(19) Octrooicentrum Nederland

(11) 2028538

(12) B1 **OCTROOI**

(21) Aanvraagnummer: **2028538**

(22) Aanvraag ingediend: **24 juni 2021**

(51) Int. Cl.:
G01N 21/31 (2021.01) **G01N 21/01** (2021.01)

(30) Voorrang:
-

(41) Aanvraag ingeschreven:
30 december 2022

(43) Aanvraag gepubliceerd:
-

(47) Octrooi verleend:
30 december 2022

(45) Octrooischrift uitgegeven:
4 januari 2023

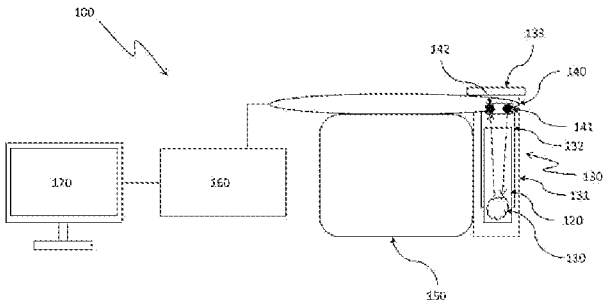
(73) Octrooihouder(s):
Clearstream Technologies Limited
te Enniscorthy, Co. Wexford, Ierland, IE

(72) Uitvinder(s):
Christopher Norris te Enniscorthy, County Wexford (IE)
Prathamesh Sharad Dhanpalwar
te Enniscorthy, County Wexford (IE)
Luke Bernard Anthony Myles te Enniscorthy, County Wexford (IE)

(74) Gemachtigde:
dr. ir. F.M. van Bouwelen te AMSTERDAM

(54) **A system for identifying a biological sample and a method for identifying a biological sample**

(57) system for identifying a biological sample in a sample holder. The system comprising a light source for emitting substantially monochrome light directed at the sample holder; a light sensor for detecting the amount of light reflected or transmitted by the biological sample and configured to output measurements indicative of the amount of light detected; and a controller connected to the light sensor and configured to identify the biological sample based on the output measurements of the light sensor.



NL B1 2028538

Dit octrooi is verleend ongeacht het bijgevoegde resultaat van het onderzoek naar de stand van de techniek en schriftelijke opinie. Het octrooischrift wijkt af van de oorspronkelijk ingediende stukken. Alle ingediende stukken kunnen bij Octrooicentrum Nederland worden ingezien.

Title: A system for identifying a biological sample and a method for identifying a biological sample

Description

Technical Field

The present invention relates to a system for identifying a biological sample in a sample holder and a method for identifying a biological sample in a sample holder.

Background of the Invention

The detection and identification of diseased tissue is of great importance in modern medicine. Cancer is still one of the leading causes of death worldwide and earlier and simpler detection and identification of tumours could save countless lives.

Cancer is often identified using a biopsy where a small sample of body tissue is taken from a patient in a medical procedure so it can be examined under a microscope. When the tissue sample is examined under the microscope, abnormal cells may be identified, which can help to diagnose a specific condition, such as a tumour. The problem with these procedures is that they are slow, expensive and they require specially trained medical staff to examine the tissue and make a determination of whether the tissue is diseased.

The present invention proposes utilizing the difference in absorption spectra between different tissues and between healthy tissue and malignant tissue to identify the tissue and make a determination of whether the tissue is diseased.

Spectrophotometers for measuring the absorption spectrum of a sample over a range of wavelengths exist in the art. However, these devices are complex and expensive and do not give an automatic identification of the biological sample and whether it relates to a diseased tissue.

There is hence a need in the art for a simple automated system which makes an accurate and quick identification of a biological sample and a determination of whether the biological sample comprises diseased tissue.

Summary of the Invention

In a first aspect of the present invention, there is provided a system for identifying a biological sample in a sample holder. The system comprises a light source for emitting substantially monochrome light directed at the sample holder;
a light sensor for detecting the amount of light reflected or transmitted by the biological sample and configured to output measurements indicative of the amount of light detected. The system further comprises a controller connected to the light sensor and configured to identify the biological sample based on the output measurements of the light sensor.

Throughout this disclosure, 'substantially monochrome' light refers to light which has a peak intensity at a predetermined wavelength and a narrow spectral bandwidth. The spectral bandwidth may be less than 200 nm, preferably 100 nm, even more preferably 50 nm. 'Substantially monochrome' light may be emitted, for example, by a laser diode or an LED.

Throughout this disclosure, the term 'identifying a biological sample' means both identifying a type of tissue, e.g. breast tissue, as well as characterising whether a type of tissue is healthy or diseased, e.g. identifying whether the breast tissue is healthy breast tissue or malignant breast tissue.

In some embodiments, this may result in a system which can automatically identify a biological sample in a cheap, simple and accurate manner.

In some embodiments, this may also allow the automatic determination of a diseased biological tissue in a quick, simple and accurate manner.

The system may further comprise a light blocking structure for holding the sample holder. The light blocking structure may be configured to block any ambient light from reaching the sample when the light blocking structure is holding the sample holder.

In some embodiments, this may result in a reduction of ambient light noise in the light measurements and thereby in a more accurate identification of the biological sample.

The light blocking structure may be non-transparent.

Throughout this disclosure, the term 'non-transparent' means that light in the visible and/or infrared spectrum is blocked.

In some embodiments, this may result in a further reduction of ambient light noise and a more accurate identification of the biological sample.

The light blocking structure may comprise a bore for accommodating the sample holder.

In some embodiments, this may result in a further reduction of ambient light noise and a more accurate identification of the biological sample.

In some embodiments, this may also allow the sample holder to be secured within the light blocking structure to give more repeatable and accurate results.

The bore may have a single opening.

The bore may comprise a first section where the bore is wider and a second section where the bore is narrower.

The second section may be disposed further away from the opening of the bore.

In some embodiments, this may allow the sample holder to be easily and quickly inserted and removed from the light blocking structure.

The second section may be configured to engage the sides of the sample holder to hold the sample holder in place.

In some embodiments, this may allow the sample holder to be secured within the light blocking structure to give more repeatable and accurate results.

The bore may have a rectangular cross section.

In some embodiments, this may allow a standard rectangular cuvette to be used as the sample holder.

The light source may be disposed at the opening of the bore and configured to emit the substantially monochromatic light into the bore.

The light detector may be disposed at the opening of the bore. The light detector may be configured to detect the substantially monochromatic light reflected or transmitted by the biological sample in the bore.

In some embodiments, this may result in a simple and robust set-up which can produce repeatable and accurate measurements.

The light blocking structure may further comprise a lid for enclosing the opening of the bore. The lid may enclose the light source and/or the lid may enclose the light detector such that ambient light is blocked from reaching the sample holder.

Some or all of the light may be blocked from reaching the sample holder.
In some embodiments, this may result in a further reduction of ambient light noise and a more accurate identification of the biological sample.

The light blocking structure may be a 3D-printed structure.

In some embodiments this may result in a simple and cheap reduction of ambient light noise.

The system may comprise the sample holder.

The sample holder may be a cuvette.

The cuvette may comprise a plurality of straight, transparent sides.

In some embodiments, this may reduce measurement errors from refraction and result in a more accurate identification of the biological tissue.

The light source may comprise an LED.

In some embodiments, this may result in a cheap and simple way to emit light with a narrow spectral bandwidth which will give more accurate results when identifying a biological sample.

The light source may comprise an infrared LED.

In some embodiments, infrared light may result in a higher absorption value from biological tissue, making it easier to distinguish between different biological samples.

The light source may comprise a laser diode. The substantially monochromatic light may be a laser light.

In some embodiments, this may result in a highly monochromatic light source which gives a more accurate identification of the biological sample.

The light source may comprise a tuneable laser.

In some embodiments, this may allow the wavelength of the emitted light to be changed such that an absorption value may be determined for a biological sample over a range of wavelengths and thereby give a more accurate identification of the biological sample.

The substantially monochromatic light emitted by the light source may have a peak intensity at a wavelength in the range of 300nm to 5000nm.

Preferably, the substantially monochromatic light emitted by the light source may have a peak intensity at a wavelength in the range of 500nm to 2000nm.

Even more preferably, the substantially monochromatic light emitted by the light source may have a peak intensity at a wavelength in the range of 800nm to 1000nm.

In some embodiments, this range of wavelengths may result in a higher absorption value from biological tissue, making it easier to distinguish between different biological samples.

The substantially monochromatic light emitted by the light source may have a spectral bandwidth below 200nm.

Preferably, the substantially monochromatic light emitted by the light source may have a spectral bandwidth below 100 nm.

Even more preferably, the substantially monochromatic light emitted by the light source may have a spectral bandwidth below 50 nm.

In some embodiments, this may result in more accurate and repeatable measurements.

The light detector may comprise a photodiode.

In some embodiments, this may result in a cheap and accurate way to detect the amount of light reflected or transmitted by the biological sample.

The photodiode may have a maximum sensitivity at a wavelength in the range of 300nm to 5000nm.

Preferably, the photodiode may have a maximum sensitivity at a wavelength in the range of 500nm to 2000nm.

Even more preferably, the photodiode may have a maximum sensitivity at a wavelength in the range of 800nm to 1000nm.

In some embodiments, this may result in maximum sensitivity of the photodiode coinciding with the peak intensity of the light emitter, giving more accurate measurements.

The light source and the light detector may be provided in a single integrated circuit package.

In some embodiments, this may allow the use of a simple and cheap off-the-shelf sensor package.

The system may further comprise a base support for holding the light source and the light detector.

In some embodiments, this may result in the light source and light detector being held securely in place, result in more repeatable and accurate measurements.

The controller may be configured to calculate an absorption value based on the ratio of the emitted light and the detected light and identify the biological sample based on the absorption value.

In some embodiments, this provides a simple and accurate way of identifying a biological sample.

The controller may be configured to calculate an absorption value based on the output measurements of the light sensor.

The controller may be configured to calculate an absorption value based on the ratio of the output measurement of the light sensor and the maximum output of the light sensor.

The controller may identify the biological tissue from a look-up table of known biological tissues based on the calculated absorption value.

The controller may be configured to make a plurality of measurements using the light sensor and calculate an average absorption value.

In some embodiments, this may result in a more accurate determination of the absorption value.

The system may further comprise a display connectable to the controller for showing the identified biological sample to the user.

In some embodiments, this may allow a user to make a quick and simple identification of the biological sample.

The controller may be further configured to show the measurements acquired by the light sensor on the display.

In some embodiments, this may allow a user to check the accuracy of the measurements.

The system may further comprise an input device connectable to the display and the controller to allow a user to begin taking the measurements of the sample, and/or load previously acquired measurements for analysis, and/or export the measurements to a different programme, and/or clear the measurements.

In some embodiments, this may provide a simple way for the user to control the system and further process the measurement data.

Identifying the biological sample may comprise identifying whether the biological sample relates to a healthy tissue or a diseased or malignant tissue.

In a second aspect of the present invention, there is provided a method for identifying a biological sample in a sample holder using a system having a light source, a light detector and a controller. The method comprises emitting a light from the light source at a sample within the sample holder; detecting an amount of light reflected or transmitted by the biological sample with the light detector; outputting measurements from the light detector indicative of the amount of light detected to the controller; and identifying the biological sample based on the output signal of the light sensor using the controller.

In some embodiments, this may result in a method which can identify a biological sample in a cheap, simple and accurate manner.

The method may further comprise blocking any ambient light from reaching the sample using a light blocking structure.

In some embodiments, this may result in a reduction of ambient light noise in the light measurements and thereby in a more accurate identification of the biological sample.

Identifying the biological sample may comprise: calculating an absorption value based on the ratio of the emitted light and the detected light; and identifying the biological sample based on the absorption value.

Identifying the biological sample may comprise: calculating an absorption value based on based on the ratio of the output measurement of the light sensor and the maximum output of the light sensor; and identifying the biological sample based on the absorption value.

The absorption value may be an average absorption value based on a plurality of measurements made by the light sensor.

In some embodiments, this may result in a more accurate determination of the absorption value.

Identifying the biological sample may comprise identifying whether the biological sample relates to a healthy tissue or a diseased or malignant tissue.

Brief Description of the Drawings

To enable better understanding of the present disclosure, and to show how the same may be carried into effect, reference will now be made, by way of example only, to the accompanying drawings, in which:

FIG. 1 shows an embodiment of a system for identifying a biological sample in a sample holder according to the present disclosure;

FIGS. 2A to 2C show different views of the body portion of a light blocking structure used in the system of FIG. 1;

FIGS. 3A and 3B show different views of the lid of a light blocking structure used in the system of FIG. 1;

FIG. 4 shows a more detailed view of the light blocking structure, base structure and sensor package of FIG. 1;

FIG. 5 shows a block diagram for a graphical user interface for controlling the system of FIG. 1.

Detailed Description

FIG. 1 shows a schematic diagram of a system 100 for identifying a biological sample 110.

The biological sample 110 may be tissue obtained from a human body in a biopsy, for example. The present system 100 can identify the type of tissue and, more importantly, identify whether the tissue is a healthy tissue or a diseased tissue based on the amount of light absorbed by the tissue.

Different tissues have different absorption spectra and absorb different amounts of light at different wavelengths. By shining light at a certain wavelength at the biological sample 110 and measuring the amount of light which is reflected or transmitted and therefore not absorbed by the biological sample 110, a determination of what type of tissue and whether the tissue is diseased can be made. The system 110 can be used, for example, to identify and detect cancerous breast tissue obtained from a biopsy. At a wavelength of 930nm, malignant breast tissue has a much lower absorption coefficient of about 0.009 mm^{-1} compared to healthy breast tissue with an absorption coefficient of about 0.02 mm^{-1}. This means that the malignant breast tissue will absorb less light which can be detected by the system 100 and used to identify and detect malignant breast tissue.

In the same manner, tumours in other types of tissues can be detected and the oxygenation levels of blood can be determined.

The biological sample 110 may be placed in a sample holder 120, which may be a cuvette or a test tube. A cuvette is preferred because a standard cuvette has a square or rectangular cross section with straight transparent sides, which reduces the effects of refraction when light is shining onto a sample inside the cuvette.

The sample holder 120 is placed inside a light blocking structure 130. The light blocking structure 130 has a body portion 131 and a lid 133 which are both non-transparent and block any ambient light in the visible and infrared spectrum from reaching the sample 110. The body portion 131 has a rectangular or square shaped bore 132 which extends from an opening on one side of the body portion 131. The sample holder 120 is placed within the bore 132 of the light blocking structure 130.

At least part of the bore 132 is dimensioned such that it engages the sides of the sample holder 120 and secures the sample holder 120 in place such that it cannot move while measurements are taken. This allows more accurate and repeatable measurements to be taken.

The light blocking structure 130 may be made from a number of materials such as a dark coloured non-transparent plastic or a metal. The light blocking structure 130 may be 3D-printed or moulded.

A sensor package 140 comprising a light source in the form of a laser diode 141, such as a Vertical Cavity Surface Emitting Laser (VCSEL), and a light detector in the form of a photodiode 142 is disposed at the opening of the bore 132 and at the top of the body portion 131. The sensor package 140 may be, for example, a Vishay VCNL36887S, which is an off-the-shelf IC package and uses a Vertical Cavity Surface Emitting Laser (VCSEL) as a light source. This allows for simple and cheap construction of the system 100. The laser diode 141 and the photodiode 142 are held in place and supported by a base structure 150. The base structure 150 may be made from plastic and may be a 3D-printed structure. The lid 133 of the light blocking structure 130 is placed over the sensor package and the opening of the bore 132 such that any ambient light is blocked from reaching the sample 110. This results in less ambient light noise when taking measurements and identifying the biological sample 110.

The laser diode 141 emits light which is substantially monochromatic and has a peak intensity at a predetermined wavelength. The light emitted by the laser diode 141 may have a peak intensity at a wavelength in the range of 300nm to 5000nm, preferably 500nm to 2000nm, even more preferably 800nm to 1000nm, even more preferably 930 nm.

It has been shown that a number of biological tissues such as sub-cutaneous human fat and post-menopausal breast tissue have an absorption peak at around 930 nm. This means that if light with a wavelength of around 930 nm is emitted through a sample of human fat or breast tissue, then a greater proportion of the light at that wavelength will be absorbed than at other wavelengths making it easier to evaluate small differences in absorption values between different tissues. A light with a wavelength of around 930 nm will therefore result in greater absorption by the biological sample 120 and more accurate identification of the biological sample 120.

The light emitted by the laser diode 141 has a narrow spectral bandwidth. The spectral bandwidth is defined as band width of the emitted light at half the maximum intensity. A narrower spectral bandwidth will result in light that is more monochromatic and therefore emits more light at a single wavelength compared to other wavelengths. The substantially

monochromatic light emitted by the light source may have a spectral bandwidth below 200nm, preferably below 100 nm, even more preferably below 50 nm. This will also result in more accurate measurements and identification of the biological sample, as the photodiode 142 is influenced by light of other wavelengths.

The photodiode 142 is preferably matched to the wavelength of the laser diode 141, such that the peak or maximum sensitivity of the photodiode 142 is close or identical to the wavelength at which the laser diode 141 emits at a peak intensity.

The photodiode 142 may therefore have a maximum sensitivity at a wavelength in the range of the 300nm to 5000nm, preferably 500nm to 2000nm, even more preferably 800nm to 1000nm, even more preferably 930 nm.

The laser diode 141 and the photodiode 142 are both connected to a controller 160. The controller may be a microcontroller such as the STM32F407VGT6 manufactured by STMicroelectronics, for example.

The controller 160 is connected to a display 170 which can show the measurements obtained by the photodiode 142 to a user. The display 160 also comprises an input device to allow a user to provide commands to the controller 160. This input device may be in the form of a touchscreen, a mouse or a keyboard, for example. The input device together with a GUI allows a user to begin the analysis of the biological sample 110 by starting measurements using the laser diode 141 and photodiode 142, load previous measurements of a biological sample, export the measurements as file to an external programme or memory, or clear the measurements (see FIG. 5).

In order to identify the biological sample and determine whether the biological sample 110 is a diseased tissue, a medical practitioner firstly obtains the biological sample 110 from a patient. The biological sample 110 is then placed into the sample holder 120 which is in turn placed into bore 132 of the body portion 131 of the light blocking structure 130. The bore 132 is sized such that it securely holds the sample holder 120 such that it cannot move while measurements are taken. The sensor package 140 comprising the laser diode 141 and the photodiode 142 is then placed over the opening of the bore 132 and the lid 133 is placed over the sensor package 140 and the opening such that no ambient light can reach the sample 110 in the bore 132.

A user can use the input device and the display 170 to start the analysis of the biological sample 110. This will cause the controller 160 to turn on the laser diode 141 which emits substantially monochromatic light directed into the bore 132 towards the biological sample 110. When the light hits the sample 110, some of the light will be absorbed by the sample 110, while some of the light will be reflected by the sample 110.

The amount of light which is reflected by the sample 110 is then detected by the photodiode 142. The photodiode 142 turns the amount of light detected into an electrical signal, which may be in the form of a voltage or a current, which is then sent to the controller 160.

The controller 160 will then calculate an absorption value for the biological sample based on the ratio of the known intensity of emitted light from the laser diode 141 and the light detected by the photodiode 142. Alternatively, the controller 160 will calculate an absorption value based on the output measurements of the photodiode 142, alone, for example, by calculating an absorption value based on the ratio of the output measurement of the photodiode 142 and the maximum output of the photodiode 142.

The photodiode 142 may take several separate measurements over a pre-determined time period and send these to the controller. The controller can then calculate an average absorption value for the biological sample 110 based on the plurality of measurements taken.

Based on the determined absorption value for the biological sample 110 and the known wavelength of light emitted by the laser diode 141, the controller 160 can then identify the biological sample 110. For example, the controller may determine whether the biological sample is healthy breast tissue or a malignant breast tissue. This can be done, for example, by the controller 160 consulting a look-up table of known absorption values and wavelengths, consulting an external database, or using pre-determined upper and lower limits for the absorption value based on empirical data.

The measurements obtained by the photodiode 142 together with the calculated absorption values and the identified biological sample 110 are then displayed on display 170. The user can then use the input device to export the data to a different programme for further processing or an external memory for storage. Alternatively, the user can clear the data and start a new

analysis of the biological sample 110 or load data from a previous analysis of a different biological sample.

The present system 100 therefore provides automated system for identifying a biological sample in a quick and accurate manner and allows a determination of whether the sample is a diseased tissue. The system 100 is simple to use, robust and cheap to make and can provide accurate determination of diseased biological tissue. The sensor package 140 and the controller 160 can be relatively cheap off-the-shelf IC components. The light blocking structure 130 and the base structure 150 can be 3D-printed structures. The present system can therefore provide an accurate and automated identification of a biological sample at a fraction of the cost of a spectrophotometer and without the training required to perform a biopsy and tissue analysis using a microscope.

FIGS. 2A to 2C show different detailed views of the body portion 131 of the light blocking structure 130. FIG.2A is a cross-sectional side view of the body portion 131 and FIG. 2B shows a cross-sectional front view of the body potion 131.

As shown in FIGS. 2A and 2B, the body portion 131 is in the shape of a cuboid and comprises a bore 132 which extends partly through the body portion 131. The bore 132 has a single opening on one side of the body portion 131. The cross-section of the bore is square or rectangular, as shown in FIG. 2C, and the bore 132 comprises a first section 132A and a second section 132B. The first section 132A starts at the opening and is wider than the second section 132B which is further away from the opening. The diagonal width of the bore of the first section 132A is therefore greater than the diagonal width of the bore of the second section 132B. The second section 132B is dimensioned to engage the sides of the sample holder 120, which in this case is a standard size cuvette. This means that the cuvette is secured inside the body portion 131 and cannot move while the measurements on the sample 110 are made. The first section 132A is wider to allow the cuvette to be easily inserted and removed from the body portion 132.

The body portion 131 further comprises a side opening 134 which is connected to the opening of the bore 132 from a side of the body portion 131. The side opening 134 may be in the form of a slit or a channel. The side opening allows the sensor package 140 including the laser diode 141 and the photodiode 142 to be placed over the opening of the bore 142. Wires from the

sensor package 140 can enter and exit the light blocking structure 130 through the side opening 134.

The body portion 131 also comprises a square indentation at the bottom, opposite the opening of the bore 132. This groove is optional but may be used to engage a corresponding raised portion to stabilise and secure the body portion 131.

FIG. 2C shows a top view of the body portion 131. This clearly shows the rectangular or square cross-section of the body portion 131 as well as the square cross-section of the first section 132A and the second section 132B and also shows that the diagonal width of the second section 132B is smaller than the first section 132A. The side opening 134 which connects the opening of the bore 132 to an orthogonal side of the body portion 131 is also shown.

As mentioned above, the body portion may be made from a non-transparent material such as a plastic or metal and may be 3D-printed or moulded, for example.

FIG. 3A shows a top view of the lid 133 of the light blocking structure. The lid is non-transparent square-shaped element which dimensioned to fit over the opening of the bore 132 and enclose the sensor package 140, including the laser diode 141 and the photodiode 142, such that no ambient light can reach the biological sample 110. The lid 133 may be provided with insignia 133A.

FIG. 3B shows a perspective side view of the lid 133.

FIG. 4 shows a schematic close-up view of the arrangement of the light blocking structure 130, sensor package 140 and base structure 150. As already mentioned with respect to FIG. 1, the biological sample 110 is placed in the sample holder 120 which is placed within the bore 132 of the light blocking structure. FIG. 4 shows how the second section 132B of the bore 132 engages the bottom of the sample holder 120 and holds it in place.

The sensor package is placed at the top of the body portion 131 over the opening of the bore 132 so that the laser diode 141 can emit light into the bore 132 and the photodiode can detect the reflected light coming from the sample 110 in the bore 132. Part of the sensor package can extend through the side opening 134 out of the light blocking structure 130 and is secured to the base structure to hold the sensor package 140 in place. Alternatively, the entire sensor

package 140 can be disposed inside the light blocking structure and only an element carrying the wires connecting the sensor package 140 to the controller 160 extends through the side opening 134 and is secured to the base structure 150. The lid 133 is placed over the opening of the bore and the sensor package 140 to block any ambient light from entering the bore 132 and reaching the sample 110.

FIG. 5 shows a block diagram for a graphical user interface (GUI) used to control the system 100.

At the start, the GUI allows the user to select a communications (COM) port of the controller 160. The controller 160 may have a plurality of COM ports which can be connected to different sensor packages 140. For example, multiple sensor packages having light sources with different wavelengths can be used, and measurements of the sample can be made at different wavelengths of light.

The controller 160 will then open the selected COM port and the GUI will present the user with a combo box. The user will then be able to select from a number of different options.

The user may select 'Begin Analysis?' which results in the controller 160 sending instructions to the sensor package 140 to start taking measurements of the biological sample 110. The display 170 will display the live measurements taken from the photodiode 142 as well as the identified biological sample.

If the user selects 'Load data', previous measurement data may be loaded and displayed as a chart on the display 170.

If the user selects 'Clear Data', the measurement data present on the GUI will be cleared and the GUI will take the user back to the start.

If the user selects 'Export to .CVS?', the measurement data obtained from the photodiode 142 and the controller 160 may be saved as a .CVS file to a memory device. The data may then be loaded into programme for reanalysis or used in a different programme for further analysis.

Various modifications will be apparent to those skilled in the art.

The sample holder 120 may be a cuvette, a test tube, or any other type of suitable vehicle for holding a biological sample.

The system 100 may not comprise a light blocking structure 130.

The light blocking structure 130 may not be cuboid shaped but may be any other suitable shape, such as, for example, spherical, pyramidal.

The bore 132 of the body portion 131 may not comprise a first section 132A and a second section 132B but rather may be a single bore with a constant width.

The light blocking structure 130 may be made from any material which is non-transparent and can block ambient visible and infrared light and is not limited to plastics or metals.

The light blocking structure 130 may be made in any suitable way and is not limited to 3D printing or moulding.

The light blocking structure 130 may not have an indentation 135 or a side opening 134.

The bore 132 is not limited to a square cross-sectional shape but may take other shapes such as a round or triangular cross-sectional shape, for example.

The light blocking structure may not comprise a lid 133.

The lid 133 is not limited to any particular shape, as long as it can block ambient light from entering the bore 132.

The system may not comprise a base structure 150.

The base structure 150 may be made from any suitable material and is not limited to plastic. The base structure 150 may also be made from any suitable manufacturing method.

The laser diode 141 and the photodiode 142 may not be provided in the same sensor package 140 but may be separate components, provided in individual packages.

The light source is not limited to a laser diode 141 but may be an LED or a tuneable laser, for example.

The light detector is not limited to a photodiode 142 but may be a different light detector such as a photoresistor, a photomultiplier tube (PMT), a charge coupled device (CCD) or any other suitable light detector.

The controller 160 may be a microcontroller or any other type of suitable processor which can store and manipulate data, such as a PC, for example.

The system 100 may not comprise a display 170.

The display 170 may be a touchscreen or a standard display 170.

The system 170 may not comprise an input device.

All of the above are fully within the scope of the present disclosure and are considered to form the basis for alternative embodiments in which one or more combinations of the above described features are applied, without limitation to the specific combination disclosed above.

In light of this, there will be many alternatives which implement the teaching of the present disclosure. It is expected that one skilled in the art will be able to modify and adapt the above disclosure to suit its own circumstances and requirements within the scope of the present disclosure, while retaining some or all technical effects of the same, either disclosed or derivable from the above, in light of his common general knowledge in this art. All such equivalents, modifications or adaptations fall within the scope of the present disclosure.

Conclusies

1. Een systeem voor identificeren van een biologisch monster in een monsterhouder, het systeem omvattende:

een lichtbron voor emitteren van in hoofdzaak monochroom licht dat naar de monsterhouder wordt gericht;

een lichtsensor voor detecteren van de hoeveelheid licht die gereflecteerd of doorgelaten is door het biologische monster en geconfigureerd om metingen uit te voeren die indicatief zijn voor de hoeveelheid gedetecteerd licht;

een besturingsinrichting die verbonden is met de lichtsensor en geconfigureerd om het biologische monster te identificeren op basis van de uitgevoerde metingen van de lichtsensor; en

een lichtblokkerende structuur voor het houden van de monsterhouder, welke geconfigureerd is om te verhinderen dat enig omgevingslicht het monster bereikt als de lichtblokkerende structuur de monsterhouder omvat,

waarbij de lichtblokkerende structuur een boring omvat voor het accomoderen van de monsterhouder,

waarbij de lichtbron opgesteld is bij de opening van de boring en geconfigureerd is om het in hoofdzaak monochromatische licht in de boring te emitteren en waarbij de lichtdetector is opgesteld bij de opening van de boring en is geconfigureerd om het in hoofdzaak monochromatische licht te detecteren dat gereflecteerd of doorgelaten is door het biologische monster in de boring.

2. Het systeem van conclusie 1, waarbij de lichtblokkerende structuur niettransparant is.

3. Het systeem van conclusies 1 of 2, waarbij de boring een enkele opening heeft.

4. Het systeem van conclusies 1,2 of 3, waarbij de boring een eerste gedeelte omvat waar de boring breder is en een tweede gedeelte waar de boring smaller is.

5. Het systeem van conclusie 4, waarbij het tweede gedeelte verder weg van de opening vande boring is aangebracht.

6. Het systeem van conclusie 4 of 5, waarbij het tweede gedeelte geconfigureerd is om aante grijpen op de zijden van de monsterhouder om de monsterhouder op zijn plaats te houden.

7. Het systeem van een van de voorgaande conclusies, waarbij de boring een rechthoekige dwarsdoorsnedeheeft.

8. Het systeem van een van de voorgaande conclusies, waarbij de lichtblokkerende structuur verder eendeksel omvat voor afsluiten van de opening van de boring, waarbij de lichtbron en/of delichtdetector zodanig zijn dat omgevingslicht wordt verhinderd de monsterhouder te bereiken.

9. Het systeem van één van de voorgaande conclusies, waarbij de lichtblokkerende structuur een3D-geprinte structuur is.

10. Het systeem van een van de voorgaande conclusies, waarbij het systeem de monsterhouder omvat.

11. Het systeem van een van de voorgaande conclusies, waarbij de monsterhouder een cuvet is.

12. Het systeem van conclusie 11, waarbij de cuvet een veelheid van rechte, transparante zijden omvat.

13. Het systeem van een van de voorgaande conclusies, waarbij de lichtbron een laserdiode omvat en waarbij het in hoofdzaak monochromatische licht een laserlicht is.

14. Het systeem van een van de voorgaande conclusies, waarbij de lichtbron een instelbare laser omvat.

15. Het systeem van conclusies 1 – 13, waarbij de lichtbron een LED omvat.

16. Het systeem van conclusie 15, waarbij de lichtbron een infrarode LED omvat.

17. Het systeem van een van de voorgaande conclusies, waarbij het in hoofdzaak monochromatische licht geëmitteerd door de lichtbron een piekintensiteit heeft bij een golflengte in het bereik van 300 nm tot 5000 nm, bij voorkeur 500 nm tot 2000 nm, en met nog meer voorkeur 800 nm tot 1000 nm.

18. Het systeem van een van de voorgaande conclusies, waarbij het in hoofdzaak monochromatische licht, geëmitteerd door de lichtbron, een spectrale bandbreedte heeft onder 200 nm, bij voorkeur onder 100 nm, en met nog meer voorkeur onder 50 nm.

19. Het systeem van een van de voorgaande conclusies, waarbij de lichtdetector een fotodiode omvat.

20. Het systeem van conclusie 19, waarbij de fotodiode een maximale gevoeligheid heeft bij een golflengte in het bereik van de 300 nm tot 5000 nm, bij voorkeur 500 nm tot 2000 nm, en met nog meer voorkeur 800 nm tot 1000 nm.

21. Het systeem van een van de voorgaande conclusies, waarbij de lichtbron en de lichtdetector voorzien zijn in een enkele geïntegreerde schakeling verpakking.

22. Het systeem van een van de voorgaande conclusies, verder omvattende een basissteun voor houden van de lichtbron en de lichtdetector.

23. Het systeem van een van de voorgaande conclusies, waarin de besturingsinrichting geconfigureerd is om:
een absorptiewaarde te berekenen op basis van de verhouding van het geëmitteerde licht en het gedetecteerde licht of een absorptiewaarde te berekenen op basis van de verhouding van de uitgevoerde meting van de lichtsensor en een maximale uitvoer van de lichtsensor;
en het biologische monster te identificeren op basis van de absorptiewaarde.

24. Het systeem van conclusie 23, waarbij de besturingsinrichting het biologische weefsel identificeert uit een opzoektabel van bekende biologische weefsels op basis van de berekende absorptiewaarde.

25. Het systeem van conclusie 23 of 24, waarbij de besturingsinrichting geconfigureerd is om een veelheid van metingen uit te voeren met behulp van de lichtsensor en om een gemiddelde absorptiewaarde te berekenen.

26. Het systeem van een van de voorgaande conclusies, verder omvattende een weergave-inrichting verbindbaar met de besturingsinrichting voor tonen van het geïdentificeerde

biologische monster aan de gebruiker.

27. Het systeem van conclusie 26, waarbij de besturingsinrichting verder geconfigureerd is om de door de lichtsensor verkregen metingen te tonen op de weergave-inrichting.

28. Het systeem van een van conclusies 26 of 27, verder omvattende een invoerinrichting verbindbaar met de weergave-inrichting en de besturingsinrichting om het voor een gebruiker mogelijk te maken om te beginnen met het nemen van de metingen van het monster, en/ofeerder verkregen metingen te laden voor analyse, en/of de metingen uit te voeren naar een ander programma, en/of de metingen te wissen.

29. Een werkwijze voor identificeren van een biologisch monster in een monsterhouder metgebruik van een systeem dat een lichtbron, een lichtdetector, een besturingsinrichting en een lichtblokkerende structuur voor het houden van de monsterhouder heeft, welke geconfigureerd is om enig omgevingslicht te verhinderen het monster te bereiken wanneer de lichtblokkerende structuur in de monsterhouder is, waarbij de lichtblokkerende structuur een boring omvat voor het accomoderen van de monsterhouder,
de werkwijze omvattende:
emitteren in de boring van in hoofdzaak monochromatisch licht van de lichtbron opgesteld bij een opening van de boring naar een monster binnen de monsterhouder;
detecteren van een hoeveelheid van in hoofdzaak monochromatisch licht die is gereflecteerd of doorgelaten in de boring door het biologische monster met de lichtdetector opgesteld bij de opening van de boring;
uitvoeren van metingen van de lichtdetector die indicatief zijn voor de gedetecteerde hoeveelheid licht naar de besturingsinrichting; en
identificeren van het biologische monster gebaseerd op het uitvoersignaal van de lichtsensor met gebruik van de besturingsinrichting.

30. De werkwijze van conclusie 29, verder omvattende verhinderen dat enig omgevingslicht het monster bereikt met gebruik van een lichtblokkerende structuur.

31. De werkwijze van conclusie 29 of 30, waarbij identificeren van het biologische monster omvat:
berekenen van een absorptiewaarde op basis van de verhouding van het geëmitteerde licht en

het gedetecteerde of berekenen van een absorptiewaarde op basis van de verhouding van de uitgevoerde meting van de lichtsensor en een maximale uitvoer van de lichtsensor; en identificeren van het biologische monster op basis van de absorptiewaarde.

32. Het systeem van conclusie 31, waarbij de absorptiewaarde een gemiddelde absorptiewaarde is op basis van een veelheid van metingen die gemaakt zijn door de lichtsensor.

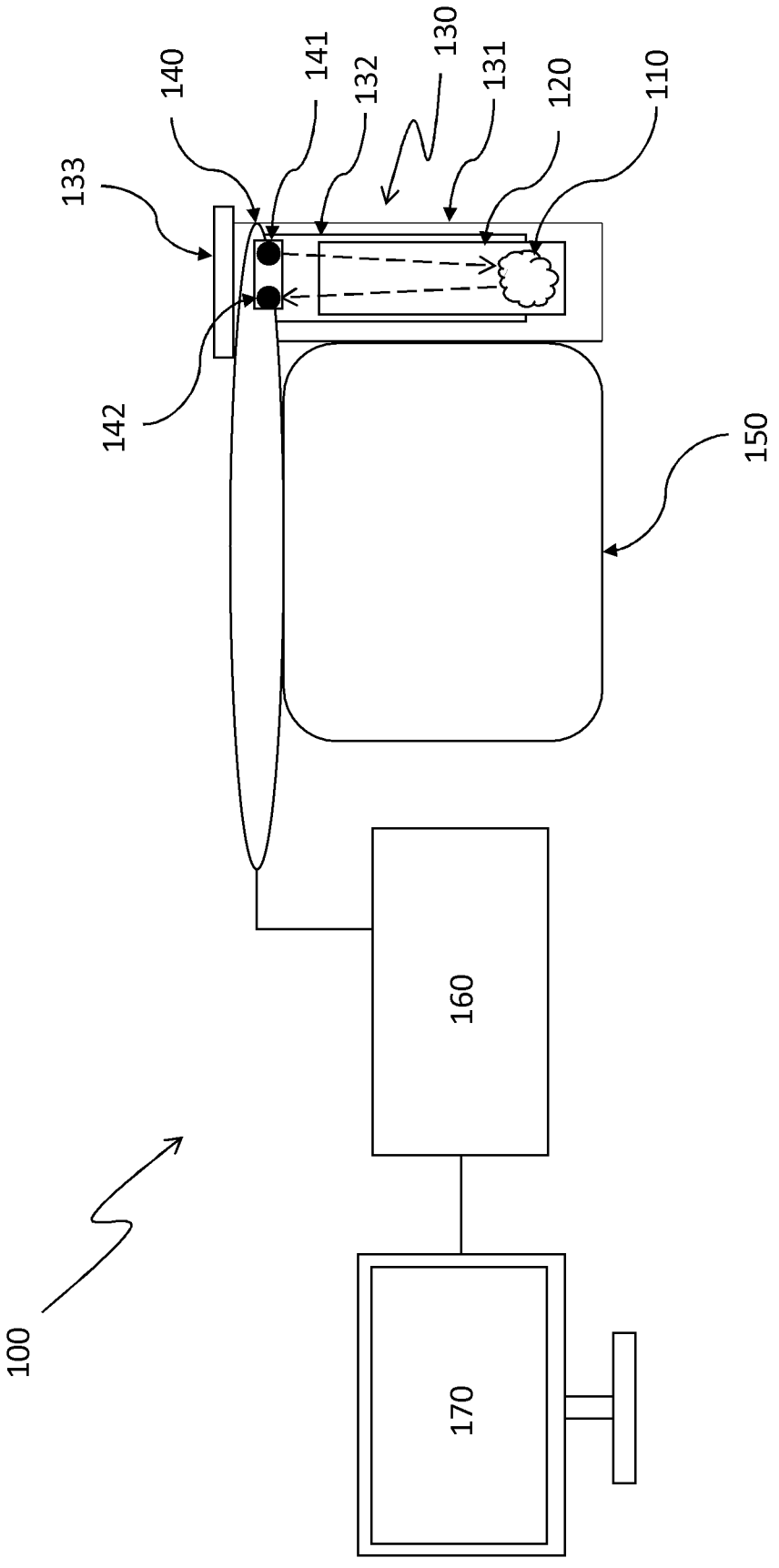


FIG. 1

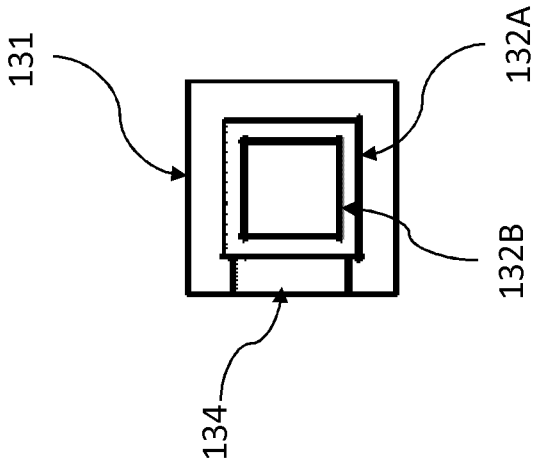


FIG. 2C

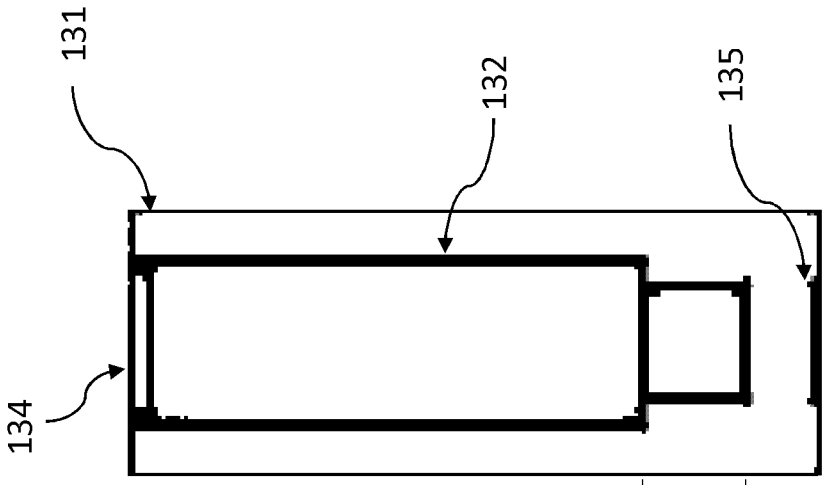


FIG. 2B

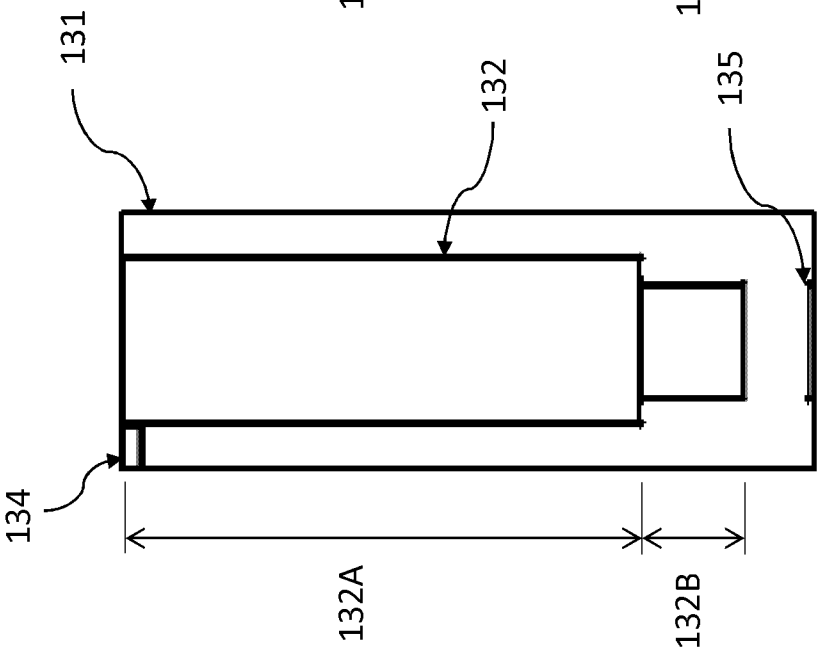


FIG. 2A

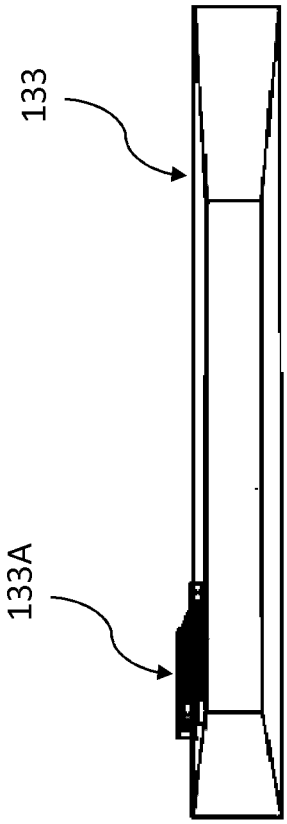


FIG. 3B

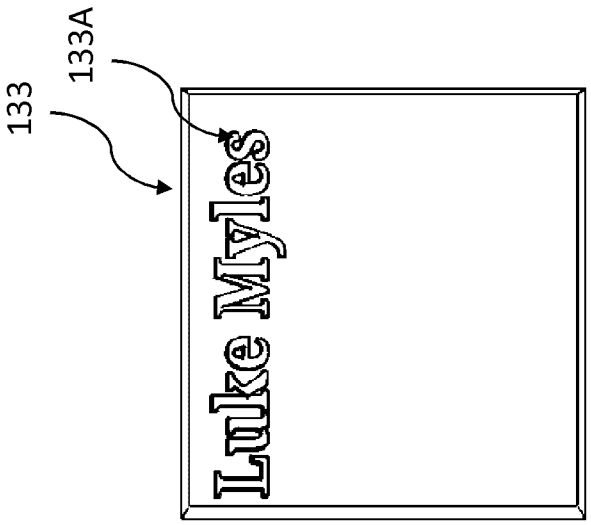


FIG. 3A

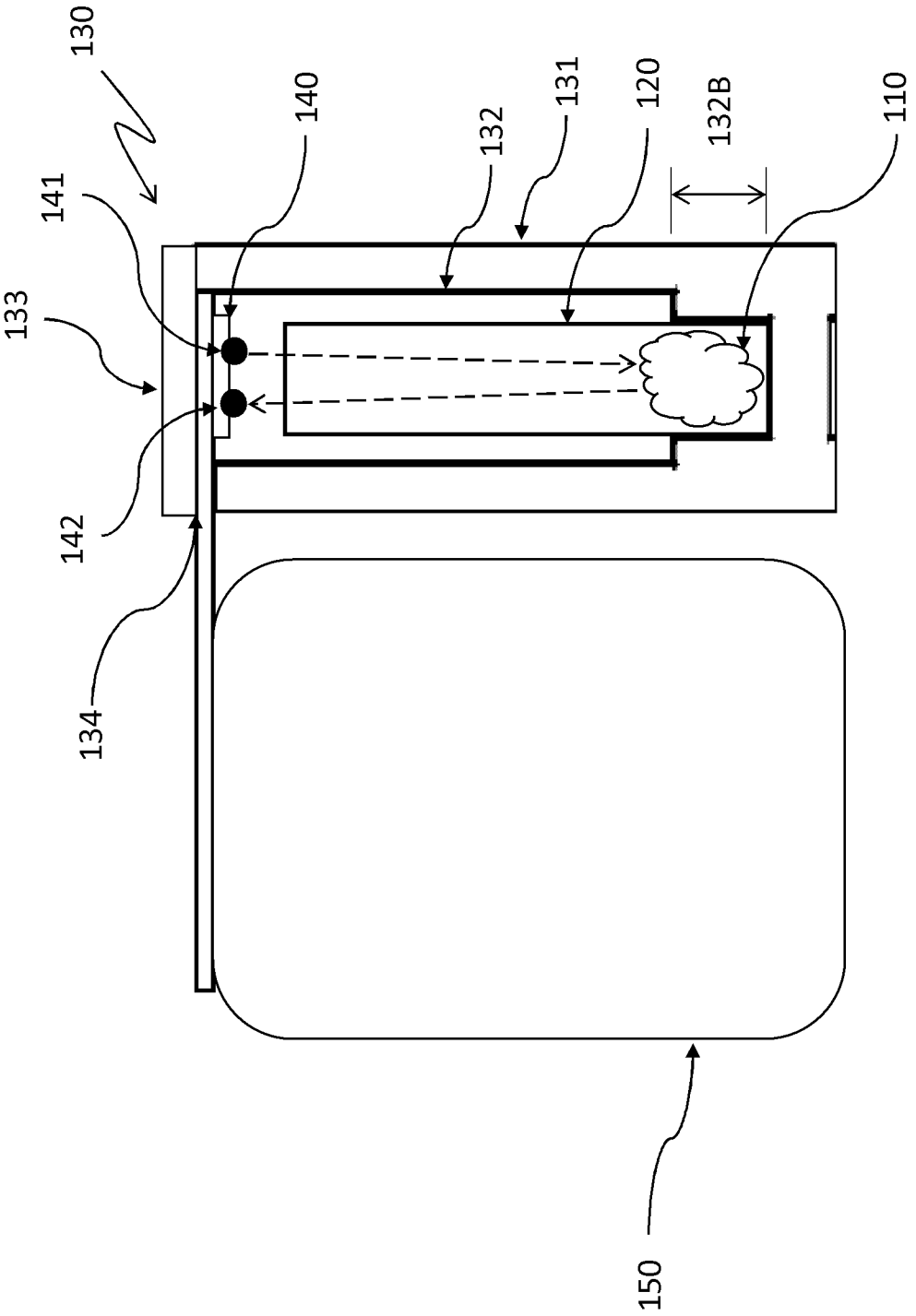


FIG. 4

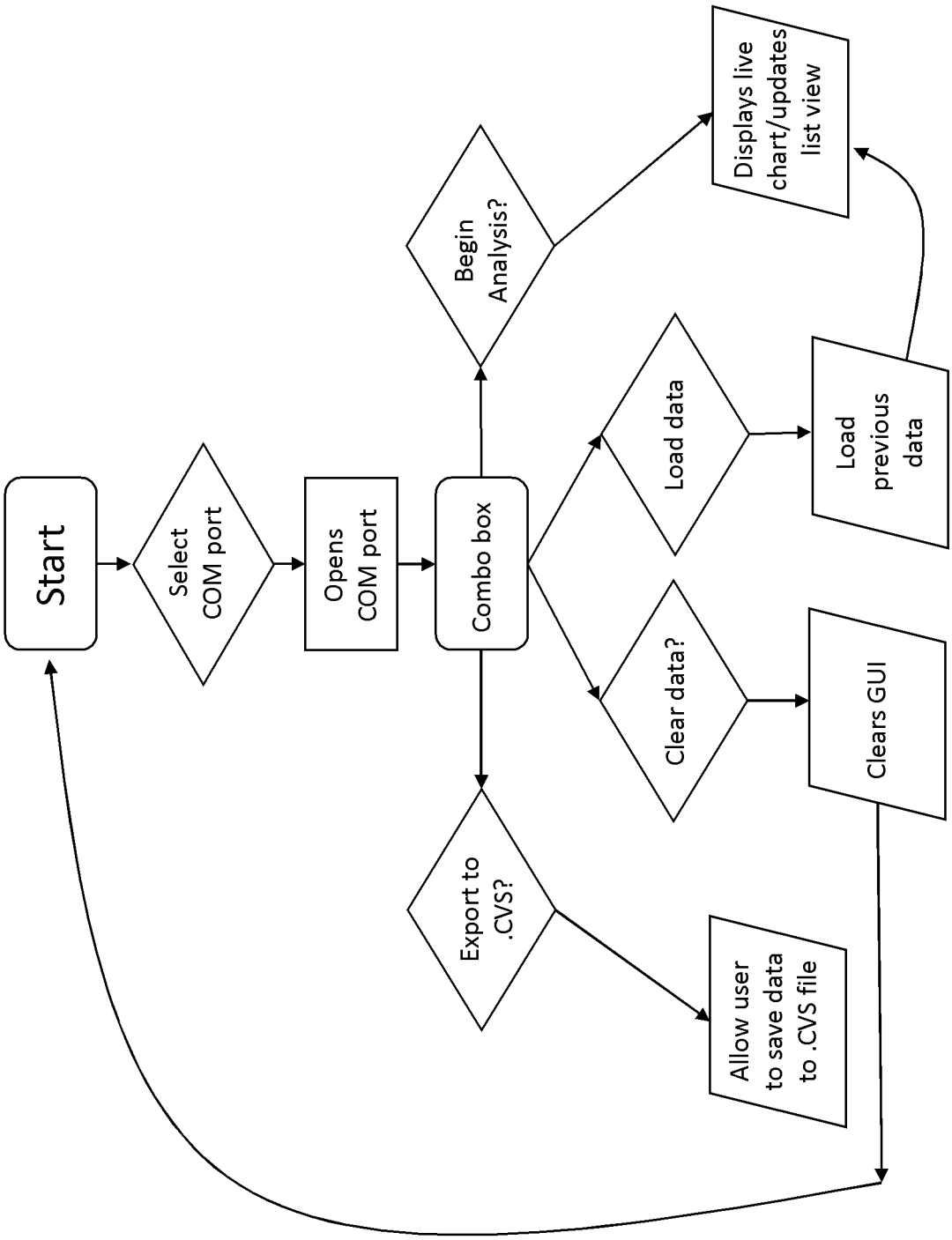

Start
Select COM port
Opens COM port
Combo box
Begin Analysis?
Displays live chart/updates list view
Load data
Load previous data
Clear data?
Clears GUI
Export to .CVS?
Allow user to save data to .CVS file

FIG. 5

SAMENWERKINGSVERDRAG (PCT)

RAPPORT BETREFFENDE NIEUWHEIDSONDERZOEK VAN INTERNATIONAAL TYPE

IDENTIFICATIE VAN DE NATIONALE AANVRAGE	KENMERK VAN DE AANVRAGER OF VAN DE GEMACHTIGDE
Nederlands aanvraag nr. **2028538**	Indieningsdatum **24-06-2021**
	Ingeroepen voorrangsdatum
Aanvrager (Naam) **Clearstream Technologies Limited**	
Datum van het verzoek voor een onderzoek van internationaal type **18-09-2021**	Door de Instantie voor Internationaal Onderzoek aan het verzoek voor een onderzoek van internationaal type toegekend nr. **SN79588**
I. CLASSIFICATIE VAN HET ONDERWERP (bij toepassing van verschillende classificaties, alle classificatiesymbolen opgeven)	
Volgens de internationale classificatie (IPC) **Zie onderzoeksrapport**	
II. ONDERZOCHTE GEBIEDEN VAN DE TECHNIEK	
Onderzochte minimumdocumentatie	
Classificatiesysteem	Classificatiesymbolen
IPC	**Zie onderzoeksrapport**
Onderzochte andere documentatie dan de minimum documentatie, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen	

III.	☐	**GEEN ONDERZOEK MOGELIJK VOOR BEPAALDE CONCLUSIES**	(opmerkingen op aanvullingsblad)
IV.	☐	**GEBREK AAN EENHEID VAN UITVINDING**	(opmerkingen op aanvullingsblad)

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Nummer van het verzoek om een onderzoek naar de stand van de techniek
NL 2028538

A. CLASSIFICATIE VAN HET ONDERWERP

INV. G01N21/01 G01N21/31

ADD. G01N21/03 G01N21/359 G01N21/3577

Volgens de Internationale Classificatie van octrooien (IPC) of zowel volgens de nationale classificatie als volgens de IPC.

B. ONDERZOCHTE GEBIEDEN VAN DE TECHNIEK

Onderzochte miminum documentatie (classificatie gevolgd door classificatiesymbolen)

G01N

Onderzochte andere documentatie dan de mimimum documentatie, voor dergelijke documenten, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen

Tijdens het onderzoek geraadpleegde elektronische gegevensbestanden (naam van de gegevensbestanden en, waar uitvoerbaar, gebruikte trefwoorden)

EPO-Internal, WPI Data

C. VAN BELANG GEACHTE DOCUMENTEN

Categorie °	Geciteerde documenten, eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
X	US 2014/233015 A1 (MANDER RICHARD IAN [US] ET AL) 21 augustus 2014 (2014-08-21)	1-4,6-9, 13-36
Y	* alineas [0002], [0009], [0016], [0017], [0042] - [0045], [0048], [0049], [0056], [0058], [0063], [0064] - [0066], [0069] - [0073], [0089], [0098]; figuren 1-13 *	5,10-12

X	RU 188 742 U1 (KOROLENKO E V) 23 april 2019 (2019-04-23)	1-4,9, 13-16, 19-28, 30-35
Y	* figuren 1-3 *	5,10-12

X	JP 2017 067719 A (USHIO ELECTRIC INC) 6 april 2017 (2017-04-06)	1-4,6-9, 13-36
Y	* samenvatting; figuren 2-6 * * alineas [0013] - [0023], [0031] *	5,10-12

	-/--	

[X] Verdere documenten worden vermeld in het vervolg van vak C.

[X] Leden van dezelfde octrooifamilie zijn vermeld in een bijlage

° Speciale categorieën van aangehaalde documenten

"A" niet tot de categorie X of Y behorende literatuur die de stand van de techniek beschrijft

"D" in de octrooiaanvrage vermeld

"E" eerdere octrooi(aanvrage), gepubliceerd op of na de indieningsdatum, waarin dezelfde uitvinding wordt beschreven

"L" om andere redenen vermelde literatuur

"O" niet-schriftelijke stand van de techniek

"P" tussen de voorrangsdatum en de indieningsdatum gepubliceerde literatuur

"T" na de indieningsdatum of de voorrangsdatum gepubliceerde literatuur die niet bezwarend is voor de octrooiaanvrage, maar wordt vermeld ter verheldering van de theorie of het principe dat ten grondslag ligt aan de uitvinding

"X" de conclusie wordt als niet nieuw of niet inventief beschouwd ten opzichte van deze literatuur

"Y" de conclusie wordt als niet inventief beschouwd ten opzichte van de combinatie van deze literatuur met andere geciteerde literatuur van dezelfde categorie, waarbij de combinatie voor de vakman voor de hand liggend wordt geacht

"&" lid van dezelfde octrooifamilie of overeenkomstige octrooipublicatie

Datum waarop het onderzoek naar de stand van de techniek van internationaal type werd voltooid	Verzenddatum van het rapport van het onderzoek naar de stand van de techniek van internationaal type
15 februari 2022	

Naam en adres van de instantie	De bevoegde ambtenaar
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	**Duijs, Eric**

2

Formulier PCT/ISA/201 (tweede blad) (Januari 2004)

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Nummer van het verzoek om een onderzoek naar de stand van de techniek
NL 2028538

C.(Vervolg). VAN BELANG GEACHTE DOCUMENTEN

Categorie °	Geciteerde documenten, eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
Y	WO 89/09390 A1 (DU PONT [US]) 5 oktober 1989 (1989-10-05) * bladzijde 5, regels 9-15; figuur 1A * * bladzijde 4, regel 26 - bladzijde 5, regel 4; voorbeeld 4 * -----	5,10-12

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Informatie over leden van dezelfde octrooifamilie

Nummer van het verzoek om een onderzoek naar de stand van de techniek

NL 2028538

In het rapport genoemd octrooigeschrift	Datum van publicatie	Overeenkomend(e) geschrift(en)	Datum van publicatie
US 2014233015 A1	21-08-2014	CA 2823481 A1	21-08-2014
		US 2014233015 A1	21-08-2014
		US 2015253244 A1	10-09-2015
		WO 2014130857 A1	28-08-2014
RU 188742 U1	23-04-2019	GEEN	
JP 2017067719 A	06-04-2017	JP 6891391 B2	18-06-2021
		JP 2017067719 A	06-04-2017
WO 8909390 A1	05-10-1989	AR 244434 A1	29-10-1993
		AU 3344189 A	16-10-1989
		BR 8907324 A	26-03-1991
		CA 1313241 C	26-01-1993
		CN 1037218 A	15-11-1989
		DK 228790 A	22-11-1990
		EP 0533653 A1	31-03-1993
		ES 2014065 A6	16-06-1990
		GR 890100175 A	19-01-1990
		JP H03503450 A	01-08-1991
		NZ 228445 A	28-05-1991
		PL 278411 A1	13-11-1989
		PT 90076 A	10-11-1989
		TR 24841 A	19-06-1992
		US 4910406 A	20-03-1990
		WO 8909390 A1	05-10-1989

WRITTEN OPINION

File No.	Filing date *(day/month/year)*	Priority date *(day/month/year)*	Application No.
SN79588	24.06.2021		NL2028538

International Patent Classification (IPC)
INV. G01N21/01 G01N21/31 ADD. G01N21/03 G01N21/359 G01N21/3577

Applicant
Clearstream Technologies Limited

This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the application
- ☒ Box No. VIII Certain observations on the application

	Examiner
	Duijs, Eric

Application number

WRITTEN OPINION

NL2028538

Box No. I Basis of this opinion

1. This opinion has been established on the basis of the latest set of claims filed before the start of the search.

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ on paper

   ☐ in electronic form

   c. time of filing/furnishing:

   ☐ contained in the application as filed.

   ☐ filed together with the application in electronic form.

   ☐ furnished subsequently for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty	Yes:	Claims	5, 10-13, 29, 36
	No:	Claims	1-4, 6-9, 14-28, 30-35
Inventive step	Yes:	Claims	
	No:	Claims	1-36
Industrial applicability	Yes:	Claims	1-36
	No:	Claims	

2. Citations and explanations

see separate sheet

WRITTEN OPINION

Box No. VII Certain defects in the application

see separate sheet

Box No. VIII Certain observations on the application

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents:

D1 US 2014/233015 A1 (MANDER RICHARD IAN [US] ET AL)

D2 RU 188 742 U1 (KOROLENKO E V)

D3 JP 2017 067719 A (USHIO ELECTRIC INC)

D4 WO 89/09390 A1 (DU PONT [US])

2 **Lack of novelty and lack of inventive step**

The present application does not meet the criteria of patentability, because the subject-matter of **claims 1-4, 6-9, 14-28, 30-35** is not new, and because the subject-matter of **claims 1-36** does not involve an inventive step:

2.1 **Independent SYSTEM claim 1**:

2.1.1 **D1** discloses een systeem 100 voor identificeren van een biologisch monster in een monsterhouder 114 (Figs. 1-13; par. 2: "evaluation systems... that evaluate characteristics of substances using electromagnetic energy"; par. 16: "biological tissue recognition, identification, verification, authentication, classification, and/or diagnostics"; par. 42: "a fluid sample or specimen analysis or evaluation device 100"; par. 48: "sample chamber 102b is sized and dimensioned to at least partially receive, as shown in FIG. 1, a specimen container referred to as a sample cuvette 114"; par. 70: "biological reactions ... bacterial growth, formation of blood clots"), het systeem omvattende:
-- een lichtbron 634 (Figs. 6, 7; par. 58: "a plurality of transducers, typically in the form of a plurality of emitters (seven shown, collectively 634)"; par. 63) voor emitteren van in hoofdzaak monochroom licht dat naar de monsterhouder 114 wordt gericht;

-- een lichtsensor 638, 640 (par. 58: "direct sensor PCBA 606 includes one or more first primary sampling detectors or sensors (four shown, collectively 638) ... backplane PCBA 608 includes one or more second primary sampling detector(s) or sensor(s) (four shown, collectively 640)") voor detecteren van de hoeveelheid licht die gereflecteerd of doorgelaten (par. 43: "detect, measure or otherwise capture electromagnetic energy reflected ... transmitted"; par. 69-70: "electromagnetic energy strikes the sample or specimen and is scattered and/or reflected therefrom") is door het biologische monster en geconfigureerd om metingen uit te voeren die indicatief zijn voor de hoeveelheid gedetecteerd licht; en

-- een besturingsinrichting 648 (par. 64: "The controller 648 may process information generated by the primary sampling detector(s) or sensor(s) 638, 640, which is indicative of the response by at least a portion of a sample or specimen to illumination by the emitters 634") die verbonden is met de lichtsensor 638, 640 en geconfigureerd om het biologische monster te identificeren op basis van de uitgevoerde metingen van de lichtsensor 638, 640 (par. 16: "biological tissue recognition, identification, verification, authentication, classification, and/or diagnostics").

Hence the subject-matter of **claim 1** is not new in view of **D1**.

2.1.2 **D2** (Figs. 1-3) also discloses een systeem voor identificeren van een biologisch monster in een monsterhouder (mounted in opaque bore or cuvette holder 3), het systeem omvattende:
-- een lichtbron 8 (LED 8) voor emitteren van in hoofdzaak monochroom licht dat naar de monsterhouder wordt gericht;
-- een lichtsensor 11 (photodiode 11) voor detecteren van de hoeveelheid licht die gereflecteerd of doorgelaten is door het biologische monster en geconfigureerd om metingen uit te voeren die indicatief zijn voor de hoeveelheid gedetecteerd licht; en

-- een besturingsinrichting (par. 24; Fig. 1: spectrophotometer housing 2 with 8-bit microcontroller, touch screen user interface 1 on which measurement results are displayed as values of optical density and relative

absorption) die verbonden is met de lichtsensor 11 en geconfigureerd om het biologische monster te identificeren op basis van de uitgevoerde metingen van de lichtsensor 11.

Hence the subject-matter of **claim 1** is also not new in view of **D2**.

2.1.3 **D3** (Figs. 2-6; abstract; par. 13-23, 31) also discloses een systeem 10 (optical measuring instrument 10) voor identificeren van een biologisch monster in een monsterhouder W (par. 18: a sample tube W loaded with a measurement sample is inserted and a tapered specimen tube receiving hole 29 having a small diameter toward the bottom is formed in the center portion), het systeem omvattende:

-- een lichtbron 24 (par. 15: light source 24) voor emitteren van in hoofdzaak monochroom licht dat naar de monsterhouder W wordt gericht;

-- een lichtsensor 28 (par. 15: light receiving section 28) voor detecteren van de hoeveelheid licht die gereflecteerd of doorgelaten is door het biologische monster en geconfigureerd om metingen uit te voeren die indicatief zijn voor de hoeveelheid gedetecteerd licht; en

-- een besturingsinrichting (implicitly disclosed in par. 13 and 23: The optical measuring instrument 10 is used for measuring the concentration or the like of a substance to be measured in a measurement sample as an absorbance; par. 31: calculating the concentration from the absorbance of the substance to be measured in the measurement sample by previously preparing a calibration curve by measuring the standard solution of the substance to be measured of known concentration as a reference sample) die verbonden is met de lichtsensor 28 en geconfigureerd om het biologische monster te identificeren op basis van de uitgevoerde metingen van de lichtsensor 28.

Hence the subject-matter of **claim 1** is also not new in view of **D3**.

2.2 **Independent METHOD claim 33**:

What has been said above with reference to system **claim 1** concerns method **claim 33** *mutatis mutandis*.

2.3 Dependent **claims 2-32 and 34-36** do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of novelty and/or inventive step:

-- **Claims 2-4, 34**: not new, see **D1** (Figs. 1, 2; par. 44-45: "housing 102", "lid 117"; par. 49: "sample cuvette 114 has a removable cuvette lid 116 that need not be transparent"; Fig. 8; par. 17, 71: "the walls of the sample chamber can be opaque, such that the sample chamber 102b has at least one opaque wall"; par. 56: "The PCBAs are typically opaque or substantially opaque, at least to electromagnetic energy that is employed in the analysis or evaluation of the samples or specimens. The PCBAs may, for example, be painted black, coated black, or may include black pigments");

-- **Claims 5, 10, 11, 12**: not inventive; it would be obvious for the skilled person of **D1**, **D2** or **D3**, all using cuvette holding bores having at least three holes (one for inserting the cuvette, one for the light source, and one for the detector) for measuring single-path absorption, scattering or reflection using a 180° transmission set-up, to use an alternative double-path absorption, scattering or reflection using a 360° transmission set-up, as suggested, for example in **D4** (p. 5, l. 9-15; FIG. 1A: light source 13a and light detector 14a above (biological food) sample holder 11a, which can be entirely opaque, for measuring sample absorbance; from p. 4, l. 26 - p. 5, l. 4 and Example 4 it is clear that the 360° set-up has the advantage that entirely opaque sample holding containers 11a can be used. The light attenuation can be detected "without the requirement that it pass through the container"). It would be clear for the skilled person of **D1**, **D2** or **D3**, that using such a 360° transmission set-up (**solution**), would allow the use of simplified bores or cuvette holders, which less risk of entering stray light via additional openings for the light source and light detector (**problem**).

-- **Claims 6, 7, 8**: not new, see **D3** (Fig. 6; par. 18: a specimen bracket 25 in which a sample tube W loaded with a measurement sample is inserted and a tapered specimen tube receiving hole 29 having a small diameter toward the bottom is formed in the center portion); not inventive, obvious shape selection in view of **D1** (Figs. 1, 12; par. 48: "While illustrated as a square cylindrical tube, the sample cuvette 114 and sample chamber 102b may take any variety of shapes");

-- **Claim 9**: not new, see **D1** (Figs. 1, 7, 8, 10: rectangular bore 102b; par. 48: "While illustrated as a square cylindrical tube, the sample cuvette 114 and sample chamber 102b");

-- **Claim 13**: product-by-process claim; obvious selection of a material for the light blocking structure(s) of **claim 2** (see the comments given above for **claim 2**);

-- **Claims 14-16**: not new, see **D1** (Figs. 1, 6-12; system 100 comprises cuvette 114; par. 48: "The sample cuvette 114 may be made of any of a large variety of materials transmissive (i.e., transparent or at least translucent) ... illustrated as a square cylindrical tube, the sample cuvette 114");

-- **Claims 17, 18**: not new, see **D1** (par. 73: "the emitters 634 may take the form of one or more lasers, for example one or more laser diodes.The lasers may, or may not, be tunable lasers"; par. 89: "If the emitters 634 are laser sources");

-- **Claims 19, 20**: not new, see **D1** (par. 9: "near-infrared (N-IR) ... light emitting diodes (LEDs), each operable to emit electromagnetic energy in a respective range or band of wavelengths"; par. 73: "The emitters 634 may, for example, take the form of one or more light emitting diodes (LEDs), including for instance organic LEDs (OLEDs)"; par. 74: "One, more, or all of the emitters 634 may be operable to emit in part or all of an “optical” portion of the electromagnetic spectrum, including the ... near infrared (N-IR) portion");

-- **Claim 21**: not new, see **D1** (par. 9: "The wavelengths may for example include some or all wavelengths in an optical portion of the electromagnetic spectrum, from near-infrared (N-IR) to near-ultraviolet (N-UV)"; par. 74: "One, more, or all of the emitters 634 may be operable to emit in part or all of an “optical” portion of the electromagnetic spectrum, including the (human) visible portion, near infrared (N-IR) portion");

-- **Claim 22**: not new, implicitly disclosed in **D1** (par. 73: "lasers, ... laser diodes"; par. 73: "light emitting diodes (LEDs)"; the spectral width of lasers and LEDs fall within the claimed ranges);

-- **Claim 23**: not new, see **D1** (par. 64: "the sensor takes the form of one or more photodiodes");

-- **Claim 24**: not new, see **D1** (par. 43: "detect, measure or otherwise capture electromagnetic energy reflected ... transmitted"; par. 9: "The wavelengths may for example include some or all wavelengths in an optical portion of the electromagnetic spectrum, from near-infrared (N-IR) to near-ultraviolet (N-UV)"; par. 74: "One, more, or all of the emitters 634 may be operable to emit in part or all of an “optical” portion of the electromagnetic spectrum, including the (human) visible portion, near infrared (N-IR) portion");

-- **Claims 25, 26**: not new, see **D1** (Fig. 9; par. 55: "four printed circuit board assemblies (PCBAs): a transducer PCBA 602, a calibrator PCBA 604, a direct sensor PCBA 606, and a backplane PCBA 608" together form a single PCB package);

-- **Claims 27, 35**: not new, see **D1** (par. 43: "detect, measure or otherwise capture electromagnetic energy reflected ... transmitted"; par. 70: "there may be observed a decrease in transmission of electromagnetic energy along the optical axis 702");

-- **Claim 28**: not new, see **D1** (par. 16: "biological tissue recognition, identification, verification, authentication, classification, and/or diagnostics"; par. 101: "the processor 1326 may compare a response to one or more reference responses. The processor 1326 may determine whether a response from a sample or specimen sufficiently matches is signature responses from a reference sample or specimen. Such may, for example, be employed to detect a presence or absence of a substance, for instance an illegal substance (e.g., cocaine), an explosive substance (e.g., nitrate based), or a toxic substance (e.g., carcinogens)");

-- **Claims 29, 36**: not inventive, although not explicitly mentioned in **D1, D2 and D3**, it would be obvious for the skilled person of **D1, D2 or D3** to use well-known averaging (**solution**) to improve the signal-to-noise ration and measurement accuracy (**problem**);

-- **Claim 30-32**: not new, see **D1** (par. 65: "the control subsystem 646 may include and/or one or more visual indicators, such ... liquid crystal displays (LCD) ... a touch sensitive LCD, which displays a graphical user interface, operable by the user of the sampling device 100"; par. 66: "the control subsystem 646 may include one or more user operable input elements, such as switches, keys or buttons"; par. 98: "processor-based device 1302 may include a user interface which may, for example include a touch-sensitive display 1312, ... The user interface may also include user selectable icons").

Re Item VII

Certain defects in the application

3 The relevant background art disclosed in **D1, D2, D3 and D4** is not mentioned in the description, nor is this document identified therein.

4 The features of the claims are not provided with reference signs placed in parentheses.

Re Item VIII

Certain observations on the application

5 The term "in hoofdzaak monochroom", used in **claim 1**, is vague and unclear. The term could have been clarified, for example, based on the subject-matter mentioned in **claims 21-22, 17 or 19**.

6 The wording "een lichtblokkerende structuur voor houden", used in **claim 2**, is incomplete and therefore unclear. It appears that the wording hould have been "een lichtblokkerende structuur die geconfigureerd is om de monsterhouder te ~~voor~~ houden".

7 The dependency of **claim 5** is not clear, since reference is made to "de boring", whereas no "boring" is mentioned in **claims 2 and 3**.

8 The dependency of **claim 7** is also not clear, since reference is made to "de opening", whereas no "opening" is mentioned in **claims 1+2+4+6**.

9 The dependency of **claim 19** is also not clear, since the claim is also dependent on **claims 17 and 18**, which define that the light source comprises a "laserdiode". It appears that a "LED" should be an alternative and not an additional light source. Hence it appears that **claim 19** should have been dependent on **claims 1-16** only.

10 The dependency of **claim 20** is also not clear, since the claim is dependent on **claim 17**, which defines that the light source comprises a "laserdiode". It appears that a "infrarode LED" should be an alternative and not an additional light source. Hence it appears that **claim 20** should have been made dependent on **claims 1-16** only, or on **claim 19** (wherein the LED comprises an infrared LED).

11 The dependency of **claim 31** is also not clear, since reference is made to "de weergave-inrichting", whereas no "weergave-inrichting" is mentioned in **claims 1 to 21**. It appears that **claim 31** should have been made dependent on **claim 30.**

12 The dependency of **claim 36** is also not clear, since reference is made to "Het systeem van conclusie 35", whereas **claim 35** is directed to a method ("werkwijze").