https://doi.org/10.1038/s41586-018-0706-x

LEDs for photons, physiology and food

P. M. Pattison[1]*, J. Y. Tsao[2], G. C. Brainard[3] & B. Bugbee[4]

Lighting based on light-emitting diodes (LEDs) not only is more energy efficient than traditional lighting, but also enables improved performance and control. The colour, intensity and distribution of light can now be controlled with unprecedented precision, enabling light to be used both as a signal for specific physiological responses in humans and plants, and as an efficient fuel for fresh food production. Here we show how a broad and improved understanding of the physiological responses to light will facilitate greater energy savings and provide health and productivity benefits that have not previously been associated with lighting.

Light is central to the biological history of our planet, both as a fuel for photosynthesis and as an environmental signal. As a fuel for photosynthesis light produces adenosine triphosphate, the universal energy currency of plants and animals. Sunlight powered the life whose fossilized remains have been human energy currency for the past two centuries, and it powers the photovoltaic- and wind-generated electricity that will become the energy sources of the future. As a signaller, light carries much of the information that enables life to adapt to its environment, and improved ability to receive that information is responsible for numerous evolutionary adaptations[1,2]. The importance of visible-light signalling for humans is demonstrated by three observations: the exquisiteness of the eye as an optical instrument; the large fraction (half) of the human brain devoted to visual signal processing; and our extreme dependence on vision technologies, such as eyeglasses[3]. Light also regulates human circadian, neuroendocrine and neurobehavioural physiology[4,5], and has an even greater effect on plants, which have more photoreceptors to process light than do humans. The importance of light as fuel and as a signaller rendered traditional lighting essential to human civilization for basic illumination; LED lighting, with its greater level of engineering control, might trigger a new world of applications.

Light for basic illumination

Lighting was among the earliest of human technologies. It expands the productive day into non-sunlit hours[6], and during the day it expands the productive space into the non-sunlit areas of enclosed spaces[7]. As illustrated in Fig. 1a, lighting technology has undergone successive fundamental improvements over the centuries, from chemical-fuel-based to vacuum-based electric lighting, culminating now in LED-based solid-state lighting[8,9].

As short an historical time as electric lighting has been available, on the horizon now are the outlines of a superior technology for basic illumination: LED-based solid-state lighting. The phosphor-converted light-emitting diode (PC-LED) approach is currently the most prevalent. A highly efficient blue LED is combined with optical down-converters, typically phosphors, which absorb a portion of the blue light and emit longer wavelengths to produce white. PC-LED white lighting has made such great progress in terms of lighting performance, efficiency and cost that there is little doubt that it will soon become the source of almost all electric lighting. This progress, which was triggered by foundational breakthroughs in the synthesis of AlInGaN semiconductors (for which the Nobel Prize in Physics was awarded[10] in 2014), is illustrated[11] in Fig. 1b. Among the key advances were the uniform and controlled epitaxial growth of InGaN LEDs by metal–organic chemical vapour deposition; thin-film flip-chip[12] and other device designs with high electrical and optical efficiencies; and robust high-quantum-yield phosphors emitting in the green–yellow and red regions of the spectrum.

LED lighting products not only use less energy and have a lower cost of ownership than other lighting technologies, but they can also possess other features that are of importance to human use of basic white-light illumination: desirable colour qualities (for example, colour rendering index and correlated colour temperature), minimal or no flicker, long life, and negligible environmental and human toxicity. The three main benefits of LED lighting are therefore a decrease in electricity consumption, a reduced cost of ownership, and improvements in lighting quality. The decrease in electricity consumption is huge because human society consumes so much electric light: around 6.5% of total global primary energy[13] was used for lighting in 2005. It is forecast[14] that in the United States alone LEDs will penetrate around 86% of electrical lighting installations by 2035, decrease electricity consumption for lighting by around 75% and save approximately 5.1 quadrillion British thermal units (5.1 quads) per year (around US$52 billion per year) in direct energy cost.

Engineered light

Even with this remarkable progress, LED lighting is only in its infancy. The historic purpose of all lighting technologies has been to provide basic illumination for visibility and vision. We now stand at the threshold of what might be called 'engineered light', in which building blocks of solid-state lighting are combined for integrated functionality beyond basic human illumination[15,16]. Four features will be especially important.

The first is spectral control. LED lighting originates in efficient narrowband blue-light emission from a semiconductor LED. This blue light can be combined with green–yellow and red optical down-converters to create various hues of white light, or with other direct-emitting LEDs (Fig. 2a, c). For the first time in history, spectral content can be customized for a wide range of applications, each with its own action spectrum. For basic illumination, the spectra can be engineered to match the human photopic visual response (the solid green curve in Fig. 2b). It can also be engineered for qualities including colour rendition, colour gamut and correlated colour temperature, and thus for controlled rendering of colours and various human visual preferences. For human health and productivity, as discussed later in this Perspective, the spectra can be engineered—as illustrated by the intrinsically photosensitive retinal ganglion cell bodies (ipRGCs) curve in Fig. 2b—for potent stimulation of ocular photoreceptors that regulate human circadian, neuroendocrine and neurobehavioural responses.

[1]SSLS, Inc., Johnson City, TN, USA. [2]Sandia National Laboratories, Albuquerque, NM, USA. [3]Thomas Jefferson University, Philadelphia, PA, USA. [4]Utah State University, Logan, UT, USA.
*e-mail: morgan@sslsinc.com

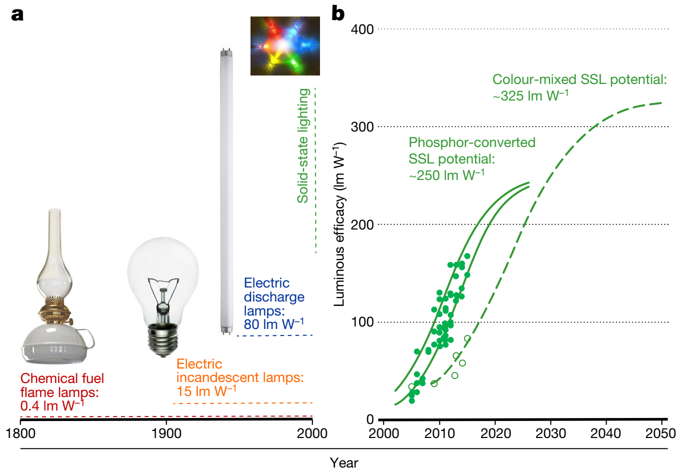

Fig. 1 | The history of lighting technology. a, The history of lighting. Chemical-fuel-based lighting was the earliest lighting technology. This was followed by electric lighting, which ushered in the modern era of electricity. Incandescent lamps, so widespread by the early twentieth century that they have now been taken for granted for generations, are an order of magnitude brighter and more efficient than gas lights. The incandescent lamp greatly reduced the volume of material that heats and emits light, thus enabling extremely high temperatures, shifting the spectrum of the black-body radiation from the infrared towards the visible. Electric discharge lamps, based on light emission from excited electronic states in controlled gas plasmas, are even more efficient—five times more so than incandescent lamps. Solid-state lighting reaches higher efficiencies still, with substantial increases expected in the future. Photo of six-colour LEDs courtesy of E. F. Schubert. **b**, Historical and projected luminous efficacies of solid-state lighting. In the past decade, luminous efficacy has tripled, from 40–60 lm W^{-1} to 140–160 lm W^{-1}, with even larger decreases in cost; in the coming decade, 325 lm W^{-1} is potentially achievable. Filled circles and solid lines, phosphor-converted LEDs; open circles and dashed line, colour-mixed LEDs; data from ref. [19].

For plants, also discussed later, the spectra can be engineered to stimulate photobiological responses that alter plant shape, increase photosynthesis and enhance nutritional value (Fig. 2d).

The second important feature of LED lighting is the precise control of the intensity of the light. Semiconductor LEDs are current-driven devices, the intensity of which can be precisely controlled across their operating range and modulated over a large range of frequencies. At the high (GHz) end of these rates, the modulation can be used for free-space visible-light communication (Li-Fi), possibly to alleviate the congestion and bandwidth limitations of Wi-Fi. In the medium range (kHz), pulse-width-modulation-controlled flicker-free dimming could help to match in real time the brightness of an illuminated scene with human visual preference. At the low (seconds–hours–days) end of these rates, modulation can be used to ensure that photons are emitted only when human eyes are available to perceive them, or to match natural, diurnal or seasonal lighting conditions.

The third feature is the control of distribution in space. Semiconductor LEDs emit light from extremely small areas and have low etendue. As such, they can be optically imaged in space with great precision or coupled efficiently into transparent waveguides with complex light-scattering surfaces. Semiconductor LEDs can also be easily arrayed and, through individual addressing and control, create pixelated 'super beams', the shapes of which are digitally controlled like a projection display.

The fourth important feature of LED lighting is its ready integration with other technologies. At the chip-and-package level, examples could include semiconductor technologies such as drivers; wireless and wired communication chips; photo, image, chemical, temperature or humidity sensors; and microprocessor and memory chips for local intelligence. At the luminaire level, other technologies could include acoustic transducers (microphones and speakers), radar- and lidar-based three-dimensional scene mappers, and occupancy sensors to enhance the functionality of the lighting products. Perhaps most importantly, such integration enables lighting that is 'connected' to the Internet of Things. Connected lighting makes use of luminaires and light fixtures as the most ubiquitous of all grid-connected appliances. Connectivity enhances the fundamental benefits of LED lighting by enabling lights to sense and respond to their environment and communicate the conditions or their status. Having sensors available everywhere a light fixture is available could allow for an unprecedented degree of spatially and temporally resolved information communicated to the Internet of Things[17], enabling new applications and advancing human productivity and safety. Even within a single building, connected controls can provide information on room utilization, improving our ability to load-schedule heating, cooling, lighting and other appliances in buildings. Such load scheduling will only grow in importance as the world's energy economy continues to electrify via renewable but intermittent sources (for example, solar and wind)[18].

These four features are catalysing a new world of engineered lighting that goes well beyond basic illumination. Although not without challenges[19], research in laboratories worldwide will continue to make these features more powerful and more affordable. They can then be combined in new ways to add value to society that is even greater than just the energy savings. We highlight two of the most important ways below.

Lighting for human health and productivity

Basic illumination enables humans to see via their primary optical tract, and hence permits productivity indoors and/or at night when sunlight is unavailable. It is now known that the primary optical tract is only one of two photoreceptor pathways between the eye and the brain. The second, illustrated in Fig. 3, is the retinohypothalamic tract, which has a primary role in supporting the light regulation of human circadian, neurobehavioural and neuroendocrine responses[4,5,20], and ultimately impacts human health and productivity.

Scientists have only recently been able to delineate the photoreceptive input to the circadian and neuroendocrine systems. In 2001, two analytical action spectra identified 446–477 nm as the most potent region for acute melatonin suppression in healthy human subjects[21,22]. Other complete analytical action spectra and studies that used selected-wavelength comparisons further indicated that circadian-phase shifting, autonomic stimulation, and the acute effects of light on alertness and performance are shifted towards the shorter wavelength—or blue-appearing—part of the visible spectrum[4,5,23]. Taken together, these results indicated that a novel ocular photosensory system, distinct from the canonical rods and cones of the visual system, is primarily responsible for regulating physiology and behaviour in humans.

At the front end of the retinohypothalamic tract is a small population of widely dispersed ipRGCs that are directly responsive to light via a vitamin A photopigment named melanopsin[24–28]. These then project through the retinohypothalamic tract to the paired hypothalamic suprachiasmatic nuclei, as well as to a number of other nuclei involved in regulating physiology and behaviour[25,27,29]. The suprachiasmatic nuclei are master oscillators in the circadian system that transmit information about lighting and circadian time to diverse loci in the nervous system, including to the pineal gland where the hormone melatonin is synthesized[4,5]. This circadian pacemaker thus synchronizes the systems of sleep- and arousal-promoting neurons in the central nervous system, and in turn the daily rhythms of sleep and wakefulness, body temperature, alertness, psychomotor performance, neurocognitive responses, and the secretion of hormones such as melatonin and cortisol[4,5,20,30].

In humans, the alerting effects of light have been assessed by subjective self-report, as well as with objective electroencephalogram measures, recordings of slow eye movements and vigilance tests[30–38]. Exposure to bright white light, as well as short-wavelength monochromatic light, has been shown to acutely enhance both subjective and objective measures of alertness[35–41]. Similarly, light stimuli can enhance human performance in terms of psychomotor vigilance and neurocognitive responses such as cognitive throughput, sustained attention

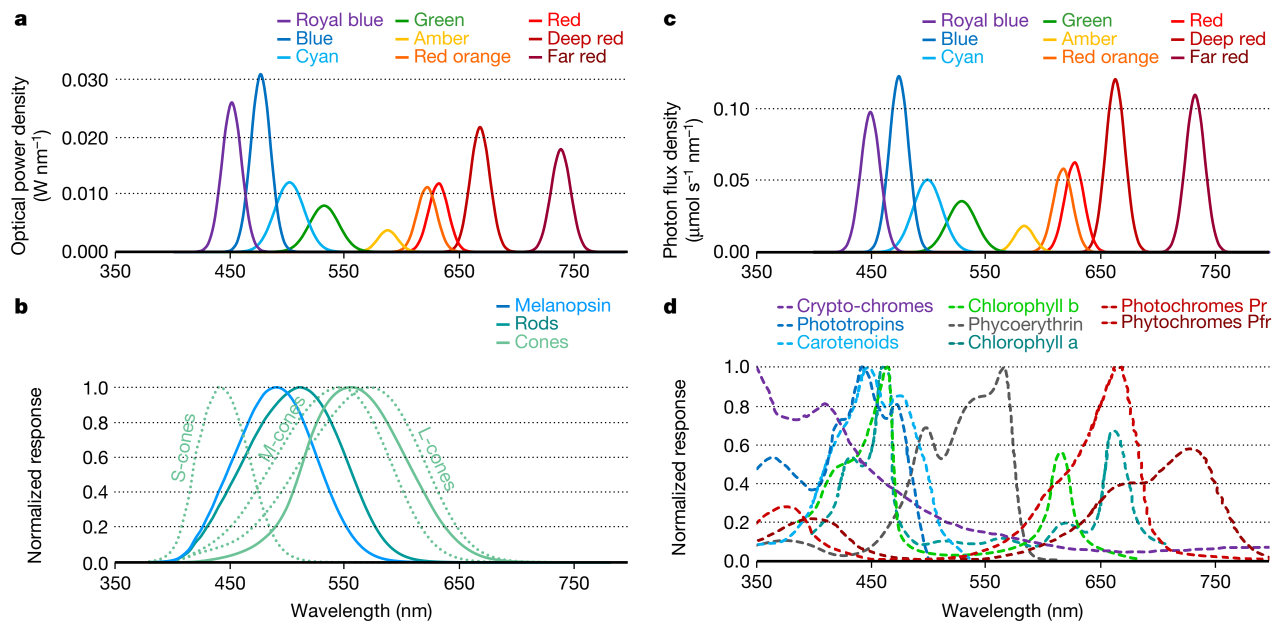

Fig. 2 | LED emission, human response and plant response spectra. **a**, Optical power distributions (obtained from ref. [92]) plotted against wavelength for state-of-the-art direct-emitting LEDs (driven at 1 W) that span virtually the entire visible spectrum, although currently with reduced efficiency in the green–amber–orange region. **b**, Human photoreceptor action spectra associated both with the primary optical tract (rods and cones, where S, M and L indicate short, medium and long wavelength) and with the intrinsically photosensitive ipRGCs at the start of the retinohypothalamic tract. Action spectra reproduced from supplementary workbook in ref. [4]. **c**, Photon flux distributions (obtained from ref. [92]) plotted against wavelength for state-of-the-art direct-emitting LEDs (driven at 1 W). Note the shift in the peak heights, compared to those in **a**, as the wavelength increases. Blue photons have higher energy than red photons, according to the Planck relation ($E = hc/\lambda$, where E is the energy, h is the Planck constant, c is the speed of light in vacuum and λ is the wavelength). **d**, Plant action spectra associated with the primary classes of photosensitive molecules in plants. Action spectra for the cryptochromes are not yet well established. Action spectrum for phycoerythrin from ref. [93]. All other plant action spectra from ref. [94].

and aspects of memory[34–41]. Not all studies, however, have found a consistent light-induced enhancement of all measures of alertness and neurocognitive responses[39–41].

Beyond alertness, a group of studies have shown that light is a regulator of many other aspects of human physiology and behaviour, and has therapeutic capacity in clinical applications such as the treatment of winter depression and selected sleep disorders[4,5,42,43]. Light therapy has been evaluated in, and is increasingly recommended for, healthy individuals who experience problems related to shift work, intercontinental jet travel and space flight[4,5,44]. A maxim for optimizing circadian regulation is increased light exposure at the beginning of and during the wake cycle, and decreased light exposure before sleep. However, many open questions remain regarding the detailed physiology of the contributing photoreceptor system and how it influences specific human neurobehavioural responses.

A first open question concerns the nature of the detailed pathways within the melanopsin-based photoreceptor system. This system is both anatomically complex at the level of the retina as well as physiologically complex in terms of regulating neural targets in the brain. All retinal photoreceptors contribute to the regulation of biological and behavioural responses to light, but the relative importance of each photoreceptor is highly labile within and between types of physiological and behavioural responses. Furthermore, the responsiveness of this photoneural system to the wavelength and the intensity of the light is fundamentally context-dependent[4,33,45–47].

A second open question considers the interactions between the retino-hypothalamic and primary optical tracts. In one direction, studies with rodents and non-human primates provide compelling evidence that ipRGCs also anatomically project to nuclei of the visual system and physiologically contribute to aspects of visual processing and image detection[4,29,48–52]. A number of studies with blind and normally sighted human subjects support a role of the melanopsin photoreceptor system in contributing to visual responses in humans[53–56]. In the other direction, studies on rodents, monkeys and humans clearly show that the visual rod and cone photoreceptors are anatomically and functionally interconnected with the ipRGCs[4,33,48–50,56]. Furthermore, there are several subtypes of ipRGCs with diverse connectivity to cells in the inner retina and differing projections to the nuclei in the brain[49,52,57–59]. We note that even the pupillary light reflex—a seemingly simple interaction between the two retinal tracts—is more complex than it appears. In all species studied, including humans, the pupillary light reflex is a rapid response of the iris to light exposure. Rodent and non-human primate studies demonstrate direct neural projections from the ipRGCs to the nuclei in the midbrain that regulate this reflex[4,27,29]. Although this reflex is dominated by melanopsin phototransduction in the ipRGCs, the rods and cones also contribute to pupillary responses, particularly at lower light levels[4,46]. Despite the direct ipRGC projection to the midbrain nuclei, elements of the pupillary light reflex exhibit diurnal rhythms.

A third open question concerns the relationship between the dose of light and physiological regulation in everyday environments. From the light-stimulus side, there are four relevant physical-exposure variables: light intensity, light spectrum, stimulus duration and stimulus timing; all of these variables are fundamentally context-dependent. These variables also depend on elements of ocular and neural physiology involved in light transduction for regulation of the human circadian, neuroendocrine and neurobehavioural systems, including conscious and reflex behaviour of the head and eyes relative to the light source; transmission of light through the ocular media; transduction of light through the iris and/or pupil; wavelength sensitivity of photoreceptors; distribution of photoreceptors; state of photoreceptor adaptation; and neural ability to integrate stimuli temporally and spatially. Controlled laboratory studies have elucidated how each element can contribute to the efficacy of a photic stimulus in eliciting a physiological or behavioural response[23,60]. There are fewer studies, however, that characterize the efficacy of lighting for physiological regulation under daily living conditions, in which people move freely about an environment that is lit by a combination of different electrical illuminants, window light and outdoor sky lighting.

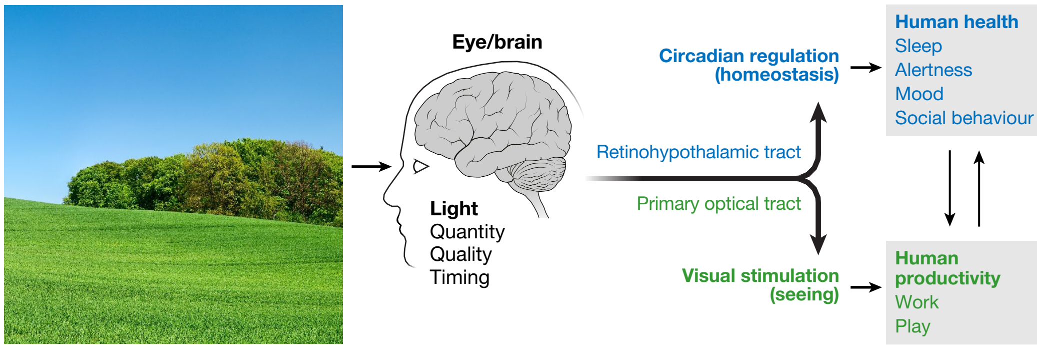

Fig. 3 | The two photoreceptor pathways between the human eye and the brain. The primary optical tract (green text) originates in the retinal rods and cones. Cone photoreceptors in the fovea provide higher-light-level photopic colour vision with a peak sensitivity in the green at a wavelength of approximately 555 nm, the colour of green foliage; rod photoreceptors provide the lower-light-level scotopic black, grey and white vision with a peak sensitivity at about 498 nm. The retinohypothalamic tract (blue text) originates with ipRGCs, the peak sensitivity of which is at about 480 nm, approximately the colour of the blue sky. This regulates the circadian, neuroendocrine and neurobehavioural systems that ultimately impact human health and productivity. Photograph from iStock/Getty.

A fourth open question asks how to frame our understanding of the positive and negative effects of light[4,5]. A basic concept of modern medicine is that agents that have the capacity to heal also potentially have the capacity to harm. Dysregulation of circadian physiology by inappropriate light exposure has been linked to several diseases and disorders. For example, epidemiological evidence indicates an association between breast and prostate cancer risk and shift work[61–63]. Shift work typically involves routine light exposure during the night time that can suppress nocturnal melatonin secretion, disrupt circadian entrainment and interfere with healthy sleep[61]. Empirical data with human tumorigenesis supports the epidemiological observations at least for breast cancer[64]. In 2007, such lines of evidence led the World Health Organization to identify long-term shift work as a probable cause of cancer[65]. Similar to the growing information on cancer risk, there is both epidemiological and empirical evidence that circadian disruption and circadian desynchrony contributes to cardiovascular disease, metabolic syndrome, diabetes, obesity and gastrointestinal disorders[66–71]. It is important to note, however, that there are limitations to the developing science related to the adverse health consequences of night-time light exposure. For example, it is not clear whether circadian disruption due to inappropriate light exposure alone increases the risk of developing cancer, cardiovascular disease or metabolic disorders. Disruption of the human circadian system usually involves disruption of sleep and/or the disruption of normal melatonin rhythms[61]. Sleep deprivation and nocturnal melatonin suppression have each been implicated in the potential health consequences associated with shift work and light exposure at night[61,65,67,69–71]. Despite such uncertainties it is noteworthy that, in 2012, the American Medical Association published a position statement on the adverse health effects of night-time lighting. Specifically, they identified a need for "further multidisciplinary research on occupational and environmental exposure to light-at-night, the risk of cancer, and effects on various chronic diseases"[72].

In parallel with research efforts to answer the above open questions, LED lighting is already being actively used in clinical and non-clinical applications. In clinical applications bright-white light therapy, which has been used since the 1980s, has proven to be an effective therapeutic intervention for patients with seasonal affective disorder (known as SAD or winter depression) and its subclinical variant, sSAD[42,43]. Additional clinical applications have been explored, including light treatment of non-seasonal depression, various sleep disorders, menstrual cycle problems, bulimia nervosa, and fatigue problems associated with senile dementia, chemotherapy and traumatic brain injury[4,5,42,43]. With the advent of LED lighting technology, therapeutic lighting devices are now being produced in which both broad and narrow bandwidths of light are emitted by LEDs. This advance has enabled light therapy equipment for clinical applications to be produced in conventionally sized light panels as well as relatively small, portable or wearable devices[60].

In non-clinical applications, light therapy has been evaluated for healthy individuals who experience problems related to shift work, intercontinental jet travel and space flight[4,5,42–44]. For example, NASA (National Aeronautics and Space Administration) has used bright white fluorescent-light treatment for improving sleep and fatigue in astronauts since 1990[73,74]. In 2007, the Phoenix Mars Lander mission provided an opportunity to test the feasibility and efficacy of LED light therapy to synchronize the circadian systems of operational ground personnel to a Mars sol of 24.6 h. Measures of circadian period demonstrated that, as part of a fatigue-management programme, timed therapy with solid-state light enabled 87% of participants to adapt to the Mars sol[75]. More recently, both ground-based and in-flight studies on the International Space Station have been testing LED luminaires for supporting vision and improving circadian entrainment, alertness and sleep in astronauts[44,76]. Compared with conventional fluorescent light sources, the advantages of LEDs that are of particular relevance to space flight include their reduced weight, power consumption and heat generation; in addition, the LEDs have a tunable spectrum, comprise fewer toxic materials, and have greater resistance to damage and a longer operational life. To date, more than half of the fluorescent light fixtures on the United States' portion of the International Space Station have been replaced with LED light assemblies that have three preset spectrum and intensity modes: general vision, alerting/circadian phase shifting, and pre-sleep.

Looking forward, there is clearly a growing interest in encouraging the development of LED lighting technologies that have the capacity to improve health, performance and well-being for healthy people in all lighting applications. As discussed above, the effects of light on enhancing alertness as well as improving cognitive and psychomotor responses may lead to advanced, daytime solid-state lighting technologies for schools, workplaces, public buildings, and almost any place that uses electric lighting. Relevant to evening and night-time lighting, a recent study compared standard fluorescent-light fixtures to solid-state sources set to an intensity typical of bedroom lighting in terms of biological and behavioural efficacy. Compared to the fluorescent light, solid-state light evoked a greater secretion of evening melatonin and reduced measures of alertness in healthy subjects, thus physiologically preparing the body for sleep[39]. Studies like this open the door for the development and application of LED-based lighting systems to benefit individuals in hospitals, care facilities and residential environments. For the general population of relatively healthy individuals, the ubiquity of electric light in the built environment provides an opportunity to tailor the lighting for individually modest health and productivity benefits that are significant when aggregated across the entire population. For healthy, at-risk (elderly, night shift, jet lag) and infirmed or recovering

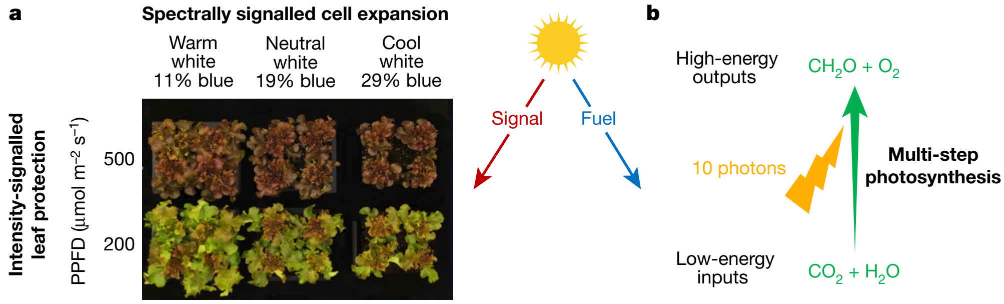

Fig. 4 | Light has both direct and indirect effects on plants. a, The indirect effect is a signal that directs plant shape, cell expansion and colour (photomorphology). The lettuce cultivar in this example is Red Salad Bowl. Light intensity triggers the synthesis of anthocyanin (red) pigments in the leaves as a protectant: a photosynthetic photon flux density (PPFD) of 200 (10% of full sunlight) was insufficient, but a PPFD of 500 (25% of full sunlight) triggered anthocyanin synthesis. The wavelength of the light affects leaf expansion: as the fraction of blue light increases (as the colour temperature shifts from warm to neutral to cool white), leaf expansion decreases. **b**, The direct effect of photons as a fuel for photosynthesis and plant growth (dry mass). Ten photons (400–700 nm) is the approximate theoretical minimum number of photons to fix one molecule of CO_2 into carbohydrate. Photosynthesis includes multiple steps (roughly 23) that turn low-energy inputs into high-energy outputs. The theoretical maximum efficiency of the process is 30%, with each individual step being about 95% efficient ($0.95^{23} \approx 0.3$).

populations, the new features of LED lighting have the potential to improve wellbeing and quality of life, provided that the fundamental questions discussed in this section can begin to be answered in order to guide specific technology and product development of LED light sources.

Lighting for plants

Plants are sentient organisms and have evolved an exquisite sensitivity to ultraviolet, photosynthetic and near-infrared radiation in their environment[77,78]. The responses of plants to light have fascinated observers since the early days of the scientific method.

Two hundred years ago, primitive light sources and coloured filters were used to characterize the effect of light colour on stem elongation. Eighty years ago, Hoover[79] found that photosynthesis used a range of wavelengths similar to those of human vision, but with increased sensitivity to blue and red light. Thirty years later, studies by McCree[80] and Inada[81] refined the early studies of Hoover. Using a monochrometer and spectral filters to achieve narrowband radiation, they found that single leaves under monochromatic red light (600–700 nm) had a 25%–35% higher quantum yield than those under blue light (400–500 nm), and a 5%–30% higher quantum yield than those under green light (500–600 nm). It is now known that these classic studies had limitations because they were conducted at low light levels on single leaves. More importantly, the use of monochromatic light did not allow for synergism among wavelengths. LEDs are enabling us to refine these spectral effects on photosynthesis by studying plant communities at higher light levels with synergistic wavelengths.

In the late 1940s, fluorescent lamps made it possible to grow plants without sunlight[82], but by today's standards the electric conversion efficacy was low. In the late 1970s, high-intensity-discharge (high-pressure sodium and metal halide) lighting made it possible to grow plants at intensities comparable to sunlight, but with a fixed spectral output.

These lighting technologies had a limited ability, however, to separately control the intensity, spectrum, and timing of the delivery of photons. Plants respond to light in more ways than do humans, and utilize more than a dozen photoreceptors to direct their growth (Fig. 2d). They live in communities and respond to light reflected from neighbouring plants. The light that reaches lower leaves is filtered by upper leaves. Plants use photons both as a fuel for photosynthesis and as a signal that directs plant shape and leaf colour (plant development) (Fig. 4). Plant shape includes leaf expansion and radiation capture, both of which increase canopy photosynthesis. LED technology is facilitating a fundamental revolution in research into the photobiology of plants. Promising research directions are discussed below.

First is the effect of the wavelength of light on the morphology of plants. It is known that the fraction of blue light has a powerful influence on morphology, but the effect varies across species (Fig. 4) and the mechanisms are not yet understood. Ultraviolet radiation has several beneficial effects on plant growth, including increased cuticle thickness, reduced intumescence[83] and increased secondary metabolism that leads to improved flavour. Ultraviolet radiation also affects the interaction between plants, fungal pathogens and insects[84]. However, these effects also vary across species. Near-infrared radiation (700–780 nm) has a powerful effect on stem elongation and the rate of leaf expansion, but although the primary receptor (phytochrome) is well characterized, significant interactions with other wavelengths are now being discovered.

A second question concerns the value of green light. Because chlorophyll absorbs green light only minimally, many researchers concluded that it was of low value for photosynthesis[85]. However, because it penetrates deeper into leaves and plant canopies, more recent studies have shown that green photons have a similar value in photosynthesis to those of other colours[77,78].

Third, the interaction between the spectrum and the intensity of light (quality and quantity) is also of interest. Early studies with LEDs were performed at a photosynthetic photon flux density (PPFD) of less than 10% of full sunlight (200 μmol m^{-2} s^{-1}), but morphological effects in low light can be reversed at higher light intensities. Blue photons, for example, interact with total PPFD to determine cell expansion (Fig. 4), elongation of the petiole, stem and leaf, and—indirectly via these morphology changes—radiation capture[78].

A fourth research direction investigates the interactions between spectra, intensity and time of exposure (time of day and stage of plant growth). The timing of the delivery of photons can help to understand the photobiological mechanisms and sites of perception. LEDs make it possible to pulse ultraviolet radiation, which can improve flavour and minimize the detrimental effects of ultraviolet radiation on DNA[86].

Finally it is important to scale from monochromatic short-term measurements on single leaves to long-term performance of plant communities. This is particularly challenging and important because plants adapt to changes in radiation by synthesizing new pigments. Changing the quality of the light also alters the shape of the plant, and multiple wavelengths interact synergistically, so defining the effects of the quality of light on photosynthesis of the whole plant and the plant community is a complex enterprise.

Even as these research directions are being pursued, LEDs are being increasingly used in a practical horticultural context. For the first time in history, photons can be precisely applied in order to grow food. Assuming the economics outlined in Box 1, the value of summer sunlight in the mid-latitudes is US$700,000 per hectare over a 100-day growing season, and about US$70,000 per hectare during the darkest 60 days of the year[87]. Although these costs are high, the value of fresh leafy greens that can be produced with supplementary LED lighting

Box 1
Economics of indoor agriculture

Lighting for plants presents unique challenges, because plants require 30–100 times higher light intensities than do humans. Efficient LED lighting reduces the photon cost and enables indoor agriculture for high-value crops. To demonstrate this, we calculate the efficacy of production (E_{dry}, in grams of dry mass produced per mole of photons) using the equation

$$E_{dry} = F_a \times QY \times CUE \times HI \times k$$

where F_a is the fraction of photons absorbed; QY is the quantum yield (moles of carbon fixed per mole of photons absorbed); CUE is the carbon use efficiency (moles of carbon incorporated into plant biomass per mole of carbon fixed); HI is the harvest index (moles of carbon in edible product per mole of carbon in plant biomass); and $k = 30$, a constant that represents the mass of CH_2O (carbohydrate) in grams per mole of carbon in edible product.

Values of the five parameters for five types of crop and the resulting production efficacies are shown in the table. We also show a calculation assuming the highest achievable values for each parameter ('potential efficacy'), which requires CO_2 levels to be increased to four times ambient levels in order to minimize photorespiration. Production efficacies of leafy microgreens approach this potential efficacy, but for other crops the efficacies are lower. Lettuce benefits from higher light levels (15% of full sunlight), which reduces QY from 0.08 to 0.07, and lettuce plants are typically spaced farther apart during early growth, which reduces radiation capture (F_a) from 0.95 to 0.65. Tomatoes benefit from even higher light levels (at least 25% of full sunlight), which reduces QY further, to 0.05, and the stems, roots and leaves of tomato plants are not edible, reducing HI to about 0.6. Vegetables such as broccoli and strawberries, and staple crops such as rice and wheat, have even lower HI.

The photon cost per dry mass is the cost per mole of photons (assumed to be US\$0.01 mol^{-1} for the most efficient LED fixtures, which have an electricity cost of US\$0.10 kWh^{-1}) divided by E_{dry}. Although the cost per mole of photons is the same for all crops, different crops have different E_{dry}, so more photons are required to create the same dry mass for some crops. The photon cost per dry mass thus varies, from a low of US\$7.5 kg_{dry}^{-1} for leafy microgreens to US\$41 kg_{dry}^{-1} for general vegetables, rice and wheat.

The market prices of the crops vary with their percentage water content. The fresh market prices vary widely, from US\$35 kg_{fresh}^{-1} for leafy microgreens to US\$0.40 kg_{fresh}^{-1} for rice and wheat. The dry market prices vary even more, because of the vast differences in the water content of the crops, from US\$700 kg_{dry}^{-1} for leafy microgreens to US\$0.40 kg_{dry}^{-1} for rice and wheat.

The final column of the table shows the ratio of the photon cost per dry mass to the dry market price, which is determined from the fresh market price and the water fraction. Leafy greens, which have the highest E_{dry} (and therefore the lowest photon cost per dry mass), also have the highest market prices. The effective photon cost thus increases rapidly with more complex crops (such as rice and wheat). The economics of simple leafy crops delivered fresh can be quite favourable. The effective cost of photons greatly exceeds the value of agronomic crops that are delivered dry and even exceeds the retail value of potatoes. Even if LEDs were 100% efficient, it would not be cost-effective to grow our staple agronomic crops with electric light. Thus, electric light input is a small cost for microgreens, a high cost for general vegetables and an unacceptable cost for staple crops. Because leafy greens are perishable and the fresh product has a high retail price, indoor farming is dominated by leafy greens.

Crop type	F_a	QY	CUE	HI	k	E_{dry}	Photon cost per dry mass (US\$ kg_{dry}^{-1})	Fresh market price (US\$ kg_{fresh}^{-1})	Water content (%)	Dry market price (US\$ kg_{dry}^{-1})	Photon cost (% of dry market price)
Potential efficacy	0.95	0.08	0.65	0.9	30	1.33	8				
Leafy microgreens	0.95	0.08	0.65	0.9	30	1.33	8	35	95	700	1
Lettuce	0.65	0.07	0.65	0.9	30	0.80	13	12	95	240	5
Tomatoes	0.60	0.05	0.65	0.6	30	0.35	29	8	95	160	18
General vegetables	0.50	0.05	0.65	0.5	30	0.24	42	4	90	40	103
Rice or wheat	0.50	0.05	0.65	0.5	30	0.24	42	0.40	3	0.40	10,000

is even higher. Seasonal combinations of sunlight and electric lights have the potential to markedly expand the range of local, year-round production of fresh greens.

An additional benefit of LED-enabled horticulture in a closed system is that water can be recycled by condensing water vapour in the air-conditioning system and returning it to the root zone. If, in the future, water were to become more expensive than energy, this would be a valuable advantage. A closed system could also reduce the need to apply pharmaceuticals owing to the limited access to pests, although lush growth in an optimal environment makes plants more susceptible to fungal pathogens such as *Pythium*. Controlled, area-intensive farming has attracted great commercial interest because it can move farming closer to urban population centres, and increase the quality of the goods by minimizing the transport time of perishable produce[88].

LEDs may also facilitate a co-evolution of plant genetics and plant environment. Plants can be engineered to better utilize the unique environment, which may, in turn, create new requirements for LEDs. This synergism between genetics and environment is the underlying reason for the marked increase in productivity of the world's agricultural system over the past 100 years. The opportunity to expand genetic potential with light has led to a new class of plants, which have been referred to as environmentally modified organisms or EMOs[89]. For example, plants have evolved self-protection mechanisms: mostly against insects and diseases, but also to cope with variations in light intensity and temperature. Exposure to ultraviolet radiation triggers the synthesis of ultraviolet-blocking pigments that prevent high-energy photons from inducing damage via the generation of reactive oxygen species[90]. If pests and ultraviolet radiation are eradicated through the use of electric lighting in a controlled environment, the need for these defence mechanisms can be reduced or even eliminated, and the efficiency of crop production might be increased.

The potential for breeding new cultivars gives rise to a great increase in scientific and technological possibilities for engineering plants for controlled environments. The tangible benefit is that health-promoting fresh produce becomes more accessible in all regions of the world in all months of the year.

Conclusions

The development of LED lighting was motivated by the promise of significant energy savings. These savings are now coming to pass. Unlike other energy-saving technologies, LED technology does not require any performance compromise, but rather improves performance while also offering new levels of control and value. Now we are entering a new world of lighting, one that includes both applications that go beyond basic illumination and value propositions that have not previously been associated with lighting.

Two primary examples are lighting for human health and productivity, and lighting for plants. The benefit of LED lighting here is not the saving of energy, although both applications will certainly benefit from improved efficiency of the light sources. The benefits here are more profound: improving human health and productivity through our emerging understanding of the physiological lighting requirements of humans, including a potential decrease in some forms of cancer and other clinical disorders; and diversifying, improving, and localizing food production in controlled environments. These nascent applications have revealed how little is known about light and physiological responses, and LEDs are providing the tools to help us better understand how humans and plants respond to light.

Even in basic lighting applications, the new levels of control offered by LED lighting have raised questions about our understanding of lighting science. Questions regarding spectral content, standard lighting levels, colour perception and preference, glare, flicker, and their impacts on visual performance are being raised. Although these issues are not fundamental shortcomings of LED lighting technology, they highlight difficulties in designing, specifying and deploying LED products when there are so many new levels of control that bring new questions. For every use of lighting, the technological possibilities of LED lighting currently outstrip our understanding of how best to use the light for the application. This situation requires research in all fields of lighting application science, concurrent with ongoing research into the underlying technology in order to achieve fully optimized lighting systems that enable the full promise of LED lighting. The promised benefits of the new world of lighting can be achieved with no obvious, fundamental downside and include vast energy savings and associated atmospheric carbon reductions, improved human health, healthier and more localized food production, and the reduced ecological impacts of light at night[91]. With these prospects at hand, the new world of LED lighting may be as profound a revolution as the transition from gas lighting to electric incandescent lighting that occurred a century ago.

Received: 26 January 2017; Accepted: 15 October 2018;
Published online 21 November 2018.

1. Parker, A. *In the Blink of an Eye: How Vision Sparked the Big Bang of Evolution* (Basic Books, New York, 2003).
2. Gerkema, M. P., Davies, W. I., Foster, R. G., Menaker, M. & Hut, R. A. The nocturnal bottleneck and the evolution of activity patterns in mammals. *Proc. R. Soc. Lond. B* **280**, 20130508 (2013).
3. Gregory, R. L. *Eye and Brain: The Psychology of Seeing* (Princeton Univ. Press, Princeton, 2015).
4. Lucas, R. J. et al. Measuring and using light in the melanopsin age. *Trends Neurosci*. **37**, 1–9 (2014).
A summary of the neurophysiology of the melanopsin ipRGC sensory pathway and of the implications for the measurement, production and application of light (includes a free measurement tool to calculate the photoreceptive inputs for circadian, neuroendocrine and neurobehavioral responses).
5. Figueiro, M. G., Brainard, G. C., Lockley, S. W., Revell, V. L. & White, R. *Light and Human Health: An Overview of the Impact of Optical Radiation on Visual, Circadian, Neuroendocrine and Neurobehavioral Responses.* Technical Memorandum IES TM-18-08 (Illuminating Engineering Society, 2008).
6. Bowers, B. & Anastas, P. *Lengthening the Day: A History of Lighting Technology* (Oxford Univ. Press, Oxford, 1998).
7. Boyce, P. R. *Human factors in lighting* (CRC Press, Boca Raton, 2014).
8. Schivelbusch, W. *Disenchanted Night: The Industrialization of Light in the Nineteenth Century* (Univ. California Press, Berkeley, 1995).
9. Steinmetz, C. P. *Radiation, Light and Illumination: A Series of Engineering Lectures Delivered at Union College* (McGraw-Hill, New York, 1918).
10. Tsao, J. Y., Han, J., Haitz, R. H. & Pattison, P. M. The blue LED Nobel prize: historical context, current scientific understanding, human benefit. *Ann. Phys.* **527**, A53–A61 (2015).
A succinct discussion of the Nobel-prize-winning breakthroughs that led to blue-LED and LED lighting and of the context of these breakthroughs in the history of semiconductor science and technology.
11. US DOE SSL Program. *Solid-State Lighting R&D Plan.* https://www.energy.gov/sites/prod/files/2018/09/f56/ssl_rd-plan_jun2016.pdf (2016).
12. Krames, M. R. et al. Status and future of high-power light-emitting diodes for solid-state lighting. *J. Disp. Technol*. **3**, 160–175 (2007).
13. Tsao, J. Y. & Waide, P. The world's appetite for light: Empirical data and trends spanning three centuries and six continents. *Leukos* **6**, 259–281 (2010).
14. US DOE SSL Program. *Energy Savings Forecast of Solid-State Lighting in General Illumination Applications*. https://energy.gov/sites/prod/files/2016/09/f33/energysavingsforecast16_2.pdf (2016).
15. Schubert, E. F. & Kim, J. K. Solid-state light sources getting smart. *Science* **308**, 1274–1278 (2005).
The first paper to discuss the potential of solid-state lighting to be 'smart', in the sense of being able not only to provide energy savings but also to adjust to the specific environments and requirements of a wide range of applications.
16. Tsao, J. Y. et al. Toward smart and ultra-efficient solid-state lighting. *Adv. Opt. Mater*. **2**, 809–836 (2014).
A comprehensive review of the state of solid-state lighting in terms of its ultimate potential to be both 'smart' and ultra-efficient.
17. Watson, B. From light to bright: San Diego is building the world's largest municipal Internet of Things. *GE Reports* https://www.ge.com/reports/light-bright-san-diego-leads-way-future-smart-cities/ (2017).
18. Tsao, J. Y., Schubert, E. F., Fouquet, R. & Lave, M. The electrification of energy: long-term trends and opportunities. *MRS Energy Sustain*. **5**, E7 (2018).
19. US DOE SSL Program. *Solid-State Lighting 2017 Suggested Research Topics Supplement: Technology and Market Context*. https://energy.gov/sites/prod/files/2017/09/f37/ssl_supplement_suggested-topics_sep2017_0.pdf (2017).
20. Dijk, D. J. & von Schantz, M. Timing and consolidation of human sleep, wakefulness, and performance by a symphony of oscillators. *J. Biol. Rhythms* **20**, 279–290 (2005).
21. Thapan, K., Arendt, J. & Skene, D. J. An action spectrum for melatonin suppression: evidence for a novel non-rod, non-cone photoreceptor system in humans. *J. Physiol*. **535**, 261–267 (2001).
22. Brainard, G. C. et al. Action spectrum for melatonin regulation in humans: evidence for a novel circadian photoreceptor. *J. Neurosci*. **21**, 6405–6412 (2001).
23. Brainard, G. C. & Hanifin, J. P. Photons, clocks, and consciousness. *J. Biol. Rhythms* **20**, 314–325 (2005).
24. Provencio, I. et al. A novel human opsin in the inner retina. *J. Neurosci*. **20**, 600–605 (2000).
25. Gooley, J. J., Lu, J., Chou, T. C., Scammell, T. E. & Saper, C. B. Melanopsin in cells of origin of the retinohypothalamic tract. *Nat. Neurosci*. **4**, 1165 (2001).
26. Berson, D. M., Dunn, F. A. & Takao, M. Phototransduction by retinal ganglion cells that set the circadian clock. *Science* **295**, 1070–1073 (2002).
27. Hattar, S., Liao, H. W., Takao, M., Berson, D. M. & Yau, K. W. Melanopsin-containing retinal ganglion cells: architecture, projections, and intrinsic photosensitivity. *Science* **295**, 1065–1070 (2002).
28. Provencio, I., Jiang, G., De Grip, W. J., Hayes, W. P. & Rollag, M. D. Melanopsin: an opsin in melanophores, brain, and eye. *Proc. Natl Acad. Sci. USA* **95**, 340–345 (1998).
A landmark paper that details the discovery of melanopsin, ultimately leading to melanopsin being identified as a functional photopigment in the retinas of mammals, including humans, with roles in the regulation by light of circadian, neuroendocrine, neurobehavioral and visual responses.
29. Hannibal, J. et al. Central projections of intrinsically photosensitive retinal ganglion cells in the macaque monkey. *J. Comp. Neurol*. **522**, 2231–2248 (2014).
30. Cajochen, C., Khalsa, S. B. S., Wyatt, J. K., Czeisler, C. A. & Dijk, D. J. EEG and ocular correlates of circadian melatonin phase and human performance decrements during sleep loss. *Am. J. Physiol*. **277**, R640–R649 (1999).
31. Cajochen, C., Zeitzer, J. M., Czeisler, C. A. & Dijk, D. J. Dose-response relationship for light intensity and ocular and electroencephalographic correlates of human alertness. *Behav. Brain Res*. **115**, 75–83 (2000).
32. Cajochen, C. et al. High sensitivity of human melatonin, alertness, thermoregulation, and heart rate to short wavelength light. *J. Clin. Endocrinol. Metab*. **90**, 1311–1316 (2005).
33. Lockley, S. W. et al. Short-wavelength sensitivity for the direct effects of light on alertness, vigilance, and the waking electroencephalogram in humans. *Sleep* **29**, 161–168 (2006).
34. Wright, K. P. Jr, Badia, P., Myers, B. L. & Plenzler, S. C. Combination of bright light and caffeine as a countermeasure for impaired alertness and performance during extended sleep deprivation. *J. Sleep Res*. **6**, 26–35 (1997).
35. Chang, A. M., Scheer, F. A., Czeisler, C. A. & Aeschbach, D. Direct effects of light on alertness, vigilance, and the waking electroencephalogram in humans depend on prior light history. *Sleep* **36**, 1239–1246 (2013).
36. Rüger, M., Gordijn, M. C., Beersma, D. G., de Vries, B. & Daan, S. Weak relationships between suppression of melatonin and suppression of sleepiness/fatigue in response to light exposure. *J. Sleep Res*. **14**, 221–227 (2005).
37. Phipps-Nelson, J., Redman, J. R., Dijk, D. J. & Rajaratnam, S. M. Daytime exposure to bright light, as compared to dim light, decreases sleepiness and improves psychomotor vigilance performance. *Sleep* **26**, 695–700 (2003).
38. Cajochen, C. et al. Evening exposure to a light-emitting diodes (LED)-backlit computer screen affects circadian physiology and cognitive performance. *J. Appl. Physiol*. **110**, 1432–1438 (2011).
39. Rahman, S. A., St Hilaire, M. A. & Lockley, S. W. The effects of spectral tuning of evening ambient light on melatonin suppression, alertness and sleep. *Physiol. Behav*. **177**, 221–229 (2017).
40. Segal, A. Y., Sletten, T. L., Flynn-Evans, E. E., Lockley, S. W. & Rajaratnam, S. M. Daytime exposure to short- and medium-wavelength light did not improve alertness and neurobehavioral performance. *J. Biol. Rhythms* **31**, 470–482 (2016).

41. Sletten, T. L. et al. Randomised controlled trial of the efficacy of a blue-enriched light intervention to improve alertness and performance in night shift workers. *Occup. Environ. Med*. **74**, 792–801 (2017).
42. Lam, R. W. & Tam, E. M. *A Clinician's Guide to Using Light Therapy* (Cambridge Univ. Press, New York, 2009).
43. Wirz-Justice, A., Benedetti, F., Terman, M. & Basel, S. Chronotherapeutics for affective disorders: a clinician's manual for light and wake therapy. *Ann. Clin. Psychiatry* **22**, 67 (2010).
44. Brainard, G. C., Barger, L. K., Soler, R. R. & Hanifin, J. P. The development of lighting countermeasures for sleep disruption and circadian misalignment during spaceflight. *Curr. Opin. Pulm. Med*. **22**, 535–544 (2016).
45. Gooley, J. J., et al. Spectral responses of the human circadian system depend on the irradiance and duration of exposure to light. *Sci. Transl. Med*. **2**, 31ra33 (2010).
46. Lall, G. S. et al. Distinct contributions of rod, cone, and melanopsin photoreceptors to encoding irradiance. *Neuron* **66**, 417–428 (2010).
47. Altimus, C. M. et al. Rod photoreceptors drive circadian photoentrainment across a wide range of light intensities. *Nat. Neurosci*. **13**, 1107–1112 (2010).
48. Dacey, D. M. et al. Melanopsin-expressing ganglion cells in primate retina signal colour and irradiance and project to the LGN. *Nature* **433**, 749–754 (2005).
49. Ecker, J. L. et al. Melanopsin-expressing retinal ganglion-cell photoreceptors: cellular diversity and role in pattern vision. *Neuron* **67**, 49–60 (2010).
50. Brown, T. M., Wynne, J., Piggins, H. D. & Lucas, R. J. Multiple hypothalamic cell populations encoding distinct visual information. *J. Physiol*. **589**, 1173–1194 (2011).
51. Brown, T. M. et al. Melanopsin-based brightness discrimination in mice and humans. *Curr. Biol*. **22**, 1134–1141 (2012).
52. Estevez, M. E. et al. Form and function of the M4 cell, an intrinsically photosensitive retinal ganglion cell type contributing to geniculocortical vision. *J. Neurosci*. **32**, 13608–13620 (2012).
53. Zaidi, F. H. et al. Short-wavelength light sensitivity of circadian, pupillary, and visual awareness in humans lacking an outer retina. *Curr. Biol*. **17**, 2122–2128 (2007).
54. Zele, A. J., Feigl, B., Adhikari, P., Maynard, M. L. & Cao, D. Melanopsin photoreception contributes to human visual detection, temporal and colour processing. *Sci. Rep*. **8**, 3842 (2018).
55. Horiguchi, H., Winawer, J., Dougherty, R. F. & Wandell, B. A. Human trichromacy revisited. *Proc. Natl Acad. Sci. USA* **110**, E260–E269 (2013).
56. Spitschan, M., Datta, R., Stern, A. M., Brainard, D. H. & Aguirre, G. K. Human visual cortex responses to rapid cone and melanopsin-directed flicker. *J. Neurosci*. **36**, 1471–1482 (2016).
57. Zhao, X., Stafford, B. K., Godin, A. L., King, W. M. & Wong, K. Y. Photoresponse diversity among the five types of intrinsically photosensitive retinal ganglion cells. *J. Physiol*. **592**, 1619–1636 (2014).
58. Prigge, C. L. et al. M1 ipRGCs influence visual function through retrograde signaling in the retina. *J. Neurosci*. **36**, 7184–7197 (2016).
59. Hannibal, J., Christiansen, A. T., Heegaard, S., Fahrenkrug, J. & Kiilgaard, J. F. Melanopsin expressing human retinal ganglion cells: Subtypes, distribution, and intraretinal connectivity. *J. Comp. Neurol*. **525**, 1934–1961 (2017).
60. Brainard, G. C. & Hanifin, J. P. *Handbook of Advanced Lighting Technology* (Springer, Berlin, 2017).
61. Stevens, R. G., Brainard, G. C., Blask, D. E., Lockley, S. W. & Motta, M. E. Breast cancer and circadian disruption from electric lighting in the modern world. *CA Cancer J. Clin*. **64**, 207–218 (2014).
A summary of the empirical and epidemiological evidence relating to the potential health consequences of inappropriate night-time light exposure disrupting human circadian physiology, melatonin production and sleep.
62. Rao, D., Yu, H., Bai, Y., Zheng, X. & Xie, L. Does night-shift work increase the risk of prostate cancer? A systematic review and meta-analysis. *OncoTargets Ther*. **8**, 2817–2826 (2015).
63. James, P. et al. Outdoor light at night and breast cancer incidence in the nurses' health study II. *Environ. Health Perspect*. **125**, 087010 (2017).
64. Blask, D. E. et al. Melatonin-depleted blood from premenopausal women exposed to light at night stimulates growth of human breast cancer xenografts in nude rats. *Cancer Res*. **65**, 11174–11184 (2005).
65. World Health Organization, International Agency for Research on Cancer. Shiftwork. *IARC Monogr. Eval. Carcinog. Risks Hum*. **98**, 561 (2010).
66. Scheer, F. A., Hilton, M. F., Mantzoros, C. S. & Shea, S. A. Adverse metabolic and cardiovascular consequences of circadian misalignment. *Proc. Natl Acad. Sci. USA* **106**, 4453–4458 (2009).
67. Buxton, O.M., et al. Adverse metabolic consequences in humans of prolonged sleep restriction combined with circadian disruption. *Sci. Transl. Med*. **4**, 129ra43 (2012).
68. Morris, C. J. et al. Endogenous circadian system and circadian misalignment impact glucose tolerance via separate mechanisms in humans. *Proc. Natl Acad. Sci. USA* **112**, E2225–E2234 (2015).
69. Morris, C. J., Purvis, T. E., Mistretta, J. & Scheer, F. A. Effects of the internal circadian system and circadian misalignment on glucose tolerance in chronic shift workers. *J. Clin. Endocrinol. Metab*. **101**, 1066–1074 (2016).
70. Leproult, R. & Van Cauter, E. in *Pediatric Neuroendocrinology* Vol. 17 (eds Loche, S. et al.) 11–21 (Karger, Basel, 2010).
71. Leproult, R., Holmbäck, U. & Van Cauter, E. Circadian misalignment augments markers of insulin resistance and inflammation, independently of sleep loss. *Diabetes* **63**, 1860–1869 (2014).
72. Blask, D. et al. *Light Pollution: Adverse Health Effects of Nighttime Lighting*. CSAPH Report 4-A-12 (American Medical Association, 2012).
73. Czeisler, C. A., Chiasera, A. J. & Duffy, J. F. Research on sleep, circadian rhythms and aging: applications to manned spaceflight. *Exp. Gerontol*. **26**, 217–232 (1991).
74. Stewart, K. T., Hayes, B. C. & Eastman, C. I. Light treatment for NASA shiftworkers. *Chronobiol. Int*. **12**, 141–151 (1995).
75. Barger, L. K. et al. Learning to live on a Mars day: fatigue countermeasures during the Phoenix Mars Lander mission. *Sleep* **35**, 1423–1435 (2012).
76. Brainard, G. C. et al. Solid-state lighting for the International Space Station: tests of visual performance and melatonin regulation. *Acta Astronaut*. **92**, 21–28 (2013).
77. Bugbee, B. Toward an optimal spectral quality for plant growth and development: the importance of radiation capture. *Acta Hortic*. **1134**, 1–12 (2016).
A comprehensive review of the current research on spectral effects on photosynthesis and plant morphology.
78. Snowden, M. C., Cope, K. R. & Bugbee, B. Sensitivity of seven diverse species to blue and green light: interactions with photon flux. *PLoS ONE* **11**, e0163121 (2016).
A review of interactions between photon flux, photosynthesis and plant morphology.
79. Hoover, W. H. The dependence of carbon dioxide assimilation in a higher plant on wavelength of radiation. *Smithson. Misc. Collect*. **95**, 1–13 (1937).
80. McCree, K. J. The action spectrum, absorptance and quantum yield of photosynthesis in crop plants. *Agric. Meteorol*. **9**, 191–216 (1971).
81. Inada, K. Action spectra for photosynthesis in higher plants. *Plant Cell Physiol*. **17**, 355–365 (1976).
82. Downs, R. J. *Controlled Environments of Plant Research* (Columbia Univ. Press, New York, 1975).
83. Kubota, C., Eguchi, T. & Kroggel, M. UV-B radiation dose requirement for suppressing intumescence injury on tomato plants. *Sci. Hortic*. **226**, 366–371 (2017).
84. Raviv, M. & Antignus, Y. UV radiation effects on pathogens and insect pests of greenhouse-grown crops. *Photochem. Photobiol*. **79**, 219–226 (2004).
85. Went, F. W. *The Experimental Control of Plant Growth* (Chronica Botanica, New York, 1957).
A classic book on the early days of photobiology.
86. Höll, J. et al. Impact of pulsed UV-B stress exposure on plant performance: How recovery periods stimulate secondary metabolism while reducing adaptive growth attenuation. *Plant Cell Environ*. (2018).
87. Bugbee, B. in *Light Emitting Diodes for Agriculture* (ed. Gupta, D.) 81–99 (Springer, Singapore, 2017).
88. Kozai, T., Fujiwara, K. & Runkle, E. S. *LED Lighting for Urban Agriculture* (Springer, Singapore, 2016).
89. Carvalho, S. D. & Folta, K. M. Environmentally modified organisms – expanding genetic potential with light. *Crit. Rev. Plant Sci*. **33**, 486–508 (2014).
A comprehensive review of spectral effects on plant growth for 20 major crops.
90. Murchie, E. H. & Niyogi, K. K. Manipulation of photoprotection to improve plant photosynthesis. *Plant Physiol*. **155**, 86–92 (2011).
91. Zielinska-Dabkowska, K. M. Make lighting healthier. *Nature* **553**, 274–276 (2018).
92. *LUXEON Rebel Color Line Product Datasheet DS68*. https://www.lumileds.com/uploads/265/DS68-pdf (Lumileds Holding B.V., 2017).
93. Roederer, M. Conjugation of monoclonal antibodies. http://www.drmr.com/abcon/ (2004).
94. Pattison, P. M., Tsao, J. Y. & Krames, M. R. Light-emitting diode technology status and directions: opportunities for horticultural lighting. *Acta Hortic*. **1134**, 413–426 (2016).

Acknowledgements P.M.P. and J.Y.T. acknowledge support from the Department of Energy through its Office of Energy Efficiency and Renewable Energy's Solid-State Lighting Program under contract DE-FE0025912. J.Y.T. acknowledges support from Sandia National Laboratories, a multi-program laboratory managed and operated by National Technology and Engineering Solutions of Sandia, LLC, a wholly owned subsidiary of Honeywell International, Inc., for the US Department of Energy's National Nuclear Security Administration under contract DE-NA0003525. The work of SSLS, Inc. is carried out on behalf of the US Department of Energy SSL Program, Washington, DC. G.C.B. acknowledges J. Hanifin for discussions, editorial review and referencing; F. Scheer, K. Roecklein and R. Lucas for insights on portions of the text; and B. Warfield for help with the design of Fig. 3. G.C.B. was supported, in part, by NASA grants NNX15AC14, NNX08AD66A and NNX09AM68G; NSF grant EEC-0812056; DOE grant DE-EE0008207; The Institute for Integrative Health; and the Philadelphia Section of the Illuminating Engineering Society. B.B. is indebted to 35 years of discussions with colleagues from around the world including T. Volk, M. van Iersel, M. Blonquist, J. Frantz, R. Heins, R. Wheeler and C. Mitchell. B.B. also acknowledges support from NASA grant NNX17AJ31G, the USDA Specialty Crop Research Initiative and the Utah Agricultural Experiment Station. Any opinions, findings and conclusions or recommendations expressed in this manuscript are those of the authors and do not necessarily reflect the views of the authors' funding agencies, including the US Department of Energy, Sandia National Laboratories and NASA.

Reviewer information *Nature* thanks J.-H. Ryou, J. Wargent and the other anonymous reviewer(s) for their contribution to the peer review of this work.

Author contributions P.M.P. outlined the overall article; J.Y.T., G.C.B., B.B. and P.M.P. wrote first drafts of the introductory, 'Lighting for human health and productivity', 'Lighting for plants' and 'Conclusions' sections, respectively; P.M.P., J.Y.T., G.C.B. and B.B. subsequently reviewed and edited all sections.

Competing interests The authors declare no competing interests.

Additional information

Reprints and permissions information is available at http://www.nature.com/reprints.

Correspondence and requests for materials should be addressed to P.M.P.