the one or more photodetectors 4 may include one or more slits 54 (Figure 15) to collimate the light 14, 15 and prevent light scattered from outside of a region of interest within the liquid flow path 2 from reaching the one or more photodetectors 4. The one or more slits 54 (Figure 15) may have a width which is greater than or equal to 1 mm. The one or more slits 54 (Figure 15) may have a width between 100 μm and 1 mm inclusive. The one or more slits 54 (Figure 15) may have a width between 300 μm and 500 μm inclusive. The one or more slits 54 (Figure 15) may have adjustable width. Optionally, one or more diffusers may be included in the optical path, for example, between the one

or more organic light emitting diodes 3 and a first slit 54 (Figure 15) and/or between a second slit 54 (Figure 15) and the one or more photodetectors 4.

The controller 5 is configured to drive the one or more organic light emitting diodes 3 at a first driving current I_d^1 and obtain a first absorbance value A_1 based on signals received from the one or more photodetectors 4. The controller 5 is also configured to drive the one or more organic light emitting diodes 3 at a second driving current I_d^2 and obtain a second absorbance value A_2 based on signals received from the one or more photodetectors 4. The controller 5 may determine the absorbance values A_1, A_2 based on a change in the measured reflectance or transmittance of the illuminated section 13. The change in reflectance or transmittance of the illuminated section 13 may be determined by reference to an initial condition prior to introduction of the liquid sample 10. Alternatively, in some examples the change in reflectance or transmittance of the illuminated section 13 may be determined by reference to a section of the liquid transport path 2 outside of a region of interest. For example, if the liquid transport path 2 is received into the assay device 1, the assay device 1 may scan the illuminated section 13 across a region of interest of the liquid transport path 2. In this way, sections of the liquid transport path 2 to one or both sides of a region of interest may be used as a reference for determining a change in reflectance or transmittance of the region of interest. A region of interest may take the form of a testing region 36 (Figure 5) or a control region 42 (Figure 15) of a lateral flow test strip 33 (Figure 5).

The controller 5 is also configured to determine the presence and/or concentration of the target analyte within the illuminated section 13 of the liquid transport path 2 in dependence on a difference of the first and second absorbance values A_1, A_2. For example, the controller 5 may determine a corrected absorbance value as $A_1 - A_2$ or $A_2 - A_1$. Alternatively, the controller 5 may determine a corrected absorbance value as $A_1 - \alpha A_2$ or $A_2 - \alpha A_1$, in which α is a weighting factor. In practice a change in driving current I_d affects the overall intensities of emitted light $E(\lambda_1)$, $E(\lambda_2)$ in addition to the ratio $E(\lambda_1)/ E(\lambda_2)$. The weighting factor α may be calibrated to compensate for the differences in the overall intensities of emitted light $E(\lambda_1)$, $E(\lambda_2)$.

By obtaining the difference between the first and second absorbance values A_1, A_2, a corrected absorbance value may be obtained which is at least partially compensated for optical scattering due to defects or other inhomogeneities in a medium, or substrate which forms all or a part of the liquid transport path 2. The light 14 at and around the

first wavelength λ_1 may be absorbed by the target analyte or by a label substance bound to the target analyte, and the light at and around the second wavelength λ_2 may be substantially not absorbed by the target analyte or the label substance bound to the target analyte. Alternatively, the light 14 at and around the second wavelength λ_2 may be absorbed by the target analyte or by a label substance bound to the target analyte, and the light at and around the first wavelength λ_1 may be substantially not absorbed by the target analyte or the label substance bound to the target analyte. Further details of the correction are discussed further hereinafter.

The one or more output devices 6 may include one or more light emitters (not shown), for example one or more light emitting diodes (LEDs) or organic light emitting diodes (OLEDs). The controller 5 may be configured to cause the one or more light emitters (not shown) of the output devices 6 to visually indicate the presence and/or concentration of the target analyte.

Alternatively, the output device 6 may include a display (not shown) such as, for example, a liquid crystal display or an organic light emitting diode display. The controller 5 may be configured to cause the display of the output device 6 to visually indicate the presence and/or concentration of the target analyte.

Additionally or alternatively, the one or more output devices 6 may include a wired or wireless communication interface (not shown). The controller 5 may be configured to cause the communication interface (not shown) of the output devices 6 to output an indication of the presence and/or concentration of the target analyte via the communication interface. For example, the controller 5 may output the indication of the presence and/or concentration of the target analyte to a data processing apparatus such as a smartphone, tablet computer, laptop or desktop computer.

The operation of the assay device 1 enables performing a dual wavelength correction using an optical path which only includes the one or more organic light emitting diodes 3, the one or more photodetectors 4 and the illuminated section 13 of the liquid transport path 2. Instead, the assay device 1 can perform a dual wavelength correction by varying drive current I_d supplied to the one or more organic light emitting diodes 3. The operation of the assay device 1 may be based on measurements at two fixed drive currents I_d, for example, a first drive current I_d^1 where the emission intensities $E(\lambda_1)$, $E(\lambda_2)$ at first and second wavelengths λ_1, λ_2 are comparable in intensity (i.e. the ratio

$E(\lambda_1)/E(\lambda_2)$ is approximately equal to one) and a second drive current I_d^2 where the ratio $E(\lambda_1)/E(\lambda_2)$ is greater than or less than one. In general, a larger difference in the ratio $E(\lambda_1)/E(\lambda_2)$ between the first and second drive currents I_d^1, I_d^2, will result in a larger improvement in signal to noise ratio by obtaining the difference of the first and second absorbance values A_1, A_2.

Alternatively, the drive current I_d may be increased or decreased in a sweep pattern, and absorbance values A may be obtained for more than two values of drive current I_d. The controller 5 may then obtain a corrected absorbance value by performing a fitting of absorbance as a function of drive current I_d.

Organic light-emitting diodes

Referring also to Figure 3, an example of an organic light emitting diode 3 stack suitable for use in the assay device 1 is shown.

The organic light emitting diode 3 is deposited onto a transparent substrate 19 in the form of a layer of polyethylene naphthalate (PEN) having a thickness of 125 μm (in the z direction shown in Figure 3). The transparent substrate 19 has first and second surfaces 20, 21 and the organic light emitting diode 3 is deposited onto the first surface 21. A foil 22 is laminated over the first surface 20 of the substrate 19 and the exemplary organic light emitting diode 3 using a layer of adhesive 23. The foil 22 is in the form of an aluminium foil having a thickness of 20 μm. The foil 22 is provided for the purpose of sealing the organic light emitting diode 3 against the environment, and the foil 22 is not used as an electrode. The adhesive 23 takes the form of a pressure-sensitive adhesive having a thickness of approximately 25 μm. An outer layer 24 is laminated over the foil 22. The outer layer 24 is in the form of a layer of polyethylene terephthalate (PET) having a thickness of 25 μm. The outer layer 24 may be chemically or thermally bonded to the foil 22, or alternatively the foil 22 may be deposited onto or chemically/thermally bonded to the outer layer 24 before the foil 22 is adhered to the substrate 19 and organic light emitting diode 3. The organic light emitting diode 3 emits light through the transparent substrate 19, i.e. from the first surface 20 towards the second surface 21 and away from the foil 22 (in the negative z direction shown in Figure 3). A transparent outer layer 25 is laminated covering the second surface 21 of the substrate 19 using a layer of transparent adhesive 26. The transparent outer layer 25 takes the form of a layer of polyethylene terephthalate (PET) having a thickness of 25 μm, and the layer of transparent adhesive 26 takes the form of a pressure-sensitive

adhesive having a thickness of approximately 25 μm. In this example, the outer layer 24 and the transparent outer layer 25 are made of the same material and the adhesive layer 23 and transparent adhesive layer 26 are made of the same material. However, only the transparent outer layer 25 and the transparent adhesive layer 26 need to be transparent. The outer layer 24 and adhesive layer 23 may be opaque.

Transparency is relative to the emission wavelengths λ_1, λ_2 of the organic light emitting diode 3. A material may be considered transparent if it transmits 70% or more of light at the emission wavelengths λ_1, λ_2 of the organic light emitting diode 3. In other examples, a material may be considered transparent if it transmits 50% or more of light at the emission wavelengths λ_1, λ_2.

The encapsulation arrangement shown in Figure 3 is exemplary only, and different encapsulation configurations may be used for the one or more organic light emitting diodes 3.

The organic light emitting diode 3 comprises an anode, a cathode and an organic light-emitting layer between the anode and the cathode. One or more further layers may be provided between the anode and cathode including, without limitation, charge-transporting layers, charge-blocking layers, interlayers, and charge-injecting layers.

Referring also to Figure 4, an example structure of a suitable organic light emitting diode 3 is shown.

The anode is provided by a transparent electrode 27 supported on the first surface 20 of the transparent substrate 19. The transparent electrode 27 provides the anode and takes the form of a layer of indium tin oxide (ITO) having a thickness of around 65 nm.

The cathode is provided by an electron injection layer 28 supported directly on a top electrode 29. The top electrode 29 takes the form of an aluminium electrode having a thickness of around 200 nm. The electron injection layer 28 has a thickness of 10 nm and comprises or consists of an n-doped, non-polymeric or polymeric electron-transporting material. The electron-transporting material is preferably a polymer comprising one or more arylene repeat units, optionally one or more repeat units selected from fluorene, phenylene and anthracene. Suitable n-dopants are 2,3-dihydro-1H-benzoimidazoles, optionally 1,3-Dimethyl-2-phenyl-2,3-dihydro-1H-

benzoimidazole (DMBI) and 4-(2,3-Dihydro-1,3-dimethyl-1H-benzimidazol-2-yl)-N,N-dimethylbenzenamine (N-DMBI). The top electrode 29 takes the form of an aluminium electrode having a thickness of around 200 nm. The electron injection layer 28 and top electrode 29 are arranged with the electron injection layer 28 facing the transparent electrode 27.

A light emitting layer 30 comprising one or more light-emitting materials is arranged between the transparent electrode 27 (anode) and the electron injection layer 28 (cathode). Light-emitting materials may be fluorescent materials, phosphorescent materials or a mixture of fluorescent and phosphorescent materials. Preferred light-emitting polymers are conjugated polymers, more preferably polyfluorenes, examples of which are described in Bernius, M. T., Inbasekaran, M., O'Brien, J. and Wu, W., Progress with Light-Emitting Polymers. Adv. Mater., 12 1737–1750, 2000, the contents of which are incorporated herein by reference. The light-emitting layer 30 may comprise a host material and a fluorescent or phosphorescent light-emitting dopant. Preferred phosphorescent dopants are row two or row three transition metal complexes, preferably complexes of ruthenium, rhodium, palladium, rhenium, osmium, iridium, platinum or gold, most preferably complexes of iridium.

The particular materials selected for the light emitting layer 30 depend on the desired emission wavelengths λ_1, λ_2 of the organic light emitting diode 3.

A hole injection layer 31 is supported on the transparent electrode 27, between the transparent electrode 27 (anode) and the light emitting layer 30. The hole injection layer 31 takes the form of a layer of a conducting organic material having a thickness of around 50 nm. Preferred conducting organic materials are polyethylenedioxythiophene (PEDOT) doped with a polyacid, for example polystyrene sulfonic acid (PSS); and polythiophenes, for example Plexcore ® available from Plextronics, Inc.

A hole transport layer 32 is supported on the hole injection layer 31, between the hole injection layer 31 and the light emitting layer 30. The hole transport layer 32 takes the form of a layer having a thickness of 22 nm and comprising or consisting of a polymeric or non-polymeric hole-transporting material. The hole-transporting material is preferably an aromatic amine or a polymer comprising arylamine repeat units.

Exemplary hole-transporting polymers are as described in WO 99/54385, WO 2005/049546 and WO 2013/108022, the contents of which are incorporated herein by reference.

In other examples of the organic light emitting diode 3, the cathode may be in direct contact with the light-emitting layer 30. In these embodiments, the cathode may comprise a first layer of a metal compound having a first surface in direct contact with the light-emitting layer and an opposing second surface in direct contact with a second layer comprising or consisting of a conducting material. Preferably, the metal compound is a metal fluoride, more preferably an alkali or alkali earth fluoride, most preferably LiF, NaF or KF.

Preferably, the second layer consists of a metal, more preferably a metal having a work function of more than 3.5 eV, preferably at least 4.0 eV, most preferably aluminium.

A third layer comprising or consisting of a metal having a work function of more than 3.5 eV, preferably at least 4.0 eV may be adjacent to the second layer.

Work functions of elemental metals are as given in the CRC Handbook of Chemistry and Physics, 87th Edition, 12-114. For any given element, the first listed work function value applies if more than one work function value is listed.

A preferred cathode is NaF / Al.

In some examples of the assay device 1, the first and second light emitting materials are comprised within the light emitting layer 30. In alternative example of the assay device 1, the first light emitting material and the second light emitting material are comprised within different layers of the organic light emitting diode. For example, the first light emitting material may be disposed within the light emitting layer 30 and the second light emitting material may be disposed within a different layer such as, for example, the hole transport layer 32 or an optional interlayer (not shown) included in the OLED 3 stack. For example, an OLED 3 may include a green light emitting material in the light emitting layer 30, and a near infrared (NIR) emitting material may be included in an interlayer (not shown) provided between the hole injection layer 31 and the light emitting layer 30. The NIR emitting material may be included in the interlayer (not

shown) by, for example, co-polymerising the NIR emitting material with the interlayer monomers.

Referring also to Figure 5, a lateral flow test strip 33 is one example of a suitable liquid transport path 2 for use with the assay device 1.

Lateral flow test strips 33 (also known as "lateral flow immunoassays") are a variety of biological testing kit. Lateral flow test strips 33 may be used to test a liquid sample, such as saliva, blood or urine, for the presence of an analyte. Examples of lateral flow test strips include home pregnancy tests, home ovulation tests, tests for other hormones, tests for specific pathogens and tests for specific drugs. Lateral flow test strips may also be used for testing food and/or drink products to determine the presence or concentration of impurities and so forth.

In a typical lateral flow test strip 33, a liquid sample 10 is introduced to the sample receiving portion 9 proximate to a first end 7 of a porous strip 34, and the liquid sample 10 is then drawn along the lateral flow test strip 33 towards the second end 8 by capillary action (or "wicking"). A portion of the lateral flow strip 33 is pre-treated with labelling particles 35 (Figure 6) which are activated with a reagent which binds to the target analyte to form a complex if the target analyte is present in the liquid sample 10. The bound complexes, and also unreacted labelling particles 35 (Figure 6) continue to propagate along the lateral flow test strip 33 before reaching a testing region 36 which is pre-treated with an immobilised binding reagent which binds complexes of analyte bound to labelling particles 35 (Figure 6) and does not bind unreacted labelling particles 35 (Figure 6). The labelling particles 35 (Figure 6) have a distinctive colour, or otherwise absorb one or more ranges of ultraviolet or visible light. The development of a concentration of labelling particles 35 (Figure 6) in the test region 36 may be measured and quantified using the assay device 1, for example by measuring the optical density of labelling particles 35 (Figure 6). The assay device 1 may perform measurements on developed lateral flow test strips 33, i.e. the liquid sample has been left for a pre-set period to be drawn along the test strip 33. Alternatively, the assay device 1 may perform kinetic, i.e. dynamic time resolved measurements of the optical density of labelling particles 35 (Figure 6).

Referring also to Figure 6, the porous strip 34 is typically formed from a mat formed of fibres 37, for example nitrocellulose fibres. Within the test region 36, the immobilised binding reagent binds complexes of analyte and labelling particles 35.

The fibres 37 scatter and/or absorb light across a broad range of wavelengths in an approximately similar way. For example, the proportion of light 14 from the first light emitting material which is scattered or absorbed by the fibres 37 is approximately the same as the proportion of light 15 from the second light emitting material which is scattered or absorbed by the fibres 37. However, the fibrous porous strip 34 is not uniform, and the density of fibres 37 may vary from point to point along the porous strip 34 (for example along the x-direction in Figures 5, 6). As explained further hereinafter, such background variations of absorbance, which are due to inhomogeneity of the porous strip 34, may limit the sensitivity of a measurement, i.e. the minimum detectable concentration of labelling particles 35.

Referring also to Figure 7, the assay device 1 may compensate for such background variations of absorbance due to the inhomogeneity of the porous strip 34, provided that the first and second wavelengths λ_1, λ_2 are selected appropriately for the labelling particles 35 used for a given lateral flow test strip 33.

For example, an ultraviolet-visible spectrum 38 of the labelling particles 35 may be obtained to determine how the absorbance of the labelling particles 35 varies with wavelength/frequency. The first wavelength λ_1 is selected to be a wavelength which is at, or close to, a peak absorbance of the labelling particles 35. The second wavelength λ_2 is selected to be a wavelength which lies substantially away from a peak absorbance of the labelling particles 35. In other words, the first and second wavelengths λ_1, λ_2 are selected such that labelling particles have relatively higher absorbance at the first wavelength λ_1 than at the second wavelength λ_2. The ratio of absorbance between the first and second wavelengths λ_1, λ_2 may be a factor of, for example, at least two, up to and including five, up to and including ten, or more than ten.

The first and second wavelengths λ_1, λ_2 may lie in the range between 300 nm and 1500 nm inclusive. The first and second wavelengths λ_1, λ_2 may lie in the range between 400 nm and 800 nm inclusive.

Referring in particular to Figure 6, light 14 from the first light emitting material, having wavelengths around the first wavelength λ_1, is absorbed by the labelling particles 35, in addition to being scattered and/or absorbed by the fibres 37. By contrast, light 15 from the second light emitting material, having wavelengths around the second wavelength λ_2, is absorbed by the labelling particles 35 only weakly or not at all.

Referring also to Figures 8 to 10, position dependent absorbance profiles $A(x)$ are shown. The absorbance profiles $A(x)$ represent that values that would be obtained if a lateral flow test strip 33 were to be passed between the one or more organic light emitting diodes 3 and the one or more photodetectors 4, and the absorbance values $A(x)$ measured as a function of position x along the porous strip 34. In other words, the absorbance profiles $A(x)$ represent that values that would be obtained by scanning the illuminated section 13 along the length of a porous strip 33 in the x-direction as illustrated in Figure 5.

Referring in particular to Figure 8, a first absorbance profile $A_1(x)$ corresponding to a first driving current I_d^1 is shown. In the first absorbance profile $A_1(x)$ corresponding to the first driving current I_d^1, the ratio $E(\lambda_1)/E(\lambda_2)$ of emission intensities at first and second wavelengths λ_1, λ_2 is substantially equal to one. The labelling particles 35 strongly absorb light 14 at and around the first wavelength λ_1 and substantially do not absorb light 15 at and around the second wavelength λ_2. Consequently, the first absorbance values $A_1(x)$ include substantial contributions from both absorption/scattering by the fibres 37 of the porous strip 34 and from absorbance/scattering by the labelling particles 35. The dashed line 39 illustrates the underlying absorbance profile resulting from the labelling particles 35.

Referring in particular to Figure 9, a second absorbance profile $A_2(x)$ corresponding to a second driving current I_d^2 is shown. In the second absorbance profile $A_2(x)$ corresponding to the second driving current I_d^2, the ratio $E(\lambda_1)/E(\lambda_2)$ of emission intensities at first and second wavelengths λ_1, λ_2 is substantially less than one. In other words, the emission intensity $E(\lambda_1)$ at the first wavelength λ_1 has decreased by more than the emission intensity $E(\lambda_2)$ at the second wavelength λ_2. Consequently, since the labelling particle 35 substantially do not absorb light 15 at and around the second wavelength λ_2, the values of the second absorbance profile $A_2(x)$ are substantially dominated by absorption/scattering by the fibres 37 of the porous strip 34. The values of the second absorbance profile $A_2(x)$ may, in practice, include some contribution from

absorbance/scattering by the labelling particles 35. Preferably, the relative contribution from absorbance/scattering by the labelling particles 35 is as small as possible using the second driving current I_d^2, which may be achieved by minimising the ratio $E(\lambda_1)/E(\lambda_2)$ of emission intensities at first and second wavelengths λ_1, λ_2.

The background level of absorbance varies with position x along the porous strip 34 due to the inhomogeneity of fibre 37 density. Absorbance signals resulting from the labelling particles 35 cannot be reliably detected unless they are at least larger than the background variance which results from inhomogeneity of the porous strip 34. This restricts the lower limit of labelling particle concentration which can be detected using a lateral flow test strip 33. The same background variance also limits the resolution of a quantitative measurement of labelling particle 35 concentration/ optical density.

However, since the fibres 37 scatter light at the first and second wavelengths λ_1, λ_2 in approximately the same way, the absorbance values $A_2(x)$ values corresponding to the second driving current I_d^2 may be subtracted from the absorbance values $A_1(x)$ corresponding to the first driving current I_d^1 to reduce or remove the variable background absorbance which results from the inhomogeneous distribution of fibres 37 in the porous strip.

Although in practice some amount of background variance in absorbance will remain when the difference $A_1(x)$ - $A_2(x)$ is obtained, the relative size of the signal which is specific to the labelling particles 35 may be increased, in some cases substantially, with respect to background variations. In this way, the lower limit of labelling particle 35 concentrations/ optical densities which may be detected may be reduced. Similarly, the resolution of a quantitative measurement of labelling particle 35 concentration/optical density may be increased.

In practice, driving the one or more organic light emitting diodes 3 at first and second driving currents I_d^1, I_d^2 will result in differences in the overall intensities of light emission, in addition to a change in colour. Consequently, it may be preferable to perform a weighted correction, i.e. $A_1(x)$ - $\alpha A_2(x)$, in order to account for variations in the overall intensity of light emission by the one or more organic light emitting diodes 3.

Through alternately driving the one or more organic light emitting diodes 3 at the first and second driving currents I_d^1, I_d^2 to provide illumination of first and second colours, the assay device 1 may perform a background correction without requiring optical components such as beamsplitters, filters or monochromators. Thus, the assay device 1 may be less bulky, simpler and less expensive to manufacture. Additionally, many optical components such as beamsplitters have wavelength dependent properties, which may restrict the choice of wavelengths λ_1, λ_2 in devices which employ more complex optical paths for dual wavelength corrections.

Referring also to Figure 11, a method of using the assay device is illustrated.

A liquid sample 10 is introduced to the sample receiving portion 9 of the liquid transport path 2 (step S1). When the liquid transport path 2 is not integrated into the assay device 1, the liquid sample 10 may be introduced either before or after the liquid transport path 2 is received into the assay device 1. For example, if a measurement of a completed assay is desired, then the liquid transport path 2 may be received by the assay device 1 once the assay is completed. Alternatively, if dynamic measurements are desired, then the liquid transport path may be received by the assay device 1 prior to introducing the liquid sample 10 into the liquid transport path 2.

The controller 5 causes the one or more organic light emitting diodes 3 to be driven at a first driving current I_d^1 (step S2). The controller 5 may cause the one or more organic light emitting diodes 3 to be illuminated immediately upon introducing the liquid sample 10 to the assay device 1. For example, if the assay device 1 is configured to perform dynamic measurements throughout the course of an assay, or when the assay device 1 measures the concentration of a target analyte directly. Alternatively, the controller 5 may cause the one or more organic light emitting diodes 3 to be illuminated after a predetermined duration has elapsed since introducing the liquid sample 10 to the assay device 1, for example, when the assay is an immunoassay which requires time to develop a concentration of labelling particles in a test region 36 disposed within the illuminated section 13 of the liquid transport path 2. In other examples, the controller 5 may cause the one or more organic light emitting diodes 3 to be illuminated in response to receiving the liquid transport path 2 into the assay device 1, either automatically or in response to input by a user.

The controller 5 receives signals from the one or more photodetectors 4 and determines a first absorbance measurement A_1 in dependence thereon (step S3).

The controller 5 causes the one or more organic light emitting diodes 3 to be driven at a second driving current I_d^2 (step S4), receives signals from the one or more photodetectors 4 and determines a second absorbance measurement A_2 in dependence thereon (step S5).

The controller 5 obtains a difference between the first and second absorbance measurements A_1, A_2, and determines the presence and/or concentration of a target analyte within the illuminated section 13 of the liquid transport path 2 in dependence on the difference $A_2 - A_1$, or the weighted difference $A_2 - \alpha A_1$.

If the assay device 1 is required to perform further measurements, then the process is repeated (step S7).

In alternative methods, additional measurements may be obtained at additional driving currents I_d. For example, a third absorbance measurement A_3 may be obtained at a third driving current I_d^3, a fourth absorbance measurement A_4 may be obtained at a fourth driving current I_d^4, and so forth. The additional measurements may be used to perform a fitting and extrapolate the contribution from absorbance of the labelling particles 35. The driving current I_d may be ramped (up or down) either continuously or in discrete steps, in order to obtain absorbance measurements A corresponding to a large number of driving currents I_d for the purpose of fitting an absorbance of the labelling particles.

Measurement geometries

The assay device 1 may be configured to use a range of organic light emitting diode 3 and photodetector 4 geometries.

Referring also to Figure 12, the assay device 1 may be configured so that the one or more photodetectors 4 receive light 14, 15 transmitted through the illuminated section 13 of the liquid transport path 2. For measurements in transmission, the one or more organic light emitting diodes 3 and the one or more photodiodes 4 may simply be spaced apart by a gap which contains or receives the illuminated section 13 of the liquid transport path 2.

Additional optical components may be included in the optical path between the one or more organic light emitting diodes 3 and the one or more photodetectors 4. For example, the light 14, 15 from the one or more organic light emitting diodes 3 may be restricted by slits 54 (Figure 15) or other apertures. Optionally, a diffuser, one or more lenses and/or other optical components may also be included in the optical path between the one or more organic light emitting diodes 3 and the one or more photodetectors 4.

Referring also to Figure 13, an assay device 1 may alternatively be configured so that the photodetector(s) 4 receive light reflected from the illuminated section 13 of the liquid transporting path 2. For example, when the liquid transport path 2 takes the form of a lateral flow test strips 33, the one or more organic light emitting diodes 3 may be arranged to illuminate a region of interest of the lateral flow test strip 33 at first angle θ_1, and the photodiode(s) 4 may be arranged to receive light reflected from the lateral flow test strip 33. Light reflected from the porous strip 34 of a lateral test strip 33 will, in general, be scattered into a wide range of different angles due to the largely random orientations of the fibres 37. Consequently, the portion of the optical path between the illuminated portion 13 and the photodetector(s) 4 may be oriented at a second angle θ_2, which does not need to be equal to the first angle θ_1. In some examples, the first and second angles θ_1, θ_2 may be equal. In some examples, the one or more organic light emitting diodes 3 and the one or more photodetectors 4 may be arranged in a confocal configuration. Light reflected from the illuminated portion 13 of the liquid transport path 2 may originate from a surface of and/or from a depth within the illuminated portion 13.

Additional optical components may be included in the optical path between the one or more light emitting diodes 3 and the one or more photodetectors 4. For example, the light from the one or more light emitting diodes 3 may be restricted by slits or other apertures. Optionally, a diffuser, one or more lenses and/or other optical components may also be included in the optical path between the one or more light emitting diodes 3 and the one or more photodetectors 4.

Referring also to Figure 14, the assay device 1 may include a number of photodetectors 4 arranged in an array to form an image sensor 40. For example, the image sensor 40 may form part of a camera. An image sensor 40 may be arranged to image all of, or a

portion of, the illuminated section 13 of the liquid transport path 2. For example, when the liquid transport path 2 takes the form of a lateral flow test strip 33, the image sensor 40 may be arranged to image one or more test regions 36 and the surrounding areas of the porous strip 34. A lateral flow test strip 33 may include one or more pairs 41, each pair 41 including a testing region 36 and a control region 42, and the image sensor 40 may be arranged to image the one or more pairs 41 at the same time. An image captured when driving the one or more organic light emitting diodes 3 using a first driving current I_d^1 may be subtracted from an image captured using a second driving current I_d^2, in order to reduce or remove the influence of background variance due to inhomogeneity of the fibres 37 making up the porous strip 34. Alternatively, an image captured when driving the one or more organic light emitting diodes 3 using the second driving current I_d^2 may be subtracted from an image captured using the first driving current I_d^1. The image difference may be weighted using a weighting factor α.

An image sensor 40 may be used to image transmitted or reflected light. Additional optical components may be included in the optical path between the one or more organic light emitting diodes 3 and the image sensor 40. For example, the light 14, 15 from the one or more organic light emitting diodes 3 which illuminates the illuminated section 13 and/or the light from the illuminated section 13 to the image sensor 40 may be restricted by slits or other apertures. Optionally, a diffuser, one or more lenses and/or other optical components may also be included in the optical path between the one or more organic light emitting diodes 3 and the image sensor 40.

Self-contained assay device

Referring also to Figure 15, the assay device 1 may take the form of a self-contained lateral flow testing device 43.

The lateral flow testing device 43 includes a liquid transport path 2 in the form of a porous strip 34 divided into a sample pad 44, a conjugate pad 45, a test pad 46 and a wick pad 47. The porous strip 34 is received into a base 48. A lid 49 is attached to the base 48 to secure the porous strip 34 and cover parts of the porous strip 34 which do not require exposure. The lid 49 includes a sample receiving window 50 which exposes part of the sample pad 44 to define the sample receiving portion 2. The lid 49 and base 48 are made from a polymer such as, for example, polycarbonate, polystyrene, polypropylene or similar materials.

The base 48 includes a recess 51 into which a pair of organic light emitting diodes 3 are received. Each organic light emitting diode 3 may be configured as described hereinbefore. The lid 49 includes a recess 52 into which a pair of photodetectors 4 are received. The photodetectors 4 may take the form of photodiodes, such as, for example, organic photodiodes. One pair of an organic light emitting diode 3 and a corresponding photodetector 4 are arranged on opposite sides of a testing region 36 formed in the test pad 46 of the porous strip 34. A second pair of an organic light emitting diode 3 and a corresponding photodetector 4 are arranged on opposite sides of a control region 42 formed in the test pad 46 of the porous strip 34. Slit members 53 separate the organic light emitting diodes 3 from the porous strip 34 to define narrow slits 54 with widths typically in the range between 300 μm to 500 μm inclusive. The slit members 53 define slits 54 which extend transversely across the width of the porous strip 34. For example, if the porous strip 34 extends in a first direction x and has a thickness in a third direction z, then the slits 54 extend in a second direction y. Further slit members 53 define slits 54 which separate the photodetectors 4 from the porous strip 34. The slits 54 may be covered by a thin layer of transparent material to prevent moisture entering into the recesses 51, 52. Material may be considered to be transparent to a particular wavelength λ, or range of wavelengths $\Delta\lambda$, if it transmits more than 75%, more than 85%, more than 90% or more than 95% of the light at that wavelength λ, or within the range of wavelengths $\Delta\lambda$. Transparent materials should be transparent at both the first wavelength λ_1 and the second wavelength λ_2. A diffuser (not shown) may optionally be included between each organic light emitting diode 3 and the corresponding slit 54.

The controller 5 is housed within the base 48. Alternatively, the controller 5 may be housed within the lid 49. The one or more output devices 6 are housed in the lid 49, or elsewhere on the lateral flow testing device 43 such that the output devices 6 are visible and/or accessible to a used when the lateral flow testing device 43 is resting on a flat surface with the sample receiving window 50 facing up. The controller 5 is connected to the OLEDs 3, photodetectors 4, output devices 6 and a battery (not shown) by suitable conductors (not shown). In other examples, the lateral flow testing device 43 may not need a battery (not shown) and may instead be powered via a communications interface of the one or more output devices 6 such as, for example, a universal serial bus (USB) connection.

A liquid sample 10 suspected of containing a target analyte is introduced to the sample receiving portion 9 through the sample receiving window 50 using, for example, a

dropper 55 or similar implement. In other examples a liquid sample 10 may be introduced by dipping the sample receiving window 50 in a container holding liquid sample 10, or by placing the sample receiving window 50 so as to intersect a flow of liquid sample 10, and so forth. The liquid sample 10 is transported along the liquid transport path 2 towards the second end 8 by a capillary, or wicking, action of the porosity of the porous strip 44, 45, 46, 47. The sample pad 44 of the porous strip 34 is typically made from fibrous cellulose filter material.

The conjugate pad 45 has been pre-treated with at least one particulate labelled binding reagent for binding an analyte which is being tested for, to form a labelled-particle-analyte complex (not shown). A particulate labelled binding reagent is typically, for example, a nanometre- or micrometre-sized label particle 35 which has been sensitised to specifically bind to the analyte, for example, using antibodies or antigens. The particles provide a detectable response, which is usually a visible optical response such as a particular colour, but may take other forms. For example, particles may be used which are visible in infrared, which fluoresce under ultraviolet light and so forth. Typically, the conjugate pad 45 will be treated with one type of particulate labelled binding reagent to test for the presence of one type of analyte in the liquid sample 10. However, lateral flow devices 43 may be produced which test for two or more analytes using two or more particulate labelled binding reagents concurrently. The conjugate pad 45 is typically made from fibrous glass, cellulose or surface modified polyester materials.

As the flow front 11 moves into the test pad 46, labelled-particle-analyte complexes and unbound label particles are carried along towards the second end 8. The test pad 46 includes one or more testing regions 36 and control regions 42 which are monitored by a corresponding organic light emitting diode 3 and photodetector 4 pair. A testing region 36 is pre-treated with an immobilised binding reagent which specifically binds the label particle-target complex and which does not bind the unreacted label particles. As the labelled-particle-analyte complexes are bound in the testing region 36, the concentration of the label particles 35 in the testing region 36 increases. The concentration increase may be monitored by measuring the absorbance of the testing region 36 using the corresponding organic light emitting diode 3 and photodetector 4. The absorbance of the testing region 36 may be measured once a set duration has expired since the liquid sample 10 was added. Alternatively, the absorbance of the

testing region 36 may be measured continuously or at regular intervals as the lateral flow strip 33 is developed.

To provide distinction between a negative test and a test which has simply not functioned correctly, a control region 42 is often provided between the testing region 36 and the second end 8. The control region 42 is pre-treated with a second immobilised binding reagent which specifically binds unbound label particles and which does not bind the labelled-particle-analyte complexes. Alternatively, the control region 42 may be pre-treated with a non-specific immobilised binding reagent which binds either unbound label particles or labelled-particle-analyte complexes. In this way, if the lateral flow testing device 43 has functioned correctly and the liquid sample 10 has passed through the conjugate pad 44 and the test pad 46, the control region 42 will exhibit a change in absorbance. The absorbance of the control region 42 may be measured by the second pair of an organic light emitting diode 3 and a photodetector 4 in the same way as for the testing region 36.

The test pad 46 is typically made from fibrous nitrocellulose, polyvinylidene fluoride, polyethersulfone (PES) or charge modified nylon materials. All of these materials are fibrous, and as such the sensitivity of absorbance measurements may be improved by obtaining a difference between absorbance values obtained using a first driving current I_d^1 and absorbance values obtained using a second driving current I_d^2.

The wick pad 47 provided proximate to the second end 8 soaks up liquid sample 10 which has passed through the test pad 46 and helps to maintain through-flow of the liquid sample 10. The wick pad 47 is typically made from fibrous cellulose filter material.

Assay reader device

Referring also to Figures 16A and 16B, the assay device 1 may take the form of a reading device 56 for receiving lateral flow test strips 33.

Referring in particular to Figure 16A, the reading device 56 includes first and second organic light emitting diodes 3a, 3b, first and second photodetectors 4a, 4b, a controller 5, an output device 6 and a battery 57, all contained within a casing 58 formed of a durable material such as plastic or metal. The casing 58 may be a single integrally formed piece, or may be formed from two or more pieces clipped or fastened together

using conventional means. The reading device 56 also includes a channel 59 for receiving a liquid transport path 2. The channel 59 may be formed as a feature of the casing 58. The channel 59 has a first end open at an exterior of the reading device 56, and a second, closed end 60.

The first organic light emitting diode 3a faces the first photodetector 4a across the channel 59 to form a first pair 3a, 4a. The illuminated section is delimited by slits 54 formed on either side of the channel 59. The slits 54 may be integrally formed as features of the casing 59. Similarly, at a distance spaced along the channel 59 from the first pair 3a, 4a, the second organic light emitting diode 3b faces the second photodetector 4b across the channel 59 to form a second pair 3b, 4b.

Referring in particular to Figure 16B, a liquid transport path 2 in the form of a lateral flow test strip 33 is received into the channel 59 and pressed into the reading device 56 until the second end 8 of the lateral flow test strip 33 abuts the closed end 60 of the channel 59. When the second end 8 of the lateral flow test strip 33 abuts the closed end 60 of the channel 59, the testing region 36 is aligned within the illuminated portion 13 corresponding to the first organic light emitting diode 3a and the control region 42 is aligned with the illuminated portion 13 corresponding to the second organic light emitting diode 3b. In this way, an absorbance of the testing region 36 may be measured using the first pair 3a, 4a and an absorbance of the control region 42 may be measured using the second pair 3b, 4b. The controller 5 determines the presence and/or concentration of the target analyte in the testing region 36, and uses the control region to verify that the assay has been performed correctly. The results are output via the output device 6 as described hereinbefore, either directly to a user using one or more light emitters and/or displays, or via a wired or wireless communications interface.

Although two pairs of organic light emitting diodes 3a, 3b and photodetectors 4a, 4b are shown, the reading device 56 may include a pair of an organic light emitting diode 3 and a photodetector 4 corresponding to each region of interest of lateral flow test strips 33 to be measured.

Alternatively, instead of receiving a lateral flow test strip 33 in a predetermined position with respect to the organic light emitting diodes 3 and photodetectors 4, the reading device 56 may include a single organic light emitting diode 3 and photodetector

4 pair, and a lateral flow test strip 33 may be passed through the illuminated section 13 to scan the whole or a part of the length of the lateral flow test strip 33. In this way, multiple regions of interest may be measured without requiring multiple organic light emitting diodes 3 and corresponding photodetectors 4.

Although Figure 16B illustrates a free-standing lateral flow test strip 33 being directly received into the reading device 56, in other examples the reading device 56 may be configured to receive lateral flow test strips 33 which are packaged within containers or cassettes (not shown). In other examples, the reading device 56 may include a moveable sample receiving stage (not shown) on or within which a packaged or free-standing lateral flow test strip 33 may be placed and/or secured. The sample receiving stage (not shown) may be moveable between a first position in which a lateral flow test strip 33 may be placed and/or secured, and one or more further positions in which one or more regions of interest are arranged within corresponding illuminated section(s) of the reading device 56. When the reading device 56 is configured to scan a lateral flow test strip 33 through an illuminated section 13, the sample receiving stage (not shown) may be motorised and controlled by the controller 5.

Measurements may be triggered automatically when a lateral flow test strip 33 is received into the reading device 56. For example, a micro-switch or light gate may determine when the second end 8 of the lateral flow test strip 33 abuts the closed end 60 of the channel 59. Alternatively, the reading device 56 may include an input device such as a switch or button which a user may actuate to trigger the controller 5 to obtain a measurement once a lateral flow test strip 33 has been loaded.

Illustrative experimental data

The preceding discussion may be better understood with reference to illustrative experimental data obtained from an example of a suitable organic light emitting diode 3. The assay devices, 1, 43, 56 described herein are not limited to the specific conditions and samples used to obtain the illustrative experimental data presented hereinafter.

Referring also to Figure 17, emission spectra of an exemplary organic light emitting diode 3 are shown for a first driving current 61, I_d^1 = 10 μA, and a second driving current 62, I_d^2 = 400 μA.

The exemplary organic light emitting diode 3 included a first light emitting material which emits first light 14 at green wavelengths λ_G centred at about 525 nm, and a second light emitting material which emits second light 15 at near infra-red wavelengths λ_{NIR} centres at about 700 nm. These wavelengths λ_G, λ_{NIR} are suitable for absorbance measurements of gold nanoparticles which are used as labelling particles 35 in many examples of lateral flow test strips 33, because the green wavelengths λ_G are strongly absorbed/scattered by the gold nanoparticles, whereas the near infra-red wavelengths λ_{NIR} are not. By contrast, the nitrocellulose fibres typically used for lateral flow test strips 33 absorb/scatter the green wavelengths λ_G and near infra-red wavelengths λ_{NIR} similarly. In the exemplary organic light emitting diode 3 used to obtain the data shown in Figure 17, the first and second light emitting materials were mixed in a single light emitting layer 30.

It may be observed that the relative intensities of green and near-infrared light 14, 15 are similar at a first driving current 61 of I_d^1 = 10 μA, i.e. the ratio $E(\lambda_{NIR})/E(\lambda_G)$ is approximately equal to one. By contrast, at a second driving current 62 of I_d^2 = 400 μA, the ratio $E(\lambda_{NIR})/E(\lambda_G)$ may be observed to have shifted significantly to a value of approximately one half.

Referring also to Figure 18, the dependence of the measured ratio of emission intensities $E(\lambda_{NIR})/E(\lambda_G)$ is shown as a function of increasing driving current I_d. Figure 18 includes data points 63 and a power law trend line 64 is included purely for the purposes of visualisation.

For the exemplary organic light emitting diode 3, the higher the drive current I_d, the lower the relative intensity of the light 15 at near-infrared wavelengths λ_{NIR} compared to the light 14 at green wavelengths λ_G.

Referring also to Figure 19, normalised photodetector 4 signals are shown corresponding to a first driving current 65 of I_d^1 = 0.5 mA and a second driving current 66 of I_d^2 = 0.05 mA. The data shown in Figure 19 were obtained using a photodetector 4 in the form of an organic photodiode (OPD), and using the same Green-NIR organic light emitting diode 3 described in relation to Figures 17 and 18. The data were obtained by scanning a lateral flow test strip 33 between the Green-NIR organic light emitting diode 3 and the organic photodiode 4. The absorbance peaks observed in Figure 19 correspond to two regions of the lateral flow test strip 33 which contained

different concentrations of gold nanoparticles. It may be observed that the signals corresponding to a region 67 between the absorbance peaks depart from the baseline values, which is attributed to inhomogeneity of the nitrocellulose fibres of the lateral flow test strip 33. When the difference 68 between the first and second driving currents I_d^1, I_d^2 is plotted, it may be observed that the anomalous signal in the region 67 is substantially reduced, which may provide improved confidence in estimating both the heights and widths of the absorbance peaks. Although the overall amplitude of the difference 68 is reduced, the signal-to-noise ratio may be increased.

Modifications

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

The examples of an integrated assay device 43 and a reading device 56 have been illustrated with reference to lateral flow test strips. However, the assay device 1 is not limited to lateral flow test strips 33, and the lateral flow test strips of any of the examples described herein may be replaced by one or more channels of a microfluidic device. The particular type of liquid transport path is not crucial, and may be selected depending on the colorimetric assay to be performed.

Examples have been described in which the absorbance of labelling particles 35 bound to a target analyte is measured. However, labelling particles 35 need not be used. In some examples, the assay device 1 may measure the absorbance of the target analyte directly, for example, by using an organic light emitting diode 3 having one or other of the first and second wavelengths λ_1, λ_2 tuned to an absorbance peak of the target analyte. In further examples, the assay device may measure the absorbance of labelling dyes, or other similar substances, which are bound to a target analyte.

Although examples have been described which are based on absorbance measurements, the present invention may alternatively be adapted for use with fluorescence measurements (i.e. fluorescence assays). For example, if the first wavelength λ_1 is used to excite fluorescence at a third wavelength λ_3 having a large enough Stokes shift $|\lambda_1-\lambda_3|$,

such that a filter (not shown) may be placed between the illuminated portion 13 and the one or more photodetectors 4, said filter being substantially transparent at the second and third wavelengths λ_2, λ_3, and attenuating the first wavelength λ_1.

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

Claims

1. An assay device for determining the presence and/or concentration of a target analyte within a liquid transport path having a first end, a second end and a sample receiving portion proximate to the first end, wherein the liquid transport path is configured to transport a liquid sample received in the sample receiving portion towards the second end, the assay device comprising:

one or more organic light emitting diodes configured to illuminate a section of the liquid transport path located between the sample receiving portion and the second end, each organic light emitting diode comprising a first light emitting material which emits light centred around a first wavelength and a second light emitting material which emits light centred around a second wavelength, wherein a ratio of emission intensity between the first and second light emitting materials varies in dependence upon a driving current supplied to the organic light emitting diode;

one or more photodetectors configured to receive light from the section of the liquid transport path illuminated by the organic light emitting diode;

a controller configured to:

drive the organic light emitting diode at a first driving current and obtain a first absorbance value based on the photodetector signal;

drive the organic light emitting diode at a second driving current and obtain a second absorbance value based on the photodetector signal;

determine the presence and/or concentration of a target analyte within the liquid transport path in dependence on a difference of the first and second absorbance values.

2. An assay device according to claim 1, wherein the first and second light emitting materials are comprised within a single layer of each organic light emitting diode.

3. An assay device according to claim 1, wherein the first light emitting material and the second light emitting material are comprised within different layers of each organic light emitting diode.

4. An assay device according to any preceding claim, configured to perform an immunoassay test.

5. An assay device according to any preceding claim, wherein the first wavelength is absorbed by the target analyte or by a label substance bound to the target analyte and wherein the second wavelength is substantially not absorbed by the target analyte or the label substance bound to the target analyte.

6. An assay device according to any one of claims 1 to 5, wherein the liquid transport path comprises a porous strip.

7. An assay device according to claim 6, wherein the porous strip is a lateral flow test strip.

8. An assay device according to any one of claims 1 to 5, wherein the liquid transport path comprises one or more microfluidic channels.

9. An assay device according to any one of claims 1 to 8, wherein the photodetector is configured to receive light transmitted through the liquid transport path.

10. An assay device according to any one of claims 1 to 8, wherein the photodetector is configured to receive light reflected and/or scattered from the liquid transport path.

11. An assay device according to any preceding claim, comprising a plurality of photodetectors arranged to form an image sensor, the image sensor configured to image all or a part of the section of the liquid transport path illuminated by the organic light emitting diode.

12. An assay device according to any preceding claims, further comprising an output device.

13. An assay device according to claim 12, wherein the output device comprises one or more output light emitters, and wherein the controller is configured to cause the one or more output light emitters to visually indicate the presence and/or concentration of the target analyte.

14. An assay device according to claim 12, wherein the output device comprises a display, and wherein the controller is configured to cause the display to visually indicate the presence and/or concentration of the target analyte.

15. An assay device according to any one of claims 12 to 14, wherein the output device comprises a wired or wireless communication interface, and wherein the controller is configured to cause the communication interface to output an indication of the presence and/or concentration of the target analyte via the communication interface.

16. An assay device according to any one of claims 1 to 15, wherein the assay device comprises the liquid transport path.

17. An assay device according to any one of claims 1 to 15, wherein the assay device is configured to receive the liquid transport path.

18. A method of using an assay device according to any one of claims 1 to 17, comprising applying a liquid sample to the sample receiving portion of the liquid transport path.

19. A method of determining the presence and/or concentration of a target analyte within a liquid transport path having a first end, a second end and a sample receiving portion proximate to the first end, wherein the liquid transport path is configured to transport a liquid sample received in the sample receiving portion towards the second end, the method comprising:

driving one or more organic light emitting diodes at a first driving current, the one or more organic light emitting diodes configured to illuminate a section of the liquid transport path located between the sample receiving portion and the second end, each organic light emitting diode comprising a first light emitting material which emits light centred around a first wavelength and a second light emitting material which emits light centred around a second wavelength, wherein a ratio of emission intensity between the first and second light emitting materials varies in dependence upon a driving current supplied to the organic light emitting diode;

obtaining a first absorbance value based on a photodetector signal received from one or more photodetectors configured to receive light from the section of the liquid transport path illuminated by the one or more organic light emitting diodes;

driving the one or more organic light emitting diodes at a second driving current;

obtaining a second absorbance value based on the photodetector signal;

determining the presence and/or concentration of a target analyte within the liquid transport path in dependence on a difference of the first and second absorbance values.

20. A method according to claim 19, further comprising applying a liquid sample to a sample receiving portion of a liquid transport path.

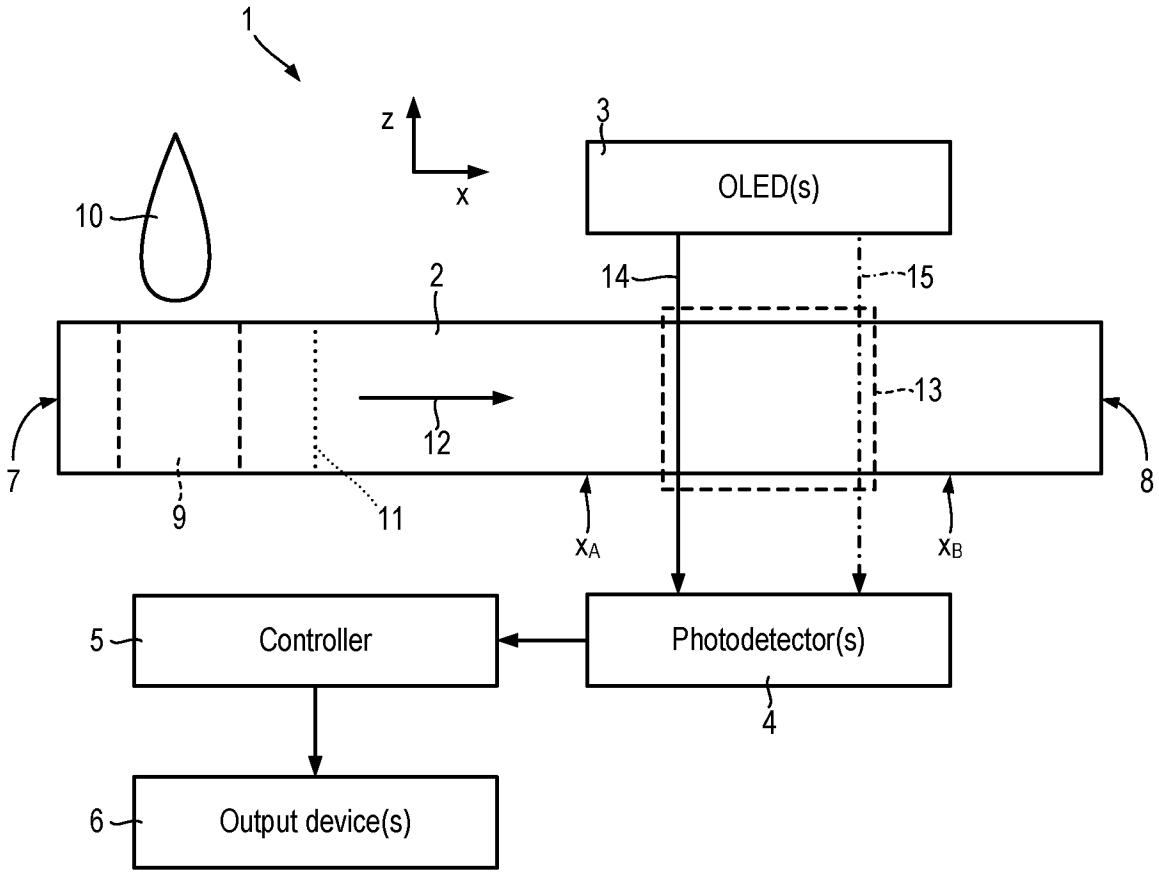

1
z
x
3
OLED(s)
10
2
14
15
13
12
7
9
11
x_A
x_B
8
5
Controller
Photodetector(s)
4
6
Output device(s)

Fig.1

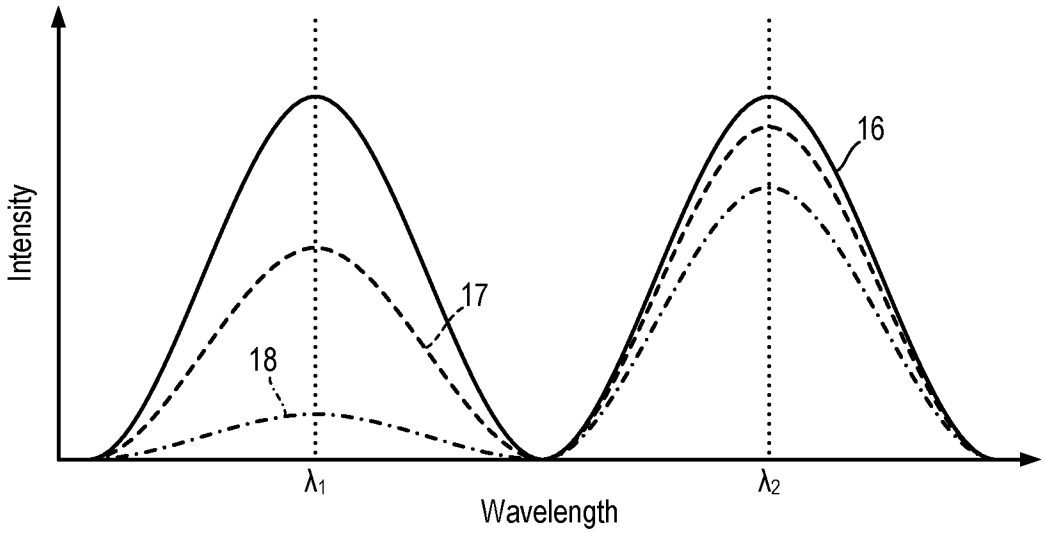

Intensity
16
17
18
λ_1
λ_2
Wavelength

Fig.2

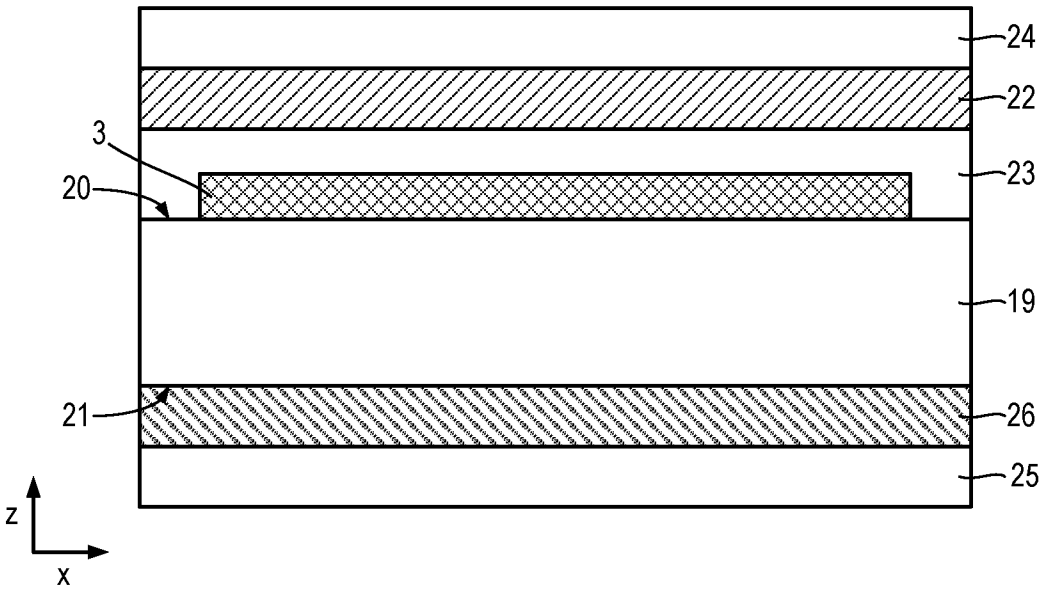


Fig.3

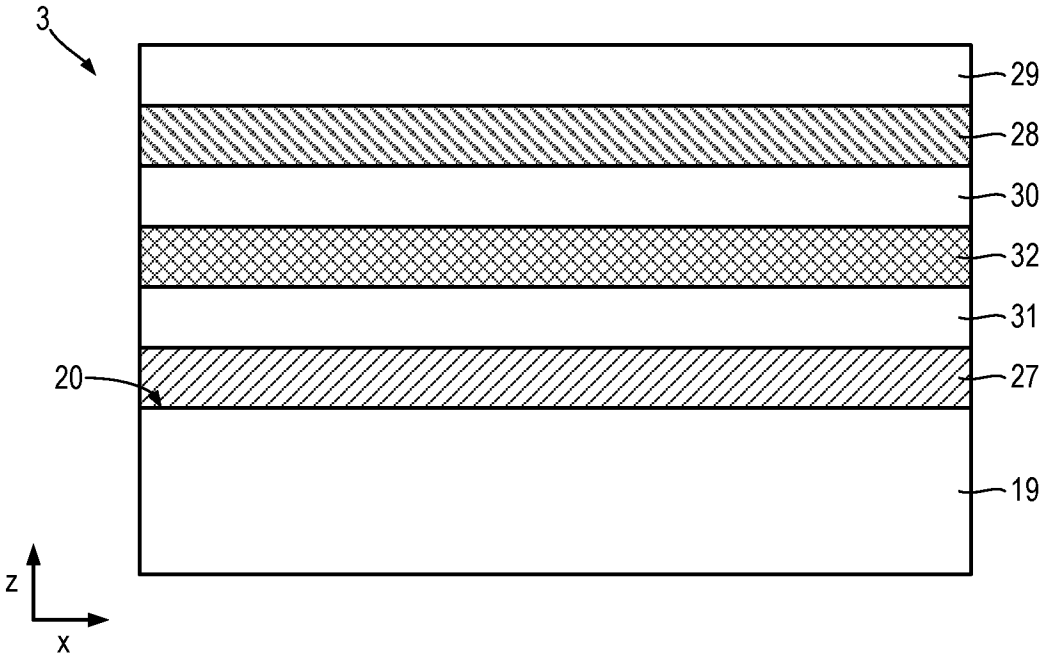


Fig.4

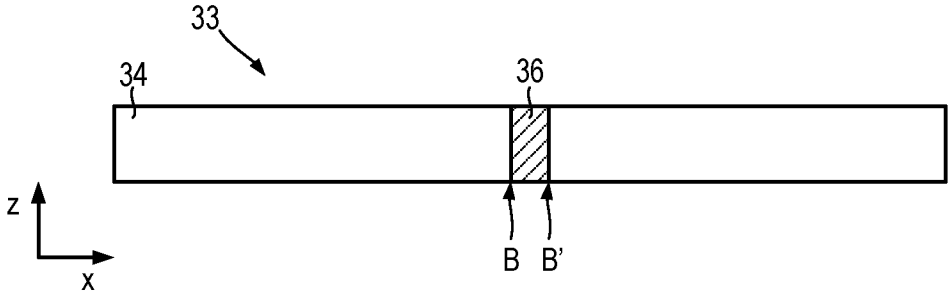


Fig.5

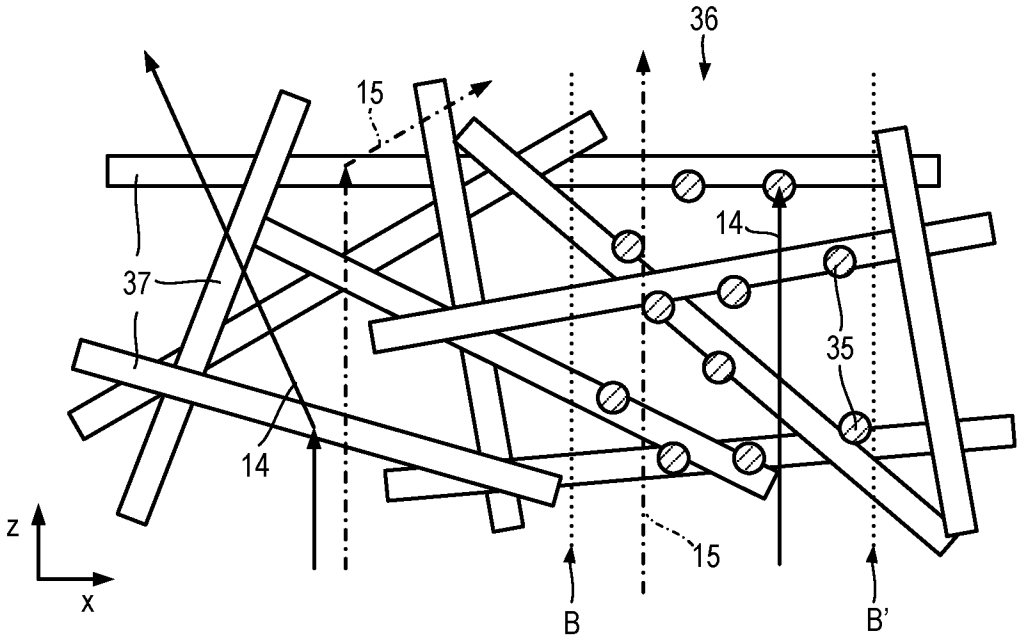


Fig.6

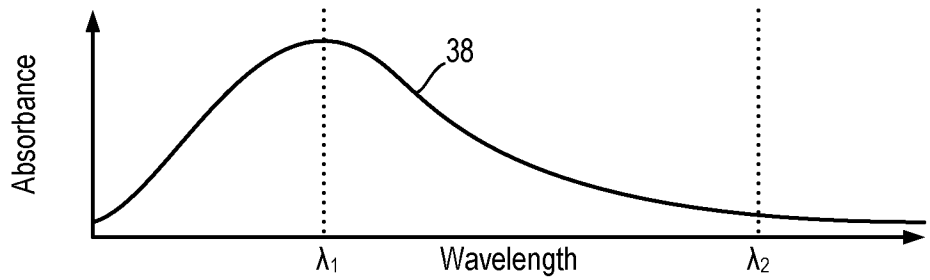


Fig.7

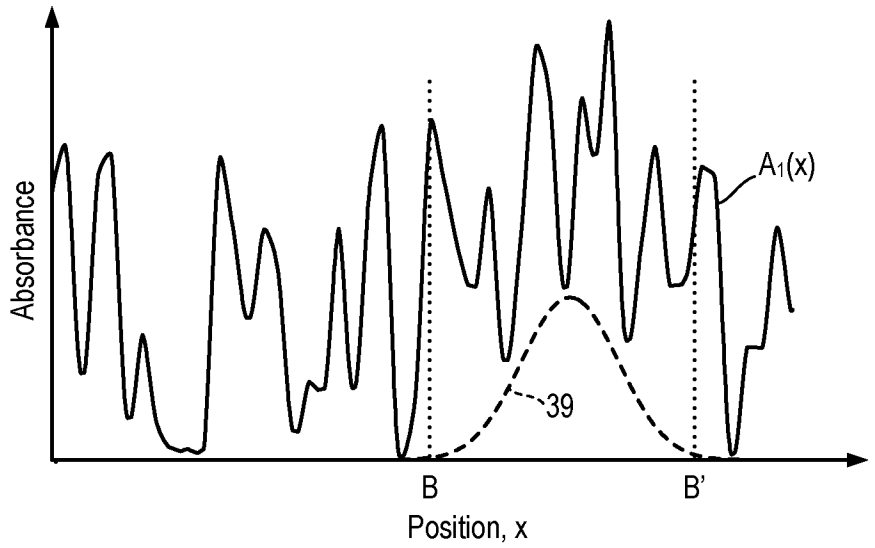


Fig.8

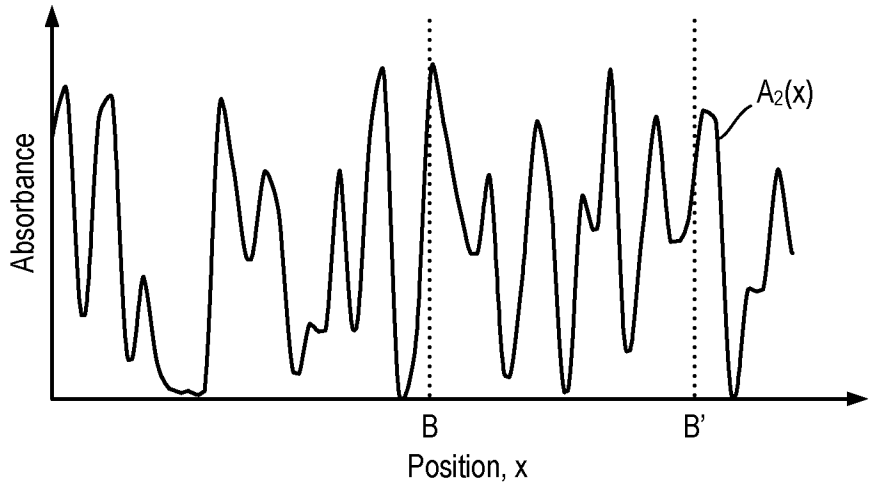


Fig.9

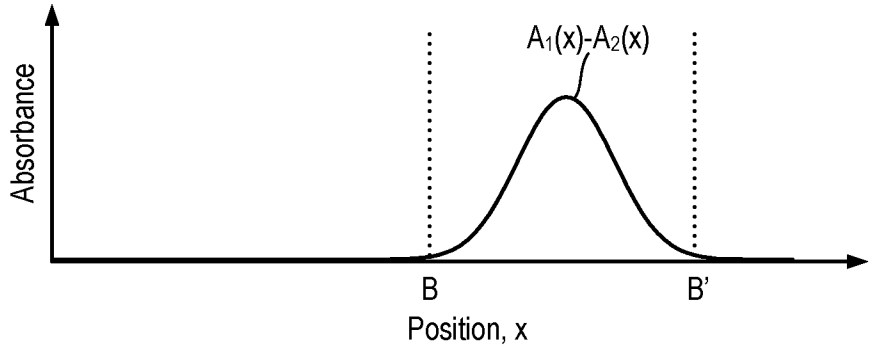


Fig.10

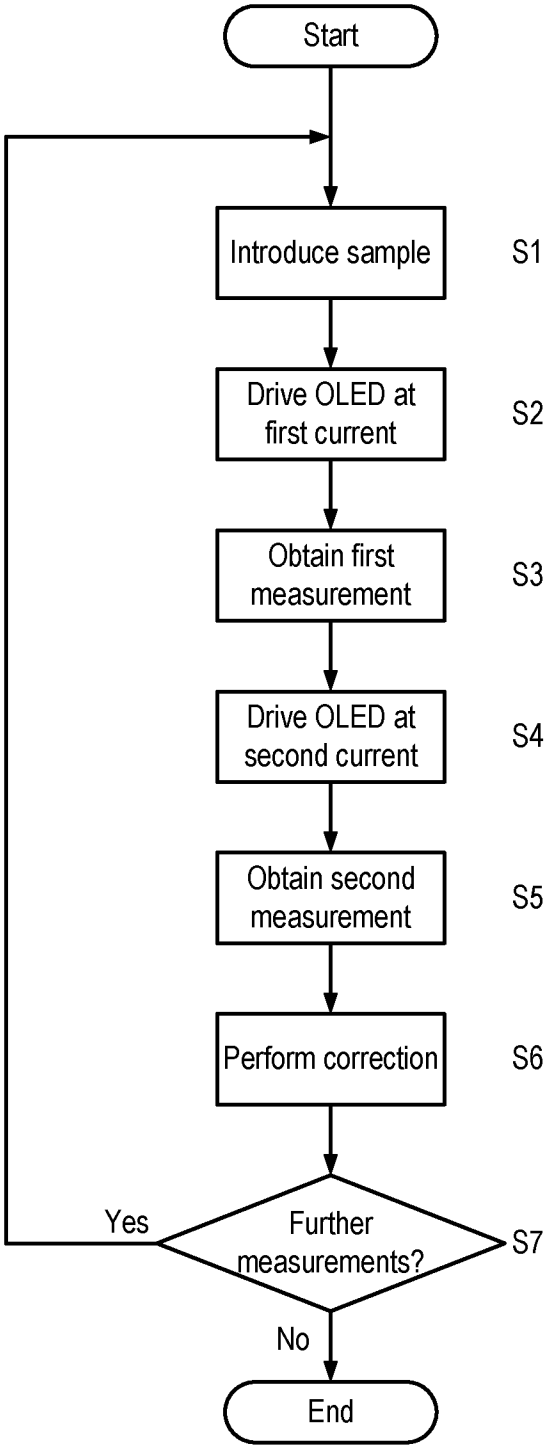

Start
Introduce sample
S1
Drive OLED at first current
S2
Obtain first measurement
S3
Drive OLED at second current
S4
Obtain second measurement
S5
Perform correction
S6
Further measurements?
S7
Yes
No
End

Fig.11

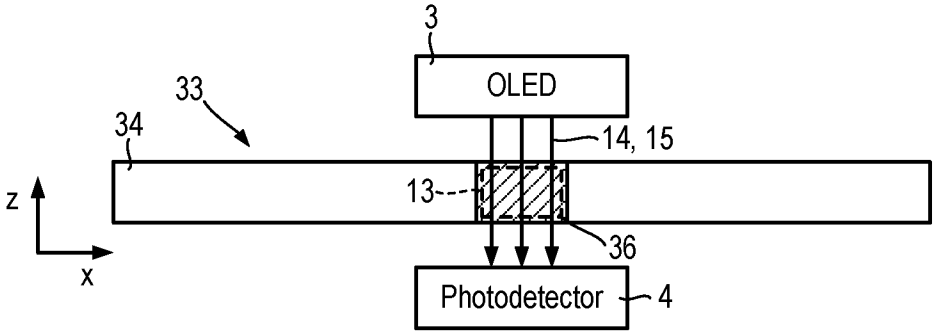


Fig.12

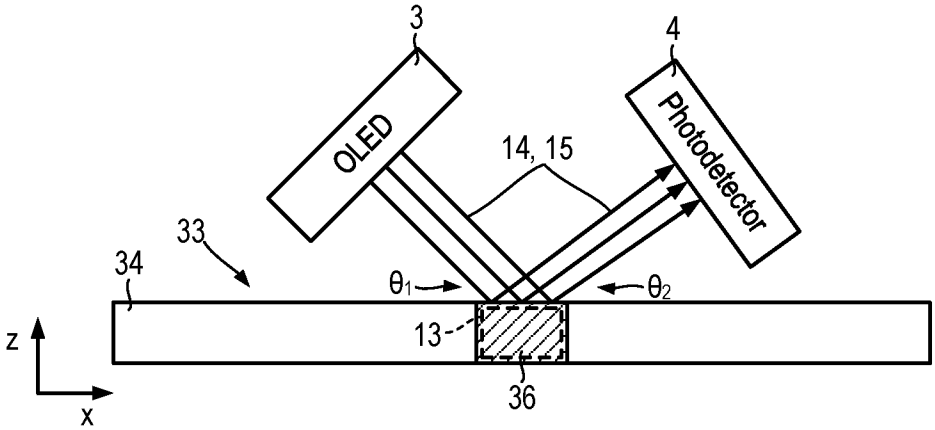


Fig.13

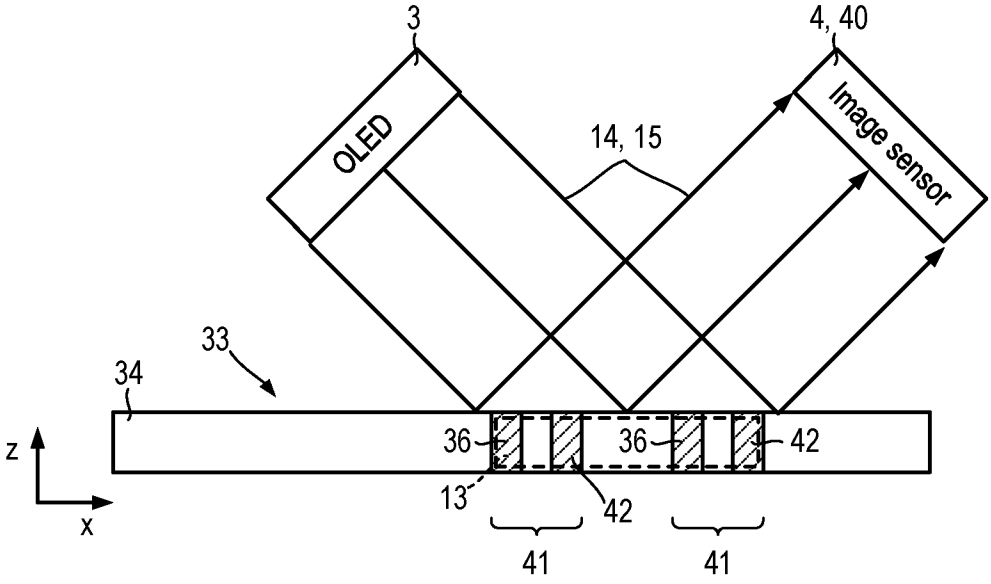
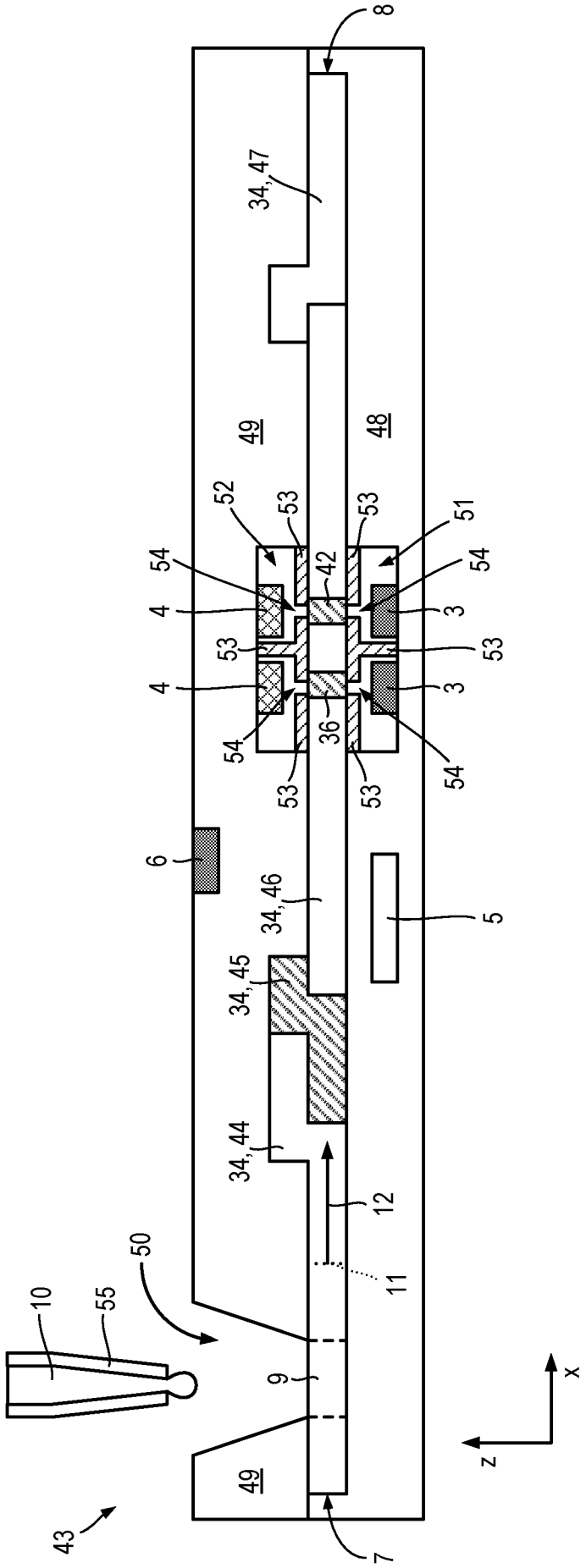


Fig.14


8
34, 47
49
48
52
53
53
51
54
42
54
4
3
53
53
4
3
36
54
53
53
54
6
34, 46
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34, 45
34, 44
12
11
50
10
55
9
49
43
7
x
z

Fig. 15

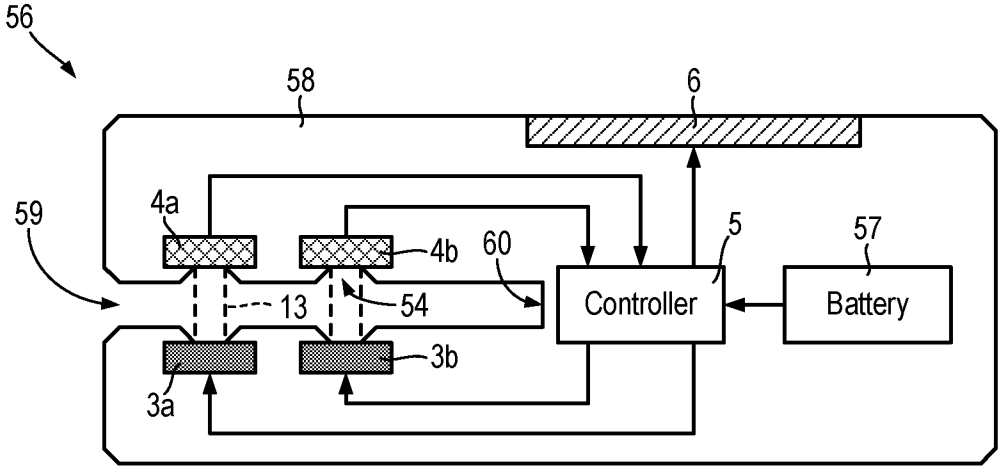

Fig.16A

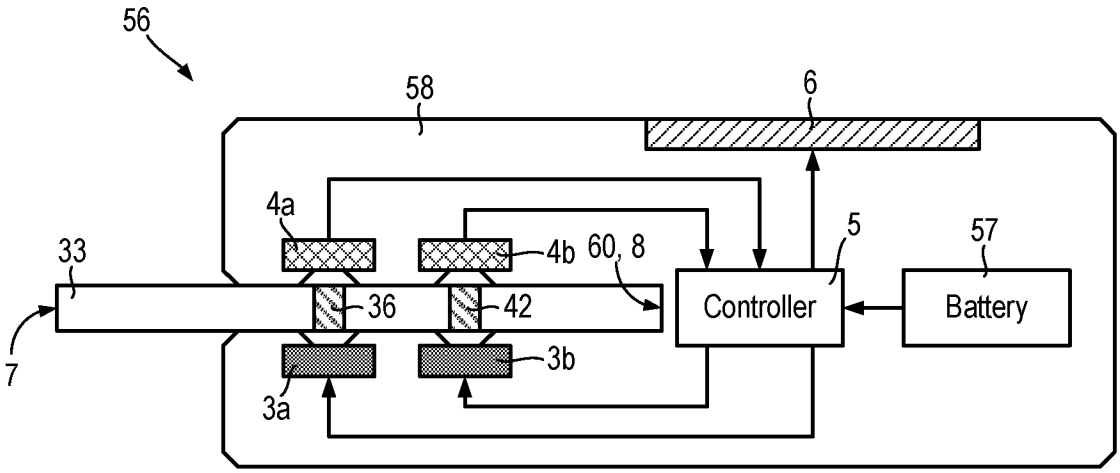

Fig.16B

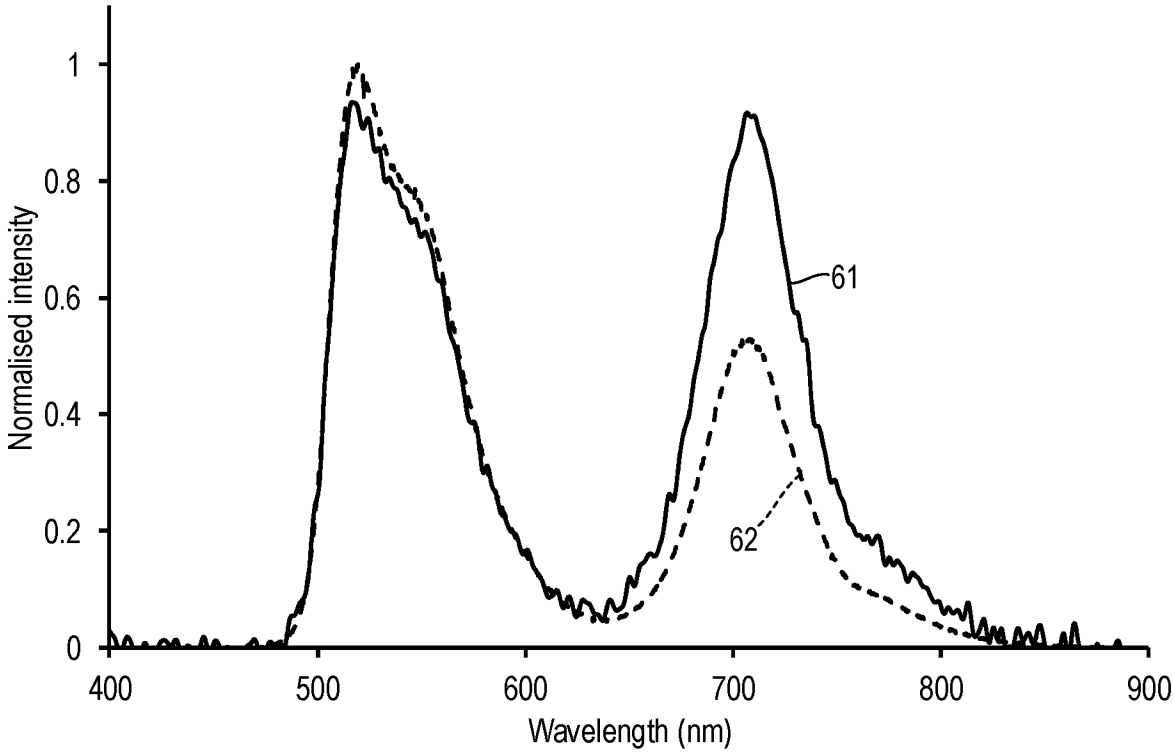
Normalised intensity
1
0.8
0.6
0.4
0.2
0
400
500
600
700
800
900
Wavelength (nm)
61
62

Fig.17

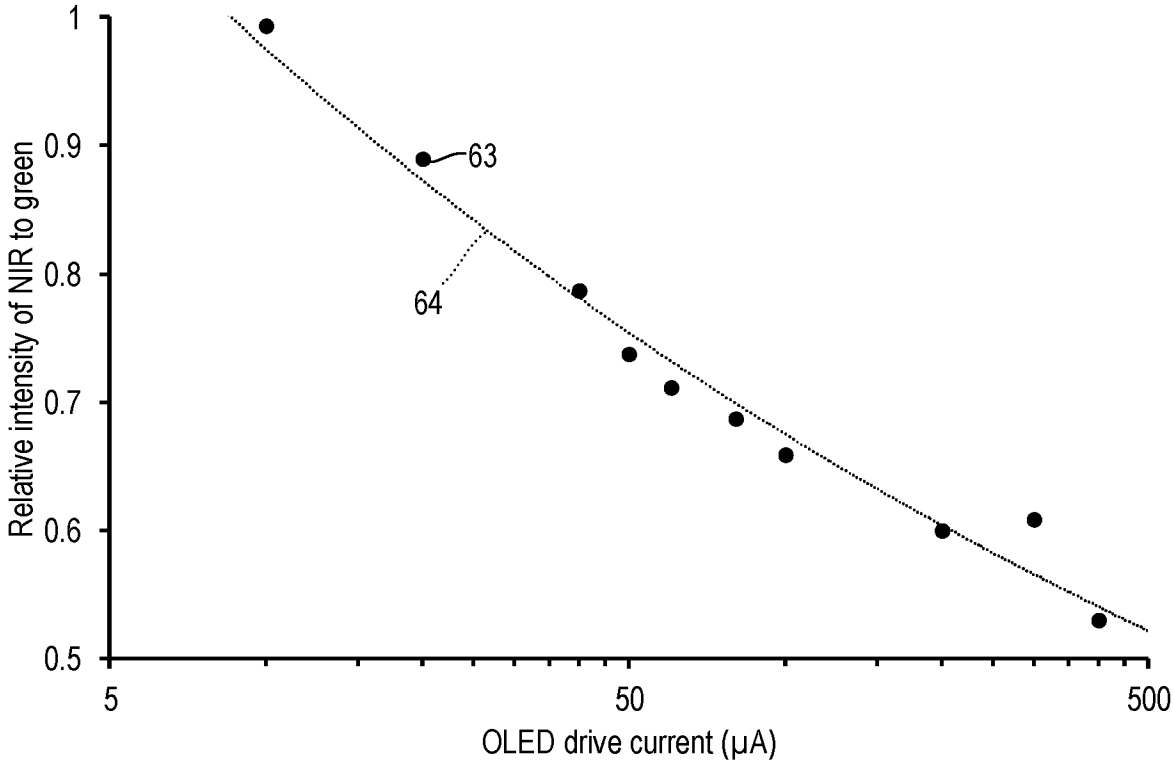
Relative intensity of NIR to green
1
0.9
0.8
0.7
0.6
0.5
5
50
500
OLED drive current (μA)
63
64

Fig.18

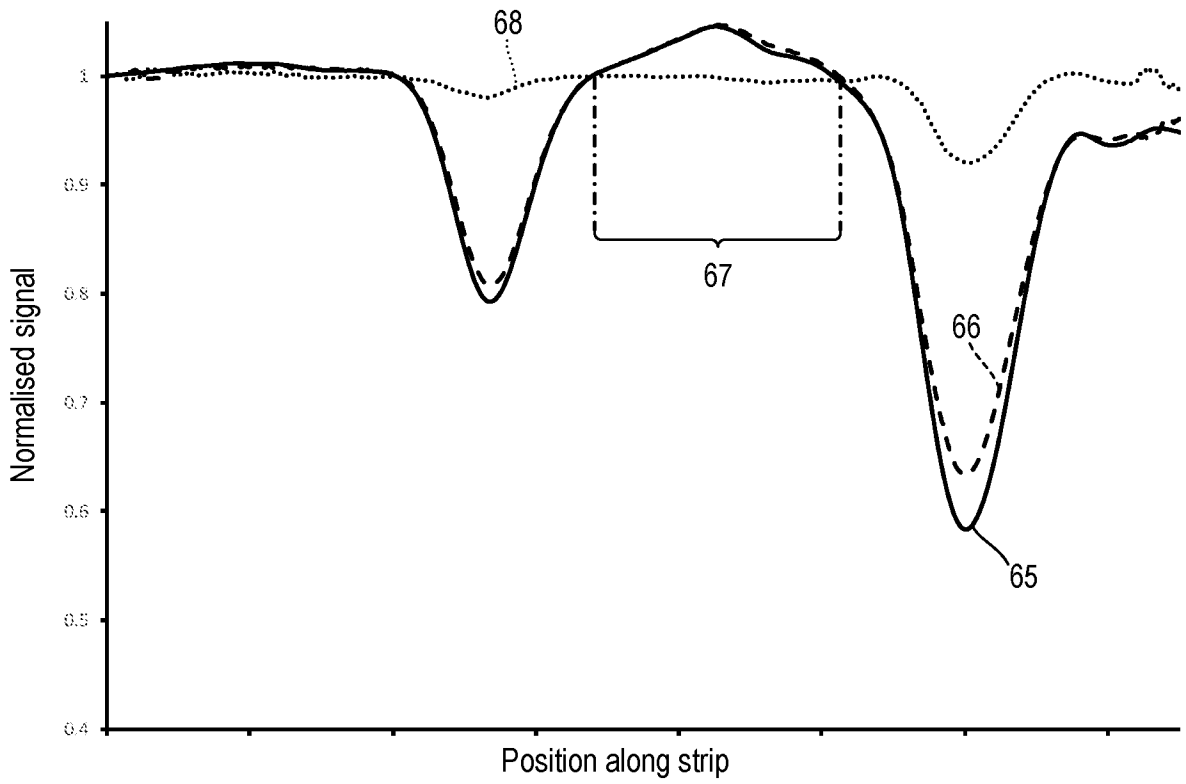
68
67
66
65
Normalised signal
Position along strip
1
0.9
0.8
0.7
0.6
0.5
0.4

Fig.19

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2018/053607

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N21/63 G01N33/53 G01N33/558
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01N B01L

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 541 425 A (MOLECULAR VISION LTD [GB]; CAMBRIDGE DISPLAY TECH [GB]) 22 February 2017 (2017-02-22)	1-20
Y	paragraph [0036] - paragraph [0043]; figures 4-5; examples 1,2	1-20

X	US 7 733 488 B1 (JOHNSON LYLE C [US]) 8 June 2010 (2010-06-08)	1-20
Y	column 7, line 16 - line 39; claims 6,7	1-20

Y	WO 00/04381 A1 (COZART BIOSCIENCE LIMITED [GB]; JONES OSBORN PIERCE [GB]; SPIVEY ROBIN) 27 January 2000 (2000-01-27) page 16, line 19 - page 17, line 2	1-20

Y	US 2016/172330 A1 (HACK MICHAEL [US] ET AL) 16 June 2016 (2016-06-16) paragraph [0044]	1-20

☐ 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	Date of mailing of the international search report
21 January 2019	01/02/2019

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Hinchliffe, Philippe

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/GB2018/053607

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