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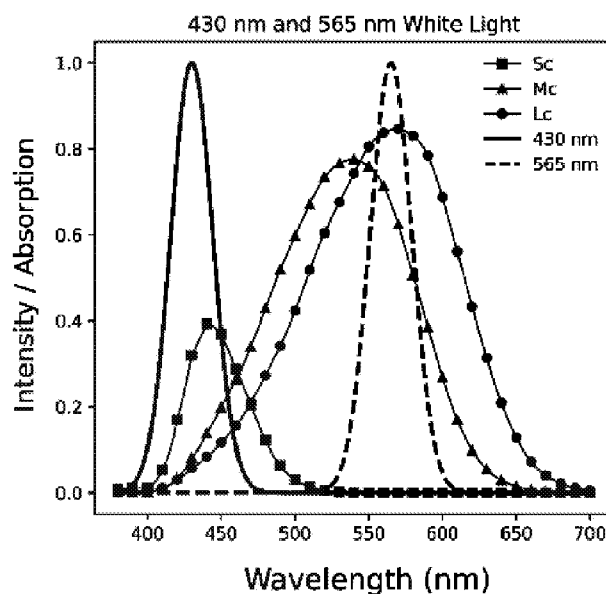


FIG. 1A

(57) Abstract: Lighting devices, systems, and methods for selectively activating S cones and L+M cones in a human retina and for regulating the phase of circadian rhythm in a human subject.

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LIGHTING DEVICES, SYSTEMS, METHODS FOR STIMULATING CIRCADIAN RHYTHMS

CROSS-REFERENCE TO RELATED APPLICATION

5 This application claims the benefit of US Application No. 62/850,493, filed May 20, 2019, expressly incorporated herein by reference in its entirety.

STATEMENT OF GOVERNMENT LICENSE RIGHTS

 This invention was made with government support under Grant No. 1RO1EY027859, awarded by the National Eye Institute. The government has certain
10 rights in the invention.

BACKGROUND OF THE INVENTION

 Despite the advances in the development of light therapies for changing the phase of human circadian rhythms and for stimulating non-image forming visual pathways involved in mood, alertness, and cognitive performance a need exists for improved
15 systems that are more effective and more practical for use in everyday, home, business, educational and healthcare settings. The present invention seeks to fulfill this need and provides further related advantages.

SUMMARY OF THE INVENTION

 The present invention provides systems, methods, and devices for using multiple
20 narrow band ranges of visible light which are modulated imperceptibly either spatially or temporally to increase the efficacy of light therapies for circadian rhythm shifts in humans.

 In one aspect, the invention provides a method for selectively activating S cones and L+M cones in a human retina and regulating the phase of circadian rhythm.

25 In certain embodiments, the invention provides a method for selectively activating S cones and L+M cones in a human retina. In one embodiment, the method comprises:

 (a) exposing a human retina to a first multi-band light consisting of a first band having a peak emission at 430 nm and a second band having a peak emission at 565 nm; and

30 (b) exposing the human retina to a second multi-band light consisting of a first band having a peak emission at 485 nm, a second band having a peak emission at 565 nm, and a third band having a peak emission at 630 nm.

In other embodiments, the invention provides a method for regulating the phase of circadian rhythm in a subject. In one embodiment, the method comprises:

(a) exposing a subject's retina to a first multi-band light consisting of a first band having a peak emission at 430 nm and a second band having a peak emission at
5 565 nm; and

(b) exposing the subject's retina to a second multi-band light consisting of a first band having a peak emission at 485 nm, a second band having a peak emission at 565 nm, and a third band having a peak emission at 630 nm.

In another aspect of the invention, lighting devices are provided.

10 In one embodiment, the invention provides a lighting device effective for the S + (L+M) retinal cone activation. In this embodiment, the lighting device comprises two light sources:

(a) a first light source that emits a first band of light having a peak emission at 430 nm; and

15 (b) a second light source that emits a second band of light having a peak emission at 565 nm.

In another embodiment, the invention provides a lighting device is effective for L+M retinal cone activation. In one embodiment, the lighting device comprises three light sources:

20 (a) a first light source that emits a first band of light having a peak emission at 485 nm;

(b) a second light source that emits a second band of light having a peak emission at 565 nm; and

(c) a third light source that emits a third band of light having a peak emission
25 at 630 nm.

In another embodiment, the lighting device comprises four light sources:

(a) a first light source that emits a first band of light having a peak emission at 430 nm;

(b) a second light source that emits a second band of light having a peak
30 emission at 565 nm;

(c) a third light source that emits a third band of light having a peak emission at 485 nm; and

(d) a fourth light source that emits a fourth band of light having a peak emission at 630 nm.

In a further aspect, the invention provides lighting systems.

In certain embodiments, the invention provides a lighting system comprising:

- 5 (a) a first lighting device, comprising two light sources,
- (i) a first light source that emits a first band of light having a peak emission at 430 nm, and
- (ii) a second light source that emits a second band of light having a peak emission at 565 nm; and
- 10 (b) a second lighting device, comprising three light sources:
- (i) a first light source that emits a first band of light having a peak emission at 485 nm;
- (ii) a second light source that emits a second band of light having a peak emission at 565 nm; and
- 15 (iii) a third light source that emits a third band of light having a peak emission at 630 nm.

In further aspects of the inventions, methods for selectively activating S cones and L+M cones in a human retina and methods for regulating the phase of circadian rhythm in a subject using the lighting devices and lighting systems are provided.

20 DESCRIPTION OF THE DRAWINGS

The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same become better understood by reference to the following detailed description, when taken in conjunction with the accompanying drawings.

- 25 FIGURES 1A and 1B compares intensity distributions of lights from a representative lighting element (solid and dashed lines) with two different modes: 430, 565 nm mode (FIGURE 1A) and 485, 565, 630 nm mode (FIGURE 1B). Square, triangle, and circle lines show the absorption spectra of the human cones. The lighting element produces white light in either mode and the two modes can be adjusted to appear
- 30 identical to human conscious perception.

FIGURES 2A-2C compare phase shift effectiveness as measured by saliva melatonin levels as a function of time in individuals in the evening and morning after subject to one hour light exposure. FIGURE 2A shows the rise in saliva melatonin levels

in individuals in the evening, which is regulated by an individual's internal circadian clock, and before and after one hour steady white light equated in intensity (dotted line shows a 1.2 minute advance). FIGURE 2B compares rise in saliva melatonin levels in individuals in the evening after 1 hour of being subject to blue light (dotted line shows an 11 minute delay). FIGURE 2C compares rise in saliva melatonin levels in individuals in the evening either after 1 hour of being subject to 430, 565 nm vs. 485, 565, 630 nm mode alternation (dotted line shows a +43 minute advance) in accordance with the present invention.

FIGURES 3A-3D depict various aspects of device and system embodiments for a light source for transmitting select narrow bands of light. FIGURE 3A is a schematic illustration of a single lighting element with circuitry to control four narrow bands of light with peak wavelengths near 430 nm, 485 nm, 565 nm and 630 nm. FIGURE 3B is a representative system that combines individual lighting elements to create array structures to provide representative lighting panels of desired shapes and sizes. FIGURE 3C illustrates a representative configuration of lighting elements combined in a cylindrical hexagonal shape (left image) for integration into a lighting fixture (left image) having a spherical shape (right image) that can be used as a table or floor lamp. FIGURE 3D is a photograph of a single lighting element emitters for the different lighting bands are located at the center of an aluminum circuit board for dissipating heat.

DETAILED DESCRIPTION OF THE INVENTION

Recent research has indicated that uptake of light by the retina of a mammalian eye includes subconscious responses to the activity of retinal ganglion cells with input circuitry from cone photoreceptors that imparts sensitivity to light with spatial and temporal properties and with spectral ranges previously not known (Patterson SS, Kuchenbecker JA, Anderson JR, Neitz M, Neitz J. A Color Vision Circuit for Non-Image-Forming Vision in the Primate Retina. *Curr Biol.* 2020 Apr 6;30(7):1269-1274.e2. doi: 10.1016/j.cub.2020.01.040.). The subconscious responses include aspects of the body's internal regulation, including, but not limited to the body's circadian rhythm. Previous study into the retina's uptake of blue wavelength light stimulation showed moderate response in terms of regulating the circadian rhythm. Presented herein are outcomes where complementary narrow bands are emitted, and combinations are used in alternating temporal and spatial fashion to present a mammalian body with visually

perceptible white light that markedly impacts regulation of some functions (e.g., circadian rhythm, mood, alertness and cognitive function).

Methods for Selective Retinal Cone Activation and Regulating Circadian Rhythm

In one aspect, the invention provides a method for selectively activating S cones
5 and L+M cones in a human retina and regulating the phase of circadian rhythm.

In certain embodiments, the invention provides a method for selectively activating S cones and L+M cones in a human retina. In one embodiment, the method comprises:

(a) exposing a human retina to a first multi-band light consisting of a first band having a peak emission at 430 nm and a second band having a peak emission at
10 565 nm; and

(b) exposing the human retina to a second multi-band light consisting of a first band having a peak emission at 485 nm, a second band having a peak emission at 565 nm, and a third band having a peak emission at 630 nm.

The bandwidth for each emission peak maximum is about 20 nm full-width at half
15 maximum (FWHM).

The peak emission wavelength may have variance: 430 nm ($\pm$ about 20 nm); 485 nm ($\pm$ about 20 nm); 565 nm ($\pm$ about 20 nm); and 630 nm ($\pm$ about 20 nm).

The first and second multi-band lights are nominally white because 430 nm and 560 nm lights are complementary colors and mixing complementary colors produces
20 white. A mixture of 485 nm and 630 nm light is a violet color like the violet color of a 430 nm light and when mixed with yellow green 560 nm light also produces white. By adjusting the relative amounts of the different bands of light in each case it is possible to change the color temperature of the whites for different environment (e.g., people often prefer warm color temperatures of about 2700K for home lighting but daylight about
25 5000K might be preferred in an art gallery).

It will be appreciated that in the methods of the invention, the only lights used are the first and second multi-band light having the specified peak emissions. However, in certain embodiments, small amounts of additional wavelength bands can be added equally to both phases in order to optimize the exact color of the whites. Usually, color
30 temperature of lights is varied along the "planckian locus" to make whites that are pleasing in color. If the whites produced by the prescribed wavelengths appears too green or too red, this can be adjusted by including some red or green wave bands to make

subtle adjustments. The methods utilize the specified first and second multi-band light having the peak emission wavelengths as described herein.

In certain embodiments of the method, exposing the retina to the first multi-band light and the second multi-band light comprises alternating exposure to the retina at a
5 frequency from about 10 to 30 Hz.

In other embodiments of the method, exposing the retina to the first multi-band light and the second multi-band light comprises exposure to one or more light sources emitting the first multi-band light and exposure to one or more light sources emitting the second multi-band light. In certain of these embodiments, the minimum number of light
10 sources for each multi-band is two. In these embodiments, the number of light sources emitting the first multi-band light and the number of light sources emitting the second multi-band light are about equal. The luminance flux would be identical in modes where L+M cone activations are kept constant between the two modes. In (S+M)-L constant mode the two are similar in lumens but not identical.

In the practice of this aspect of the method of the invention, there are two modes
15 where the first and second lights are alternated invisibly. In a first mode, L+M cone activation is kept constant between the first and second lights and only activation of S-cones is modulated between first and second lights. The transition between modes is imperceptible because S-cones are insensitive to temporal modulation. In a second mode,
20 (S+M)-L cone activations are kept constant between the first and second lights. This can be imperceptible because conscious perception of blue vs. yellow is based on circuitry in the visual system that compares activation of (S+M) cones to L cones.

In other embodiments, the invention provides a method for regulating the phase of circadian rhythm in a subject. In one embodiment, the method comprises:

25 (a) exposing a subject's retina to a first multi-band light consisting of a first band having a peak emission at 430 nm and a second band having a peak emission at 565 nm; and

(b) exposing the subject's retina to a second multi-band light consisting of a first band having a peak emission at 485 nm, a second band having a peak emission at
30 565 nm, and a third band having a peak emission at 630 nm.

In certain embodiments, exposing the retina to the first multi-band light and the second multi-band light comprises alternating exposure to the retina at a frequency from about 15 to about 19 Hz.

In other embodiments, exposing the retina to the first multi-band light and the second multi-band light comprises exposure to one or more light sources emitting the first multi-band light and exposure to one or more light sources emitting the second multi-band light.

5 In certain embodiments of the methods described herein, the subject's retina is exposed to the first multi-band light and the second multi-band light for at least about 15 minutes to about 60 minutes per day (e.g., 20-30 minutes). In certain embodiments, exposure is for a full day (i.e., 8 hours). A minimum of 20 minutes in the morning while going through a normal routine, such as in the bathroom or kitchen, will help with social
10 jet lag and reduce morning fatigue. At the other extreme, exposure for a full day, starting at home in the morning and then continuing throughout the productive part of the day at school or work until about 4 PM is anticipated to optimize circadian rhythms health and happiness. This would be like the experience of our prehistoric ancestors who lived outside and enjoyed a whole day of bright light exposure. However, in the late afternoon
15 the lights should switch to "non-circadian disrupter mode" where the S-cone activation differential between the two modes is reduced to zero.

In the methods of the invention, the phase of circadian rhythm may be determined by measuring the subject's saliva melatonin levels. In certain embodiments, and as described herein, the subject's saliva melatonin levels are measured before and 12 hours
20 after exposure to the first multi-band light and the second multi-band light.

Lighting Devices

In another aspect of the invention, lighting devices are provided.

In one embodiment, the invention provides a lighting device effective for the S + (L+M) retinal cone activation. In this embodiment, the lighting device comprises two
25 light sources:

- (a) a first light source that emits a first band of light having a peak emission at 430 nm; and
- (b) a second light source that emits a second band of light having a peak emission at 565 nm.

30 In certain embodiments, the first and second bands of light are emitted from a single point source. In certain embodiments, the lighting device has a luminosity flux from about 200 to about 5000 lumens.

In another embodiment, the invention provides a lighting device is effective for L+M retinal cone activation. In this embodiment, the lighting device comprises three light sources:

- 5 (a) a first light source that emits a first band of light having a peak emission at 485 nm;
- (b) a second light source that emits a second band of light having a peak emission at 565 nm; and
- (c) a third light source that emits a third band of light having a peak emission at 630 nm.

10 In certain embodiments, the first, second, and third bands of light are emitted from a single point source. In certain embodiments, the lighting device has a luminosity flux from about 200 to about 5000 lumens.

The lighting devices described herein are useful for implementing the methods of the invention. In certain embodiments, a single lighting device is capable of both modes and includes all four light sources (e.g., light-emitting devices, LEDS) 430 nm, 565 nm, 15 485nm, and 630 nm. In these embodiments, the lighting device is a single light bulb or lighting element capable of temporally switching between modes. Also, individual elements could be incorporated into an array with half the elements in one mode and half in the other at any one moment. Each element includes the light sources (e.g., LEDS) at 20 430 nm, 565 nm, 485nm, and 630 nm as active components but may also include light sources emitting at additional wavelengths where small amounts of light can be used to improve aesthetics or color rendering.

Thus, in another embodiment, the invention provides a lighting device, comprising four light sources:

- 25 (a) a first light source that emits a first band of light having a peak emission at 430 nm;
- (b) a second light source that emits a second band of light having a peak emission at 565 nm;
- (c) a third light source that emits a third band of light having a peak emission at 485 nm; and
- 30 (d) a fourth light source that emits a fourth band of light having a peak emission at 630 nm.

The lighting devices of the invention do not include any light source(s) other than specified above. The lighting devices do not include any other light source that emits light at a wavelength other than specified above. It will be appreciated that each light source's peak emission wavelength may have some variance (i.e., 430 nm ($\pm$ about 20 nm); 485 nm ($\pm$ about 20 nm); 565 nm ($\pm$ about 20 nm); and 630 nm ($\pm$ about 20 nm)) and a bandwidth (full-width at half maximum about 20 nm).

It will be appreciated that in the lighting devices, the only lights used are the light bands having the specified peak emissions. However, in certain embodiments, small amounts of additional wavelength bands can be added equally to both phases in order to optimize the exact color of the white light.

Lighting System

In a further aspect of the invention, lighting systems are provided.

In certain embodiments, the invention provides a lighting system comprising:

- (a) a first lighting device, comprising two light sources,
 - (i) a first light source that emits a first band of light having a peak emission at 430 nm, and
 - (ii) a second light source that emits a second band of light having a peak emission at 565 nm; and
- (b) a second lighting device, comprising three light sources:
 - (i) a first light source that emits a first band of light having a peak emission at 485 nm;
 - (ii) a second light source that emits a second band of light having a peak emission at 565 nm; and
 - (iii) a third light source that emits a third band of light having a peak emission at 630 nm.

In certain embodiments, the lighting system comprises two or more first lighting device and two or more second lighting devices. In certain of these embodiments, the lighting system comprises about the same number first lighting devices and second lighting devices.

In certain embodiments of the lighting system, L+M cone activation is kept constant between the first and second lighting devices and only activation of S-cones is temporally modulated between first and second lighting devices.

In other embodiments of the lighting system, (S+M)-L cone activations are kept constant between the first and second lighting devices.

As described above for the lighting devices, the lighting systems of the invention do not include any light source(s) other than specified above. The lighting systems do not include any other light source that emits light at a wavelength other than specified above. It will be appreciated that each light source's peak emission wavelength may have some variance (i.e., 430 nm ($\pm$ about 20 nm); 485 nm ($\pm$ about 20 nm); 565 nm ($\pm$ about 20 nm); and 630 nm ($\pm$ about 20 nm)) and a bandwidth (full-width at half maximum about 20 nm).

It will be appreciated that in the lighting systems, the only lights used are the light bands having the specified peak emissions. However, in certain embodiments, small amounts of additional wavelength bands can be added equally to both phases in order to optimize the exact color of the white light.

The lighting system can be deployed in a low natural light environment or in an environment of a human subject in need of a phase shift to regulate the subject's circadian rhythm. All indoor lighting environments are examples where light intensities fall well short of direct-sunlight or cloud-covered sunlight intensities, such that they provide insufficient intensity to drive the circadian system effectively. Specific examples are artificial lighting for the home, commercial, industrial, medical, and classroom/school spaces. For example, homes--bedrooms, bathrooms, living rooms, kitchens; commercial--lobbies, stairways, offices, retail sales rooms, lounges, laboratories; industrial--cafeterias, work rooms, offices; Medical--patient rooms, nurses stations, day rooms; schools--classrooms, corridors, study halls, cafeterias.

The lighting systems can be used in the methods of the invention: a method for selectively activating S cones and L+M cones in a human retina; or a method for regulating the phase of circadian rhythm in a subject.

As noted above, in one aspect, the present invention includes methods, devices, and systems for manipulating circadian rhythms in humans. In certain embodiments, the devices and systems emit a first complementary multi-band white light (color temperature between 2700K and 5000K) that activates S-cones in the retina (a band having a maximum at about 430 nm) and that simultaneously activates L and M cones in the retina (a band having a maximum at about 565 nm). See FIGURE 1A. In other embodiments, the devices and systems emit a second complementary multi-band light having band

maxima at 485, 565, and 630 nm. See FIGURE 1B. The multi-band light emits lights in narrow bandwidths specified by full width-at-half-maximum (FWHM) about each emission maximum. The approximate bandwidth for each emission peak is set forth in parentheses after each peak: 430 nm (20 nm $\pm$ 20 nm), 485 nm (25 nm $\pm$ 20 nm), 565 nm (30 nm $\pm$ 20) and 630 nm (35 nm $\pm$ 20 nm).

FIGURES 1A and 1B compare intensity distributions of lights from a representative lighting element (solid and dashed lines) with two different modes: 430, 565 nm mode (FIGURE 1A) and 485, 565, 630 nm mode (FIGURE 1B). Square-, triangle-, and circle-labeled lines show the absorption spectra of the human retinal cones (i.e., S-, M-, and L-cones, respectively). The lighting element produces white light (over a range of color temperatures between 2700K and 5000K) in either mode and the two modes can be adjusted to appear identical to human conscious perception. However, when the two modes are presented in either spatial or temporal alternation they powerfully but subconsciously stimulate ganglion cells in the retina of eye that regulate mood, arousal, cognitive performance and the phase of the circadian clock. This regulation is based on the very different activation of S vs. (L + M) cone activation between the modes (FIGURE 1A, 430 + 565 nm, S+L+M; FIGURE 1B, 485 + 565 + 630 nm, L+M only). Modulating S vs. L+M cone activation activates the newly discovered Color Vision Circuit for Non-Image-Forming Vision in the Primate Retina (Ref: Curr Biol. 2020 Apr 6;30(7):1269-1274.e2. doi: 10.1016/j.cub.2020.01.040). The two light sources can be presented in either spatial or temporal alternation. In the method of the invention, alternation of white light sources in space or time is not perceptible to human conscious vision change but it can be a powerful stimulus for intrinsically photosensitive retinal ganglion cells (ipRGCs). The strength of the activation of the ipRGCs depends on the magnitude of the difference in S vs (L+M) cone activation between the two light sources. The light sources are equipped with WIFI controlled computers that are programmed to adjust the magnitude of the difference in S vs (L+M) cone activation between the two modes, and thus activations of ipRGCs, at different times of day. The effect can vary from strong to none as appropriate to maximize the health and happiness of users. For example, strong activation in the morning combats "social jet lag" and stimulates alertness. Strong activation in the middle of the day in the workplace or school can enhance alertness and cognitive capacity. However, weak or no activation in the evening promotes relaxation and uninterrupted circadian rhythms. The

transition between the two modes can be rendered imperceptible in one of two ways. One way is to keep the quantal catch for the L+M cones constant between the two modes thus only modulating the S-cones in the transition between the two modes. The other way is to keep the quantal catch for (S+M)-L cones silent between the two modes. The most appropriate method depends on the exact details of the spatial, temporal and spectral characteristics of the lights.

Melatonin levels in human saliva are an indication of the body's circadian rhythm. During the day and exposure to sun, melatonin secretion is reduced and at night when the sun has set melatonin secretion increases. Disruption of the one's normal melatonin cycle is an indication of the disruption of one's internal circadian rhythm. Monitoring melatonin levels provides insight into one's circadian rhythm. One aspect of a person's circadian rhythm is the phase of the circadian clock which can be assessed by measuring the dim light melatonin onset (DLMO).

FIGURES 2A-2C compares saliva melatonin levels as a function of time in individuals in the evening and morning after subject to one-hour light exposure (FIGURE 2A, white light; FIGURE 2B, blue light; FIGURE 2C, multi-band light in accordance with the invention).

FIGURES 2A-2C provide a demonstration of the very strong effectiveness of 430, 565 nm vs 485, 565, 630 nm mode alternation against blue light and a steady white light equated in melanopic lux intensity. Results are the average for 3 subjects (error bars plus & minus one SEM). Shown in all graphs is the rise in saliva melatonin. Evening rise in melatonin secretion is regulated by our internal circadian pacemaker and it is used as an indicator of the phase of the internal clock. This experiment was carried out over three evenings. On the first evening, a baseline melatonin curve was obtained (gray dots and solid lines in FIGURES 2A, 2B, and 2C). The following morning subjects viewed a steady white light for 1 hr (FIGURE 2A), a blue light for 1 hr (FIGURE 2B), or multi-band light in accordance with the present invention (happy light) for 1 hr (FIGURE C). That evening a second melatonin curve was determined (unfilled circles and black dashed lines in FIGURE 2A, 2B, and 2C). Only a 1.2 minute (non-significant) phase advance was observed in response to a white light stimulus, an 11 minute delay (non-significant) was observed in response to blue light, and a 43 minute advance (significant) was achieved in response to the 430, 565 nm vs 485, 565, 630 nm mode alternation mode. This phase advance shown in FIGURE 2C demonstrates the powerful effects of the multi-

band light in accordance of the invention compared to steady white light (FIGURE 2A) and blue light (FIGURE 2B).

In this experiment, the 430, 565 nm vs 485, 565, 630 nm modes were alternated temporally (alternating at 17 Hz for 1 hr). However, the same effect can be achieved using spatial patterns of 430, 565 nm vs 485, 565, 630 nm lighting elements and viewing the lighting elements or viewing the illumination of surfaces illuminated by the lighting elements with an alternating spatial pattern. Here, 17 Hz was chosen because normal eye movements across the patterned light are expected to produce a virtual temporal alternation on the retina of near 17 Hz. The light used was adjusted to have the same intensity which was defined as having the same time averaged effect on the intrinsic photopigment melanopsin.

Narrow band blue light with peak wavelengths near 480 nm has been shown to be 10-15 times more effective than white light at stimulating cells in the retina responsible for circadian entrainment. However, as demonstrated herein blue light is still relatively ineffective compared to the method of the invention. Moreover, in order to be effective, the blue lights have to narrow band and must be presented in isolation in the absence of exposure to wavelengths outside the narrow band. For example, white lights have blue light as a component but white lights that contain the same amount of blue light as a narrow band blue light that is effective on its own are not themselves effective. Narrow band blue lights cannot be used as standard lighting in home, school, health care or business settings, as can the present invention. The results demonstrate the vast superiority of the invention described here to blue lights designed to influence circadian rhythms.

Importantly, the present invention can be used as standard white lighting in residential, business and healthcare settings. Moreover, the effect on circadian rhythms can be modulated at different times of day to maximize positive effects on health.

FIGURES 3A-3D depict representative embodiments of devices and systems transmitting the select multi-band light in accordance with the methods of the invention.

FIGURE 3A is a schematic illustration of a single lighting element with input / output connections such that an individual lighting element may be configured in series or parallel. Circuitry to control four narrow bands of light then controls intensity of four narrow bands of light with peak wavelengths near 430 nm, 485 nm, 565 nm, and 630 nm.

Alternating 430, 565 nm vs. 485, 565, 630 nm modes produces powerful effects on neural circuits in the eye that control circadian rhythms, mood, alertness, and cognitive capacity.

Referring to FIGURE 3A, the single lighting element includes circuit board 100 (e.g., aluminum or other material effective at transferring heat away from the digital light emitters) on which are mounted pads 101 and 102 for plastic interconnection (101) or
5 direct soldering (102) to LED packages 103 shown in a typical layout. The single lighting element shown in FIGURE 3A contains five individual LED emitters inside two LED packages. The larger LED package (left) is a 4-in-1 LED package containing a red, green, blue, and white LEDs (Cree XLamp XM-L series, part number XMLCTW-A2-
10 0000-00C2AAAB1 from Cree). The smaller LED package (right) is a single LED emitter package containing a violet LED (Lumiled Luxeon UV U2 series manufacturer part number L1F3-U410200014000 from Luxeon).

FIGURE 3B illustrates two configurations of four single lighting elements, where a single lighting element consists of multiple LED emitters from the center of an
15 aluminum heat sink: a vertical checkerboard ("even") configuration (200A) and an offset ("odd") configuration (200B). The representative systems combine individual lighting elements to create array structures to provide representative lighting panels of desired shapes and sizes that can be configured to conform to current lighting in residential, school, business, and medical settings.

FIGURE 3C illustrates a representative configuration of lighting elements combined in a cylindrical hexagonal shape (left) for integration into a lighting fixture having a spherical shape (right image) that can be used as a table or floor lamp. Other arrays may be configured to suit use in fixed indoor lighting systems, wearable devices, or aircraft cabin lighting.

Referring to FIGURE 3C, configuration 300A includes six individual lighting elements forming the upper row of a hexagonal shape in a lamp implementation (and six individual lighting elements forming the lower row of a hexagonal shape in a lamp implementation) (each upper row lighting element shown as 300A). Interconnect 301A (plastic) provides an electrical connection with the individual LEDs, whereas in 302A are
25 unused, and LED driver board 303A drives the individual LED wavelengths. This hexagonal configuration of driver circuitry and spatial LED arrangement can be positioned inside spherically-shaped glass diffuser 300B to provide a lamp emitting light perceived by the human eye as white light.
30

FIGURE 3D is an illustration of a single lighting element located at the center of a circuit board for dissipating heat. For reference, the area of a single lighting element as shown is about 40 mm by 40 mm, though this embodiment's design may be adapted to suit other installments.

5 Referring to FIGURE 3D, single lighting element 400 with LED connections made via soldered wires 401 on pads 402. In this embodiment, plastic interconnects were not used in favor of direct solder pads. As shown in FIGURE 3A, element 400 includes two LED packages: the left LED package contains four LEDs in one package, and the right LED package contains one LED.

10 As used herein, the "about" refers to $\pm 5\%$ of the specified value.

While illustrative embodiments have been illustrated and described, it will be appreciated that various changes can be made therein without departing from the spirit and scope of the invention.

CLAIMS

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A method for selectively activating S cones and L+M cones in a human retina, comprising:

(a) exposing a human retina to a first multi-band light consisting of a first band having a peak emission at 430 nm and a second band having a peak emission at 565 nm; and

(b) exposing the human retina to a second multi-band light consisting of a first band having a peak emission at 485 nm, a second band having a peak emission at 565 nm, and a third band having a peak emission at 630 nm.

2. The method of Claim 1, where exposing the retina to the first multi-band light and the second multi-band light comprises alternating exposure to the retina at a frequency from about 10 to 30 Hz.

3. The method of Claim 1, where exposing the retina to the first multi-band light and the second multi-band light comprises exposure to one or more light sources emitting the first multi-band light and exposure to one or more light sources emitting the second multi-band light.

4. A method for regulating the phase of circadian rhythm in a subject, comprising:

(a) exposing a subject's retina to a first multi-band light consisting of a first band having a peak emission at 430 nm and a second band having a peak emission at 565 nm; and

(b) exposing the subject's retina to a second multi-band light consisting of a first band having a peak emission at 485 nm, a second band having a peak emission at 565 nm, and a third band having a peak emission at 630 nm.

5. The method of Claim 4, where exposing the retina to the first multi-band light and the second multi-band light comprises alternating exposure to the retina at a frequency from about 15 to about 19 Hz.

6. The method of Claim 4, where exposing the retina to the first multi-band light and the second multi-band light comprises exposure to one or more light sources emitting the first multi-band light and exposure to one or more light sources emitting the second multi-band light.

7. The method of any one of Claims 4-6, wherein the subject's retina is exposed to the first multi-band light and the second multi-band light for about 15 to about 60 minutes per day.

8. The method of any one of Claims 4-7, wherein the phase of circadian rhythm is determined by measuring the subject's saliva melatonin levels.

9. The method of Claim 8, wherein the subject's saliva melatonin levels are measured before and 12 hours after exposure to the first multi-band light and the second multi-band light.

10. A lighting device, comprising two light sources:

- (a) a first light source that emits a first band of light having a peak emission at 430 nm; and
- (b) a second light source that emits a second band of light having a peak emission at 565 nm.

11. The lighting device of Claim 10, wherein the first and second bands of light are emitted from a single point source.

12. The lighting device of Claims 10 or 11, wherein the lighting device has a luminosity flux from about 200 to about 5000 lumens.

13. A lighting device, comprising three light sources:

- (a) a first light source that emits a first band of light having a peak emission at 485 nm;
- (b) a second light source that emits a second band of light having a peak emission at 565 nm; and
- (c) a third light source that emits a third band of light having a peak emission at 630 nm.

14. The lighting device of Claim 13, wherein the first, second, and third bands of light are emitted from a single point source.

15. The lighting device of Claims 13 or 14, wherein the light device has a luminosity flux from about 200 to about 5000 lumens.

16. A lighting device, comprising four light sources:

(a) a first light source that emits a first band of light having a peak emission at 430 nm;

(b) a second light source that emits a second band of light having a peak emission at 565 nm;

(c) a third light source that emits a third band of light having a peak emission at 485 nm; and

(d) a fourth light source that emits a fourth band of light having a peak emission at 630 nm.

17. The lighting device of Claim 16, wherein the first, second, third, and fourth bands of light are emitted from a single point source.

18. The lighting device of Claims 16 or 17, wherein the light device has a luminosity flux from about 200 to about 5000 lumens.

19. A lighting system, comprising:

(a) a first lighting device, comprising two light sources,

(i) a first light source that emits a first band of light having a peak emission at 430 nm, and

(ii) a second light source that emits a second band of light having a peak emission at 565 nm; and

(b) a second lighting device, comprising three light sources:

(i) a first light source that emits a first band of light having a peak emission at 485 nm;

(ii) a second light source that emits a second band of light having a peak emission at 565 nm; and

(iii) a third light source that emits a third band of light having a peak emission at 630 nm.

20. The lighting system of Claim 19, comprising two or more first lighting device and two or more second lighting devices.

21. The lighting system of Claims 19 or 20, comprising about the same number first lighting devices and second lighting devices.

22. The lighting system of Claim 19, wherein L+M cone activation is kept constant between the first and second lighting devices and only activation of S-cones is temporally modulated between first and second lighting devices.

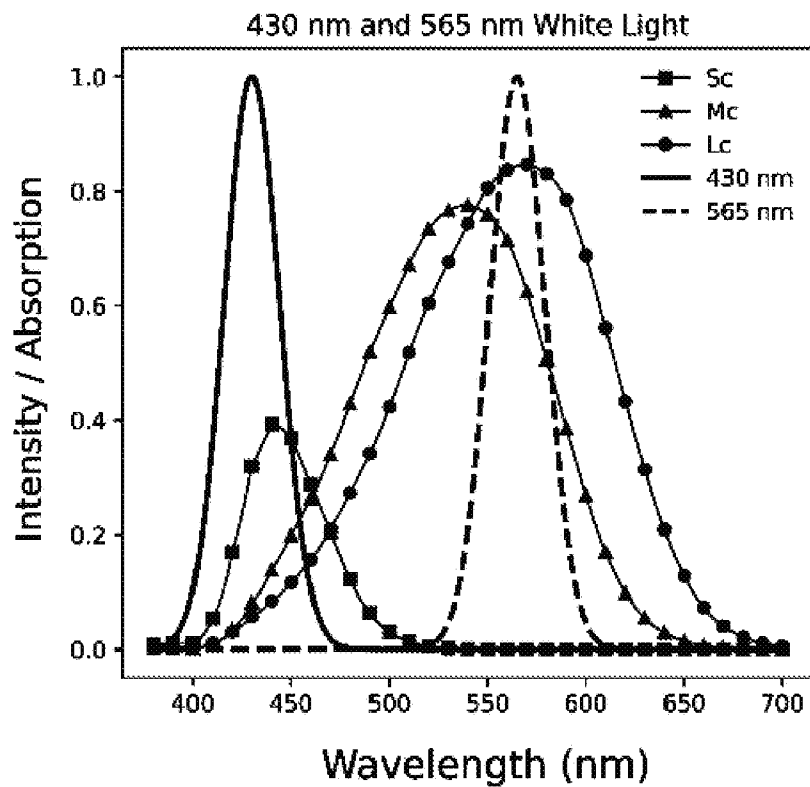
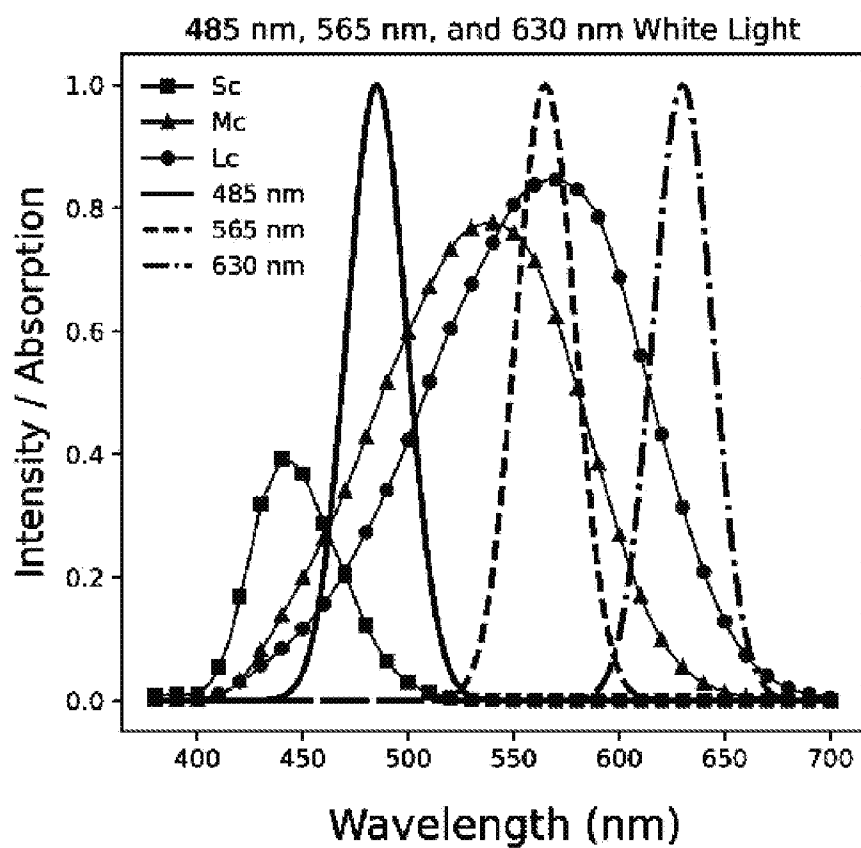
23. The lighting system of Claim 19, wherein (S+M)-L cone activations are kept constant between the first and second lighting devices.

24. The lighting system of any one of Claim 19-23, wherein the system is deployed in a low natural light environment.

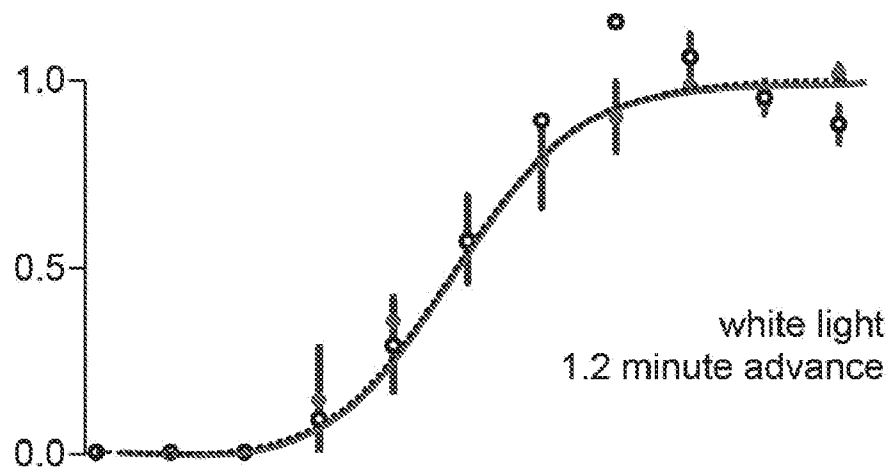
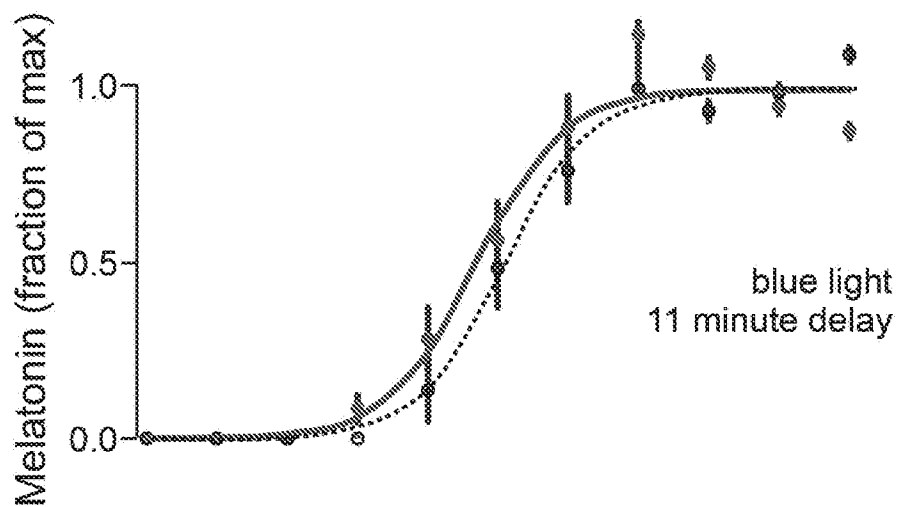
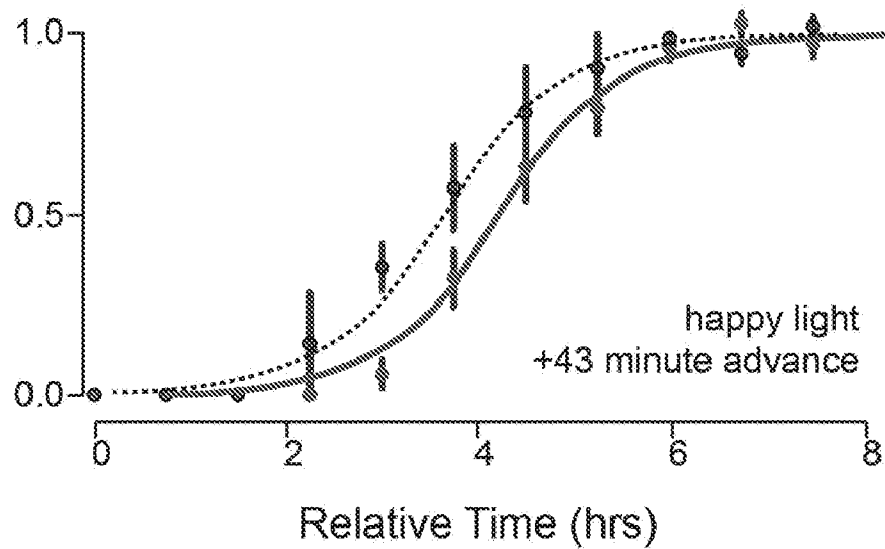
25. The lighting system of any one of Claim 19-23, wherein the system is deployed in an environment of a human subject in need of a phase shift to regulate the subject's circadian rhythm.

26. A method for selectively activating S cones and L+M cones in a human retina using the lighting system of any one of Claims 19-23.

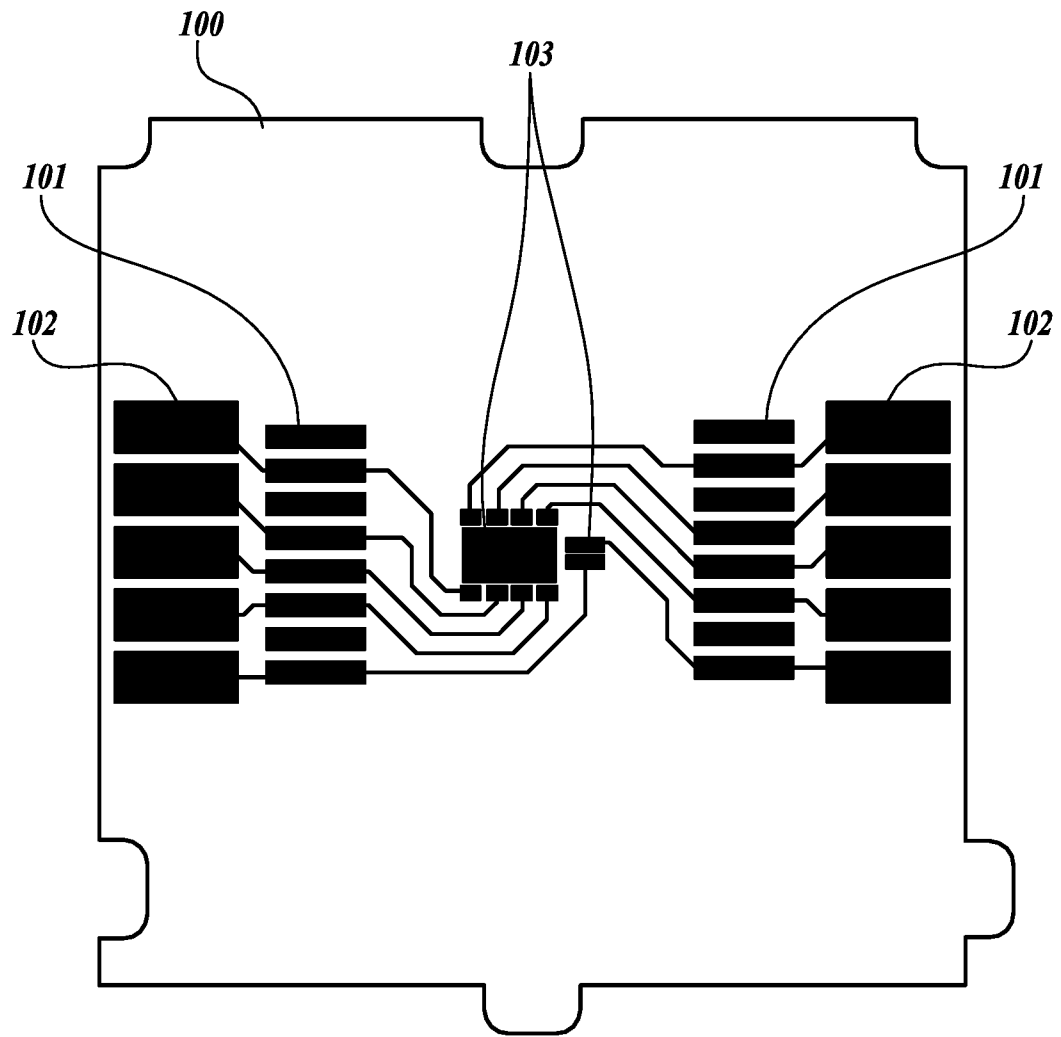
27. A method for regulating the phase of circadian rhythm in a subject using the lighting system of any one of Claims 19-23.

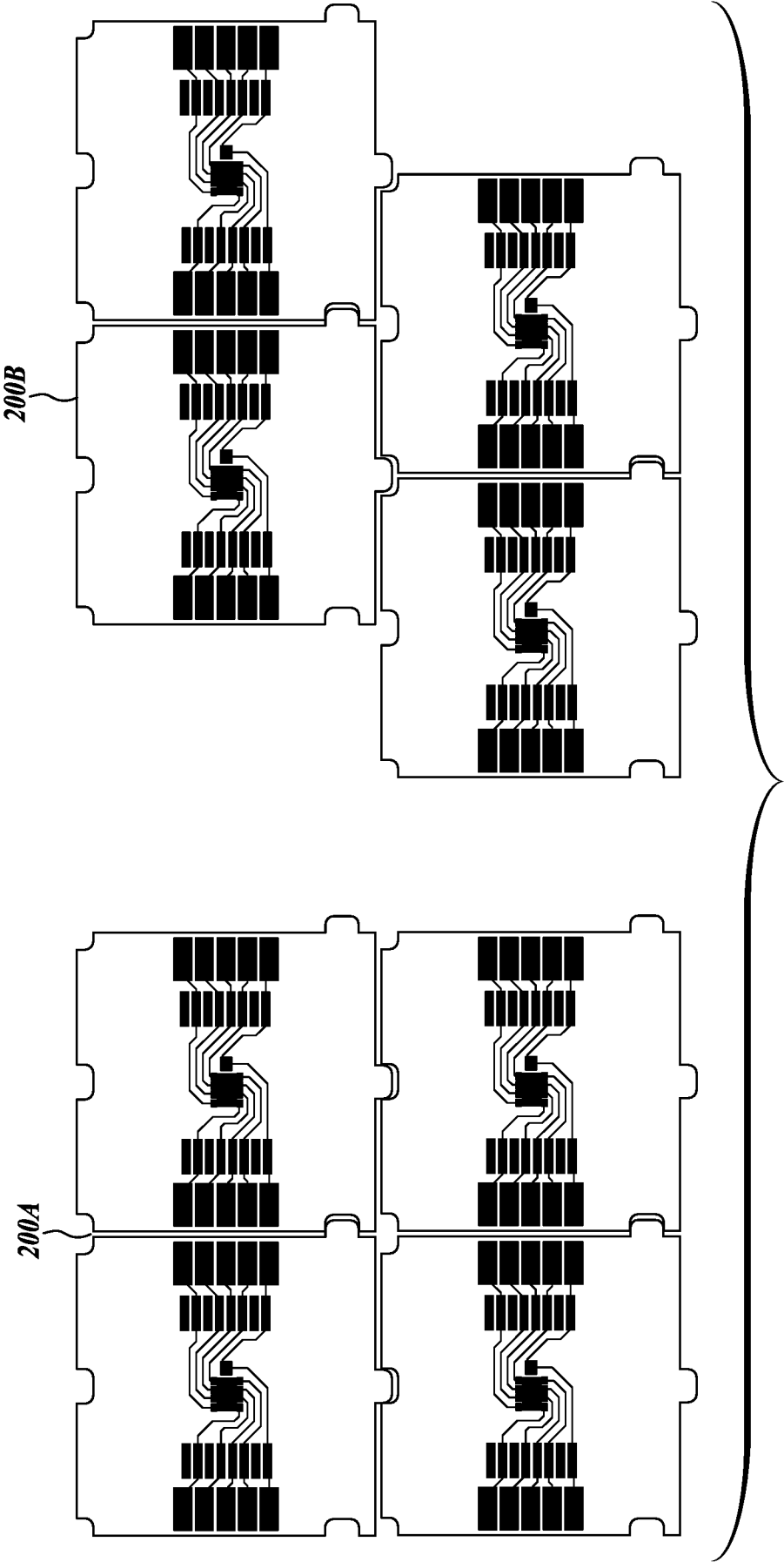
1/6**FIG. 1A****FIG. 1B**

2/6

**FIG. 2A****FIG. 2B****FIG. 2C**

3/6

**FIG. 3A**



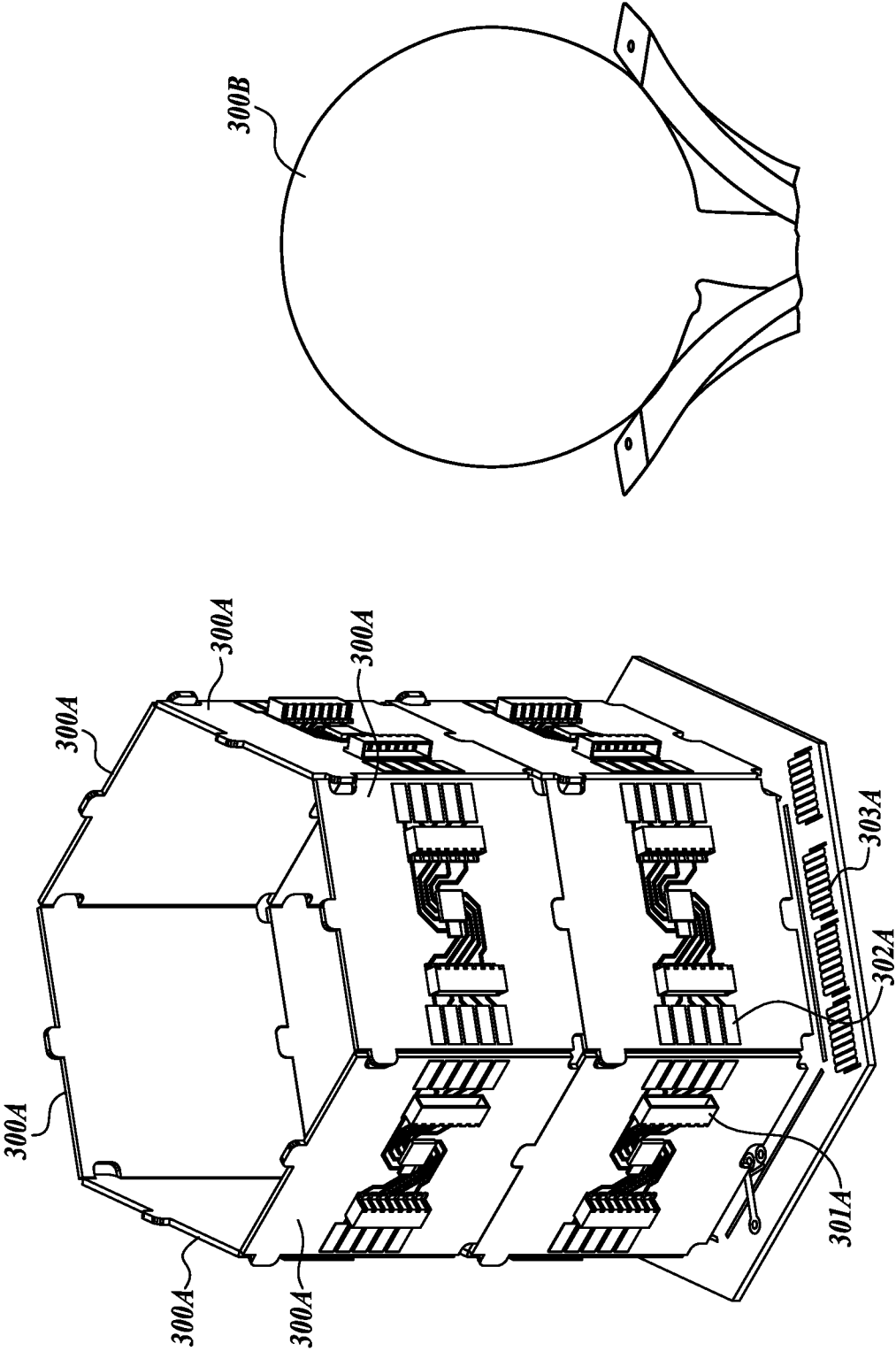


FIG. 3C

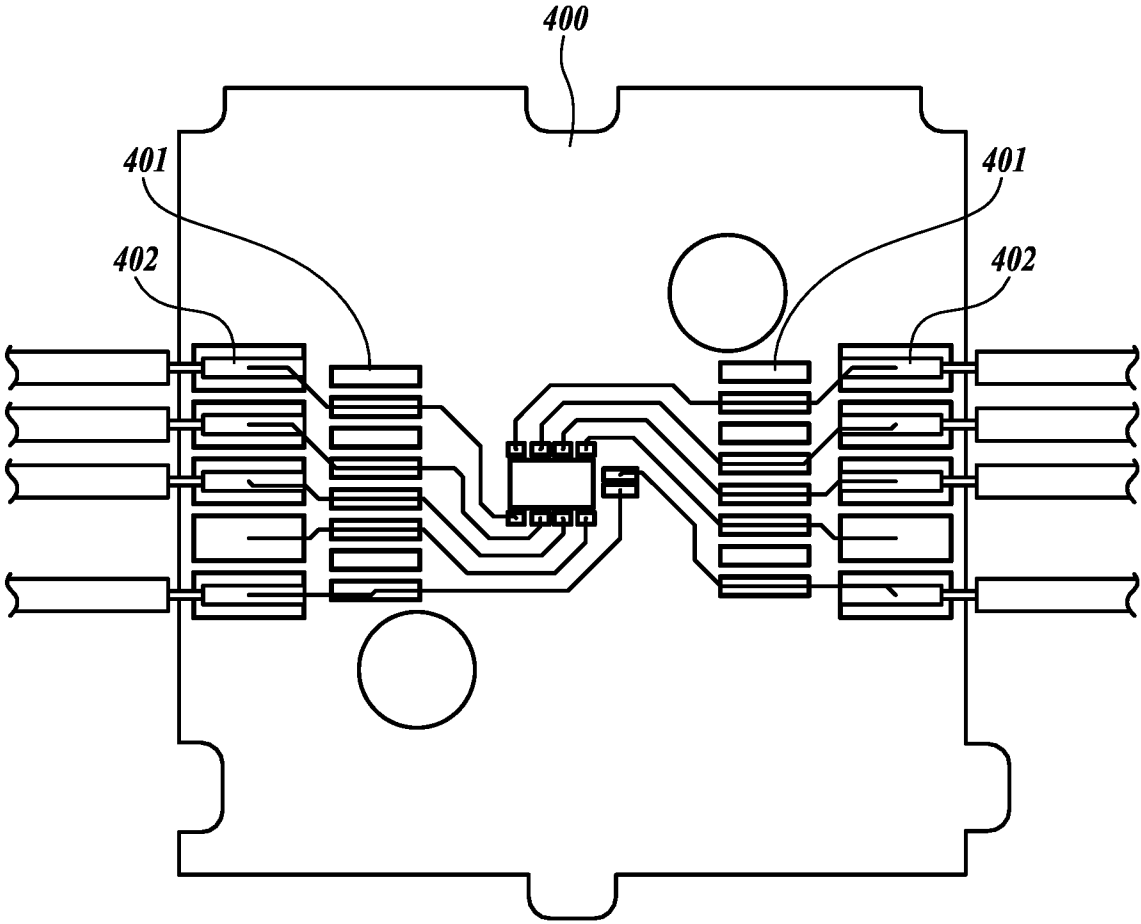


FIG. 3D

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2020/033844

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - F21V 9/02; F21V 9/00; F21V 9/40; F21V 99/00 (2020.01)

CPC - F21V 9/02; F21V 9/00; F21V 9/40; F21V 99/00 (2020.05)

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

R. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

see Search History document

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

see Search History document

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

see Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---	WO 2018/212819 A1 (PAULSEN et al) 22 November 2018 (22.11.2018) entire document	10 ---
Y		1-7, 11-21
Y	US 4,176,299 A (THORNTON, JR.) 27 November 1979 (27.11.1979) entire document	1-7, 13-21
Y	Crowley, et al. Phase advancing human circadian rhythms with morning bright light, afternoon melatonin, and gradually shifted sleep: can we reduce morning bright light duration? Sleep Med. February 2015. [Retrieved 27 July 2020]. Retrieved from internet: < https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4344919/pdf/nihms650769.pdf > entire document	7
Y	US 2017/0238401 A1 (INNOSYS, INC.) 17 August 2017 (17.08.2017) entire document	11, 14, 17
Y	US 2014/0306620 A1 (BIOLOGICAL ILLUMINATION, LLC) 16 October 2014 (16.10.2014) entire document	12, 15, 18

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"D" document cited by the applicant in the international application

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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

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

"&" document member of the same patent family

Date of the actual completion of the international search

29 July 2020

Date of mailing of the international search report

23 SEP 2020

Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2020/033844

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 8, 9, 24-27
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.