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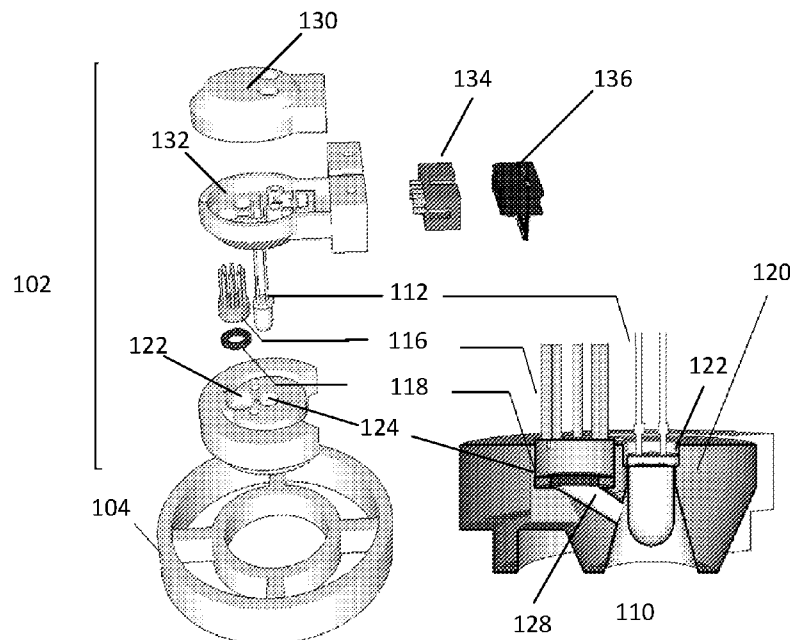


Fig. 1a

Fig. 1b

(57) Abstract: Embodiments generally relate to an electromagnetic radiation module or light source module. The light source module includes at least one light source for illuminating a sample, a photodetector configured to measure a light intensity of the at least one light source and to generate an output signal corresponding to the light intensity measured and a module housing or holder having slots for supporting the at least one light source and the photodetector.



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MULTI-SPECTRAL CALIBRATED LIGHT SYSTEMS

BACKGROUND

[0001] Various optical methods to provide light stimulus of appropriate wavelength have been employed for optical excitation of a sample, including cells. However, these conventional optical methods suffer from various limitations. For example, the conventional optical methods are provided as separate units and are not integrated with optical instruments. Moreover, the light intensities of a light source provided by these optical methods are not calibrated and the light intensities may not be uniform to provide for accurate dose of light for optical stimulation of the sample.

[0002] It is desirable to equip optical instrument or apparatus with standardized, controlled electromagnetic radiation or light source modules with defined, calibrated and uniform light intensities and fluences on a predefined area and level to test reproducibly effect of electromagnetic radiation on a sample for both short and long term studies.

SUMMARY

[0003] Embodiments of the present disclosure generally relate to light source modules with defined, calibrated and uniform light intensities and fluences on a predefined area and level to test reproducibly effect of electromagnetic radiation on a sample for both short and long term studies.

[0004] In one aspect, the present disclosure provides a light source module for use in microscopy or any other kind of monitoring device to test reproducibly effect of light on a live or organic/anorganic sample. The light source module includes a module housing which includes at least first and second slots and at least one light source. The light source is fitted into the first slot and the light source generates light. The light module also includes a light sensor. The light sensor is fitted into the second slot. The first slot is configured to direct light in a first direction to illuminate a test sample and the second slot is configured to be in

communication with the first slot to detect an intensity of the light from the light source. The light sensor facilitates in-situ monitoring and controlling light exposure by the light source.

[0005] In another aspect, the present disclosure provides an optical microplate system. The optical microplate system includes at least one light source module for use in microscopy to test reproducibly effect of light on a sample. The at least one light source module includes a module housing which includes at least first and second slots, at least one light source and a light sensor. The light source is fitted into the first slot and the light source generates light while the light sensor is fitted into the second slot. The first slot is configured to direct light in a first direction to illuminate a test sample and the second slot is configured to be in communication with the first slot to detect an intensity of the light from the light source. The light sensor facilitates in-situ monitoring and controlling light exposure by the light source. The optical microplate system includes a support plate having at least one slot for holding the at least one light source module and a well plate having a plurality of wells for holding test sample. The support plate is aligned to the well plate through a plurality of alignment posts. The optical microplate system also includes a cover disposed over and partially seals the at least one light source module, the support plate and the well plate.

[0006] In a further aspect, the present disclosure provides a method for testing reproducibly effect of light on a sample. The method includes providing a light source module having a module housing which includes at least first and second slots, at least one light source and a light sensor. The light source is fitted into the first slot and the light source generates light while the light sensor is fitted into the second slot. The first slot is configured to direct light in a first direction to illuminate a test sample and the second slot is configured to be in communication with the first slot to detect an intensity of the light from the light source. The light sensor facilitates in-situ monitoring and controlling light exposure by the light source.

[0007] In a further aspect, the present disclosure provides a method for assembling a light source module. The method includes providing a module housing which includes at least first and second slots, at least one light source and a light sensor. The light source is fitted into the first slot and the light source generates light. The light sensor is fitted into the second slot. The first slot is configured to direct light in a first direction to illuminate a test sample and the second slot is configured to be in communication with the first slot to detect an intensity of the light from the light source, the light sensor facilitates in-situ monitoring and controlling light exposure by the light source.

[0008] These and other advantages and features of the embodiments herein disclosed, will become apparent through reference to the following description and the accompanying drawings. Furthermore, it is to be understood that the features of the various embodiments described herein are not mutually exclusive and can exist in various combinations and permutations.

BRIEF DESCRIPTION OF THE DRAWINGS

[0001] The accompanying drawings, which are incorporated in and form part of the specification in which like numerals designate like parts, illustrate preferred embodiments of the present disclosure and, together with the description, serve to explain the principles of various embodiments of the present disclosure.

[0002] Fig. 1a shows a schematic diagram illustrating various components of a light source assembly for a microscope and a microscope adapter;

[0003] Fig. 1b shows a cross-sectional view of an example arrangement of an electromagnetic radiation source, electromagnetic radiation detector and an aperture in a holder of a light source module;

[0004] Fig. 2 shows a screen capture of exemplary LED control software for an optical instrument;

[0005] Figs. 3a-3b show examples of an integration of the light source module to various inverted microscopes;

[0006] Fig. 3c shows an example arrangement of a Metamorph® workstation and the LED control software;

[0007] Fig. 4a shows an embodiment of an optical microplate system and Figs. 4b-4d show various components of the optical microplate system;

[0008] Figs. 5a-5c show various views of a light source module implemented in the optical microplate assembly;

[0009] Fig. 6 shows an example implementation of the light source module for an integrated incubator optical instrument;

[0010] Figs. 7a-7b show various views of an example setup inside a standard incubator;

[0011] Fig. 8 shows a screen capture of exemplary LED control software for an integrated incubator optical instrument; and

[0012] Fig. 9 shows an example of relationship between different wavelengths of light source with depth of skin.

DESCRIPTION

[0009] Embodiments in this disclosure generally relate to calibrated light sources which include light emitting diode (LED) for optical instruments, such as but not limited to microscopes and devices for long term kinetic live cell monitoring in an incubator, including IncuCyte™. Embodiments in this disclosure may also be applied to any suitable high throughput monitoring device, including microfluidic and chip like solutions.

Light source module for microscopes outside incubators

[0010] An embodiment of an electromagnetic radiation or light source module as will be described below is suitable for use in optical stimulation of various cell types or other

biological or non-biological material for, for example and not restricted to calcium imaging, electrophysiology, chemiluminescence, fluorescence or Raman spectroscopy characterization through an inverted microscope over a short duration outside an incubator. The light source module may also be suitable for use in short term studies for material research outside incubators. It is understood that the light source module may be employed for other suitable uses and other suitable types of microscope outside incubators. The light source module is fitted onto existing microscopes without interfering with their original imaging or characterization functions.

[0011] Figs. 1a-1b show an embodiment of a light source module. Fig. 1a shows schematic diagram illustrating the various components of the light source for microscopes which includes a light source assembly 102 and a microscope adapter 104. Fig. 1b shows a cross-sectional view of an example arrangement of an electromagnetic radiation source 112, such as a light emitting diode (LED) or semiconductor laser, electromagnetic radiation detector or sensor 116 such as photodiode, and an aperture 118 in a module housing or holder 120 of a light source module 110.

[0012] For simplicity and for illustration purpose, LED is used as an example light source throughout this disclosure. It is understood that the electromagnetic radiation source or light source, for example, may include any suitable light sources with wavelengths ranging from UV to the near infrared. For example, the electromagnetic radiation source or light source may include laser sources such as small semiconductor lasers with tunable wavelengths. Other suitable light sources with other wavelengths may also be useful.

[0013] Referring to Figs. 1a-1b, the light source assembly includes a cover 130 which protects a wiring housing 132 and a light source module 110. The wiring housing accommodates wiring connectors 134, such as insulation-displacement contact (IDC) connector and wiring cables 136 which provide electrical connection between a control system (not shown)

and the light source module 110. The light source module, for example, includes a module housing or holder 120 having slots 122 and 124 for holding a LED 112 and a detector 116, such as photodiode, which can be clipped into an adapter 104 on a microscope condenser lens (not shown). The photodiode, which is disposed in the same holder as the LED, detects an intensity of the LED and facilitates in-situ monitoring and controlling the exposure of the LED. Although one LED is shown in Figs. 1a-1b, it is understood that there could be one or more LEDs and additional slots provided in the holder for holding the LEDs. The holder 120 may be made of any suitable materials which does not absorb and does not interfere with the light of the LED light source. For illustration purpose, the adapter 104 as shown in Fig. 1a is customized for Nikon Diaphot 300 microscope. It is understood that the adapter, for example, may be customized for different makes or types of microscope.

[0014] From the cross-sectional view of the holder shown in Fig. 1b, it can be seen that the slot 122 is configured for fitting the LED and directing light from the LED in a first direction while the slot 124 is configured for fitting the photodiode and in communication with the slot 122. As shown, the light from the LED 112 is sampled or directly detected by the photodiode 116 through a small channel 128 which is fitted with an aperture 118. The aperture, for example, controls an opening for light to the photodiode. The diameter of the aperture may include any suitable diameter which avoids saturation and ensures that the photodiode is operated in a linear range. The output signal of the photodiode is calibrated to read the light intensity at the focal point at a target sample (not shown), such as a target cell or a target material, disposed in a sample holder of a microscope. From the knowledge of the light intensity at the focal point, the actual light dosage delivered to the target cell can be directly computed.

[0015] Fig. 2 shows a screen capture of a user interface screen 200 of an exemplary LED control software for an optical instrument, such as microscope. As shown in Fig. 2, the LED control software may be generated by, for example, a software application which runs on

a computer device, such as a personal computer, or a mobile application which runs on other suitable mobile or portable devices. The user interface screen 200 may display various user input control elements 210, 220 and 230 which allow a user to perform various operational functions. The user interface screen allows the user to select the correct calibration file for a LED light source. For example, the user interface screen includes a drop down menu 210 which lists all the file locations available in a repository of the computer device. Each light source module has a calibration file, based on the measured power at the focus spot of the target cell or material. This ensures variations due to manufacturing batches and module assembly are accounted for. The user may select the correct calibration file associated with the LED light source from a file location from the drop down menu 210, as shown.

[0016] As shown in Fig. 2, the user interface screen of the LED control software allows the user to set the desired light power. The LED light power is controlled by the duty cycle of light pulses with constant injected current amplitude. When the user enters a set point for the light power in the user editable field 220, the proportional integral derivative (PID) controller automatically adjusts the duty cycle based on the feedback from the photodiode, actively compensating for heat or aging effects or electrical fluctuations in the electric circuit.

[0017] Referring to Fig. 2, the user interface screen also enables synchronization with the microscope imaging camera through a radio button 230. In one implementation, it may be connected to existing microscope image management software, such as but not limited to Metamorph®, via RS232, to allow the LED to be turned off during fluorescence imaging. This is to avoid secondary fluorescence or over-exposing the CCD, especially for wavelengths close to the fluorescence wavelengths.

[0018] Furthermore, the LED control software also allows the user to set operation parameters for pulse frequency and PID controller. The optimized value for the frequency of light pulse is about, for example, 5kHz while the values for P, I and D parameters are about, for

example, 100, 100 and 50 respectively. The P, I and D parameters control the dynamic response of the LED in tracking the set point light intensity values. Depending on the specific application conditions, other optimal values of P, I and D may be chosen to ensure fast and stable LED response.

[0019] Fig. 3a shows an example of an integration 310 of the light source module 110 to Nikon Diaphot 300 Inverted Microscope 315 for opto-electrophysiology cellular measurements, and Fig. 3b shows another example of an integration 330 of the light source 110 module to a Zeiss Inverted Microscope 335 for opto-calcium imaging of cells. The light source module may be integrated or used in any suitable types of inverted microscope and for any suitable uses. The LED light source has an ON and OFF switching latency of less than, for example, 10 ms. The switching control, for example, may be integrated into an existing MetaMorph® Microscopy Automation and Image Analysis Software to synchronize fluorescence image capture without interference from LED light. For illustration purpose, Fig. 3c shows a MetaMorph® workstation 340 having the MetaMorph® Microscopy Automation and Image Analysis Software which runs on a computer device on the left and a workstation 350 having the LED control software 200 which runs on another computer device on the right. It is understood that the LED control software may be integrated into any other suitable image analysis software.

Light source module for microscopes inside incubators

[0020] Another embodiment of a light source module 410 which is suitable for use with integrated incubator optical (or non-optical) instrument or apparatus for long term cell or material monitoring will be described below. The light source module 410 as will be described below is suitable for use in long term studies (e.g., days to weeks) on behavior of living cells or for material research after exposure to well defined, calibrated and uniform light intensities and

fluences on a predefined area and level with multi-well plates inside an incubator. It is understood that the light source module may be employed for other suitable uses and other suitable types of optical or non-optical devices for long term follow up of reaction of cells or organic/anorganic matter to various light qualities and quantities (optics, spectroscopy, impedance, etc.) under defined temperature and gas conditions (e.g., cell culture incubator).

[0021] Fig. 4a shows an embodiment of an optical microplate system 400 illustrating the arrangement of a support plate or light plate 405 and a plurality of light source modules 410 being assembled together with a well plate 440. The optical microplate system, as shown, includes a transparent cover 430 which reduces evaporation and does not fully seal the optical microplate system. Fig. 4b shows a closer view of one of the plurality of light source modules 410 disposed on the light plate 405 shown in Fig. 4a. Fig. 4c shows an example light plate 405 with a plurality of slots 445 for holding the plurality of light source modules and Fig. 4d shows the assembled light plate 405 with light source modules 410.

[0022] In one example, the optical microplate system 400 is designed to work with a standard 96-well plates which are divided into 8 rows of 12 wells. For illustration purpose, 6 wells 448 are used as shown in Fig. 4a. The other wells are left empty to provide isolation and prevent cross-contamination of light across the wells. As shown, 6 light source modules 410 are mounted onto a light plate 405 which is placed above a well plate 440. The light plate is self-aligned to the well plate through the use of alignment posts and spacers 407. The light plate 405 includes at least one hollow channel 447 which is aligned with a vertical hollow channel 426 of the holder 420 of the light source module and one of the wells 448 of the well plate. The optical microplate system is flexible and may be designed to work with other suitable well plates with suitable number of wells. It is understood that other suitable number of wells and other suitable numbers of light source modules may be employed as long as sufficient isolation is provided to avoid cross-contamination of light across the wells. The plurality of

light source modules which are mounted onto a light plate which is placed above a well plate may operate in the same or different wavelengths.

[0023] Fig. 5a shows a detailed schematic view of one of the plurality of light source modules 410 implemented in the optical microplate assembly 400 shown in Fig. 4a. The light source module 410, as shown in Fig. 5a, includes a module housing or holder 420 with slots 422 and 424 for holding at least one light source 412 and a photodiode 416 and includes a main channel or vertical hollow channel 426 for microscopy imaging. As shown, the holder includes a plurality of slots 422 configured to fitting a plurality of LEDs and directing light from the LEDs in a first direction while the slot 424 is configured for fitting the photodiode 416 and in communication with the slots 422. The light source module 410 further includes a plurality of light sources 412, such as but not limited to LEDs, inclined at an angle and a photodiode 416 with aperture 418. The aperture, for example, controls an opening for light to the photodiode. Fig. 5b shows cross-sectional view taken at A-A' of the light source module 410 shown in Fig. 5c. Fig. 5c illustrates the relative positions of the LEDs 412 and the vertical hollow channel 426. The vertical channel walls, in one embodiment, are tapered at an angle to allow reflection of LED light to fall directly onto the bottom of the well plate 440. The vertical hollow channel 426, for example, should have suitable diameter and size which corresponds to the diameter or size of the underlying well 448 in the well plate 440.

[0024] Each light module 410 assembles together a plurality of LEDs 412 and a photodiode 416 as shown in Fig. 5a. The photodiode, which is disposed in the same holder as the LEDs, detects total intensities of the LEDs and facilitates in-situ monitoring and controlling the exposure of the LEDs. For illustration purpose, 4 LEDs 412 and a photodiode 416 are included in a light source module 410 as shown in Fig. 5a. It is understood that the light source module may include any suitable number of LEDs. An aperture 418 is used to restrict the amount of light reaching the photodiode to avoid saturation and ensure linear operation.

[0025] The light source module is designed and is configured to maintain a vertical light path for microscope imaging. For instance, the area above the holder is kept clear of obstruction of the microscope light path as shown in Figs. 5a-5b. The light source module is configured to deliver a uniform illumination over a defined area and distance from light source. The surface of the LED encapsulation, for example, is roughened to diffuse the light. Uniform distribution of the light on a predefined area and level is further achieved by distributing the LEDs equally around the target well, and using the slightly tapered walls of the vertical hollow channel or vertical light bore along the center of the holder to reflect light from the LED onto the bottom of the target well. The light source module is configured to deliver controlled and calibrated dose of light. For example, the plurality of LEDs are used to deliver the necessary intensity of light. Additional LEDs can be used if necessary to increase the light intensity. The light power at the bottom of the well or an other defined distance from light source is measured with a calibrated light power meter and the reading related directly to the photodiode signal. Each light module has a calibration file to account for differences in manufacturing batches and differences in cell assembly.

[0026] The plurality of LEDs 412 in each light source module 410 are connected in series and driven by the same current. The mode of operation is similar to the microscope system. The photodiode 416 samples the intensity provided by the plurality of LEDs 412 and the PID controller adjusts the duty cycle of the light pulses to maintain the desired set point. Fig. 6 shows an example of the implementation 600 of the optical microplate system 400 with an integrated incubator optical instrument 610, such as IncuCyte™ FLR which is an integrated microscope for standard incubators while Figs. 7a-7b show the corresponding arrangement inside the incubator.

[0027] Fig. 6 shows an example implementation 600 of the light source module 410 for an integrated incubator optical instrument 610, such as IncuCyte™ FLR which is a commercial

system for long-term, kinetic live-cell imaging. As shown, the top cover of the IncuCyte™ FLR is opened, showing 3 well plates with light plates above them. The intensity of the LEDs can be varied using the computer device 640 on the left while the scheduling of microscope imaging can be done using the computer device 650 on the right. Figs. 7a-7b show views of an example setup inside a standard incubator 610. The controller 670 for IncuCyte™ FLR and the power supply for the LED control system, as shown, are located on top of the incubator. It is understood that the light source module 410 may be implemented with other suitable types of integrated incubator optical instrument and the arrangement of the controller and the power supply for the LED control system may be suitably arranged as desired.

[0028] Fig. 8 shows a screen capture of a user interface screen 800 of an exemplary LED control software for an integrated incubator optical instrument 610, such as the IncuCyte™ FLR. As shown in Fig. 8, the LED control software may be generated by, for example, a software application which runs on a computer device, such as a personal computer, or a mobile application which runs on other suitable mobile or portable devices. The LED control software, as shown, provides operation control of the light source modules 410. The user interface screen 800 may display various user input control elements which allow a user to perform various operational functions. For example, the user interface screen includes a drop down menu 810 which lists all the file locations available in a repository of the computer device. The user interface screen 800 allows a user to select the correct calibration file for light source module 410. Each light source module has a calibration file, based on the measured power at the bottom of the well plate. This ensures variations due to manufacturing batches and module assembly are accounted for. The user may select the correct calibration file associated with the LED light source from a file location from the drop down menu 810, as shown.

[0029] As shown in Fig. 8, the user interface screen of the LED control software allows the user to set the desired light power. The LED light power is controlled by the duty cycle of light pulses with a constant injected current. When the user enters a set point for the light power, the PID controller automatically adjusts the duty cycle based on the feedback from the photodiode, actively compensating for heat or aging effects or electrical fluctuations in the electric circuit. The system, for example, allows configuration of up to 18 independent channels, and can be upgraded for 36 channels. The functions of selecting the correct calibration file for light source module 410 and setting the desired light power are similar to that of the microscope system.

[0030] The LED control software as shown in Fig. 8 also enables scheduling to match the microscope imaging camera. In one example implementation, a scheduler controls the ON/OFF functionality of the light source module during fluorescence imaging. This is needed to avoid secondary fluorescence or over-exposing the CCD, especially for wavelengths close to the fluorescence wavelengths.

[0031] Furthermore, the LED control software also allows the user to set operation parameters for PID controller and pulse frequency. The default values for P, I and D parameters are, for example, 50, 50 and 20 respectively and the frequency of the light pulse is, for example, 5kHz. Depending on the specific application conditions, other optimal values of P, I and D may be chosen to ensure fast and stable LED response.

[0032] In one embodiment, the plurality of LEDs in each light source module are operated in the same wavelength. In another embodiment, the LEDs in each light source module may operate in different wavelengths. For example, the slots 422 in the holder 420 may be segmented into at least first and second groups. The first group, for example, may be configured to hold at least one LED of a first light wavelength and the second group is configured to hold at least one LED of a second light wavelength, different than the first light

wavelength. Furthermore, at least one LED of the first group is configured to be activated at a different time than at least one other LED of the second group for testing effects of the first light wavelength and second light wavelength on the test sample. In such case, each of the LEDs in the light source module may be controlled and excited independently as desired in order to provide accurate spectral dose delivery.

Light sources

[0033] As described, for illustration purpose, LED is used as an example light source throughout this disclosure. It is understood that other suitable types of light source with suitable wavelengths may also be useful. The LEDs that are used in a light source module for use with an optical instrument, such as microscope and IncuCyte™ systems, are similar to provide consistency of light sources for short and long term studies. The wavelengths of LEDs, for example, cover the entire UV, visible and infrared spectrum at 20-40 nm intervals, which is comparable to the FWHMs of the individual LED emissions. The chosen wavelengths and their respective specifications are tabulated in Table 1 below as examples, but is not restricted to these chosen wavelengths.

Table 1

Color	Wavelength λ (FWHM) [nm]	Typical Operating Parameters				Example of Supplier Part Number
		Voltage V_F [V]	Current I_F [mA]	Luminous Int. (Abs. Irradiance) [mcd (μ W)]	Viewing angle [deg]	
UV-B	310 (10)	5.5	30	(500 μ W)	10	SETI UVTOP310T018BL
UV-A	355 (15)	4.5	30	(800 μ W)	10	SETI UVTOP310T018BL
UV-A	380 (12)	3.5	30	(30 mW) ^a	15	Super Bright LEDs Inc. RL5-UV0315-380
UV-A	400 (12)	3.5	30	1,000	15	Super Bright LEDs Inc. RL5-UV430-400

Blue	470 (26)	3.5	20	5,500 ^a	15	Super Bright LEDs Inc. RL5-B5515
Aqua	505 (30)	3.6	20	9,000 ^a (5591)	18	Super Bright LEDs Inc. RL5-A9018
Green	525 (30)	3.5	30	13,000 ^a	8	Super Bright LEDs Inc. RL5-G13008
Yellow	588 (n.a.)	2.2	50	10,000	8	Super Bright LEDs Inc. RL5-Y10008
Orange	605 (n.a.)	2.2	20	5,000 ^a	15	Super Bright LEDs Inc. RL5-05015
Red	627 (n.a.)	2.3	50	12,000 ^a	8	Super Bright LEDs Inc. RL5-R12008
Red	660 (n.a.)	1.9	30	2,400 ^a	15	Super Bright LEDs Inc. RL5-2415
Red	680 (30)	1.7	350	(60 mW) ^b	75	Roithner Laser Technik APG2C1-680

^a Test conditions $I_F = 20$ mA

^b Test conditions $I_F = 350$ mA

The values in Table 1 are exemplary. Other suitable values may also be useful. Together with the holder design, the choice of wavelength, power and viewing angle can be tailored to suit specific application needs.

[0034] The LEDs for both embodiments of light source modules as described above are excited by a train of high-frequency pulses of current. A consistent spectral light output intensity is maintained by varying the duty cycle of the current pulses at a constant voltage. The frequency of the pulses can be tuned for various applications (continuous or sequenced). The light output is monitored by a photodetector in real-time that allows feedback to achieve defined, calibrated and uniform light fluence and intensity. A microprocessor averages the detected light pulses and provides a feedback signal to a closed PID loop to control the light intensity. For example, the LEDs are controlled by a pulse-width modulated (PWM) electrical signal and the feedback circuit is configured to vary a duty cycle of the PWM electrical signal to adjust the intensity of the LEDs.

[0035] The embodiments as described above result in advantages. The light source modules as described in this disclosure are unique and cover an unmet need in photobiology and photomedicine to have very standardized devices with features described in paragraphs [0036] and [0037] below.

[0036] For example, light source modules 110 and 410 that have very defined light spectral distribution and fluence/intensity for short and long-term comparison studies are provided. The light source module, for example, may be designed to work with standard or any suitable well-plates and inverted microscopes that are widely used in cell studies. The light source module can deliver accurately calibrated dose of light to the target wells and actively compensate for LED aging effects using a photodiode within the light assembly and directly measures the intensity of high frequency light pulses and computes the average light intensity over a time duration. This approach is accurate, especially when the light source is to be operated over a wide range of frequencies.

[0037] In addition, choice of LED as light source provides various advantages. For example, LED has a very compact and robust packaging, which is crucial for small spaces inside the incubator-microscope. The compact packaging is advantageous for wavelengths with weak emission where multiple LEDs can be employed to increase the intensity. Moreover, the wavelengths of light emitted from LEDs are monochromatic with a typical FWHM of, for example, 10-30 nm and spans across the entire UV to infrared spectrum. The narrow band emission eliminates the need for monochromators or filters. LEDs are more efficient compared to other lamp sources and emit less heat. This is crucial for an incubator where temperature needs to be kept constantly at 37°C. LEDs generally have long life expectancy, typically in the range of 10,000 to 50,000 hours, exceeding that of other lamp sources which are usually about 5,000 hours. This minimizes lamp replacement and recalibration routines. Furthermore, LEDs offer consistent color with age. For instance, LEDs

maintain their color and intensity well with age. A slight change can arise due to aging of the resin of the LED. In comparison, traditional lamp sources red-shift with age. Additionally, LEDs support for pulsed operation. The shift in the dominant emission wavelength of a LED shifts less under pulsed operation (1-2 nm) than continuous operation (5-15 nm). By using pulse-width-modulation to control the intensity while maintaining a constant injection current, a higher intensity and a highly reproducible emission spectrum can be maintained over a long duration of time. In comparison to traditional lamps which can only operate in continuous operation mode, intensity can only be varied by changing the injected current which affects its spectral distribution.

[0038] The light source modules as described above may be implemented with any suitable optical or non-optical instrument or apparatus to test reproducibly effect of electromagnetic radiation on a sample for both short and long term studies. The light source modules as described can be used with, for example, any suitable well plates and inverted microscopes, to provide accurately calibrated dose of light to various test samples. In one example, the light source module may be implemented in an optical instrument to test reproducibly effect of different light qualities on skin which could be useful in photodynamic therapy in cosmetics and skin disorders. An example of relationship between different wavelengths of light source with depth of skin is shown in Fig. 9. The embodiments thus provide in-vitro light sources with complete range of wavelengths (e.g., UV-visible-infrared) for short term and long term exposure and enable standardized tests for basic and cosmetic research. In addition, the embodiments can also be applied in various suitable fields of technology where the effect of light intensity, exposure time and mode, and wavelength dependence on the material properties are to be studied.

[0039] The inventive concept of the present disclosure may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The

foregoing embodiments, therefore, are to be considered in all respects illustrative rather than limiting the invention described herein. Scope of the invention is thus indicated by the appended claims, rather than by the foregoing description, and all changes that come within the meaning and range of equivalency of the claims are intended to be embraced therein.

[0040] What is claimed is:

CLAIMS

1. A light source module for use in microscopy or any other kind of monitoring device to test reproducibly effect of light on a live or organic/anorganic sample comprising:
 - a module housing which comprises at least first and second slots;
 - at least one light source, wherein the light source is fitted into the first slot, the light source generates light;
 - a light sensor, wherein the light sensor is fitted into the second slot, wherein
 - the first slot is configured to direct light in a first direction to illuminate a test sample, and
 - the second slot is configured to be in communication with the first slot to detect an intensity of the light from the light source, the light sensor facilitates in-situ monitoring and controlling light exposure by the light source.
2. The light source module of claim 1 wherein the at least one light source comprises a light emitting diode (LED) or semiconductor laser.
3. The light source module of claim 1 comprising an aperture fitted to the light sensor, the aperture controlling an opening for light to the light sensor.
4. The light source module of claim 1 comprising:
 - a plurality of first slots configured for fitting a plurality of light sources and directing light from the light sources in the first direction; and
 - wherein the second slot is configured to be in communication with the first slots.
5. The light source module of claim 4 wherein:

the plurality of first slots are fitted with light sources; and
the light sensor detects the sum of light intensity from the light sources.

6. The light source module of claim 4 wherein the light sources generate light in a first light wavelength.
7. The light source module of claim 4 wherein the first slots are segmented into at least first and second groups, wherein the first group is configured to hold at least one first light source of a first light wavelength and the second group is configured to hold at least one second light source of a second light wavelength.
8. The light source module of claim 7 wherein the at least one first light source is configured to be activated at a different time than the at least one second light source for testing effects of the first light wavelength and second light wavelength on the test sample.
9. The light source module of any of claims 1-7 further comprises an adapter for mounting onto an inverted type microscope.
10. The light source module of claim 9 wherein the adapter fits the light source module onto a condenser of the inverted type microscope.
11. The light source module of any of claims 1-7 wherein the module housing comprises a main channel through a body of the housing, wherein the main channel provides a line of sight between external imaging light sources and optics and the test sample.

12. The light source module of claim 11 wherein:
the one or plurality of first slots are configured at an angle vis-à-vis the main channel for directing light from the one or plurality of light sources in the first direction.
13. The light source module of claim 11 wherein the main channel is a hollow channel and comprises tapered sidewalls.
14. The light source module of claim 11 comprising an adapter for mounting onto a well plate holding the test sample.
15. The light source module of any of claims 1-7 comprising a feedback circuit configured to adjust the light intensity of the at least one or plurality of light sources based on output signal of the light sensor.
16. The light source module of claim 15 wherein the at least one or plurality of light sources are controlled by a pulse-width modulated electrical signal, and wherein the feedback circuit is configured to vary a duty cycle of the PWM electrical signal to adjust the light intensity of the at least one or plurality of light sources.
17. The light source module of any of claims 1-16 wherein the at least one light source comprises a wavelength in a region of a light spectrum ranging from UV to near infrared.
18. An optical microplate system comprising:
at least one light source module for use in microscopy to test reproducibly effect of light on a sample comprising

a module housing which comprises at least first and second slots,
at least one light source, wherein the light source is fitted into the first slot, the light source generates light,
a light sensor, wherein the light sensor is fitted into the second slot, wherein the first slot is configured to direct light in a first direction to illuminate a test sample, and
the second slot is configured to be in communication with the first slot to detect an intensity of the light from the light source, the light sensor facilitates in-situ monitoring and controlling light exposure by the light source;
a support plate having at least one slot for holding the at least one light source module;
a well plate having a plurality of wells for holding test sample, wherein the support plate is aligned to the well plate through a plurality of alignment posts; and
a cover disposed over and partially seals the at least one light source module, the support plate and the well plate.

19. The optical microplate system of claim 18 wherein the at least light source module comprises a feedback circuit configured to adjust light intensity of the at least one light source based on output signal of the light sensor.

20. The optical microplate system of claim 19 wherein the module housing comprises a main channel through a body of the housing, wherein the main channel provides a line of sight between microscope objectives and the test sample.

21. The optical microplate system of claim 20 wherein the support plate comprises at least one hollow channel which is aligned with the main channel of the module housing and one of the wells of the well plate.
22. A method for testing reproducibly effect of light on a sample comprising:
providing a light source module comprising
a module housing which comprises at least first and second slots,
at least one light source, wherein the light source is fitted into the first slot,
the light source generates light,
a light sensor, wherein the light sensor is fitted into the second slot, wherein
the first slot is configured to direct light in a first direction to illuminate a test sample, and
the second slot is configured to be in communication with the first slot to detect an intensity of the light from the light source, the light sensor facilitates in-situ monitoring and controlling light exposure by the light source.
23. The method of claim 22 comprising attaching the light source module to an optical instrument outside of an incubator.
24. The method of claim 22 comprising attaching the light source module to an incubator optical instrument.
25. A method for assembling a light source module comprising:
providing a module housing which comprises at least first and second slots;

providing at least one light source, wherein the light source is fitted into the first slot, the light source generates light; and

providing a light sensor, wherein the light sensor is fitted into the second slot, wherein

the first slot is configured to direct light in a first direction to illuminate a test sample, and

the second slot is configured to be in communication with the first slot to detect an intensity of the light from the light source, the light sensor facilitates in-situ monitoring and controlling light exposure by the light source.

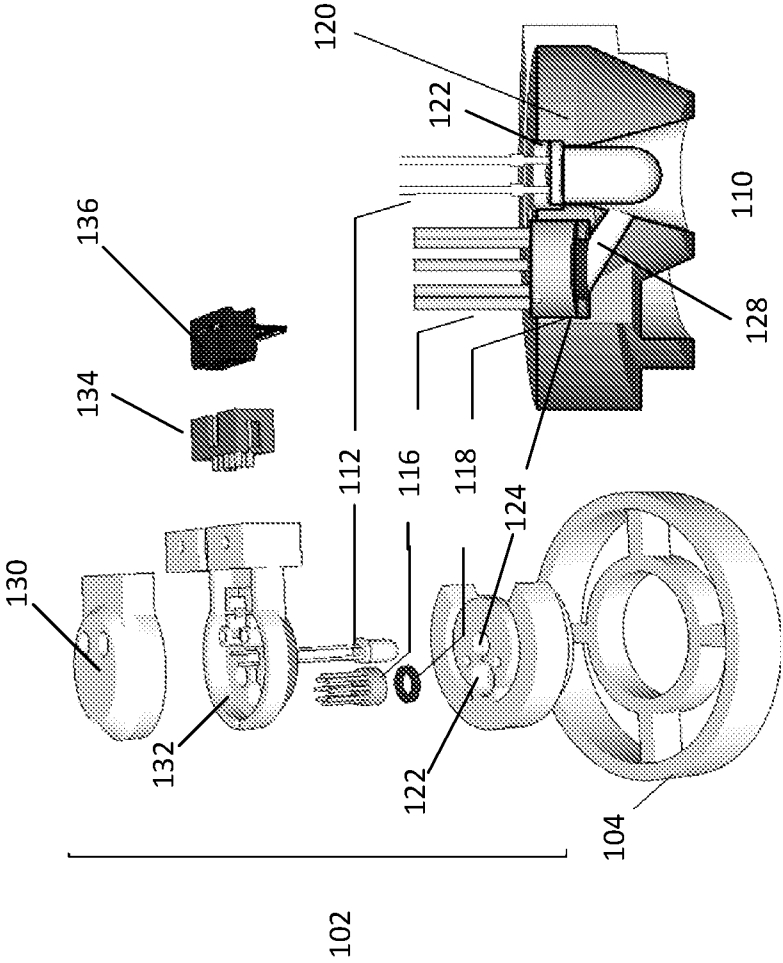
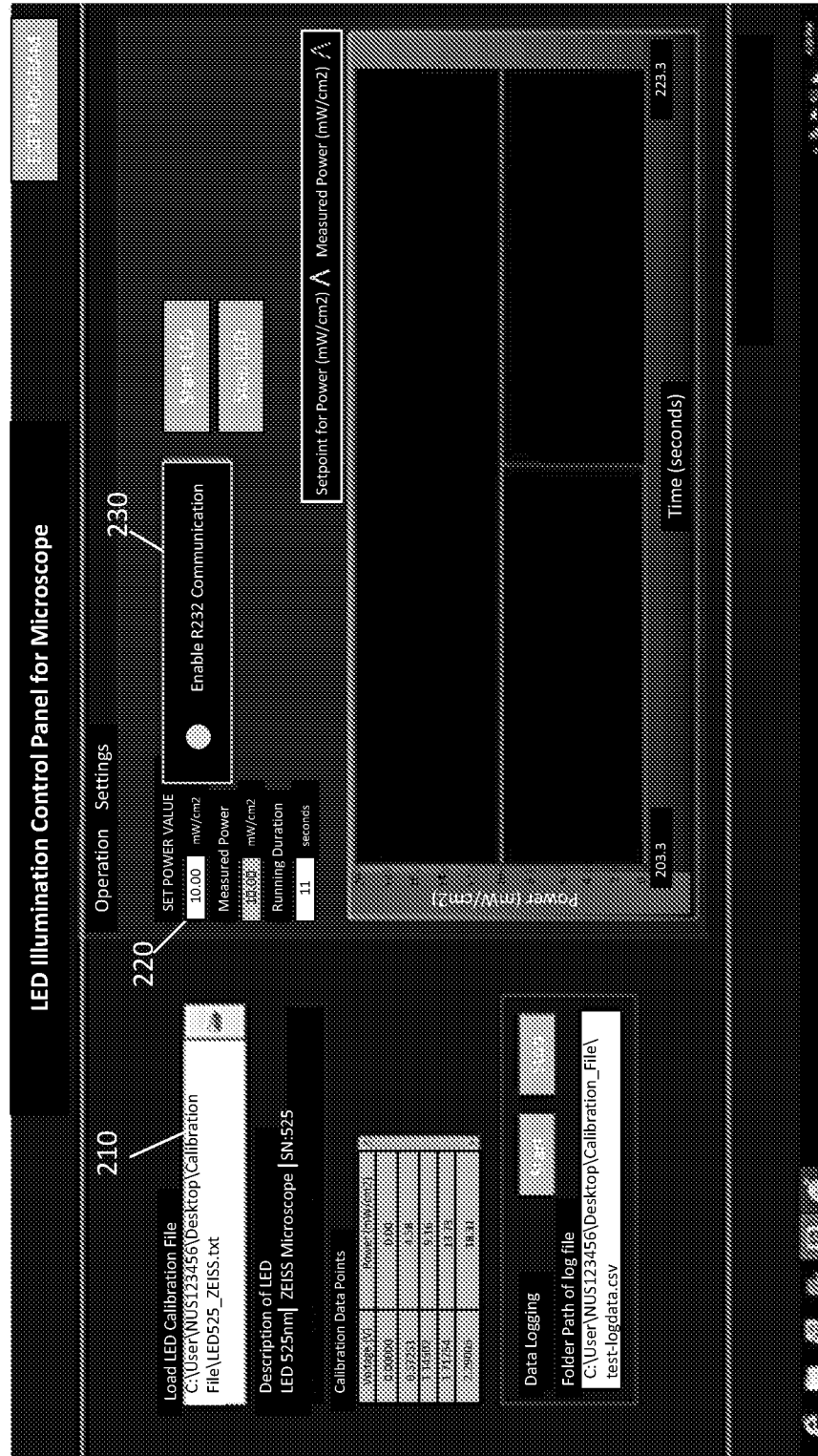


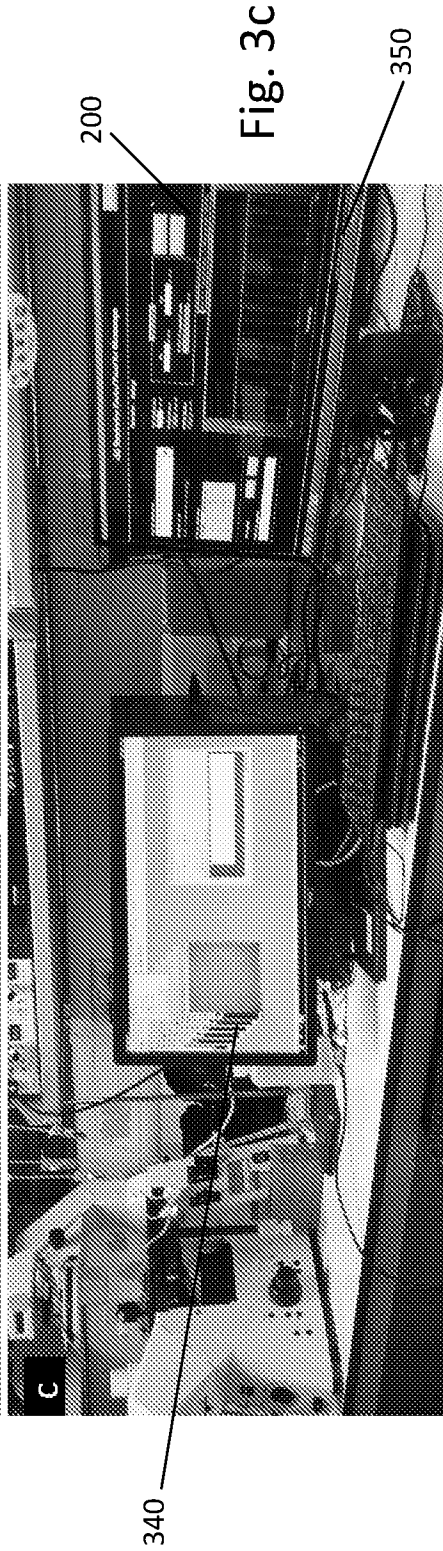
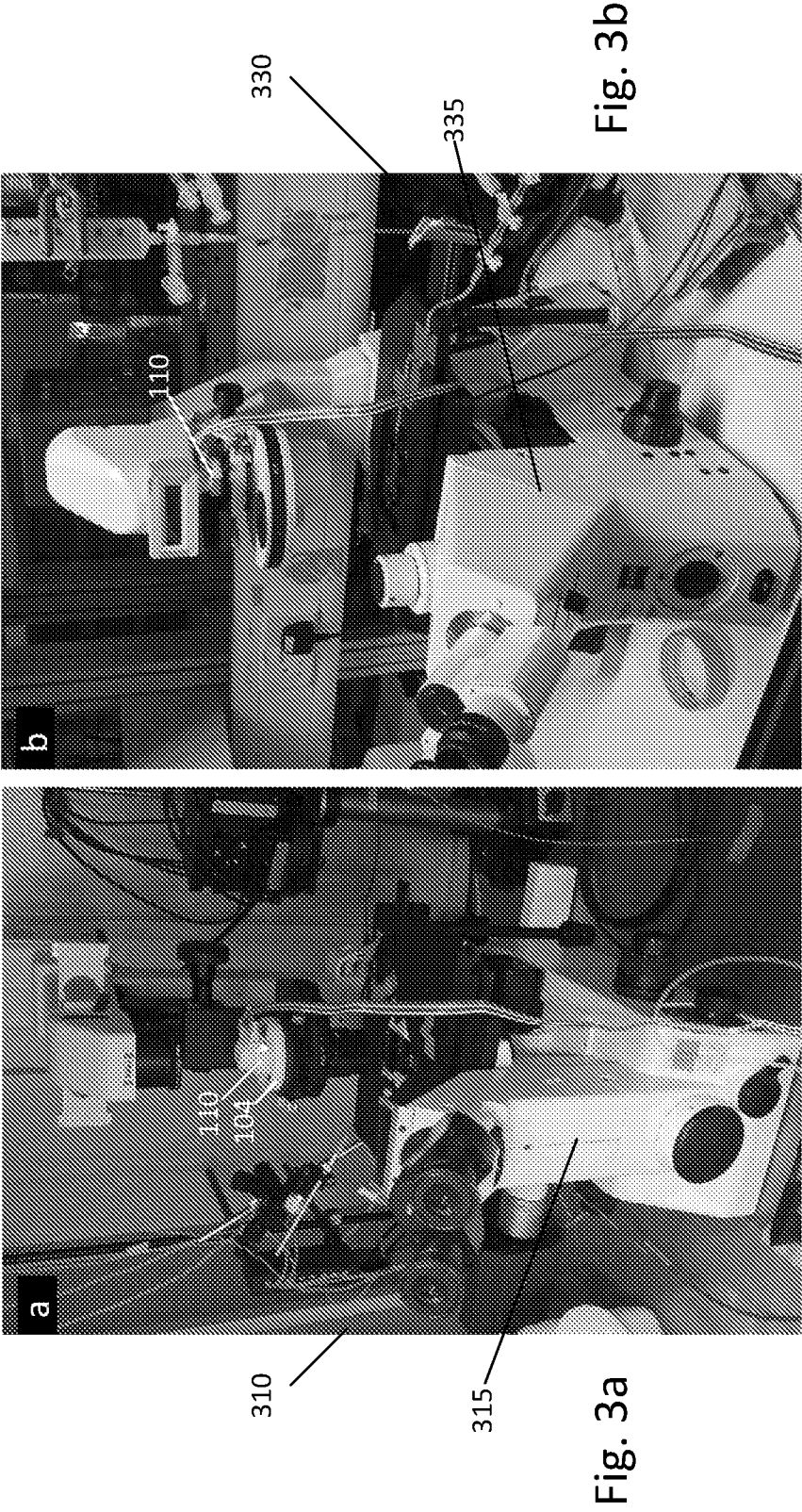
Fig. 1a

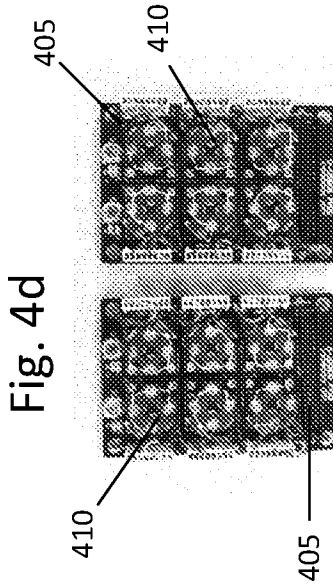
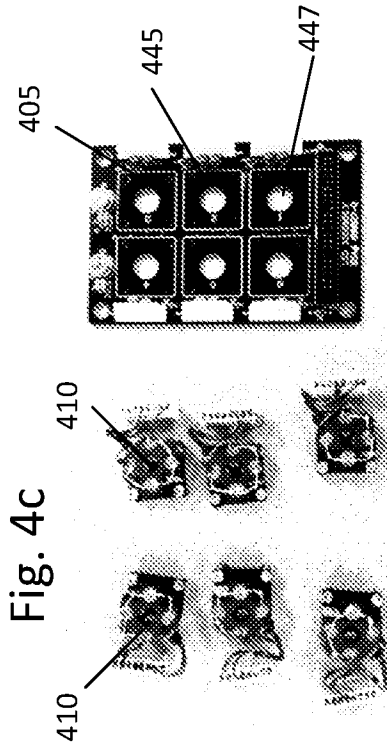
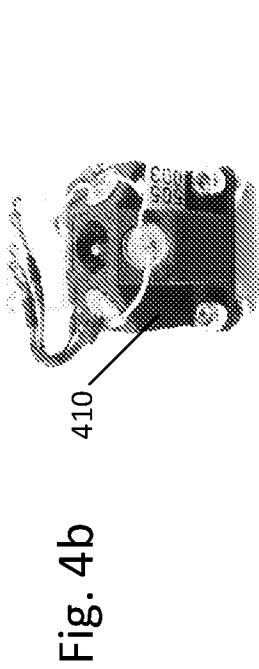
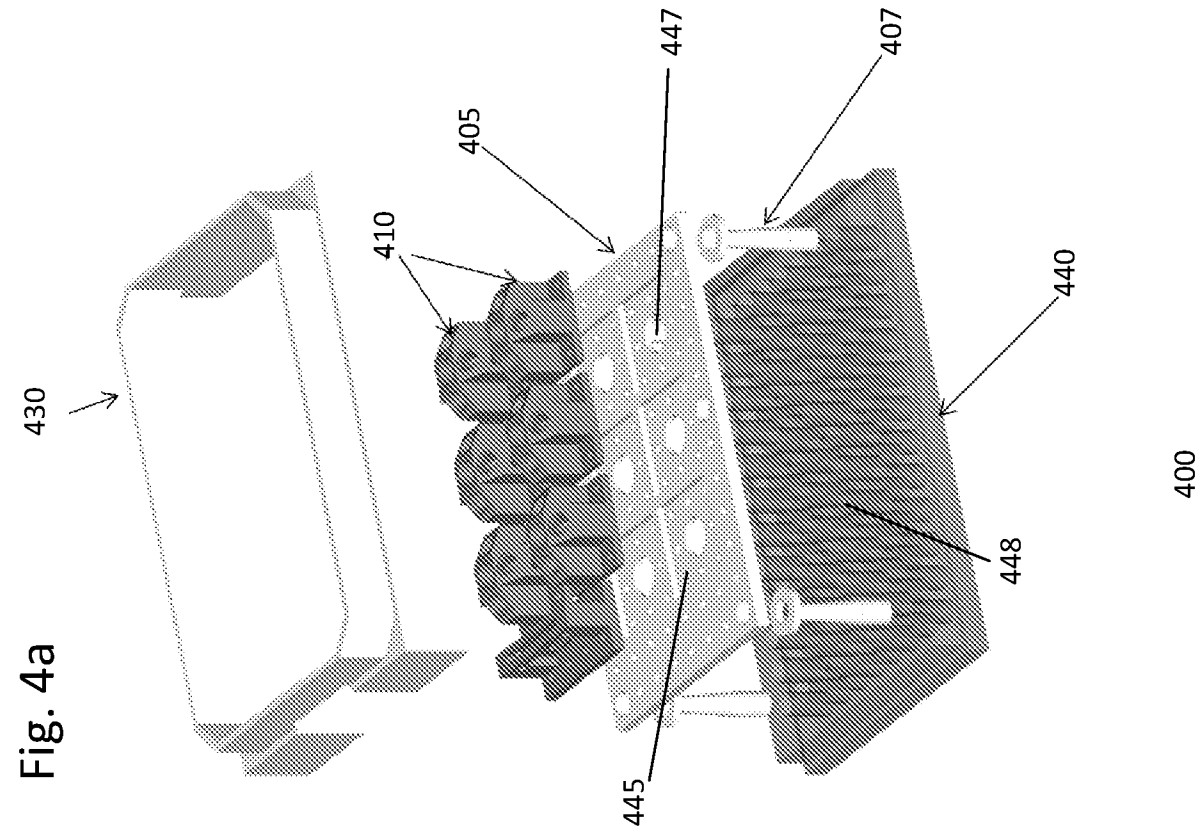
Fig. 1b

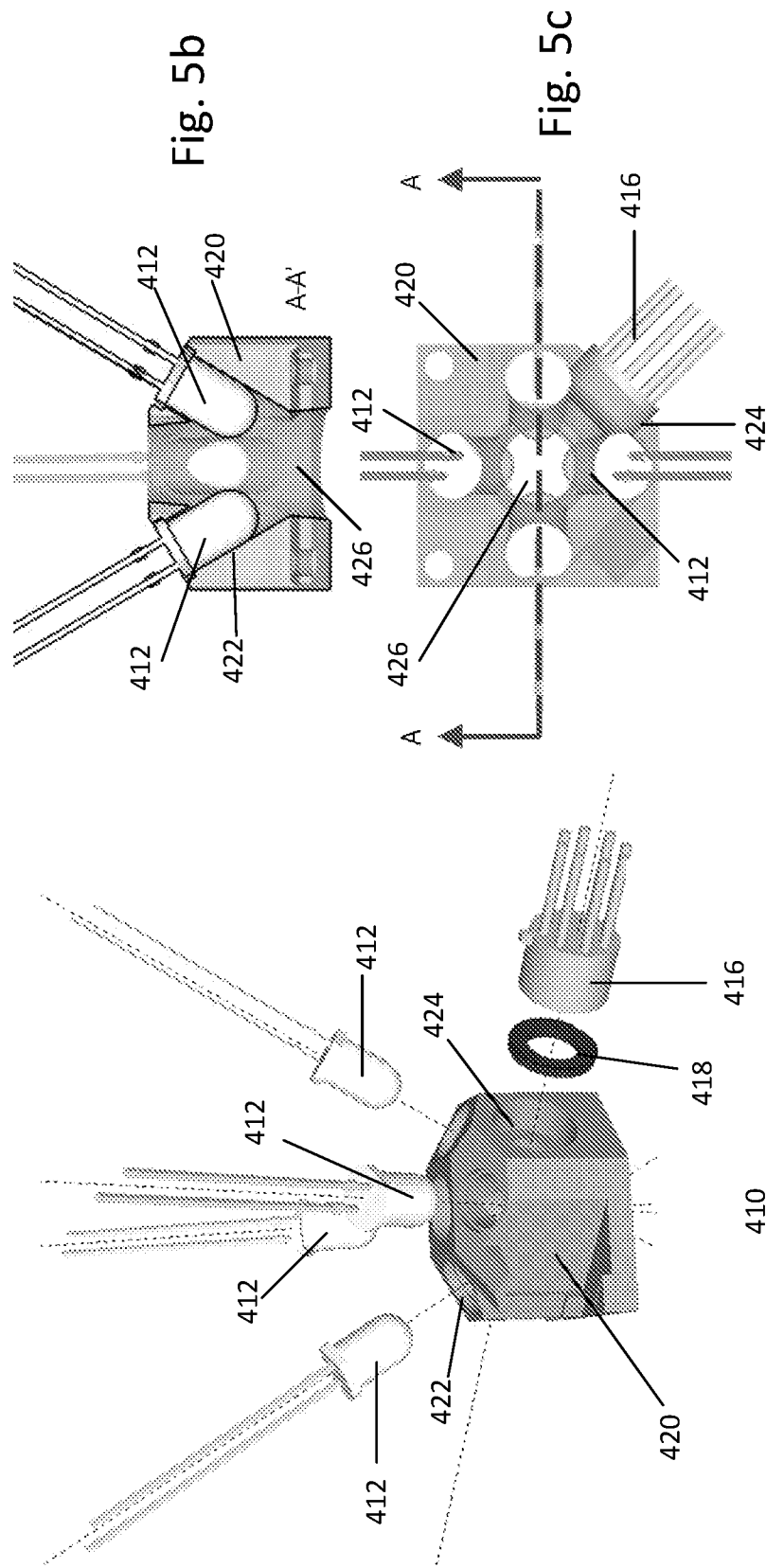


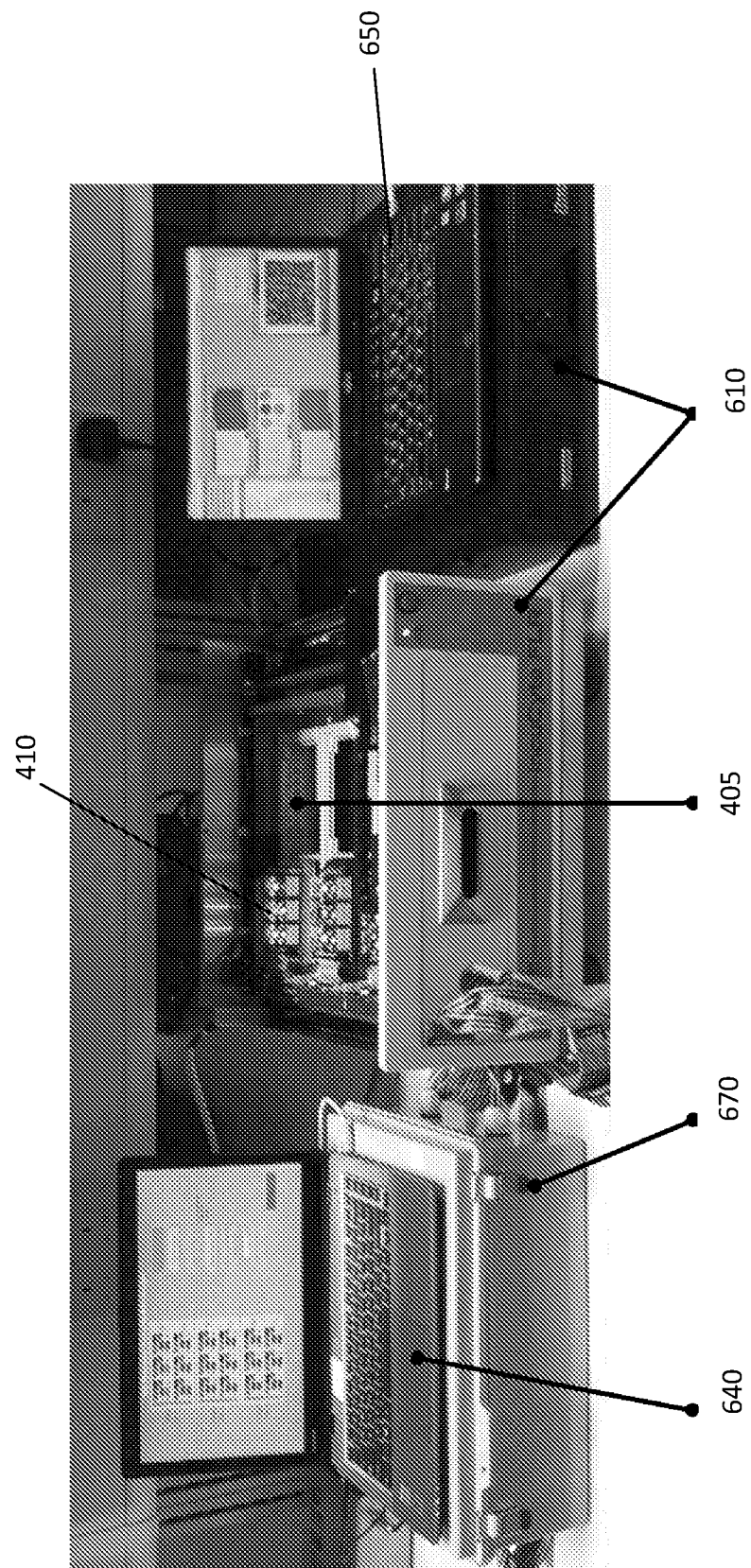
200

Fig. 2









600

Fig. 6

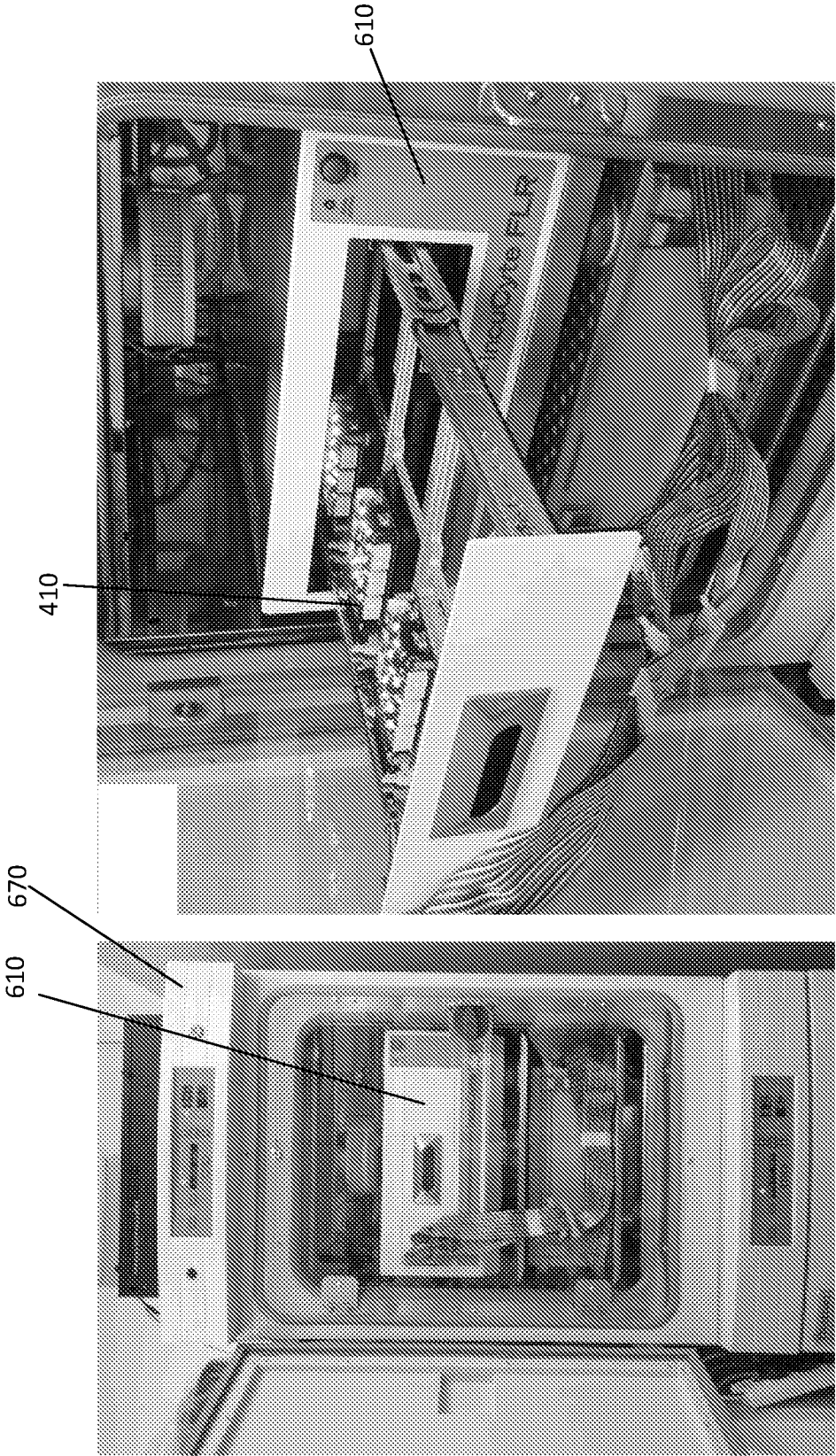
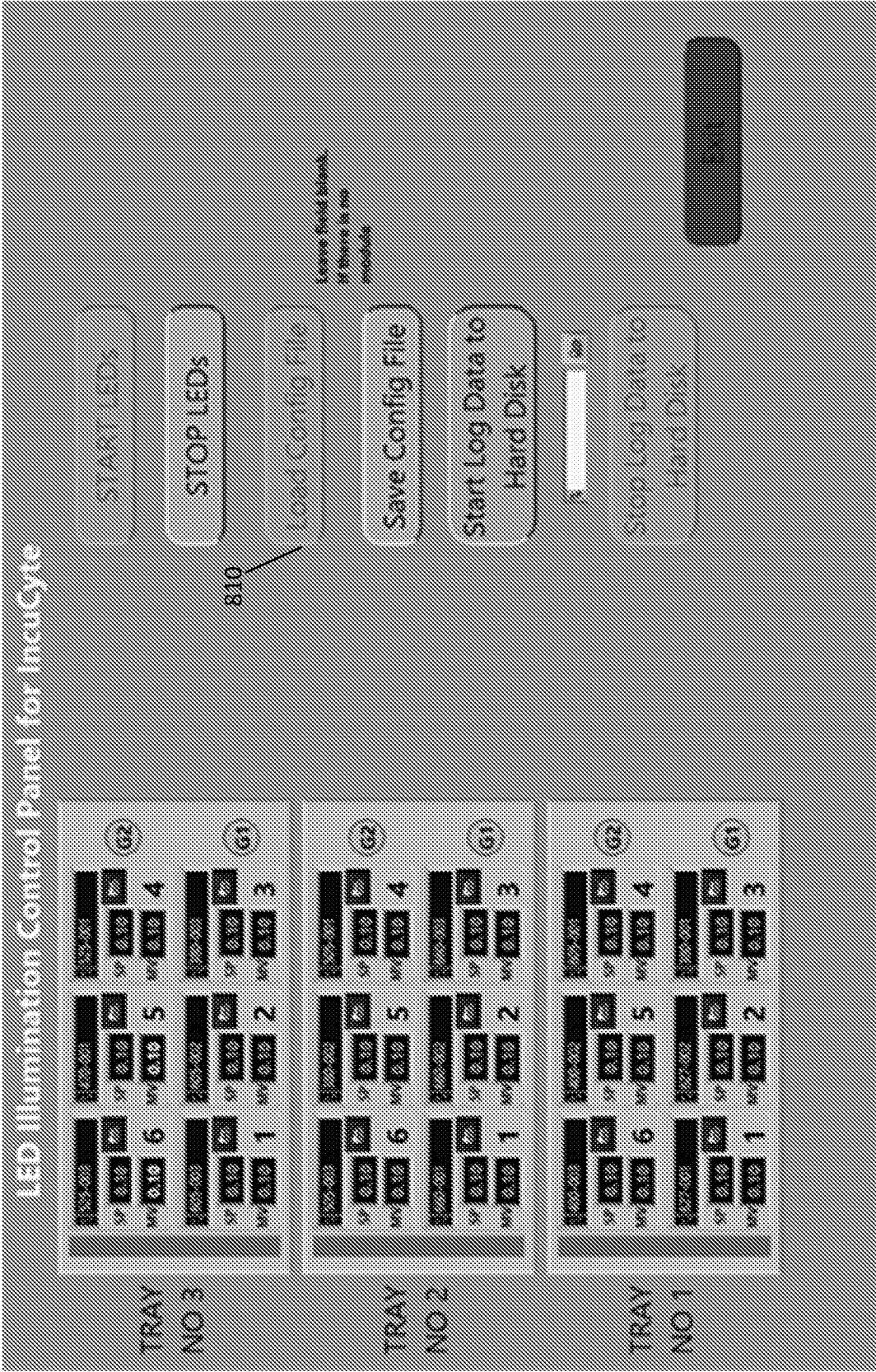


Fig. 7b

Fig. 7a



800

Fig. 8

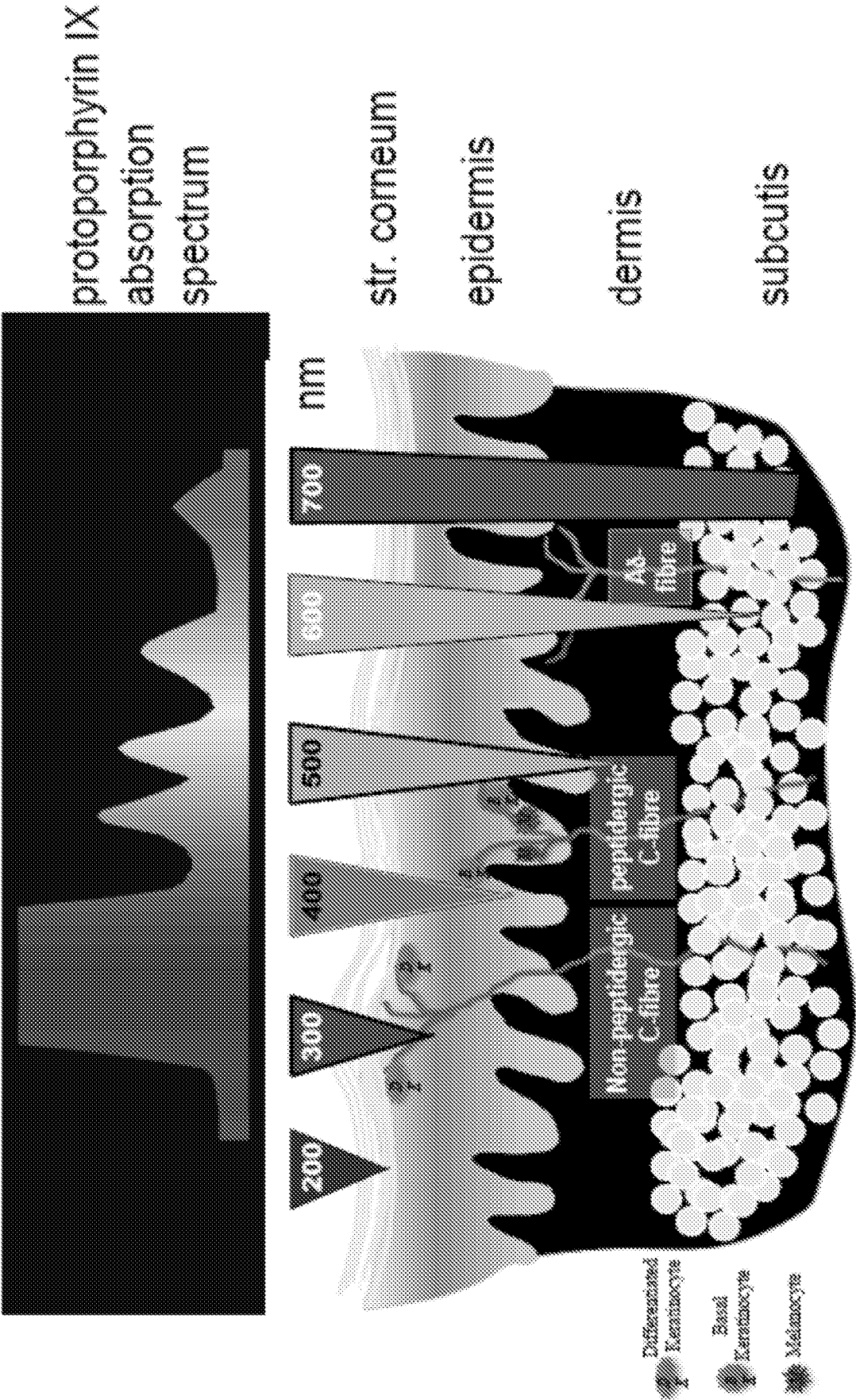


Fig. 9

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG2016/050102

A. CLASSIFICATION OF SUBJECT MATTER

G01J 3/02 (2006.01) G01J 3/10 (2006.01) G01N 21/01 (2006.01) G01N 21/31 (2006.01)

According to International Patent Classification (IPC)

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

G01J, G01N

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

FamPat: LED, optical, light, module, housing, slots, aperture, monitoring, control and like terms.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/0001035 A1 (ENGSTRAND B. W.) 6 January 2011 Whole document, especially paras. [0076]-[0079], [0093], Figs. 1-2	1-25
X	US 2006/0192125 A1 (YOGANANDAN S. N. ET AL.) 31 August 2006 Paras. [0008]-[0011], Figs. 1-2	1-3, 8-10, 13-16, 18-25
X	US 2002/0179816 A1 (HAINES J. P. ET AL.) 5 December 2002 Paras. [0016]-[0020], Figs. 1-2	1-3, 8-10, 13-16, 18-25
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A	US 2004/0257808 A1 (BJORNSON T. ET AL.) 23 December 2004 Whole document	

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

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Date of the actual completion of the international search

17/05/2016

(day/month/year)

Date of mailing of the international search report

27/05/2016

(day/month/year)

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/SG2016/050102

Note: This Annex lists known patent family members relating to the patent documents cited in this International Search Report. This Authority is in no way liable for these particulars which are merely given for the purpose of information.

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