Innovation, Sciences et Développement économique Canada
Office de la Propriété Intellectuelle du Canada

Innovation, Science and Economic Development Canada
Canadian Intellectual Property Office

CA 2913474 C 2023/04/18

(11)(21) 2 913 474

(12) BREVET CANADIEN
CANADIAN PATENT

(13) C

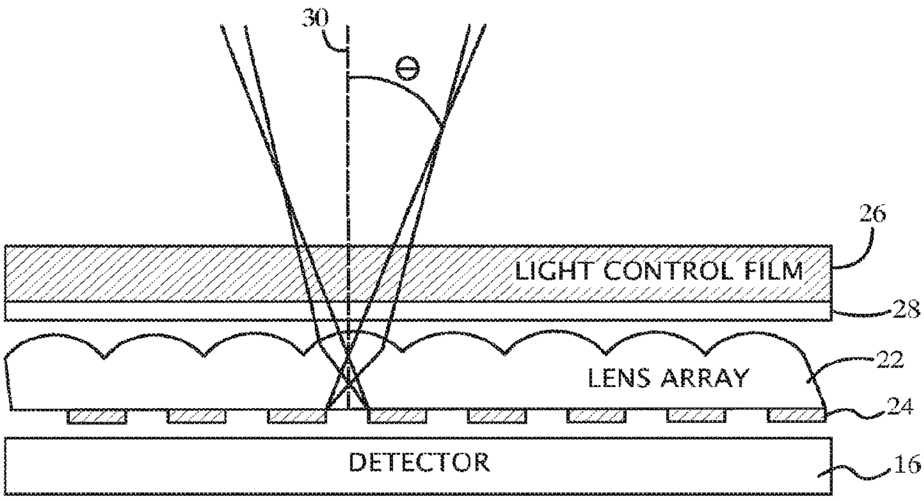
(86) Date de dépôt PCT/PCT Filing Date: 2014/06/06
(87) Date publication PCT/PCT Publication Date: 2014/12/11
(45) Date de délivrance/Issue Date: 2023/04/18
(85) Entrée phase nationale/National Entry: 2015/11/24
(86) N° demande PCT/PCT Application No.: US 2014/041284
(87) N° publication PCT/PCT Publication No.: 2014/197786
(30) Priorités/Priorities: 2013/06/06 (US61/832,065); 2013/06/06 (US61/832,078)

(51) Cl.Int./Int.Cl. *A61B 5/1459* (2006.01)
(72) Inventeurs/Inventors:
MCMILLAN, WILLIAM A., US;
WISNIEWSKI, NATALIE A., US;
KINTZ, GREGORY J., US

(73) Propriétaire/Owner:
PROFUSA, INC., US

(74) Agent: BORDEN LADNER GERVAIS LLP

(54) Titre : APPAREIL ET PROCEDES POUR DETECTER DES SIGNAUX OPTIQUES A PARTIR DE CAPTEURS IMPLANTES
(54) Title: APPARATUS AND METHODS FOR DETECTING OPTICAL SIGNALS FROM IMPLANTED SENSORS



(57) Abrégé/Abstract:
Some embodiments described herein relate to an apparatus including a light source configured to transmit an excitation optical signal to an implanted sensor and a detector configured to detect an analyte-dependent optical signal emitted from an implanted sensor. The apparatus can include a lens configured to focus at least a portion of the analytedependent optical signal onto the detector.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
11 December 2014 (11.12.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/197786 A3

(51) International Patent Classification:
A61B 5/00 (2006.01)

(21) International Application Number:
PCT/US2014/041284

(22) International Filing Date:
6 June 2014 (06.06.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/832,065 6 June 2013 (06.06.2013) US
61/832,078 6 June 2013 (06.06.2013) US

(72) Inventors; and
(71) Applicants : **KINTZ, Gregory J.** [US/US]; 211 Heath Street, Santa Cruz, California 95060 (US). **MCMILLAN, William A.** [US/US]; 23 Cuesta Real, La Honda, California 94020 (US). **WISNIEWSKI, Natalie A.** [US/US]; 1219 18th Street, San Francisco, California 94109 (US).

(74) Agents: **MILLS, John R.** et al.; Cooley LLP, 1299 Pennsylvania Ave., Suite 700, Washington, District of Columbia 2004 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(88) Date of publication of the international search report:
29 January 2015

(54) Title: APPARATUS AND METHODS FOR DETECTING OPTICAL SIGNALS FROM IMPLANTED SENSORS

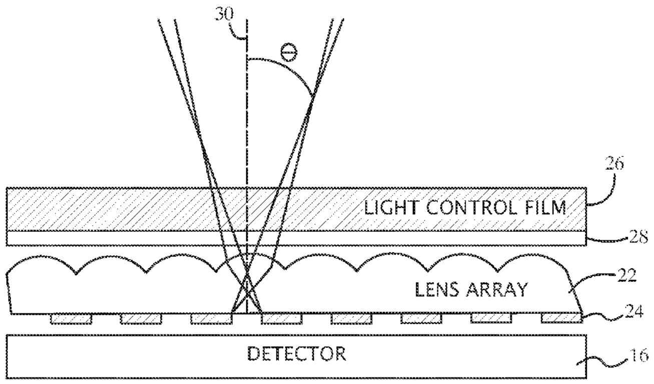


Fig. 2

(57) Abstract: Some embodiments described herein relate to an apparatus including a light source configured to transmit an excitation optical signal to an implanted sensor and a detector configured to detect an analyte-dependent optical signal emitted from an implanted sensor. The apparatus can include a lens configured to focus at least a portion of the analytedependent optical signal onto the detector.

WO 2014/197786 A3

APPARATUS AND METHODS FOR DETECTING OPTICAL SIGNALS FROM IMPLANTED SENSORS

[0001]

Background

[0002] Some embodiments described herein relate to apparatus and methods for monitoring an implant, and in particular to apparatus and methods for detecting optical signals emitted from an implant with restriction of off-axis light.

[0003] Some embodiments described herein relate to apparatus and methods for monitoring an implant, and in particular to apparatus and methods for detecting optical signals through a relatively large surface area of tissue relative to a surface area of tissue through which an excitation optical signal is supplied.

[0004] The monitoring of the level or concentration of an analyte, such as glucose, lactate, oxygen, etc., in certain individuals is important to their health. High or low levels of glucose, or other analytes, may have detrimental effects or be indicative of specific health states. The monitoring of glucose is particularly important to persons with diabetes, a subset of whom must determine when insulin is needed to reduce glucose levels in their bodies or when additional glucose is needed to raise the level of glucose in their bodies.

[0005] A conventional technique used by many persons with diabetes for monitoring their blood glucose level includes the periodic drawing of blood, the application of that blood to a test strip, and the determination of the blood glucose level using calorimetric, electrochemical, or photometric detection. This technique does not permit continuous or automatic monitoring of glucose levels in the body, but typically must be performed manually on a periodic basis. Unfortunately, the consistency with which the level of glucose is checked varies widely among individuals. Many persons with diabetes find the periodic

Date Reçue/Date Received 2020-10-19

testing inconvenient, and they sometimes forget to test their glucose level or do not have time for a proper test. In addition, some individuals wish to avoid the pain associated with the test. Unmonitored glucose may result in hyperglycemic or hypoglycemic episodes. An implanted sensor that monitors the individual's analyte levels would enable individuals to monitor their glucose, or other analyte levels, more easily.

[0006] Some known devices perform in situ monitoring of analytes (e.g., glucose) in the blood stream or interstitial fluid of various tissues. A number of these devices use sensors that are inserted into a blood vessel or under the skin of a patient. Communicating and/or retrieving data from such known and/or proposed devices, however, can be challenging. For example, an implanted sensor may be able to communicate with a detector or receiver using radio frequency (RF) transmissions. Such a sensor, however, may require electronics, batteries, antennae, and/or other communication hardware which may increase the bulk of the implanted sensor, may require frequent inconvenient recharging, and/or may decrease the longevity or reliability of the implant.

[0007] A need therefore exists for apparatus and methods for detecting optical signals from an implanted sensor, such that a fluorescent sensor can be used. A fluorescent sensor may not require electric charging and/or transmission electronics. Such implanted sensors, however, may be difficult to read or to monitor optically because of low levels of florescence in the presence of high scatter due to dynamic changes in skin conditions (e.g., blood level and hydration). The skin is highly scattering, and the scattering may dominate the optical propagation. Scatter is caused by index of refraction changes in the tissue, and the main components of scatter in the skin are due to lipids, collagen, and other biological components. The main absorption is caused by blood, melanin, water, and other components.

[0008] Devices and apparatus described herein are suitable for providing accurate and consistent measurement of an analyte by monitoring an implantable sensor in such low-signal, high-scattering environments.

Summary

[0009] Some embodiments described herein relate to an apparatus including a light source configured to transmit an excitation optical signal to an implanted sensor and a detector configured to detect an analyte-dependent optical signal emitted from an implanted sensor. The apparatus can include a lens configured to focus at least a portion of the analyte-dependent optical signal onto the detector.

[0010] Some embodiments described herein relate to an array of lenses. Each lens from the array of lenses can be configured to transmit an analyte-dependent optical signal from an implanted sensor to a detector. A plurality of light-blocking elements can be disposed within a substrate of the array of lenses. Each light blocking element from the array of light-blocking elements can be configured to prevent or inhibit a photon having an angle of incidence greater than a predetermined angle of incidence from passing through the substrate.

[0011] Some embodiments described herein relate to an apparatus including a detector configured to detect an analyte-dependent optical signal from an implanted sensor. A lens can be configured to focus at least a portion of the analyte-dependent optical signal onto the detector. A filter can be configured to attenuate light having wavelengths shorter than the analyte-dependent optical signal.

[0012] Some embodiments described herein relate to an implant capable of emitting, in response to excitation light in at least one excitation wavelength range, at least one analyte-dependent optical signal in at least one emission wavelength range. A device including at least one light source can be arranged to transmit the excitation light through tissue surrounding the implant. The device can include at least one detector arranged to detect light emitted from implanted sensor and transmitted through the tissue in the emission wavelength range. The device can also include an array of lenses arranged with an array of apertures to restrict transmission of off-axis light to the detector. The arrays of lenses and the array of apertures can be positioned with respect to the detector to restrict the light emitted from the tissue that travels to the detector based on the incidence angle of the emitted light. At least one layer of light control film can be arranged with the lens and aperture arrays to restrict the light emitted from the tissue that travels to the detector based on the incidence angle of the emitted light relative to the film. The device can further include at least one filter positioned

to restrict transmission of light to the detector to wavelengths substantially within the emission wavelength range.

[0013] Some embodiments described herein relate to an optical detection device is for monitoring an implant embedded in tissue of a mammalian body. The implant is capable of emitting, in response to excitation light in at least one excitation wavelength range, at least one analyte-dependent optical signal in at least one emission wavelength range. The device can include at least one light source arranged to transmit the excitation light through the tissue to the implant. At least one detector is arranged to detect light emitted from the tissue in the emission wavelength range. The device can also include an array of lenses arranged with an array of apertures to restrict transmission of off-axis light to the detector. The arrays of lenses and the array of apertures are positioned with respect to the detector to restrict the light emitted from the tissue that travels to the detector according to an input angle of the emitted light. Light-blocking elements are arranged between the apertures to block propagation of incident light rays through the apertures. The light-blocking elements are positioned to block the incident light rays in accordance with an increase in incident angle of the light rays with respect to optical axes of the apertures. The device further comprises at least one filter arranged to restrict the transmission of the emitted light to the detector to wavelengths substantially within the emission wavelength range.

[0014] Some embodiments described herein relate to a method for monitoring an implant embedded in tissue of a mammalian body. The implant is capable of emitting, in response to excitation light in at least one excitation wavelength range, at least one analyte-dependent optical signal in at least one emission wavelength range. The method can include transmitting the excitation light through the tissue to the implant and detecting light emitted from the tissue in the emission wavelength range. The light in the emission wavelength range is transmitted through an array of lenses and an array of apertures arranged to restrict the light emitted from the tissue that travels to at least one detector according to an input angle of the emitted light. The light in the emission wavelength range is also transmitted through at least one layer of light control film arranged with the lens and aperture arrays to restrict the light emitted from the tissue that travels to the detector according to an incident angle of the emitted light relative to the film. The light in the emission wavelength range is also transmitted through at least one filter positioned to restrict transmission of light to the detector to wavelengths substantially within the emission wavelength range.

[0015] Some embodiments described herein relate to a method for monitoring an implant embedded in tissue of a mammalian body. The implant is capable of emitting, in response to excitation light in at least one excitation wavelength range, at least one analyte-dependent optical signal in at least one emission wavelength range. The method can include transmitting the excitation light through the tissue to the implant and detecting light emitted from the tissue in the emission wavelength range. An array of apertures arranged with an array of lenses restricts the light emitted from the tissue that travels to at least one detector according to an input angle of the emitted light. The method can also include blocking propagation of incident light rays through the apertures using light-blocking elements positioned between the apertures to block the incident light rays having an angle of incidence greater than a threshold angle of incidence based on, for example, the optical axes of the apertures. The method can further include filtering the emitted light to wavelengths substantially within the emission wavelength range.

[0016] Some embodiments described herein relate to an optical detection device for monitoring an implant embedded in tissue under skin. The implant is capable of emitting, in response to excitation light in at least one excitation wavelength range, at least one analyte-dependent optical signal in at least one emission wavelength range. The device can include at least one light source arranged to transmit the excitation light through a first surface area of the skin to the implant embedded in the tissue. One or more detectors can be arranged to detect light that is emitted from at least a second surface area of the skin, wherein the light source and one or more detectors are arranged such that the ratio of the surface area of the skin through which the detected light passes as it travels to the one or more detectors to the surface area of the skin through which the excitation light is transmitted is at least 4:1.

[0017] Some embodiments described herein relate to a method for monitoring an implant embedded in tissue under skin. The implant can be capable of emitting, in response to excitation light in at least one excitation wavelength range, at least one analyte-dependent optical signal in at least one emission wavelength range. The method can include transmitting the excitation light through a first surface area of the skin to the implant embedded in the tissue and detecting light that is emitted from at least a second surface area of the skin. The ratio of the surface area of the skin through which the detected light passes as it travels to one or more detectors to the surface area of the skin through which the excitation light is transmitted is at least 4:1.

Brief Description of the Drawings

[0018] Fig. 1 is a schematic side view of an optical detection device for monitoring an implant, according to an embodiment.

[0019] Fig. 2 is a schematic side view of an optical detection device for monitoring an implant, according to an embodiment.

[0020] Fig. 3 is a plan view of an aperture array, according to an embodiment.

[0021] Fig. 4 is a schematic plan view of an optical detection device, according to an embodiment.

[0022] Fig. 5 is a schematic exploded view of an optical detection device, according to an embodiment.

[0023] Fig. 6 is a schematic side view of an optical detection device for monitoring an implant, according to an embodiment.

[0024] Fig. 7 is a schematic side view of an optical detection device for monitoring an implant, according to an embodiment.

[0025] Figs. 8A-8D depict a lens and aperture array with light-blocking elements in various stages of fabrication, according to an embodiment.

[0026] Fig. 9 is a schematic plan view of an optical detection device, according to an embodiment.

[0027] Fig. 10 is a schematic plan view of an optical detection device, according to an embodiment.

[0028] Fig. 11 is a schematic plan view of an optical detection device, according to an embodiment.

Detailed Description

[0029] According to some embodiments described herein, an optical detection device is provided for monitoring an implant embedded in tissue of a mammalian body. The implant can include a fluorophore-labeled target capable of emitting, in response to excitation light in at least one excitation wavelength range, at least one analyte-dependent optical signal in at least one emission wavelength range. The optical detection device can be operable to illuminate the implant with light whose wavelength content falls within an absorption band and/or collect light whose wavelength content is in an emission band.

[0030] The optical detection device can include excitation optics including a light source and/or optics operable to generate illumination in the absorption band. The optical detection device can also include emission optics operable to collect fluorescent emissions from the implant. Because in some instances, it may be difficult to obtain, design, and/or implement a light source that has a spectral content (i.e., wavelength range) that exactly matches every fluorophore absorption band, an optical filter or filters (usually band-pass filters) can be used along with the light source to limit the range of illuminating wavelengths to that of the absorption band and/or to reduce illuminating wavelengths of the emission band. Similarly, the emission optics can include another filter or filters operable to allow substantially only light with wavelengths in the emission band to reach the detector and/or to attenuate light with other wavelengths (e.g., light in the absorption band). Similarly stated, the optical detection device can include an optical system design operable to allow substantially only photons with wavelengths in the absorption band reach the target, and substantially only photons with wavelengths in the emission band reach the detector. Without proper optics, photons from the light source may be reach the detector and induce a measurement error.

[0031] Properly designing an optical system for an optical detection device can be complicated in instances in which the amount of emitted fluorescence to be detected is much less than the amount of excitation light scattered (e.g., not absorbed) by an intermediate surface (e.g., skin or tissue disposed between the optical detection device and the implant). One challenge is that the amount of excitation light that reaches the implant may be low because of the absorption and scattering caused by the various body parts (skin, tissue, etc.). The low amount of emitted fluorescence is further reduced by absorption and scattering as it makes its way out of the body towards the detector. Existing optical filter technology, which may provide rejection of unwanted photons on the order of (10^{-6}) may be insufficient in these situations. Another challenge is that the difference between excitation and detection wavelengths (e.g., Stokes shift) may be quite small. A further challenge is that dichroic filters cause shifting (e.g., the "blue shift") of filter wavelengths as a function of the angle of light rays transmitted through the filter. Because of these challenges, standard fluorescence methods would allow through high background levels and, in turn, result in low Signal-to-Background (SBR) and Signal-to-Noise (SNR) ratios.

[0032] Some embodiments described herein relate to a compact device that can accurately and consistently monitor an implanted sensor. Such a device can be worn by a user substantially continuously and/or may not substantially restrict movements or activities of the user. The device and the sensor can collectively allow for continuous and/or automatic monitoring of an analyte and can provide a warning to the person when the level of the analyte is at or near a threshold level. For example, if glucose is the analyte, then the monitoring device might be configured to warn the person of current or impending hyperglycemia or hypoglycemia. The person can then take appropriate actions.

[0033] In the description contained herein, it is understood that all recited connections between structures can be direct operative connections or indirect operative connections through intermediary structures. A set of elements includes one or more elements. Any recitation of an element is understood to refer to at least one element. A plurality of elements includes at least two elements. Unless clearly indicated otherwise, any described method steps need not be necessarily performed in a particular or illustrated order. A first element (e.g. data) derived from a second element encompasses a first element equal to the second element, as well as a first element generated by processing the second element and optionally other data. Making a determination or decision according to a parameter encompasses making the determination or decision according to the parameter and optionally according to other data. Unless otherwise specified, an indicator of some quantity/data may be the quantity/data itself, or an indicator different from the quantity/data itself. Some embodiments described herein reference a wavelength, such as an excitation wavelength or an emission wavelength. Unless clearly indicated otherwise, a wavelength should be understood as describing a band of wavelengths including the wavelength. Computer programs described in some embodiments of the present invention may be stand-alone software entities or sub-entities (e.g., subroutines, code objects) of other computer programs. Computer readable media encompass non-transitory media such as magnetic, optic, and semiconductor storage media (e.g. hard drives, optical disks, flash memory, DRAM), as well as communications links such as conductive cables and fiber optic links. According to some embodiments, the present invention provides, inter alia, computer systems comprising hardware (e.g. one or more processors and associated memory) programmed to perform the methods described herein, as well as computer-readable media encoding instructions to perform the methods described herein.

[0034] The following description illustrates embodiments of the invention by way of example and not necessarily by way of limitation.

[0035] Fig. **1** is a schematic side view of an optical detection device **10** for monitoring an implanted sensor or implant **12**, according to an embodiment. The implant **12** is embedded in tissue **15** of a mammalian body (which may be a piece of tissue that is attached or unattached to the rest of the body in various embodiments). The implant **12** can be embedded under a surface of skin **14**. The implant **12** can be embedded and/or positioned in the subcutaneous tissue (e.g., in the range of 1 to 4 mm under the surface of the skin **14**). The implant **12** is capable of emitting, in response to excitation light within an excitation wavelength range, at least one analyte-dependent optical signal within an emission wavelength range. The analyte may be, for example, glucose or other analytes in the tissue **15**. Suitable optical signals include, without limitation, luminescent, bioluminescent, phosphorescent, autoluminescence, and diffuse reflectance signals. In some embodiments, the implant **12** contains one or more luminescent dyes (e.g., fluorescent dyes) whose luminescence emission intensity varies in dependence upon the amount or presence of target analyte in the body of the individual (e.g., in tissue **15**).

[0036] A light source **18** is arranged to transmit excitation light within the excitation wavelength range from the surface of the skin **14**, through the tissue **15**, and to the implant **12**. Suitable light sources include, without limitation, lasers, semi-conductor lasers, light emitting diodes (LEDs), and organic LEDs. Detectors **16**, **20** are arranged with the light source **18** to detect light emitted from the tissue in the emission wavelength range. Suitable detectors include, without limitation, photodiodes, complementary metal–oxide–semiconductor (CMOS) detectors or charge-coupled device (CCD) detectors. Although multiple detectors are shown, a single and/or universal detector can be used.

[0037] The detectors can be **16**, **20** filtered (e.g., with dichroic filters or other suitable filters) to measure the optical signals emitted within the wavelength ranges. For example, a suitable luminescent dye sensitive to glucose concentration is Alexa Flour ® 647 responsive to excitation light (absorption) in the range of about 600 to 650 nm (absorption peak 647 nm) and within an emission wavelength range of about 670 to 750 nm with an emission peak of about 680 nm. Thus, in an embodiment in which the sensor includes Alexa Flour ® 647, the detectors **16**, **20** can be filtered from light having a wavelength shorter than about 650 nm or shorter than about 670 nm.

[0038] In some embodiments, the implant **12** is further capable of emitting, in response to excitation light within a second excitation wavelength range, at least one analyte-independent optical signal within a second emission wavelength range. For example, the implant **12** can contain an analyte-independent luminescence dye that functions to control for non-analyte physical or chemical effects on a reporter dye (e.g., photo bleaching or pH). Multiple dyes may be used. The analyte-independent optical signal is not modulated by analyte present in the tissue **15** and provides data for normalization, offset corrections, or internal calibration. The analyte-independent signal may compensate for non-analyte affects that are chemical or physiological (e.g., oxygen, pH, redox conditions) or optical (e.g., water, light absorbing/scattering compounds, hemoglobin). Alternatively, the analyte-independent signal may be provided by a stable reference dye in the implant **12**. Suitable stable reference materials include, but are not limited to, lanthanide-doped crystals, lanthanide-doped nanoparticles, quantum dots, chelated lanthanide dyes, and metal (e.g., gold or silver) nanoparticles. The stable reference dye may provide a reference signal for other signals (e.g., to determine photo bleaching).

[0039] In the operation of device **10**, the light source **18** is activated to transmit excitation light within the excitation wavelength range from the surface of the skin **14**, through the tissue **15**, and to the implant **12**. The dye in the implant **12** absorbs some of the excitation light and emits fluorescence that depends on glucose or other analyte properties. The light may be emitted from the implant **12** in all directions, and scattered by the tissue **15**. Some of the light that is emitted from the implant **12** is transmitted through the tissue **15** and detected by at least one of the detectors **16**, **20**. This can provide the primary analyte-dependent optical signal. In embodiments in which a reference optical signal is used for normalization, the light source **18** (or a second light source) is activated to transmit second excitation light from the surface of the skin **14** to the implant **12**. At least one of the detectors **16**, **20** measures, in response to the second excitation light, a second optical signal emitted from the tissue **15** through the surface of the skin **14**.

[0040] The second optical signal may be used to normalize the primary analyte-dependent optical signal for scattering of light emitted from the implant **12**. At least one corrected signal value may be calculated in dependence upon the measured optical signals. In one example, the primary analyte-dependent signal from the implant may be normalized by the analyte-independent optical signal emitted from the implant **12**. Prior to executing optical reads for the analyte-dependent signal and/or the analyte-independent signal, a dark reading may be taken to account for background or ambient light, and this reading may be used to further correct the signals, e.g., by background subtraction.

[0041] In some embodiments, an analyte value (e.g., glucose concentration) is determined from the analyte-dependent signal and/or a ratio of multiple optical signals including one or more reference signals. In one example, the signal from the glucose sensitive fluorophore (e.g., Alexa Flour ® 647) is normalized by the signal from a glucose insensitive fluorophore (e.g., Alexa Flour ® 700). One suitable dye for the analyte-independent signal is Alexa Flour ® 750 which is responsive to excitation light within an excitation wavelength range of about 700 to 760 nm (excitation peak 750 nm) and has an emission wavelength range of about 770 to 850 nm with an emission peak of about 780 nm.

[0042] An analyte value can be determined based on the optical signal(s) using, for example, a look-up table or calibration curve. Determining the analyte value can be implemented in software (executing on a processor) and/or hardware. For example, the optical device **10** can include a microprocessor. In some embodiments, the microprocessor is programmed to store measured optical signal values in a memory and/or to calculate normalized signal values and analyte concentrations. Alternatively, these functions may be performed in a separate processor or external computer in communication with the optical device **10**. The external processor or computer can receive data representative of the measured optical signals and calculates the corrected signal value and analyte concentration. Alternatively, multiple processors may be provided, e.g., providing one or more processors in the optical device that communicate (wirelessly or with wires) with one or more external processors or computers.

[0043] In some embodiments in which two implant dyes (e.g., luminescent dyes) are utilized, it is possible that the implant dyes may share or overlap excitation (absorption) or emission wavelength ranges. In one example, the emission wavelength range of the first dye, which provides the analyte-dependent luminescence signal, shares or overlaps the excitation wavelength range of the second dye, which provides the analyte-independent luminescence signal. In another embodiment, the first and second dyes may share or overlap excitation wavelength ranges (so that a common light source may be used) and emit optical signals within different emission wavelength ranges. In another embodiment, the first and second dyes may be excited by light within different excitation wavelength ranges and emit optical signals within the same or overlapping emission wavelength range(s).

[0044] The implant **12** can be embedded in subcutaneous tissue (e.g., 1 to 4 mm under the surface of the skin **14**). In some embodiments, the implant **12** comprises hydrogel scaffolds embedded with glucose-sensing nanospheres. The design of the implant **12** can use injectable, tissue-integrating, vascularizing scaffolds as the sensor. Embedded nanospheres emit luminescence that changes intensity and lifetime in response to the presence or concentration of the analyte (e.g., interstitial glucose). The spacing distances between each of the detectors **16**, **20** and the light source **18** determine the depths of the respective light paths for detecting optical signals from the implant **12**. The combination of an excitation light source and a detection band is an optical channel. The light source **18** and detectors **16**, **20** can be arranged such that a surface area of skin **14** through which the excitation light is transmitted is located between substantially surrounding surface areas of skin **14** through which the detected light passes as it travels from the tissue **15** to one or more detectors **16**, **20**.

[0045] Although only one light source **18** and two detectors **16, 20** are shown in Fig. **1**, in some embodiments, the optical device **10** can have any number of light sources and any number of detectors. The optical device **10** can have multiple possible combinations of spacing distances between multiple light sources and detectors. Such a multiple light source and/or multiple detector implementation can allow increased flexibility of the optical device **10**. For example, since the depth of the implant **12** may be application-specific, an optical device **10** having multiple light sources and/or multiple detectors can be used for multiple applications.

[0046] The optical device **10** can be configured to ensure that substantially only photons with wavelengths in the excitation wavelength range(s) reach the implant **12**, and substantially only photons with wavelengths in the emission wavelength ranges(s) reach at least one of the detectors **16**, **20**. Such an arraignment can minimize photons from the light source **18** reaching the detectors **16**, **20,** which can result in measurement error.

[0047] Fig. **2** is a schematic side view of an optical detection device for monitoring an implant, according to an embodiment. An array of lenses **22** is aligned with an array of apertures **24** to restrict transmission of off-axis light to the detector **16**. The lens arrays **22** and the aperture array **24** are positioned with respect to the detector **16** to collectively restrict the light emitted from the tissue that travels to the detector **16** based on an input angle **θ** (also referred to herein as incident angle) of the emitted light relative to optical axes **30** of the apertures. The optical axes **30** of the apertures can be substantially perpendicular to the surface of the detector **16**. Each aperture from the array of apertures **24** can be substantially aligned with a lens from the array of lenses **22**. Similarly stated the optical axes **30** of the apertures can be substantially coaxial with the center and/or axes of the lenses. For example, a substantially opaque portion of the array of apertures **24** can be positioned below the edges of the lenses.

[0048] At least one layer of light control film **26** is arranged with the lens array **22** and the aperture array **24**. The light control film **26** can restrict the light emitted from the tissue from entering the lens array **22** and/or the aperture array **24** based on the incident angle of the emitted light relative to the film **26**. In one example, the light control film **26** is Vikuti™ optical grade micro-louver privacy film commercially available from 3M™, which can block light having an incident angle greater than desired (e.g., greater than 24 degrees) relative to a perpendicular line through the film **26**. This privacy film comprises a set of microlouvers that prevent light from large incident angles from reaching the lens array **22**. In other embodiments, the film **26** comprises alternating transparent and opaque layers in an arrangement which is similar to a Venetian blind. Light propagating from angles greater than a desired incident angle can be absorbed and/or reflected.

[0049] At least one filter **28** (e.g., a dichroic or dielectric filter) is positioned to restrict transmission of light to the detector **16** to wavelengths substantially within the desired emission wavelength range. Because the detection of optical signals is dominated by low levels of return signals relative to the excitation light, the filter **28** can prevent scattered excitation light from blinding the detector **16**. Suitable filters include band-pass, low-pass, and high pass filters depending upon the desired emission wavelength range for an application. Some modern optical filters have demonstrated 10^{-9} light rejection due to improvements in coating technologies. Additionally, intermediate layers of the optical detection system (e.g., the lens array **22**, the aperture array **24**, etc.) can include anti-reflective coatings to reduce or prevent light leaking through to the detector **16**.

[0050] Due to fundamental properties of dichroic filters, maintaining a high level of light rejection requires careful design. One property of dichroic filters that detracts from light rejection is the "blue shift" as a function of input angle, where the transmittance wavelengths of dichroic filters change as a function of input angle. For the detection light emitted from the implant, there is a trade off between the input angle and the absolute optical signal. The light leaving the tissue is highly scattered and may form a lambertian distribution by the time it reaches the surface of the skin. The collection efficiency of the emitted light is proportional to $\sim NA^2$, where NA=Numerical Aperture = n sin **θ**, and **θ** is the input angle. To improve the collection efficiency, the allowable input angle θ can be increased without increasing the angle so much to allow excitation light though the filter **28**.

[0051] The lens array **22** and the aperture array **24** control the input angle **θ** of light traveling to the detector **16**. The lens array **22** and an aperture array **24** restrict the light to an input angle less than **θ**, which in some embodiments is selected to be +/- 20 degrees. The input angle **θ** can be controlled by varying the size of the apertures and the focal length of the micro lenses in the lens array **22**. The smaller the aperture, then the smaller is input angle **θ**. The longer the focal length, then the smaller is input angle **θ**. Although not shown, a spacer can be used to maintain separation between the surface of the aperture array **24** and the lens array **22**.

[0052] Fig. **3** is a plan view of the aperture array **24** having a plurality of apertures **25**. In some embodiments, the aperture array **24** is constructed by patterning a metal mask on the surface of a silicon detector, such as the detector **16** shown in Fig. **2**. The lens array **22** may be fabricated as etched glass or molded plastic. In some embodiments, the lens array **22** is a custom micro-lens array commercially available from JENOPTIK Optical Systems.

[0053] Fig. **4** is a schematic plan view of an optical detection device, according to an embodiment. The optical detection device of Fig. **4** is configured as a patch **32**. At least one light source (not shown in Fig. **4**) and detector **38** are arranged in an optical reader, such that the patch **32**, that is configured to be placed on the skin. A light source is arranged to transmit the excitation light through a central via **34** in the patch **32**, and a single universal detector **38** substantially surrounds the central via **34**. In other embodiments, instead of the single detector **38**, a plurality of detectors can be used, for example, substantially encircling the central via **34** to detect the emitted light in a plurality of emission wavelength ranges. In some embodiments, the optical detection device includes at least one light guiding component **36** in the central via **34**. The light guiding component **36**, such as a waveguide or optical fiber, is arranged to guide the excitation light to the skin. In some embodiments, a plurality of light sources (not shown for clarity in Fig. **4**) are arranged to transmit the excitation light through the central via **34** (e.g., by means of one or more waveguides or optical fibers) in a plurality of different excitation wavelength ranges.

[0054] As one possible example, one or more light sources may be arranged to transmit excitation light to the skin through the central via **34** having a circular cross-section to transmit the excitation light through a substantially circular surface area of the skin having a diameter of about 1 mm and a corresponding excitation surface area of about 0.8 mm^2. The detector **38** has a square cross-section and is positioned to detect light emitted from a substantially square surface area of the skin through which the detected light passes as it travels to the detector **38**. The detection surface area is substantially square with sides of 10 mm length, so that the total detection surface area is (10 mm x 10 mm) - 1 mm^2 = 99 mm^2. Accordingly, in this example, the ratio of detection surface area to excitation surface area is greater than 120:1.

[0055] Fig. **5** is a schematic exploded view of the patch **32**. The patch **32** includes multiple layers. Dimensions of the patch **32** may be, for example, a diameter of about 16 mm and a thickness T of about 1.6 mm. In some embodiments, the layers may include a plastic cover **40** having a thickness of about 200 um, the light control film **26** having a thickness of about 100 um, the filter **28** having a thickness of about 200 um, the lens array **22** having a thickness of about 100 um, and the aperture array **24** patterned on a silicon detector layer **48** having a thickness of about 200 um. The layers can also include a printed circuit board (PCB) **50** having a thickness of about 400 um, a battery **52** having a thickness of about 300 um, and a case **54** having a thickness of about 200 um. The PCB **50** can include one or more light sources. The PCB **50** can also include processing electronics and/or a microprocessor in communication with one or more detectors in the detector layer **48** to receive data representative of the light detected in the emission wavelength range and programmed to determine at least one analyte value in dependence upon the data. The central via **34** may be formed through a stack of the layers (e.g., etched or drilled through the stack in the assembly process).

[0056] Fig. **6** is a schematic side view of an optical detection device for monitoring an implant showing an arrangement of detection optics **60**, according to an embodiment. In this embodiment, light emitted from the implant and tissue in the emission wavelength range is transmitted through at least two layers of light control films **62**, **64**. The two layers of light control films **62**, **64** can restrict the light emitted from the tissue from entering the lens array **22** and/or the aperture array **24** based on the incident angle of the emitted light relative to the films **62**, **64**. In one example, the light control film **62** comprises alternating transparent and opaque layers in an arrangement which is similar to a Venetian blind. Light propagating from angles greater than a desired incident angle is absorbed. The light control film **64** may include Vikuti™ optical grade micro-louver privacy film commercially available from 3M™, which blocks light having an incident angle greater than desired (e.g., greater than 24 degrees) relative to a perpendicular line through the film **64**.

[0057] In some embodiments, the light control film **62** and/or **64** may be operable to restrict light emitted from the tissue from entering the lens array **22** and the aperture array **24** based on a combination of incident angle and azimuth. For example, in an embodiment where the light control film **62** and/or **64** includes multiple micro-louvers, the light control film **62** and/or **64** may be effective at blocking high angle-of-incidence light having an azimuth substantially perpendicular to the micro-louvers, but may be relatively ineffective at blocking high angle-of-incidence light having an azimuth substantially parallel to the micro-louvers. In some such embodiments, two layers of light control film **62**, **64** can be cross-hatched or otherwise disposed such that louvers or other light control elements are non-parallel such that the light control film **62**, **64** are collectively effective at blocking high angle-of-incidence light having different azimuths.

[0058] In some embodiments, the films **62**, **64** may be substantially the same as each other, or comprises different types of privacy film. Additionally, the filter **28** (e.g., a dichroic or dielectric filter) may be positioned between the aperture array **24** and the detector **16** to restrict the transmission of the emitted light to the detector **16** to wavelengths substantially within the emission wavelength range(s). The operation of the embodiment of Fig. **6** can be similar to the operation of the embodiment of Figs. **1-2** previously described.

[0059] Fig. **7** is a schematic side view of an optical detection device for monitoring an implant. An array of lenses **122** is aligned with an array of apertures **24** to restrict the transmission of off-axis light to the detector **16**. The lens arrays **122** and the aperture array **24** are positioned with respect to the detector **16** to restrict the light emitted from the tissue that travels to the detector **16** according to an input angle **θ** of the emitted light relative to optical axis **30** of the apertures. The optical axis **30** of the apertures can be substantially perpendicular to the surface of the detector **16**.

[0060] The lens array **122** includes light-blocking elements **72**. The light-blocking elements **72** can be disposed between the apertures **25** to block propagation of off-axis light rays **74**, **76** through the apertures **25**. The light-blocking elements **72** can include black resin, metal, and/or metal film deposited in cavities of a substrate **123** of the lens array **122** positioned. At least one filter **28** is positioned to restrict the transmission of the emitted light to the detector **16** to wavelengths substantially within the emission wavelength range. Optionally, one or more layers of light control film may be included in this embodiment. The operation of the embodiment of Fig. **7** can be similar to the operation of the embodiment of Figs. **1-2** previously described.

[0061] Figs. **8A-8D** depict a lens array **122** with light-blocking elements in various stages of fabrication, according to an embodiment. Fig. **8A** shows a side view of the lens array **122** which may be fabricated as etched glass or molded plastic. In some embodiments, the lens array **122** is a micro-lens array commercially available from JENOPTIK Optical Systems. Fig. **8B** shows cavities **78** which can be, for example, etched or integrally molded into a substrate portion **123** of the lens array **122**. As shown in Fig. **8C**, the cavities 78 can be filled with a substantially opaque material to form light-blocking elements **72**. The light-blocking elements 72 can be constructed of, for example, black resin, metal, and/or metal film. As shown in Fig. **8D**, the aperture array **24** may be positioned adjacent to the lens array **122** (with a spacer in some embodiments) such that light-blocking elements **72** are positioned between the apertures **25**. In some embodiments, the aperture array **24** is constructed by patterning a metal mask on the surface of a silicon detector and positioning the detector with aperture array **24** adjacent to the lens array **22** with light-blocking elements **72** such that the light-blocking elements **72** are positioned between the between apertures **25**.

[0062] Fig. **9** is a schematic plan view of an optical detection device **210**, according to an embodiment. The optical detection device **210** includes four detectors **216**, **220**, **222**, and **224** and a light source **218**. The optical detection device **210** has a relatively large ration of detector surface area to light source surface area (also referred to herein as "surface area ratio"). The large surface area ratio can improve detection of implant signals, when the implant is embedded in subcutaneous tissue (e.g., 1-4 mm under the surface of the skin). In particular, the light source **218** and four detectors **216**, **220**, **222**, **224** are arranged such that the ratio of the surface area of the skin through which the detected light passes as it travels to the detectors **216**, **220**, **222**, **224** to the surface area of the skin through which the excitation light is transmitted is at least 4:1. For example, in one embodiment the light source **218** has a circular cross-section and is positioned to transmit the excitation light through a substantially circular surface area of the skin having a diameter of about 3 mm, a radius of about 1.5 mm, and an excitation surface area of about 7 mm^2. The four detectors **216**, **220**, **222**, **224** have square cross-sections and are positioned to detect light emitted from four substantially square surface areas of the skin, through which the detected light passes as it travels to the detectors. Each of the four detection surface areas is substantially square with sides of 3 mm, so that the total detection surface area is $4 \times 9\ mm^2 = 36\ mm^2$. Accordingly, in this example, the ratio of detection surface area to excitation surface area is slightly greater than 5:1.

[0063] In some embodiments, the optical detection device **210** can be configured to detect implant signals at a lateral distance at least twice the depth of the implant. For example, at least a portion of at least one of the detectors **216**, **220**, **222**, **224** can be at least twice as far away from the implant laterally as that portion is from the implant distally. For example, in an instance where the light source **218** is centered over an implant that is embedded under 4 mm of tissue, at least a portion of at least one of the detectors **216**, **220**, **222**, **224** can be 8 mm away from the center of the light source **218**. Similarly stated, the furthermost edge or corner of at least one of the detectors **216**, **220**, **222**, **224** can be at least twice as far away from the center of the light source **218** as the implant is deep. In an alternate embodiment, such as an embodiment having a single or universal detector, the detector can have a radius at least twice the depth of the implant. In other embodiments, the optical detection device **210** can be configured to detect implant signals at a lateral distance at least three times, at least five times, or any other suitable multiple of the depth of the implant. An optical detector device **210** operable to detect implant signals a relatively large lateral distance from the implant may be able to detect a larger portion of an emitted signal, particularly in a high-scattering environment. Capturing a larger portion of the emitted signal can improve detection accuracy.

[0064] Fig. **10** is a schematic plan view of an optical detection device **310**, according to an embodiment. As compared to the optical detection device 210, in this embodiment, the four detectors **316**, **320**, **322**, **324** are positioned closer to the light source **318** as they surround or encircle the light source **318**, and the ratio of detection surface area to excitation surface area is larger. For example, the light source **318** may have a circular cross-section and is arranged to transmit the excitation light through a substantially circular surface area of the skin having a diameter of about 2 mm, a radius of about 1 mm, and an excitation surface area of about 3.14 mm^2. The four detectors **316**, **320**, **322**, **324** have square cross-sections and are positioned to detect light emitted from four substantially square surface areas of the skin, through which the detected light passes as it travels to the detectors. Each of the four detection surface areas is substantially square with sides of 6 mm, so that the total detection surface area is 4 x 36 mm^2 = 144 mm^2. Accordingly, in this example, the ratio of detection surface area to excitation surface area is slightly greater than 45:1.

[0065] Fig. **11** is a schematic, plan view of aspects of an optical detection device **410**, according to another embodiment. In this embodiment, five circular-shaped detectors **428A**, **428B**, **428C**, **428D**, and **428E** surround or encircle a central via **434**. The central via **434** may be a hole in the device **410**. A plurality of light sources **426** are arranged to transmit excitation light in a plurality of different wavelength ranges through the central via **434**. As one possible example, the light sources **426** may be arranged to transmit excitation light to the skin through the central via **434** having a circular cross-section to transmit the excitation light through a substantially circular surface area of the skin having a diameter of about 3 mm and a corresponding excitation surface area of about 7 mm^2. The five detectors **428A**, **428B**, **428C**, **428D**, and **428E** have circular cross-sections and are positioned to detect light emitted from five substantially circular surface areas of the skin, through which the detected light passes as it travels to the detectors. Each of the five detection surface areas is substantially circular with a diameter of 5 mm, so that the total detection surface area is 5 x 19.6 mm^2 = 98 mm^2. Accordingly, in this example, the ratio of detection surface area to excitation surface area is slightly greater than 13:1.

[0066] It will be clear to one skilled in the art that the above embodiments may be altered in many ways without departing from the scope of the invention. For example, many different permutations or arrangements of one or more light sources, one or more detectors, filters, and/or light guiding elements connecting the optical components may be used to realize the device and method of the invention. For example, alternative embodiments may have different dimensions and/or wavelengths. Embodiments may include cabled or wireless hand-held readers, wireless skin patch readers, bench-top instruments, imaging systems, smartphone attachments and applications, or any other configuration that utilizes the disclosed optics and algorithms.

[0067] In some embodiments described herein, a monitoring device can be operable to simultaneously emit an excitation optical signal and detect an emission signal. For example, the detector of such a monitoring device can be shielded from reflected or back-scattering excitation light using apertures, light-blocking elements, filters, light control film, etc. In other embodiments, a monitoring device can be operable to emit an excitation optical signal during one period of time, and detect an emission signal during another period of time in which the excitation optical signal is deactivated.

[0068] Tissue optical heterogeneity in some cases may be significant. Thus, it may be advantageous to utilize a single light source and a single detector to assure that every color passes through the same optical pathway through the tissue. In one embodiment, a light source can be positioned with a set of moveable filters between the light source and the surface of the skin. Similarly a single photodetector can be utilized in place of separate discrete detector elements. The detector may be used to detect different wavelength ranges by using moveable or changeable filters to enable multiple wavelengths to be measured. Changing or moving filters may be accomplished by a mechanical actuator controlling a rotating disc, filter strip or other means. Alternatively, optical filters may be coated with a material that, when subjected to current, potential, temperature or another controllable influence, changes optical filtering properties, so that a single photodetector can serve to detect multiple wavelength ranges.

[0069] In some embodiments, the devices and methods of the present invention make use of wafer-based micro-optics. These systems are created lithographically, but can be replicated at low cost. The technology allows for layers of optics and detectors to be bonded at the wafer level and then diced into individual detector systems. Suitable components include etched refractive lenses, polymer replicated refractive lenses, etched binary lenses, replicated binary lenses, replicated holograms, and replicated volume holograms.

[0070] In some embodiments, a complementary metal–oxide–semiconductor (CMOS) detector may be used as an integral part of the optical system. The advantage of a CMOS sensor is the ability to integrate the detection, excitation, and digital filtering circuitry into a single piece of silicon. A new technology was recently announced, sCMOS, where researchers have been able to greatly reduce the noise in CMOS detectors to be comparable to charge charge-coupled device (CCD) detectors. Another benefit to a CMOS integrated solution is the ability to perform lock-in detection and digital filtering on the signals to reduce or eliminate the impact of ambient light.

[0071] While various embodiments have been described above, it should be understood that they have been presented by way of example only, not limitation, and various changes in form and details may be made. Any portion of the apparatus and/or methods described herein may be combined in any combination, except mutually exclusive combinations. The embodiments described herein can include various combinations and/or sub-combinations of the functions, components and/or features of the different embodiments described.

What is claimed is:

1. An apparatus, comprising:

a printed circuit board;

a light source coupled to the printed circuit board and configured to transmit an excitation optical signal to an implanted sensor;

a plurality of detectors coupled to the printed circuit board and configured to detect an analyte-dependent optical signal emitted from the implanted sensor in response to the implanted sensor being illuminated by the excitation optical signal; and

a plurality of lenses, each lens from the plurality of lenses configured to focus at least a portion of the analyte-dependent optical signal onto a detector from the plurality of detectors.

2. The apparatus of claim 1, further comprising:

an aperture configured to inhibit a photon having an angle of incidence greater than a predetermined angle of incidence from striking a detector from the plurality of detectors.

3. The apparatus of claim 1, wherein the plurality of lenses is from an array of lenses, each lens from the array of lenses defining a substantially parallel and non-coaxial lens axes.

4. The apparatus of claim 1, wherein the plurality of lenses is from a monolithically formed array of lenses.

5. The apparatus of claim 1, wherein the plurality of lenses is from an array of lenses, the apparatus further comprising:

an array of apertures, each aperture from the array of apertures being substantially aligned with a center of a lens from the array of lenses.

6. The apparatus of claim 1, further comprising:

a filter configured to attenuate optical signals having wavelengths associated with the light source.

Date Reçue/Date Received 2022-04-07

7. The apparatus of claim 1, further comprising:

a filter configured to attenuate optical signals having wavelengths associated with the light source, the filter configured to transmit the analyte-dependent optical signal with substantially no attenuation.

8. The apparatus of claim 1, further comprising:

a dichroic filter configured to attenuate optical signals having wavelengths associated with the light source, the dichroic filter configured to blue shift analyte-dependent optical signals towards the wavelength associated with the light source as a function of an angle of incidence, a detector from the plurality of detectors not being configured to detect a blue-shifted analyte-dependent optical signal.

9. The apparatus of claim 8, wherein a portion of the excitation optical signal is scattered by tissue surrounding the implant, the apparatus further comprising:

an aperture, (1) a lens from the plurality of lenses, (2) the aperture, and (3) the dichroic filter are collectively configured to inhibit the portion of the excitation optical signal from entering a detector from the plurality of detectors.

10. The apparatus of claim 1, wherein:

the implanted sensor is implanted at a depth, and

at least a portion of a detector from the plurality of detectors is configured to be disposed a lateral distance from the implant, the lateral distance being at least twice the depth.

11. The apparatus of claim 1, wherein:

the light source is configured to be disposed directly above the implanted sensor,

the implanted sensor is implanted at a depth, and

at least a portion of a detector from the plurality of detectors is a distance from the light source, the distance being at least twice the depth.

Date Reçue/Date Received 2022-04-07

12. The apparatus of claim 1, wherein the light source is configured to transmit the excitation optical signal through a first surface area of skin to the implant, and the plurality of detectors is configured to detect the analyte dependent optical signal from a second surface area of the skin, the second surface area of the skin being at least four times the first surface area of the skin.

13. The apparatus of claim 1, wherein further comprising:

the printed circuit board defining a via, the light source configured to transmit the excitation optical signal to the implanted sensor through the via, the plurality of detectors substantially surrounding the via.

14. An apparatus, comprising:

an array of lenses, each lens from the array of lenses configured to transmit an analyte-dependent optical signal from an implanted sensor to a detector disposed behind that lens, the array of lenses including a substrate; and

a plurality of light-blocking elements disposed within the substrate of the array of lenses, each light-blocking element from the plurality of light-blocking elements configured to inhibit a photon having an angle of incidence greater than a predetermined angle of incidence from passing through the substrate.

15. The apparatus of claim 14, wherein each lens from the array of lenses has an edge and a center defining a lens axis such that the array of lenses includes a plurality of lens axes, and each light-blocking element from the plurality of light-blocking elements is disposed between the lens axes.

16. The apparatus of claim 14, further comprising an array of apertures coupled to the array of lenses, the array of apertures and the plurality of light-blocking elements collectively configured to inhibit the photon having the angle of incidence greater than the predetermined angle of incidence from passing through the substrate.

Date Reçue/Date Received 2022-04-07

17. The apparatus of claim 14, further comprising:

a light source configured to transmit an excitation optical signal to the implanted sensor; and

a filter, the filter and the plurality of light-blocking elements collectively configured to substantially eliminate a portion of the excitation optical signal scattered onto the array of lenses from passing through the substrate.

18. The apparatus of claim 14, further comprising:

a detector coupled to the array of lenses, the detector configured to measure light that exits the substrate.

19. The apparatus of claim 14, wherein the photon is a first photon having a first angle of incidence, and the predetermined angle of incidence is a first predetermined angle of incidence, the apparatus further comprising:

a layer of light control film coupled to the array of lenses, the layer of light control film configured to inhibit a second photon having a second angle of incidence greater than a second predetermined angle of incidence from entering the substrate.

20. The apparatus of claim 14, wherein the photon is a first photon having a first angle of incidence, the apparatus further comprising:

a first layer of light control film coupled to the array of lenses, the first layer of light control film configured to inhibit a second photon having a second angle of incidence and a first azimuth from entering the substrate; and

a second layer of light control film configured to inhibit a third photon having a third angle of incidence and a second azimuth reaching the first layer of light control film.

21. The apparatus of claim 20, wherein the second angle of incidence is less than the first angle of incidence, the second angle of incidence is substantially equal to the third angle of incidence, and the second azimuth is ninety degrees different from the third azimuth.

Date Reçue/Date Received 2022-04-07

22. The apparatus of claim 21, wherein the first photon has a third azimuth forty-five degrees different from the second azimuth.

23. The apparatus of claim 14, further comprising:

a light source coupled to the array of lenses, the light source configured to transmit an excitation optical signal to the implanted sensor; and

a detector coupled to the array of lenses, the detector configured to measure light that exits the substrate, the array of lenses having an anti-reflective coating configured to inhibit the excitation optical signal from being reflected to the detector.

24. An optical detection device for monitoring an implant embedded in tissue of a mammalian body, the implant being capable of emitting, in response to excitation light in at least one excitation wavelength range, at least one analyte-dependent optical signal in at least one emission wavelength range, the device comprising:

a) at least one light source arranged to transmit the excitation light through the tissue to the implant;

b) at least one detector arranged to detect light emitted from the tissue in the emission wavelength range, the ;

c) an array of lenses disposed in front of and parallel to a plane to which the at least one light source and the at least one detector are coupled;

d) an array of apertures arranged with the array of lenses to restrict transmission of off-axis light to the detector, wherein the array of lenses and the array of apertures are positioned with respect to the detector to restrict the light emitted from the tissue that travels to the detector according to an input angle of the emitted light;

e) at least one layer of light control film arranged with the lens and aperture arrays to restrict the light emitted from the tissue that travels to the detector according to an incident angle of the emitted light relative to the film; and

f) at least one filter positioned to restrict transmission of light to the detector to wavelengths substantially within the emission wavelength range.

Date Reçue/Date Received 2022-04-07

25. The device of claim 24, further comprising at least one processor arranged to receive data representative of the light detected in the emission wavelength range and programmed to determine at least one analyte value in dependence upon the data.

26. The device of claim 24, wherein the at least one light source and detector are arranged such that a surface area of skin through which the excitation light is transmitted is located between substantially surrounding surface areas of skin through which the detected light passes as it travels from the tissue to one or more detectors.

27. The device of claim 24, wherein the at least one light source and detector are arranged in an optical reader adapted to be placed on skin, the light source is arranged to transmit the excitation light through a central via in the optical reader, and the one or more detectors substantially surround the central via.

28. The device of claim 27, further comprising at least one light guiding component in the central via arranged to guide the excitation light to the skin.

29. The device of claim 27, wherein the device comprises a plurality of light sources arranged to transmit the excitation light through the central via in a plurality of different excitation wavelength ranges.

30. The device of claim 27, wherein the device comprises a plurality of detectors substantially encircling the central via to detect the emitted light in a plurality of emission wavelength ranges.

31. The device of claim 24, wherein the device includes at least two layers of light control film arranged with the lens and aperture arrays to restrict the light emitted from the tissue that travels to the lens and aperture arrays according to the incident angle of the emitted light.

32. The device of claim 24, wherein the filter comprises a dichroic filter.

Date Reçue/Date Received 2022-04-07

33. The device of claim 24, wherein the at least one light source and detector are arranged to monitor the implant embedded in tissue at a depth in the range of 1-4 mm under a surface of skin.

34. An optical detection device for monitoring an implant embedded in tissue of a mammalian body, the implant being capable of emitting, in response to excitation light in at least one excitation wavelength range, at least one analyte-dependent optical signal in at least one emission wavelength range, the device comprising:

a) at least one light source arranged to transmit the excitation light through the tissue to the implant;

b) at least one detector arranged to detect light emitted from the tissue in the emission wavelength range, the at least one light source and the at least one detector coupled to a planar substrate;

c) an array of lenses disposed in front of the at least one detector and parallel to the planar substrate;

d) an array of apertures arranged with the array of lenses to restrict transmission of off-axis light to the detector, wherein the array of lenses and the array of apertures are positioned with respect to the detector to restrict the light emitted from the tissue that travels to the detector according to an input angle of the emitted light;

e) light blocking elements arranged between the apertures to block propagation of incident light rays through the apertures, wherein the light blocking elements are positioned to block the incident light rays in accordance with an increase in incident angle of the light rays with respect to optical axes of the apertures; and

f) at least one filter arranged to restrict the transmission of the emitted light to the detector to wavelengths substantially within the emission wavelength range.

35. The device of claim 34, further comprising at least one processor arranged to receive data representative of the light detected in the emission wavelength range and programmed to determine at least one analyte value in dependence upon the data.

Date Reçue/Date Received 2022-04-07

36. The device of claim 34, wherein the at least one light source and detector are arranged such that a surface area of skin through which the excitation light is transmitted is located between substantially surrounding surface areas of skin through which the detected light passes as it travels from the tissue to one or more detectors.

37. The device of claim 34, wherein the at least one light source and detector are arranged in an optical reader adapted to be placed on skin, the light source is arranged to transmit the excitation light through a central via in the optical reader, and the one or more detectors substantially surround the central via.

38. The device of claim 37, further comprising at least one light guiding component in the central via arranged to guide the excitation light to the skin.

39. The device of claim 37, wherein the device comprises a plurality of light sources arranged to transmit the excitation light through the central via in a plurality of different excitation wavelength ranges.

40. The device of claim 37, wherein the device comprises a plurality of detectors substantially encircling the central via to detect the emitted light in a plurality of emission wavelength ranges.

41. The device of claim 34, further comprising at least one layer of light control film arranged with the lens and aperture arrays to restrict the light emitted from the tissue that travels to the lens and aperture arrays according to an incident angle of the emitted light.

42. The device of claim 34, wherein the filter comprises a dichroic filter.

43. The device of claim 34, wherein the light blocking elements comprise resin or metal deposited in cavities of a lens array substrate positioned adjacent the aperture array.

Date Reçue/Date Received 2022-04-07

44. The device of claim 34, wherein the at least one light source and detector are configured to monitor the implant embedded in tissue at a depth in the range of 1-4 mm under a surface of skin.

45. A method for monitoring an implant embedded in tissue of a mammalian body, the implant being capable of emitting, in response to excitation light in at least one excitation wavelength range, at least one analyte-dependent optical signal in at least one emission wavelength range, the method comprising:

a) transmitting the excitation light from at least one light source through the tissue to the implant;

b) detecting light emitted from the tissue in the emission wavelength range, wherein the light in the emission wavelength range is transmitted through:

i) an array of lenses and an array of apertures arranged to restrict the light emitted from the tissue that travels to at least one detector according to an input angle of the emitted light, the array of lenses disposed in front of at least one detector and parallel to a plane defined by the at least one light source and the at least one detector;

ii) at least one layer of light control film arranged with the lens and aperture arrays to restrict the light emitted from the tissue that travels to the detector according to an incident angle of the emitted light relative to the film; and

iii) at least one filter positioned to restrict transmission of light to the detector to wavelengths substantially within the emission wavelength range.

46. The method of claim 45, further comprising the step of employing at least one processor to receive data representative of the light detected in the emission wavelength range and to determine at least one analyte value in dependence upon the data.

47. The method of claim 45, wherein a surface area of skin through which the excitation light is transmitted is located between substantially surrounding surface areas of skin through which the detected light passes as it travels from the tissue to one or more detectors.

Date Reçue/Date Received 2022-04-07

48. The method of claim 47, wherein the excitation light is transmitted through a central via in an optical reader adapted to be placed on skin.

49. The method of claim 48, wherein the excitation light is further transmitted through at least one light guiding component in the central via arranged to guide the excitation light to the skin.

50. The method of claim 45, wherein the light in the emission wavelength range is transmitted through at least two layers of light control film to restrict the light emitted from the tissue that travels to the lens and aperture arrays according to the incident angle of the emitted light.

51. The method of claim 45, wherein the filter comprises a dichroic filter.

52. The method of claim 45, wherein the implant is embedded in tissue at a depth in the range of 1-4 mm under a surface of skin.

53. A method for monitoring an implant embedded in tissue of a mammalian body, the implant being capable of emitting, in response to excitation light in at least one excitation wavelength range, at least one analyte-dependent optical signal in at least one emission wavelength range, the method comprising:

a) transmitting the excitation light at least one light source through the tissue to the implant;

b) detecting light emitted from the tissue in the emission wavelength range, wherein the detecting step includes:

i) employing an array of apertures arranged with an array of lenses to restrict the light emitted from the tissue that travels to a plurality of detectors according to an input angle of the emitted light, the array of lenses disposed in front of the plurality of detectors and parallel to a plane defined by the at least one light source and the plurality of detectors;

Date Reçue/Date Received 2022-04-07

ii) blocking propagation of incident light rays through the apertures using light blocking elements positioned between the apertures to block the incident light rays in accordance with an increase in incident angle of the light rays with respect to optical axes of the apertures; and

iii) filtering the emitted light to wavelengths substantially within the emission wavelength range.

54. The method of claim 53, further comprising the step of employing at least one processor to receive data representative of the light detected in the emission wavelength range and to determine at least one analyte value in dependence upon the data.

55. The method of claim 53, wherein a surface area of skin through which the excitation light is transmitted is located between substantially surrounding surface areas of skin through which the detected light passes as it travels from the tissue to the plurality of detectors.

56. The method of claim 53, wherein the excitation light is transmitted through a central via in an optical reader adapted to be placed on skin.

57. The method of claim 56, wherein the excitation light is further transmitted through at least one light guiding component in the central via arranged to guide the excitation light to the skin.

58. The method of claim 53, wherein the light in the emission wavelength range is transmitted through at least one layer of light control film to restrict the light emitted from the tissue that travels to the lens and aperture arrays according to an incident angle of the emitted light relative to the film.

Date Reçue/Date Received 2022-04-07

59. The method of claim 53, wherein the light in the emission wavelength range is transmitted through at least two layers of light control film to restrict the light emitted from the tissue that travels to the lens and aperture arrays according to an incident angle of the emitted light relative to the at least two layers of light control film.

60. The method of claim 53, wherein the filter comprises a dichroic filter.

61. The method of claim 53, wherein the implant is embedded in tissue at a depth in the range of 1-4 mm under a surface of skin.

62. The method of claim 53, wherein the light blocking elements comprise resin or metal deposited in cavities of a lens array substrate positioned adjacent the aperture array.

Date Reçue/Date Received 2022-04-07

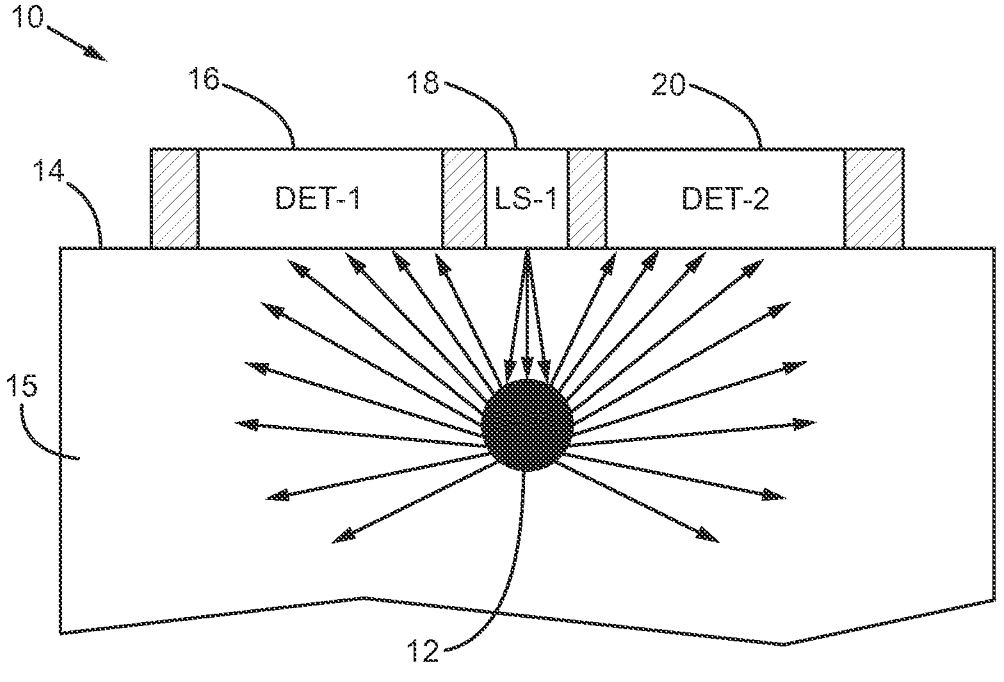


Fig. 1

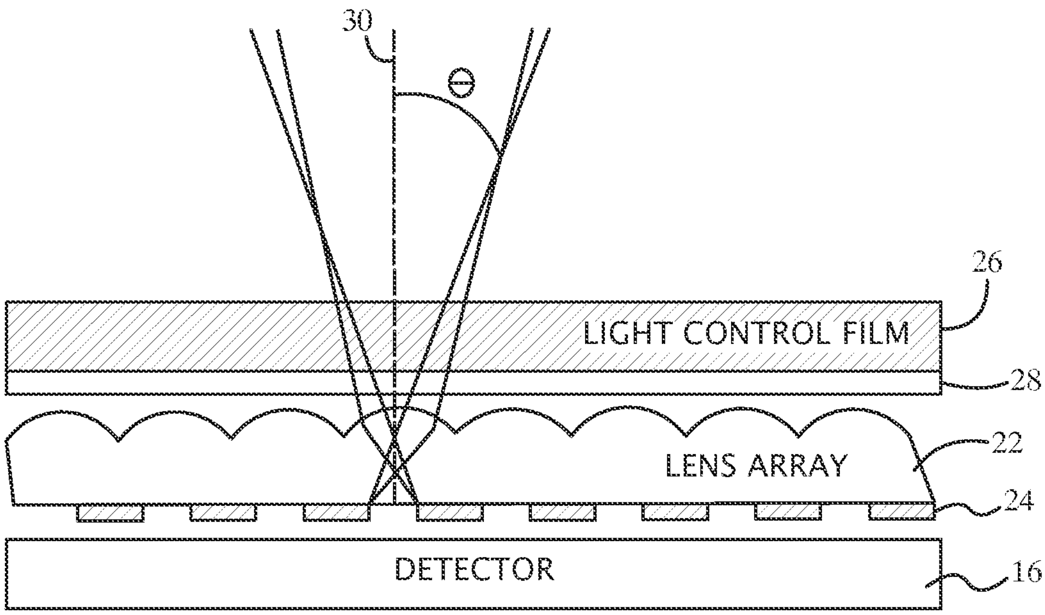


Fig. 2

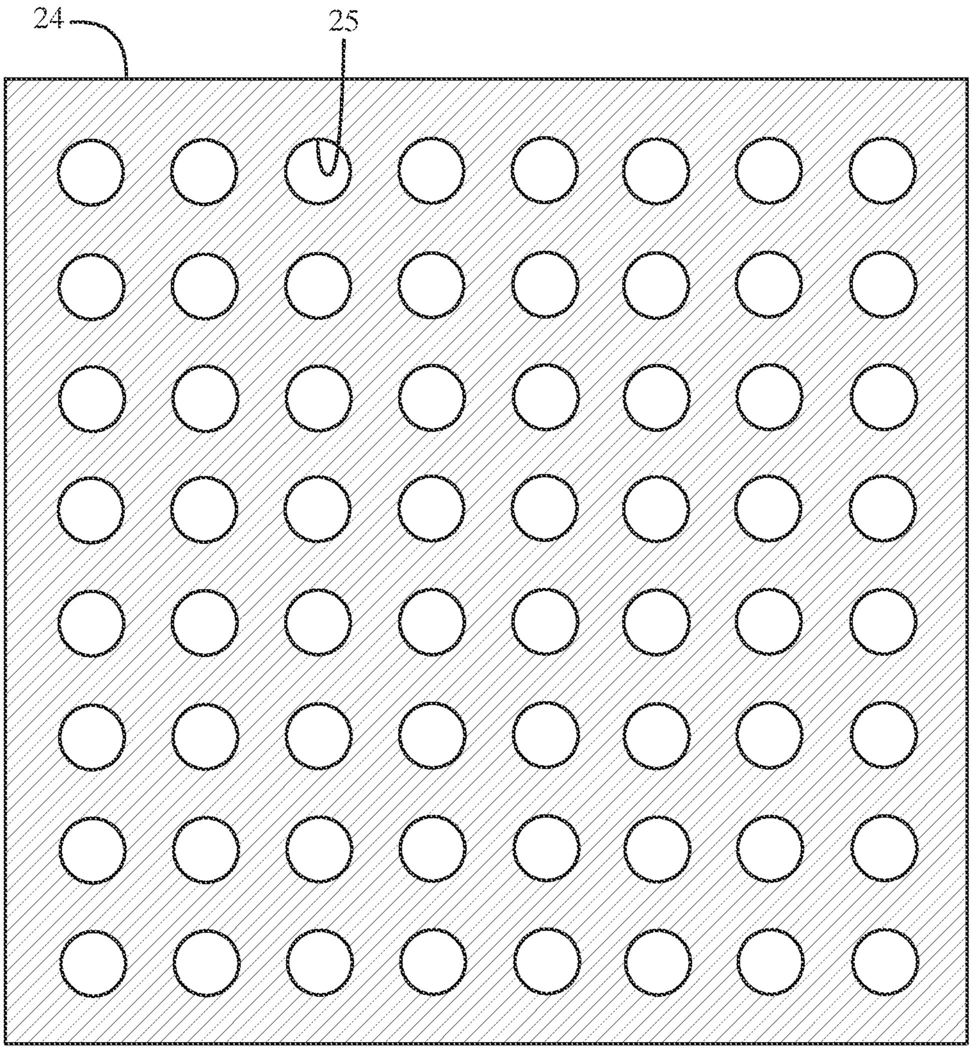


Fig. 3

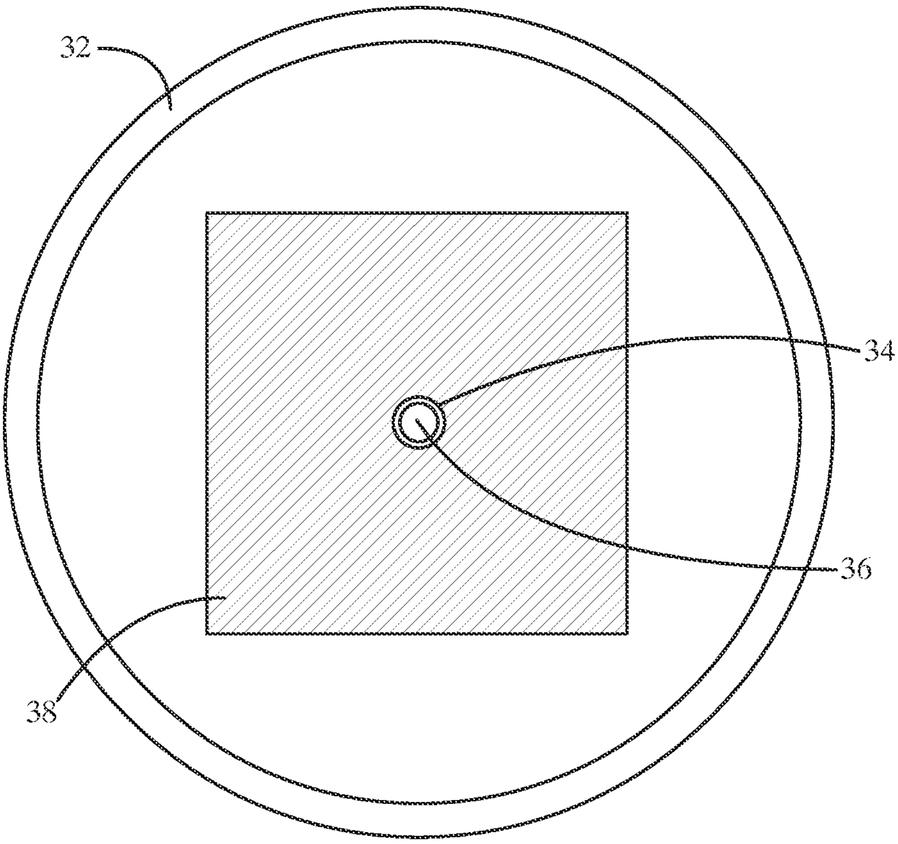


Fig. 4

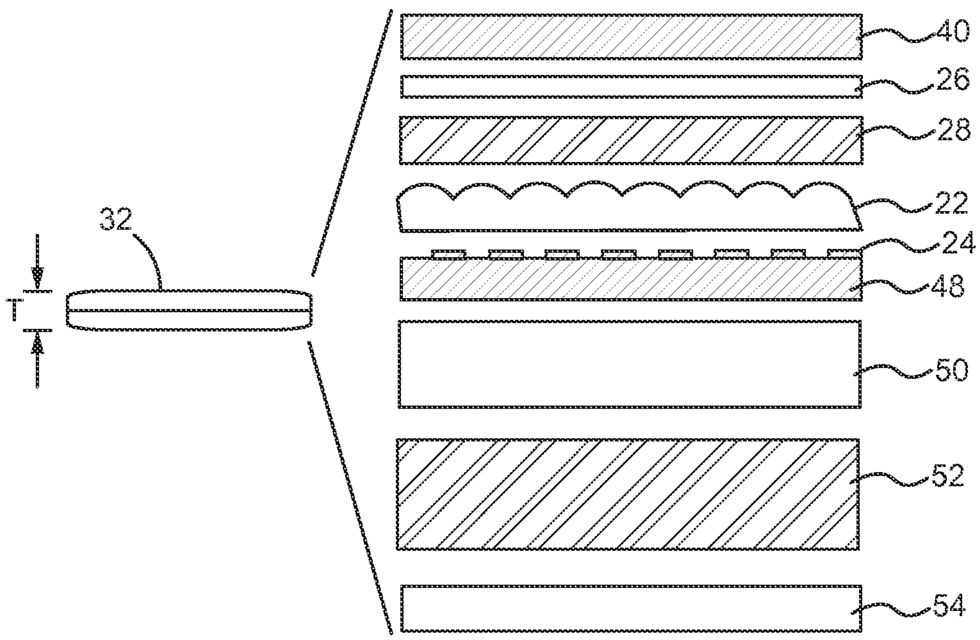


Fig. 5

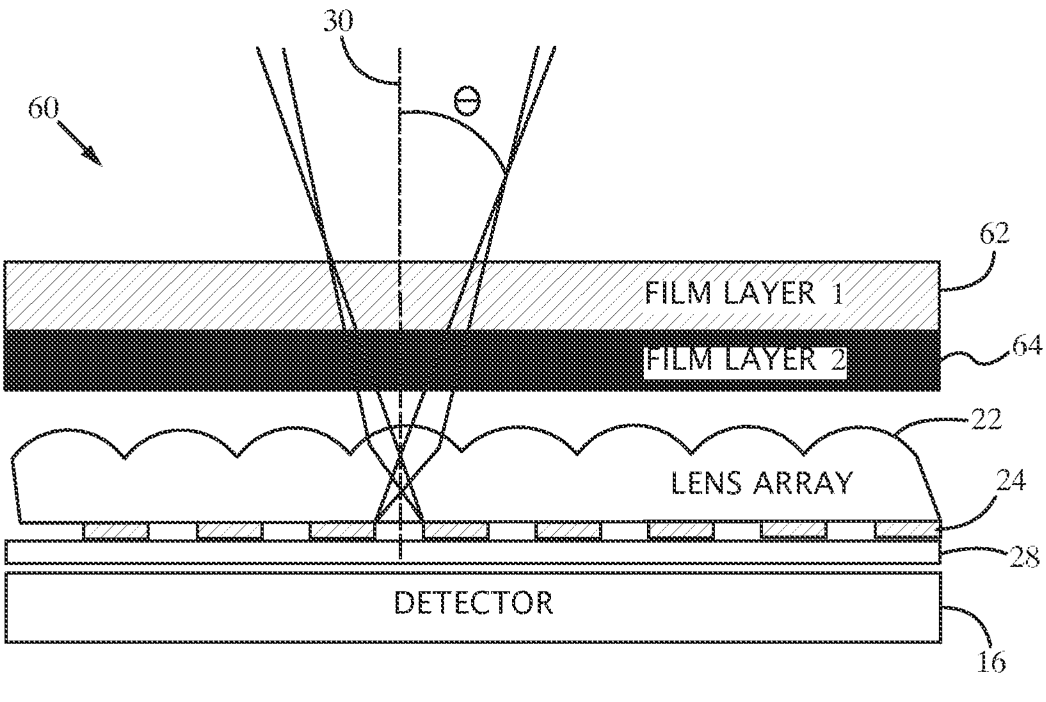

30
Θ
60
62
FILM LAYER 1
64
FILM LAYER 2
22
LENS ARRAY
24
28
DETECTOR
16

Fig. 6

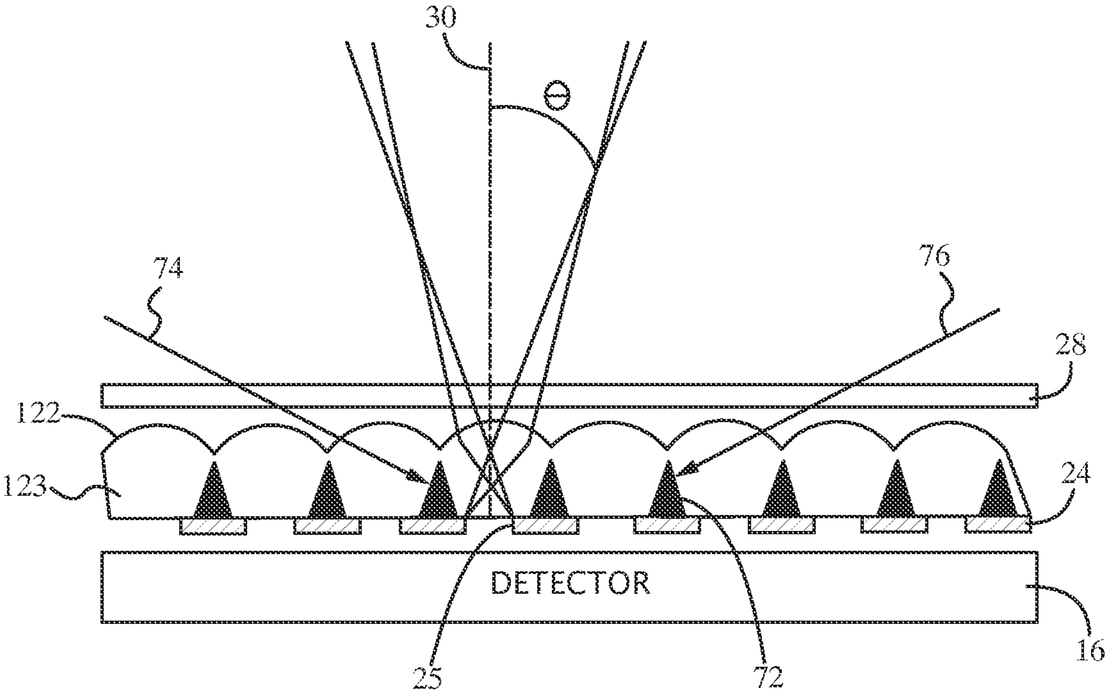


Fig. 7

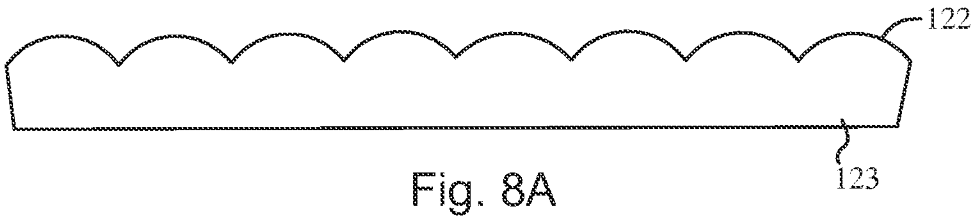


Fig. 8A

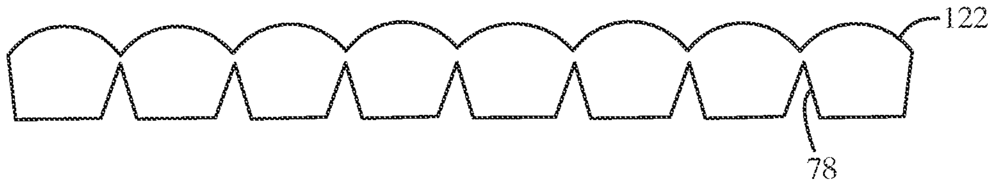


Fig. 8B

Fig. 8C

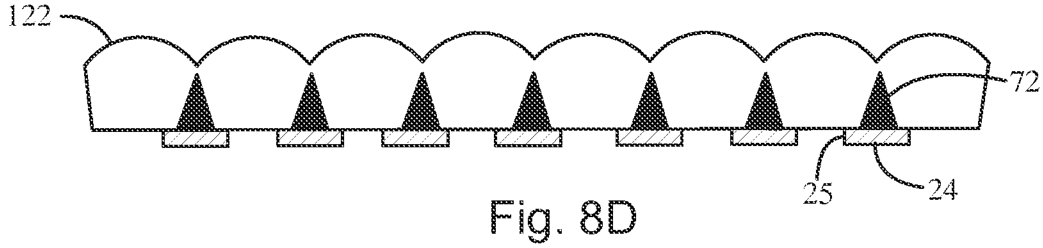


Fig. 8D

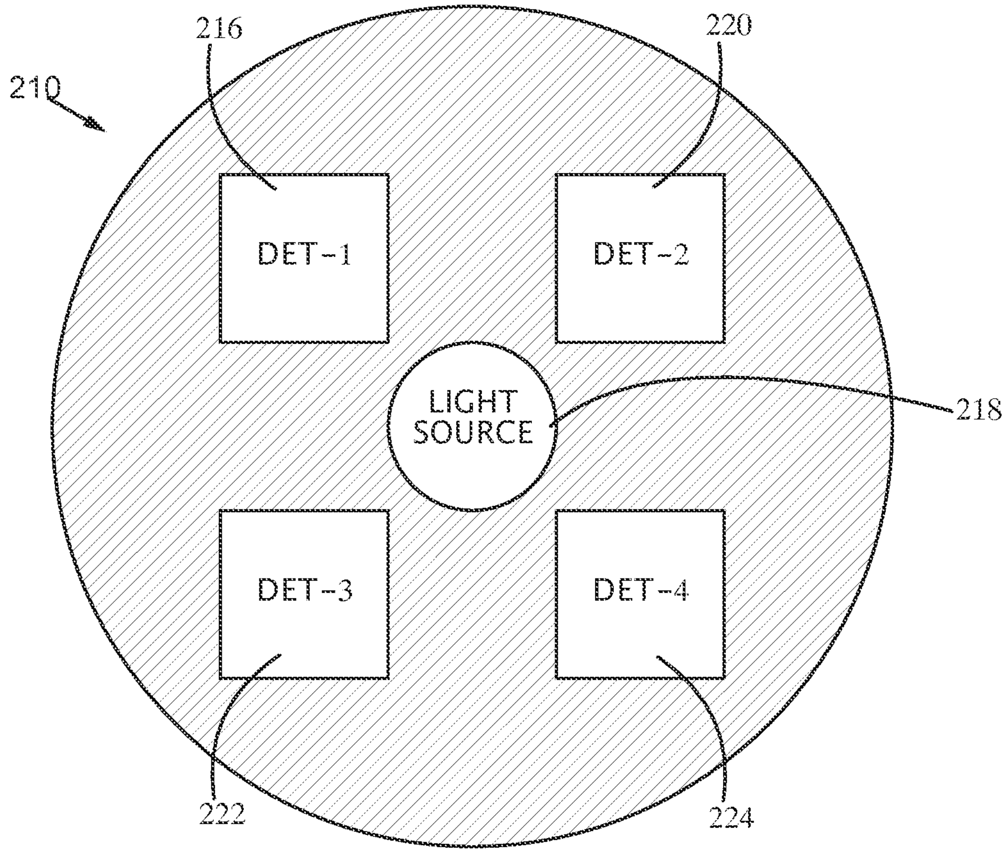


Fig. 9

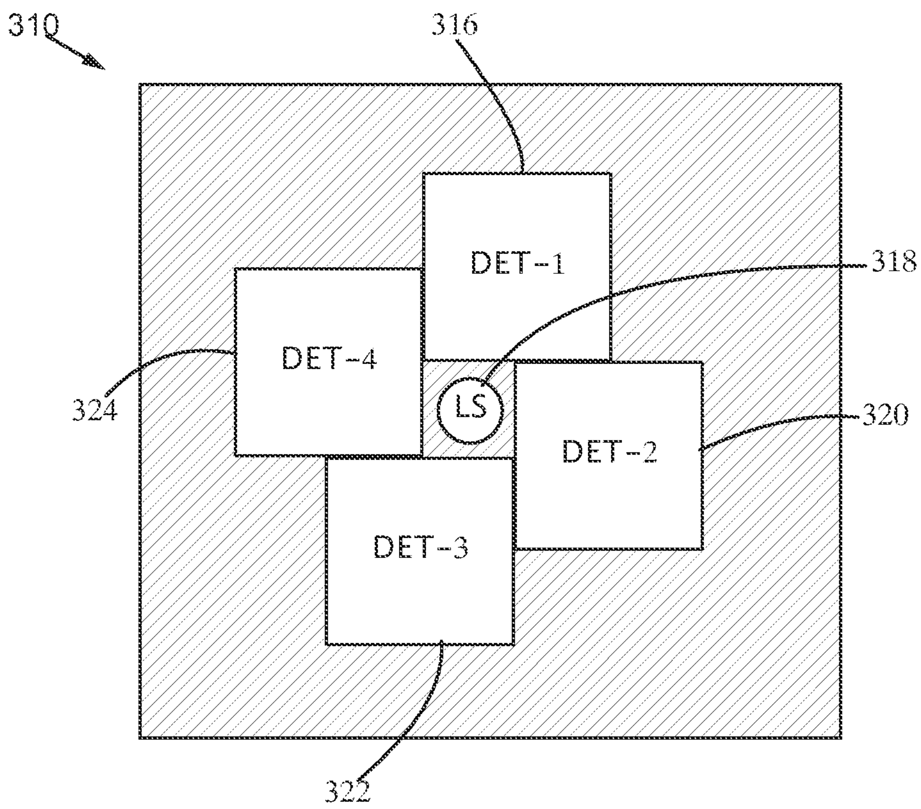


Fig. 10

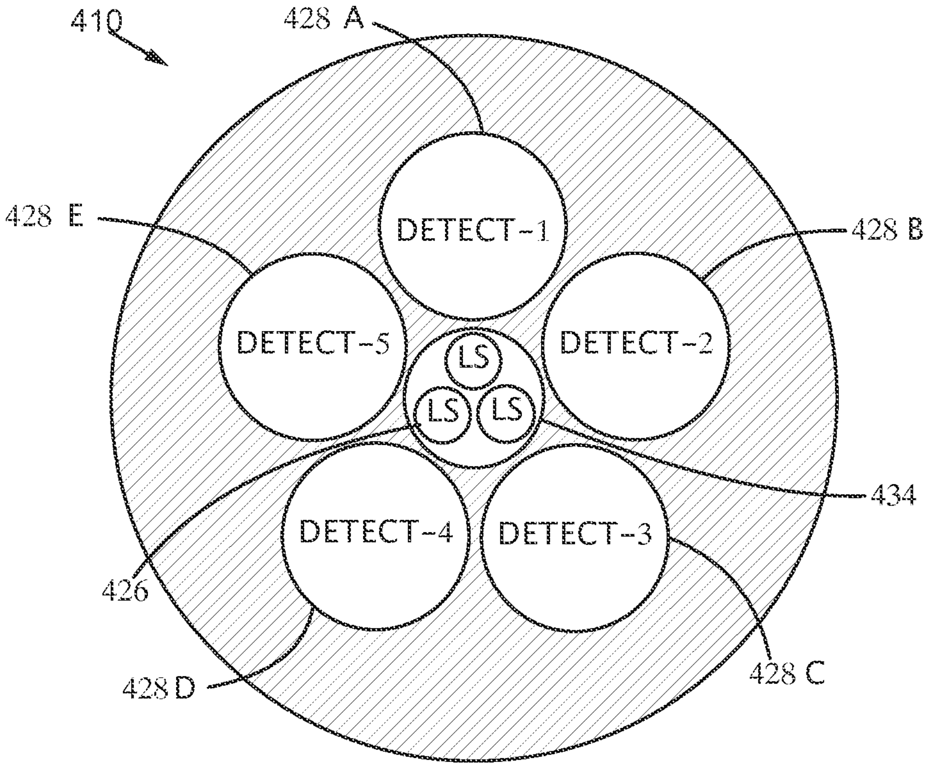
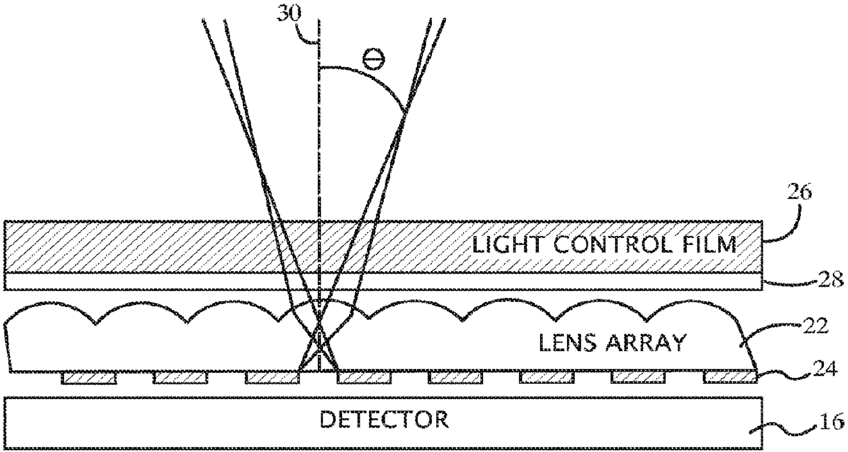

410
428 A
428 E
428 B
DETECT-1
DETECT-5
DETECT-2
LS
LS
LS
434
DETECT-4
DETECT-3
426
428 C
428 D

Fig. 11


30
Θ
26
LIGHT CONTROL FILM
28
22
LENS ARRAY
24
DETECTOR
16