Beyond Vision: Light’s Effectiveness in Eliciting Human Responses

Thesis

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Beyond vision:
Light’s effectiveness in eliciting
human responses

Submitted for the degree of Doctor of Philosophy by Published
Work in Physical Sciences and Health Sciences

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Abstract

Optical radiation affects health via diverse and interconnected mechanisms. The skin and eyes support multiple actinic processes, exploiting environmental optical radiation, including light, to the benefit of the whole body. Sub-optimal exposures can disrupt these processes and in extreme scenarios may cause tissue damage. Natural and artificial lighting can lead to both beneficial and unwanted responses; understanding how to achieve a healthy balance relies on quantitative exposure data and dose-response relationships based on physical measurements.

Through non-visual retinal photoreception, light has a profound effect on daily patterns of human physiology and behaviour. This thesis reviews the spectral weighting function, or action spectrum, for the regulation of plasma melatonin, and its relation to photoreceptors, melanopsin, circadian rhythms, standardisation, health advice and eye safety.

In my portfolio, I have contributed to understanding human non-visual responses to light. The human photoreceptor calculation tool I constructed is widely used and supports an International Standard. I published a revised circadian light-drive model based on melanopsin photoreception, and coordinated multidisciplinary advice on shift work health studies.

Short-wavelength light synchronises day and night time activities with the environment. Bright artificial light at night can interfere with this process, and high radiance blue light can cause retinal lesions. I have contributed practical advice on the efficacy of bright light therapy products, confirmed the eye safety of display screens, and raised concerns about the modulation or flicker from some LED lighting.

My published advice is based on field measurements of human exposures to light and experience gained of gathering exposure data. In the final section of my portfolio, my work has included characterising the performance and use of wearable broadband dosimeters and light-weight CCD array spectroradiometers, proposing performance requirements for wearable sensors and developing the closest-matching melanopic light-logger from an existing product.
I went to sleep; and now I am refresh’d,
A strange refreshment: for I feel in me
An inexpressive lightness, and a sense
Of freedom, as i were at length myself,
And ne’er had been before. How still it is!
I hear no more the busy beat of time,
No, nor my fluttering breath, nor struggling pulse;
Nor does one moment differ from the next.

The Dream of Gerontius, John Henry Newman
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PART I – The covering paper

1. Introduction

1.1 The public health context

Light has widespread effects on everything we do, from supporting vision and our understanding of the immediate environment, through to regulating both activity patterns, whereby the vital resources for a full life can be obtained, and our rest and sleep, allowing our bodies and minds to recover from the insults and stresses of activity and develop resilience. Healthy activity, rest and sleep are fundamental components of well-being. Research is also revealing how the non-visual system supports mental performance, learning and development.

The full range of the impacts of light on health, the underlying biological mechanisms and the optimal light conditions for health are still a long way from being fully understood. By relating the health effects of exposures to measurable quantities of light, both public health advice and clinical interventions can be developed to improve our light environment, avoiding potential hazards and promoting longer life.

The papers in Part II investigate the metrology, dosimetry and analysis to relate light exposures systematically when addressing such vitally important public health questions, with a strong emphasis on the metrology of non-visual retinal photoreception.

![Spectrum of light](image)

Figure 1.1: The spectrum of light. Light is optical radiation that elicits visual sensations (see Definitions). The adult lens is increasingly opaque below 380 nm and visual pigment sensitivity gradually declines above 600 nm, so there are arguably no meaningful fixed wavelength boundaries for visible light. Colour designations are similarly subjective: visible violet light overlaps with ultraviolet radiation (UVR), which runs up to 400 nm; and visible red light overlaps with infrared radiation (IRR), which runs from 700 nm.
1.2 An introduction to the published works

The study of light as a physical agent in health research cannot be accomplished without an appreciation for the human aspects. The scope of the work is multidisciplinary in the truest sense, encompassing not just multiple areas such as physical, environmental, behavioural and physiological sciences, epidemiology, photobiology and photochemistry; it influences clinical and industrial practice relating to intraocular lens implants, electronics, lighting manufacture, lighting design and architecture. Ultimately, the work feeds into policy and regulation, including on working hours, education, street-lighting and healthcare.

Much health research is concerned with the progression of one or more diseases, applying specialist medical or biological expertise. Another valid approach is to understand and measure the presence in the living environment of a physical, chemical or biological agent that may have an influence over a wide range of diseases. This is the technique taken in my work.

I have divided my portfolio into three categories, which broadly speaking correspond to the benefits, hazards and measurement of light (see Definitions for terms in bold) and optical radiation in general (Figure 1.1). The common factor is the connection between exposures to light and health and well-being, which is ultimately what is studied in each of my publications.

1.1 Light exposure, circadian rhythms and health

Section 3.1 details three papers, reproduced in Part II, that tackle various aspects of translating laboratory results on the effects of light exposure on circadian rhythms into health advice.

Artificial lighting is widely used as a surrogate for solar radiation in the modern world, and light in both its natural and artificial forms are as unavoidable as they are necessary (Figure 1.2; Wyszecki & Stiles, 1982). Light has a systemic biological function in regulating daily routines or circadian rhythms, as well as being the basis of vision. Not only are these routines not purely socially determined, they are intrinsic to underlying human (and animal) biology and we fundamentally need to have both light and darkness at the right time.
Figure 1.2: The spectral distribution of three of the International Commission on Illumination’s (CIE) standard illuminants. These are examples of artificial, natural and theoretical light, respectively: illuminant A is an incandescent lamp (dashed), resembling a Planckian radiator with a colour temperature of 2,856 K; illuminant D65 (solid) represents a typical phase of daylight (sunlight plus skylight) for a clear sky at midday (standardised at 5 nm intervals, the Fraunhofer lines are not resolved); and illuminant E (dotted) has an ideal uniform photometric distribution, also called the equi-energy spectrum.

1.2 The optical hazards of visible light

Section 3.2 details three more papers, reproduced in Part II, on the topic of balancing the positive effects of light such as visual performance and circadian rhythms against potential phototoxicity and the problems of temporal light modulation (TLM).

Visible light varies in intensity, distribution, duration, spectrum and the extent to which it is accompanied by two further components found in sunlight: ultraviolet and infrared radiation. The relative sensitivity to monochromatic light or optical radiation for a given response is known as an action spectrum. Three standard action spectra (respectively CIE, 2002; Publication 1 or Publication A8; Gibson & Tyndall, 1923) are shown in Figure 1.3, using the radiometric system. The graph in the photon system would look very similar, with the curves skewed less than 5 nm to the left.

There are several mechanisms by which too much light can be harmful to eyes, skin, clothes and even our brains, for example the immediate and permanent photochemical, or phototoxic, damage that can result when high levels of short-wavelength light are concentrated on a small area of the retina – the blue light hazard (BLH), and symptoms ranging from visual discomfort to light-induced epilepsy caused by fluctuations and oscillations in light intensity, i.e. caused by TLM.
Figure 1.3: Three human action spectra. The absorbing chemicals for the phototoxic action spectrum, \( h(\lambda) \), are not known with certainty (peak at 450 nm). Melanopsin is a photopigment discovered in 1998, with the melanopic sensitivity curve, \( 
u_{mel}(\lambda) \), involved in circadian rhythm regulation (490 nm). At light levels supporting colour vision, the cones mediate visibility, resulting in the sensitivity curve shown, \( v(\lambda) \), known as the spectral luminous efficiency function for photopic vision (555 nm). These responses are most sensitive to different visible wavelength regions, but the regions overlap significantly.

1.3 CCD array and dosimeter performance for field measurement

Section 3.3 details five papers reproduced in Part II, three connected to the performance of wearable dosimeters for non-visual (NV) applications, and two connected to the optical performance of portable charge-coupled device array (CCD array) spectroradiometers (or spectrometers) for use in field studies related to general health applications.

Laboratory studies of the physiological effects of light and circadian rhythms in animals and humans have helped to establish important principles about the NV system of photoreception and associated action spectra, as will be reviewed in Section 2. However, field studies are a powerful means for translating such findings into effective public health advice. If lifestyle advice, light therapy and other interventions that influence light exposures are to be validated, it is important to measure both the baseline profiles of exposure to light in the everyday living environment, and the changes brought about. However, collecting reliable time-series data from dosimeters or portable CCD array spectrometers in uncontrolled environments relies on understanding how they behave under different conditions, and how the data collected relate to phototransduction processes in the human eye.
1.4 Conclusions and summaries of the publications

Section 4 offers conclusions and deals with future directions in the use of light-emitting technology and research into its impact on health and well-being, ranging from GPS-based exposure estimates, to targeted methods for stimulating light-activated pharmaceuticals inside the human body. Section 5 details my personal contributions to the eleven publications comprising the portfolio, and their impact. For completeness, Appendix A summarises some of my other publications, and how they relate to the portfolio. In Appendix B, definitions are given for selected terminology and measures used in the covering paper; some terms derive from the portfolio, and have been formalised in other related publications. Finally, selected wording from my introduction to the topic of NV responses in Appendix C is reproduced in the next section.
2. A review into light exposure, circadian rhythms and health

The review in this section briefly covers the historic background of artificial light and some unintended consequences of the quantitative definition of light. Within this context, the effect of light on physiology, sleep and circadian rhythms is explored, and developed by considering the results of progressive experiments on human subjects since the 1980s and the implications of the discovery of a previous unknown class of photoreceptor around the turn of the century. After assessing the research, the review will turn to the question of redefining quantities of light with new standard quantities.

Some of the published works include detailed reviews in a similar area, especially in Section 3.1, so I have tried to ensure this review is self-contained whilst being complementary to these publications. To achieve this, I have concentrated on developments over recent years concerning the action spectrum of melatonin suppression, and on high-level implications for standardisation, energy efficiency, lighting practice and health.

To conclude, any additional relevant existing literature is reviewed for the topics of the later papers in Sections 3.2 and 3.3 concerned with advice about exposure to artificial light sources and assessments of field measurement technology.

2.1 Light, lighting and its first international definition

The origins of controlled artificial light generated by combustion are pre-historic. Public street lighting was introduced by several ancient civilisations and electric artificial light was invented and developed in the form of incandescent light in the 19th century. This enabled indoor lighting to become ubiquitous in developed regions wherever a supply of electricity is available for public subscription. The technology used in electric lighting continues to develop.

The international standard for quantifying light, the photometric system, is based on a 1923 study and review of the effect of wavelength on visibility (Gibson & Tyndall, 1923). Luminous flux expressed in lumens (e.g. produced by a light bulb) is calculated as the sum of its spectral radiometric power weighted for the intensity of the luminous sensation at each wavelength of radiation of equal power. The weighting function is known variously as $V(\lambda)$, spectral luminous efficiency, or the $V(\lambda)$ function for photopic vision (see Figure 1.3). $V(\lambda)$ can be used analogously to calculate other photometric quantities, including illuminance expressed in lux and luminance expressed in candelas per square metre.
The emphasis in the second half of the 20th century, continuing in the 21st, has been to reduce the energy needed to generate the same level of light, according to \( V(\lambda) \). This is often based on the illuminance produced on a horizontal surface, such as a desk at a standard height. Sodium, metal halide, fluorescent and increasingly LED technologies can all out-perform incandescent lighting based on this criterion (Boyle, 2014). However, there are problems with this approach to determining energy efficiency.

Firstly, \( V(\lambda) \) is underweight for light which stimulates the short-wavelength cones (Wyszecki & Stiles, 1982). Although widely accepted, the difference is modest and mainly of academic interest to visual scientists. It does not constitute a strong enough practical justification to modify the curve.

A second problem is that photopic calculations described above do not deal with the range of spectral distribution of light. The preferred approach is simply to assess colour rendering qualities independently of photopic measures of light.\(^*\) For instance, sodium street lighting has a monochromatic orange colour unsuitable for indoor lighting, as it would not allow for the colours of objects to be perceived (see Figure 2.1). Provided it is sufficiently bright, an illuminant with a broad visible light spectrum similar either to daylight or certain Planckian radiation (e.g. incandescent lighting) tends to achieve acceptable object colours, partly due to having a high spectral entropy (Publications A1 & A7).

Thirdly, the finding that vision is only one of the functions of phototransduction in the eye calls into question the fundamental definition of light using visibility (Publication 1). The action spectrum for visibility \( V(\lambda) \) is unlikely to be spectrally appropriate for a broader definition of light based on retinal photoreception, because it ignores the NV functions of the receptors. Moreover, no single static action spectrum will reflect the changes repeated every 24 hours to the utility of NV exposures, particularly the changes between day and night. My portfolio deals extensively with situations where \( V(\lambda) \) is not the appropriate weighting for measuring light, or is relevant only in combination with other weighting functions (see Publications 1-5, 7, 10, 11).

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\(^*\) Whiteness only predicts colour rendering quality. Any colour can be created with combinations of three narrowband sources that correctly balance the responses of the three classes of cones. A white light produced this way can noticeably distort the colours associated with an object’s spectral reflectance. Hence, perceptual whiteness should not be conflated with the concept of white noise, which relates to an auditory stimulus containing a continuous range of frequencies with near equal intensities, i.e. one with high spectral entropy.
Figure 2.1: Three typical artificial lighting spectra (e.g. Publication AS). Low pressure sodium (LPS) light appears orange. White light from a compact fluorescent lamp (CFL) has gaps in the spectrum. The LED light bulb shown appears white, due to combining a blue LED and a yellow-orange phosphor, but is concentrated in the central visible spectrum. The more spectrally selective the light, in comparison to natural light, the lower its quality in terms of colour rendering performance, and the less well illuminance predicts NV responses.

2.2 Light and circadian rhythms

Regardless of technology, the artificial illumination levels favoured indoors are consistently lower than outdoor levels during daylight hours by one to two orders of magnitude (see Figure 2.2). By the 1970s, it was already known from animal experimentation that serum melatonin levels at night could be suppressed with light, and that the nocturnal melatonin rhythm and other circadian rhythms (see Definitions) could be shifted if the light was correctly timed. This review concentrates on action spectra, and Arendt (1996, 2019) is recommended reading for further information concerning melatonin’s role in circadian rhythms, and its use as a marker of circadian timing.¹

Lewy et al. (1980) showed that if the illumination levels were increased above normal indoor levels, artificial light would also lead to the suppression of pineal melatonin secretion in humans. Although humans appeared less sensitive to dim light than some animal models, these findings immediately suggested a similar mechanism existed in humans as in animals whereby access to daylight plays an important role in circadian...

¹ Melatonin itself was discovered in 1958. It is secreted into the blood stream at night by the pineal gland in mammals. Often described as a sleep hormone, its relationship with sleep is largely associative rather than being strongly causal. For instance, in nocturnal mice, serum melatonin levels also rise at night, during wakefulness (Barrentette et al., 2004).
regulation, and that bright artificial light might serve as an alternative. A much lower threshold for human sensitivity was later demonstrated (Brainard et al., 1988) using narrowband light peaking at 509 nm, and human circadian rhythms are now considered to be "exquisitely sensitive" to light using constant dim light routines in circadian rhythm protocols (Czeisler & Gooley, 2007).

Figure 2.2: Natural daylight is typically much brighter than artificial illumination, and can reach approximately 120,000 lux when measured in the horizontal plane, compared to daytime office lighting which may be approximately 100 lux on working surfaces away from windows (own photo, Trough of Bowland, UK). Similar differences relate to the light reaching the eye in outdoor vs indoor environments, with computer screens 100 times dimmer than skylight (see Publication 5).

The discovery of human melatonin suppression and light sensitivity accorded with the more established picture of NVC function and the regulation of circadian rhythms in mammals. Light detected by retinal photoreceptors produces signals that travel to various brain targets. Arriving at the suprachiasmatic nuclei (SCN), these signals coordinate the timing of multiple genetic clocks or oscillators, each one contained in an individual SCN neuron.

Remarkably, each SCN neuron has its own period and in the absence of light the clock will continue to run at a fixed rate. These periods are distributed around approximately 24 hours. As the neurons interact, the clocks are coupled to form a master clock with a typical period of 24.18 ± 0.13 hours in continuous darkness (Czeisler et al., 1999). Exposure to bright light early in the night-time delays the timing on subsequent days, whereas exposure to bright light late in the night-time (early morning hours) advances the timing (Khalsa et al., 2003). When these timing shifts become largely balanced, the clock is said to be
“entrained” to the “light:dark cycle” (see entrainment, Definitions). Someone whose master clock has a natural period of shorter than 24 hours would tend to choose to wake earlier and have a morning preference for activity and in contrast a longer period is associated with late wake times and an evening preference (Duffy et al., 2001).

The SCN send signals to the pineal gland, controlling the timing of secretion of melatonin so that it coincides with the dark period of the natural cycle of light and dark (Klein, 1985). In addition to these phase shifts, pineal secretion of melatonin is also acutely inhibited by exposure to bright light at night, due to signals received via the SCN, but not by sufficiently dim light. The late evening onset of melatonin secretion under dim light conditions (dim light melatonin onset, DLMO) is an accurate indicator for the phase, and a person’s “chronotype” (i.e. the extent of their morning or evening preference; Lewy & Sack, 1989).

The central nervous system and endocrine system are profoundly influenced by SCN activity, and they transmit its timing information around the body. Cells found in almost all tissues and organs also contain genetic clocks, known as peripheral oscillators, which are coordinated directly in this way, and indirectly by feeding times determined by the SCN control over the rest-activity rhythm (Schibler et al., 2003). Other notable circadian rhythms include serum levels of the hormone cortisol, core body temperature, sleep and activity, but this is far from an exhaustive list.

Many researchers considered the findings of Lewy et al. (1980) of interest owing to the implications for pathology and treatment of depressive disorders (e.g. Lewy et al., 1981; Kripke et al., 1983; Rosenthal et al., 1984; Wirz-Justice, 1987). However, Price et al. (1983) showed circadian rhythms in cortisol levels appear by the third month of a baby’s life, with the limited range of evening cortisol values observable from the eighth week. This suggests daylight may benefit circadian development in healthy newborns, just as it is subsequently of key importance to circadian regulation throughout life.

Daily exposure to daylight is now seen as part of a healthy way of life for children and adults alike, rather than simply for medical care (e.g. Wright et al., 2013; Baczynska et al., 2019). Architects increasingly incorporate daylighting for health and well-being, and lighting manufacturers market consumer products programmed to change in spectra and intensity depending on time of day, or even to mimic the appearance of skylights (Canazé et al., 2017). It is curious with the benefit of hindsight, why it took the discovery of a new human
photopigment and photoreceptor (detailed in the next section) before the wider opportunities to improve public health with light-based interventions came to wider notice.

2.3 Unseen photoreception

“Prior to 1998, the possibility of a third class of photoreceptor in the human eye was deeply contentious, although it was known that in many mammalian species circadian rhythms could be shifted by exposure to light, with a peak sensitivity that did not match to rods or cones. At that time, the photopigment melanopsin was discovered in a species of frog, and subsequently shown to be present in mammals and humans at several locations including the hypothalamus and retina (Provencio et al., 1998; Provencio et al., 2000). It was quickly recognised to be a candidate for the photopigment of a third mammalian photoreceptor that might be relevant in human physiology (Berson et al., 2002).” (Adapted from my own conference paper, see Appendix C)

Figure 2.3: Extrinsic factors governing the sensitivity of suppression of nocturnal melatonin secretion by light. Intrinsic factors, such as SCN circadian clock state (primarily phase angle φ), are important for circadian-type responses. A) incident angle θ: ipRGC distribution in macaque (Dacey et al., 2005; based on 3.4° per mm), B) wavelength λ: action spectrum (Brainard et al., 2001 blue, Thapan et al., 2001 grey; Publication 7 fitted curve), C) melanopic irradiance Emel: continuous 6.5 h exposures (Zeitzer et al., 2000, based on 0.7625 mW·lm⁻¹), and D) duration t: continuous bright light exposures (Chang et al., 2012; Publication 2 fitted curve).

Zeitzer et al. (in 2000; see Figure 2.3 Panel C) returned to the sensitivity of the suppression of melatonin secretion to light of different irradiance levels, using white light rather than
narrowband light at 509 nm (Brainard et al., 1988). They considered a wider range of
irradiance, a longer 6.5 h exposure, rather than 1 h, and based circadian phase-shifting on
DLMO. Given the methodological differences, the results were in reasonable agreement.

Later in 2001, two action spectra studies confirmed that the response could not be
explained by the spectral sensitivities of the rods or cones (Brainard et al., 2001; Thapan et
al., 2001; see Figure 2.3 Panel B). Each article suggested the responses might be explained
by a novel human photoreceptor, and fitted opsin templates to their data to estimate the
peak photopigment responses at wavelengths of 464 nm and 459 nm, respectively. A
similar action spectrum was published (Hankins & Lucas, 2002) of delayed cone responses
to light flashes following 15 min duration adapting light exposures at night, which also could
not be explained by the spectral sensitivities of the rods or cones, with a peak fitted
response at 483 nm.

The presence of melanopsin was confirmed in retinal ganglion cells that project to the SCN,
the circadian master clock (Gookey et al., 2001). Further work has shown melanopsin is
responsible for direct responses to light in these intrinsically-photoreceptive retinal
ganglion cells (ipRGCs) (e.g. Hattar et al., 2002; Dacey et al., 2005). In Publication 1 (Lucas
et al., 2014) the central role of ipRGCs in circadian timing and NV responses to light was
confirmed by the consensus and literature review of invited international experts. ipRGCs
are a small proportion of all retinal ganglion cells (RGCs), but there are at least five ipRGC
subtypes known as M1-M5 (Zhao et al., 2014; Sonoda & Schmidt, 2016), suggesting a
variety of specialised functions. Melanopsin photoreception in ipRGCs has characteristics
that are distinct from photoreception of the rods and cones in spectral, temporal and
spatial domains: it is maximal at around 490 nm in vivo, between the rods and the short-
wavelength cones; light exposure (or dose) is integrated over time, so that responses are
relatively slow to react to changes in light levels; ipRGCs and their dendrites are spread
across relatively large regions of the retina (e.g. Figure 2.3 Panel A), so that ipRGCs cannot
form sharp images. As ipRGCs receive signals from rods and cones, as illustrated by the
schematic retinal diagram in Figure 2.4, ipRGC-influenced responses to light (IIL responses)
combine some of the characteristics of rod and cone photoreception with melanopsin
photoreception.
Although the timing of melatonin secretion in darkness is dependent on circadian timing, secretion can be suppressed by exposure to bright light and the circadian regulation of secretion is unmasked on return to darkness (Lewy et al., 1980; Chang et al., 2012). Hence, melatonin suppression is an example of an acute response to light, whereas a phase shift in the timing of the onset of melatonin secretion in dim light is an example of a circadian response to light regulated by SCN timing signals. In the absence of further phase-shifting exposures, changes to timing persist in the following days and weeks (Czeisler & Gooley, 2007). I will refer to Figure 2.5 further in discussing Publication 3, and how it illustrates the various connections between light entrainment of circadian rhythm regulation and health.

Interestingly, adjunct to their role in circadian rhythms and neuroendocrine physiology, ipRGCs are involved functionally in regulating so-called classical vision (Allen et al., 2014; Hankins & Hughes, 2014), but the lack of temporal or spatial resolution and the higher thresholds meant their influences went undetected. In hindsight, protocols relating to visual function were optimised to remove the complexity ipRGCs add to responses to light.
As well as spectrum and irradiance, duration of light exposure predicts melatonin suppression and phase shifting. The effects are subadditive for long durations (Chang et al., 2012; see Figure 2.3 Panel D), and the spectral sensitivity shifts towards the melanopsin sensitivity curve from longer-wavelength sensitivity mediated by the medium- and long-wavelength cone classes (M-cones and L-cones) (Gooley et al., 2010).

2.4 Standardisation

Following the 2001 action spectra (by Brainard et al. and Thapan et al.), there was interest from many organisations and researchers in codifying the data into a standard. The CIE, the foremost authority on “standards and procedures of metrology in the fields of light and lighting”, hosted a Symposium on “Light and Health: non-visual effects” in 2004 (CIE, 2004). At least three different approaches were proposed and are detailed below: the Gall function, an approach allowing for spectral-opponency and a melanopic function based on ipRGC sensitivity due to melanopsin.

The “Gall function”, denoted $c(\lambda)$, was based on averaging and smoothing the shape of underlying data in the two melatonin suppression action spectra studies (Gall, 2002). This brute force approach was described as empirical. The purpose was to standardise a
spectrally-weighted quantity of light, separate from its visual effects, supposed to have circadian regulation and health-giving properties, effects which were not generally agreed. The concept was used for marketing of health-related lighting products. Indeed, the Gall function was adopted by the German standards body DIN (Deutsches Institut für Normung) as the basis for a pre-standard, but attempts to adopt this as a national and European standard were later abandoned.  

Spectral opponency theory holds that the colour of a light stimulus, as observed by the three cone types, influences the contribution of the five different photoreceptor types. To explain the melatonin suppression responses, a spectral opponency model was proposed, with a sharp increase in efficacy when a light becomes sufficiently blue (Rea et al., 2005). Like the Gall function, the data were interpreted as applying to all NV responses. One problem with this proposal is its complexity, as melatonin suppression, like many other measures of melanopsin responses, is subject to large uncertainties, and the data are not sufficiently precise to derive the multiple parameters independently. It was also agreed at an expert workshop on human action spectra held in Manchester in 2013 (Publication A3; Publication 1), that there were insufficient data to demonstrate spectral opponency in any practical sense in human NV responses. Three of the model’s authors have published a range of alternative theories as their view has developed over time (Rea et al., 2001, 2002, 2010; Publication A6), but the 2005 model was the first incorporating spectral opponency in the interpretation of data of melatonin suppression (Figueiro et al., 2004).

The melanopic approach derives from the early action spectra papers (Brainard et al., 2001; Thapan et al., 2001; Hankins & Lucas 2002), which fitted opsin templates to their data. Further data in primates and humans (Dacey et al., 2005; Gamlin et al., 2007) confirmed the peak sensitivity of human melanopsin to be approximately 480 nm to individual photons arriving at the retina, which converts to a peak of approximately 490 nm for light measured using the radiometric system in the environment. This shift is accounted for by

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Footnote: I presented at a DIN "Expert panel on the effect of light on humans" (Normenausschuss Lichttechnik (FNL) im DIN NA 058-00-27 AA "Wirkung des Lichts auf den Menschen", 2012) about how clinical decisions between lighting intervention options could differ, or even be reversed, based on following the different competing action spectra proposals, reanalysing data from Publication 4. The presentation emphasised the risks of standards that were not sufficiently evidence-based. As an observer in a strategic meeting that evening, DIN representatives appeared concerned and considered abandoning the Gall function for the first time.
the spectral transmittance of pre-receptoral media in the eye (al-Enezi et al., 2011) as well as the conversion from the photon system to the radiometric system (Publication A9).

The melanopic model is a component of the spectral opponency model. When comparing models, applying the spectral opponency model either to narrowband or polychromatic light offers no practical advantage in explaining melatonin suppression data over the melanopic model (Publication 1). The evidence for opponency is mixed, but whilst cones play a role in responses to shorter exposure durations (Gooley et al., 2010), there is no cone input in circadian responses following light adaptation (Lall et al., 2010). Probably the conclusive evidence against the theory is a recent report showing no evidence for short-wavelength cones contributing to NV responses, including melatonin suppression; a key aspect of the theory is simply lacking in nature (Spitschan et al., 2019).

For context, visual responses are mediated by cones at high photopic light levels, rods take over this role completely at very low or scotopic light levels, and rods combine with cones at intermediate or mesopic light levels. At 498 nm (Bowmaker & Dartnell, 1980), the peak spectral sensitivity of the photopigment rhodopsin found in rods is close to melanopsin’s, so distinguishing rhodopsin and melanopsin responses with polychromatic light is challenging. Ill responses have a high threshold, and it is thought that the responses of rods are extinguished, or greatly attenuated, due to bleaching of the photopigment rhodopsin in most relevant conditions. As there is also little difference between spectra that activate the two photopigments, there might be little practical advantage for the field of lighting design in determining the contribution of rods to the overall responses.

Publication 1 represents the current scientific consensus on measuring light in respect of ill responses, and is the basis for the recent International Standard CIE S 026:2018 (Publication A8). It recommends that studies and applications quantify light in respect of all five of the photoreceptor types in the NV system, namely ipRGC responses due to melanopsin, rod responses and the contribution of the three types of cones in the peripheral retina. The standard recommends a system of action spectra (see Figure 3.1), quantities, units and related metrics, closely following the consensus view in Publication 1. Publication 10 followed these recommendations, but in contrast, the assessments in Publications 2, 4, 7 and 11 were based on quantifying NV responses using the melanopsin response alone, and where appropriate this is combined, compared or contrasted with the visual response to ambient light (resulting from the cones).
This largely concludes the review of IIL responses, but it is worth listing some important subtleties to be considered in deriving standard action spectra for reference purposes:

- contrary to some older publications, the values of dimensionless action spectra change when applied to quantities measured in different spectral systems, such as the (actinometric) photon system and the radiometric system (Price & Peirson, 2014; Publication A9);
- the peak in vitro response of a photopigment is modified in vivo by pre-receptoral filtering between the external environment and the location of the photopigment (Norren & Vos, 1974; CIE, 2012);
- due to the variability of IIL responses, the standard melanopsin action spectrum is based on a template of opsin spectral sensitivity (Publication 1; Publication A8);
- although the single univariant opsin spectral sensitivity model has been codified, melanopsin may be a bi-stable or tri-stable photopigment (Brainard et al., 2008; Rollag, 2008; Emanuel & Do, 2015), and to date there are insufficient data to demonstrate meaningful differences in IIL responses in vivo (just as with spectral opponency);
- those classical photoreceptors that provide signals to ipRGCs are found in the peripheral retina, and different optical photopigment densities and pre-receptoral filtering determine their responses than those that relate to foveal vision (Publication 1; Publication A3);
- photoreceptor spectral sensitivities exhibit significant inter-individual variation, so a standard for a whole population can only represent an average (e.g. see Asano et al., 2016);
- with similar consequences, pre-receptoral filtering varies with age becoming less transparent to shorter wavelengths over time, and the extent of this change also shows large inter-individual variation (Pokorny et al., 1987; Barker & Brainard, 1991; CIE, 2012);
- the sensitivity of IIL responses may vary according to the broad direction from which the light is incident (Lasko et al., 1999; Visser et al., 1999; Glickman et al., 2003); and
- the absolute sensitivity and relative contribution of different photoreceptor types may be subject to inter-individual, seasonal and age-related changes, along with known diurnal changes (Najjar et al., 2014; Hankins & Lucas, 2002).
2.5 Hazards

Optical radiation can cause hazards to skin and eye tissues, but does not normally penetrate to harm other tissues. For light and lighting the dominant hazards are widely thought to relate to safety via visual performance and to the effects of short-wavelength light on the retina. However, there is a possibility that oscillating light may also have an adverse effect based on responses to high frequencies not directly related to visual performance (Berman et al., 1991).

Photochemical damage to the retina, such as from staring at the sun, or from arc welding sources, was at one time attributed to thermal damage. However, research culminating in the 1970s (Ham jr et al., 1976) established the role of actinism in this response, meaning these effects cannot be explained by the absorbed energy alone. The term “blue light hazard” (BLH) was coined, and several standards and even legislation were published over the following years which specify dose thresholds or limits, and assessment methods, notably at international and European level, published by (with relevant references):

- International Commission on Non-Ionizing Radiation Protection ICNIRP (ICNIRP, 2013; updated from 1997);
- International Commission on Illumination CIE (CIE, 2002; updated from 2000 and published jointly with International Electrotechnical Commission IEC in 2006); and

The guidelines all include effectively the same BLH assessments, although the context and interpretation varies substantially, with the EU Directive establishing the ICNIRP threshold, that includes a substantial margin for avoiding the adverse effects of the BLH, as a legally-binding safety limit for workplaces. Further, the BLH codified in these guidelines is for acute effects (Type II effects, arising from exposures of up to a few hours). There was too much uncertainty about the evidence for long-term effects (Type I effects, arising from repeated exposures on consecutive days, or over much longer periods). It is possible the guidelines provide sufficient protection against any long-term effects, and no additional assessments are suggested. There are some concerns about this, and about the hypothesised possibility that lifetime exposures to blue light are a risk factor for age-related macular degeneration.
Figure 2.6: A blue LED lamp for treating seasonal affective disorder (own photo). Exposure programmes of up to 1 h (note that contraindications apply to this therapy). Under assessment at a realistic worst case viewing distance, the lamp generates BLW-weighted radiance of approximately 60% of the international guideline safety threshold (ICNIRP, 2013) for extended viewing (e.g. several hours in a day).

This question was considered in Publication 4, where I carried out assessments using an approach to estimate the dose from repeated daily exposures to devices such as the treatment lamp shown in Figure 2.6.

There have been reports of negative affect with artificial lighting, that appears to be linked to the TLM in some LEDs. LEDs are not inherently unstable, but the electronics used to drive them from regular and intermittent mains electricity variations, create a range of new modulation phenomena, which can include modulation depths of 100% at twice the mains frequency (Publication 8), and at other frequencies where retinal responses were demonstrated.

Visual responses to TLM include flicker (direct sensation of modulation), motion illusions (rotational and non-rotational stroboscopic effects) and array effects (saccadic and non-saccadic). As well as retinal responses, research has shown TLM to be associated with adverse health effects, even in the absence of visual responses (Wilkins et al., 1989). It is thought however, that these sub-perception adverse health effects are related to one of these perceptual visual responses. Some even propose to use visibility thresholds directly to counter the adverse health effects. To do this, however, they will now have to ignore or reject the findings and the collected evidence reviewed in a recent wide specialist
consensus including industry and researchers (IEEE, 2015). For this reason, in Publication 6, I set out an alternative approach to the regulation of TLM.

Natural light, and even artificial lighting, can have greatly beneficial effects for health via NV responses, as well as functional benefits from visual responses. But the responses governing the quality of light are complex, and it is here that artificial lighting, together with the way it is used or misused, can often fall short of daylight.

2.6 Research objectives and public health

The purpose of the research in the portfolio is to develop and apply systematic methods to quantify light and exposures to light for their photobiological effects.

A primary objective in this high-level program is to understand what constitutes a healthy daily light exposure, and what might be detrimental to health. To do this it is fundamental to understand what representative light exposures are in the population and in sub-groups such as children or shift-workers. A second objective would then to be to test and improve that understanding by changing the light environment in field research and studying the impact on people’s lives, mental well-being and physical health. It is clearly an important ultimate objective to make positive changes that will have the widest and greatest positive impacts.

The three sections of the portfolio are broadly linked to these three public health objectives (respectively section 3, 1 and 2), and are positioned to achieve their impact and influence through international communities concerned with health research.
3. Measuring and assessing light exposures for human responses

3.1 Light exposure, circadian rhythms and health (Publications 1-3)

Results showing that short-wavelength light exposure and bright artificial light could regulate circadian rhythms (see Definitions), sleep and even be used to treat medical conditions have prompted a strong public interest in blue light. The range of competing action spectra and response models for ILL responses, themselves derived and extrapolated largely from laboratory studies under controlled conditions and extended fixed posture and dim light protocols, make it unclear how to give even the broadest advice about light exposure and lighting choices to inform the public's questions about light and health. This has given rise to a need for a consensus and coherent approach to ILL responses, with the endorsement of the best scientific expertise.

The descriptions of what light different people are exposed to were limited. Studies routinely employed spot measurements of lighting, historic lamp model numbers, and loose indications of lighting type. Where exposure profiles were available, these were often based on measurements with unknown sources of systematic and random errors (see Section 3.3), frustrating comparisons and reconciliations of the data. The data further suffered from being based on quantities relating to image-forming vision, such as illuminance and correlated colour temperature (CCT) that were already known to be inadequate to predict non-image-forming (NIF) responses.

To answer these questions, studies need to collect data on the 24-hour exposure of the eyes related to the photoreceptors' spectral weighting functions (action spectra) and the eyes' directional and dynamic optical response characteristics. In translational work, models of dose-response relationships need to agree with laboratory results and be usable with complex uncontrolled exposure scenarios as the input. There is still a need for much more exposure data relating to babies, children and adults in settings such as schools, hospitals and in the home environment, and data relating to the impact of indoor work and shift work on exposures and ultimately health outcomes.

Further, small experimental study sizes can lead to seemingly contradictory results, as the statistical power of the findings may be relatively weak. There are many confounders for light exposure and its timing, such as chronotype, UVR exposure, and other variables that can be associated with outdoor behavioural routines, such as working hours, existing health, age, exercise and physical labour. These and many more aspects are interlinked in
complex relationships, making it difficult to ascribe experimental results to causal mechanisms in less controlled exposure conditions (i.e. real life), whilst making translating results directly from a limited set of controlled exposure protocols less plausible.

Overall, health advice relating to light and IL responses including circadian rhythms will require coherent, larger scale studies using traceable metrology and more robust analysis of light exposures. The complexity of translational work suggests prospective studies of health outcomes require a multidisciplinary approach, and places clear limitations on the interpretation of retrospective studies with unsuitable proxies for non-visual (NV) light exposure profiles.

Publications 1 and 3 are reviews and consensuses about how coherent and systematic approaches to NV research can increase the comparability and generalisability of research findings. Publication 2 provides the only melanopic-based model to date for NV dose-responses that applies to general 24-hours-a-day circadian light exposure patterns, and has been applied in Publication A10, showing the preliminary circadian analysis of light exposures in shift working nurses for the first time. The background work to the metrology in Publication A10 is discussed in Section 3.3, confirming it as the first large-scale study with spectrally-matched melanopic light exposure time-series data. More details are given in Appendix A about my publications numbered A1 to A11, which do not form part of the portfolio, but are included for completeness and context.

3.1.1 Publication 1: Measuring and using light in the melanopsin age
Publication 1 was the first to recommend using an agnostic system of photoreceptor-based action spectra and quantities to investigate circadian and neurophysiological responses to light (see Figure 3.1). It has two parts: the recommendations were based on a thorough consensus review of the literature on NV responses to light (Part 1), and the recommended action spectra and quantities were provided within a spreadsheet toolbox to facilitate their use (Part 2).

The recommendations have found wide acceptance and the toolbox has been equally widely used in both photobiological laboratory and daylighting experiments as well as in lighting design. The melanopic quantity was adopted in an international building standard (IWBI, 2014), and incorporated in some handheld spectrometers. The CIE has included the recommended approach in an international measurement standard (Publication A8), with
the participation of the first author and myself. With the first two authors and myself have produced a version of the toolbox adapted for use in research on rodent NV responses.

Some other research groups have since proposed similar systems amounting to minor modifications or additions, but the original recommendations, now as codified by CIE in its international standard, continue to predominate over any alternative unified system and any other multi-receptor model. A second IWCNP workshop was held Manchester in 2019 and aimed to produce practical recommendations about exposure to light for health and well-being in people. I continue to be heavily involved in this project.

![Figure 3.1: Left panel as Figure 2.4 and Publication 1: Rods (turquoise [R]) and three cone types (green (MC), red (LC) and blue (SC)) provide signals to the ipRGCs (purple (M)]. Phototransduction in all five cell types can influence the NIF signals produced via the ipRGCs, on which all NV responses to light depend by definition (as NV and NIF are used as synonyms). Right panel as Publication 1: The boxes show the five spectral sensitivity curves (sensitivity vs wavelength), which due to the principle of unvariance reduce the incident spectral information down to five channels. Melanopsin bistability (or multistability) was assumed, by consensus, to have a negligible effect on human NV response to light in vivo.](image)

Note that the review in Publication 1 relates primarily to the responses of ipRGCs, but the Manchester workshop arose out of a project to standardise the action spectrum for circadian responses to light. This was recognised to be narrower, and broadened from the outset of the workshop, whereas it forms the central theme of the literature review in Section 2. As a result, it is hoped that my personal review in Section 2 complements the consensus review in Publication 1.
3.1.2 Publication 2: On the role of exponential smoothing in circadian dosimetry

The measurement methods and data collection for Publication 2 were completed to provide data to assist the development of a model of how light in retired people’s homes effects circadian rhythms. Retired people are freer to organise their time according to their preference, and so make a good group to collect such data without the biases and routines imposed by work or similar schedules. Two groups were used in this study: data from the homes of retired employees of the former National Radiological Protection Board were used to investigate the type of models that were ultimately considered; residents in private homes with the retirement community at Whitley Village in Surrey were used to parameterise the model. The Surrey data were also used in a collaboration to investigate the impact on sleep of LED lighting; spectral measurements confirmed that the LED lighting intervention would make no significant difference to the melanopic exposures compared to the previous lights.

The manuscript was around 90% developed before attendance at the 2013 Manchester workshop, and the model produced was distinct from the action spectra discussions, as it focussed on time-series and the use of 24 h variable light exposures to predict responses to light. Laboratory protocols often refer to light pulses and photoperiods with three variables – strength of stimulus, start time and duration – because the stimuli are generally constant, and periods before and after stimuli are effectively dark. In field work, variable light exposures have no clear start time, length or strength, so the aim was to create a model that for a range of realistic daily exposure patterns would produce one such photoperiod measure per day.

Prior to Publication 2, other published photoreceptive models of circadian response to variable light had not been updated to account for the persistent response to light after a light stimulus ends, or reduces in strength. There is still very little activity towards this goal, partly due to the adequacy of previous models, which depends on two main points:

- Circadian oscillators are chaotic system, specifically they are modelled as a Van der Pol oscillator, systems where small differences to inputs can produce very different results, but also where a range of different stimulus patterns can produce comparable results and repetitive features. Entrainment depends on exploiting the latter property, although the former can be demonstrated too. Consequently, many different models could predict circadian responses.
Previous models contain many stages and parameters, some being justified according to biological mechanisms, others according to the measured responses. The model in Publication 2 replaces the first stages of the main previous model (Kronauer et al., 1999) with a smoothing mechanism based only on a half-life, reflecting the response persistence. Figure 3.2 illustrates how the light exposure pattern (top left) is converted into the updated light-drive (top right), and the effect on different values for the smoothing parameter (bottom panels).

Figure 3.2: Melanopic-weighted irradiance time-series collected at several points in a room used during the day and evening in a house in Whitley Village, Surrey (top left panel), and shown with exponential smoothing of different half-lives (top right: 90 min; bottom left: 5 min; bottom right: 24 h) (data from Publication 2), shown on a logarithmic axis. The original time-series noise is evident with too short a half-life, whereas with a long half-life most of the timing information in the profile is lost. A moderate half-life, e.g. 90 min, enables measures of phase, photoperiod and amplitude to be determined that may help predict impacts of non-laboratory light exposure profiles on circadian rhythms (and/or other NV responses to light).

The half-life might be set according to the measured responses, e.g. those of Chang et al. (2012), but Publication 2 primarily used a non-biologically informed systems approach. The two methods were shown to agree remarkably closely to a half-life parameter of around 90 minutes. It is also remarkable that this model, permitting variable light exposure patterns, predicts the response to different durations of fixed stimulus strength light
exposure at least as well as the four-parameter model in favour that cannot be generalised to variable light exposure patterns (see Figure 2.3 Panel D).

As the model in Publication 2 is only a first stage of a larger model, there is extensive work required to validate it in the context of circadian behaviour. Publication 2 illustrated one example of how this might be achieved using existing qualitative data on the boundary between circadian phase resetting behaviours (where similar light stimuli with small differences in their timing can lead to qualitatively different outcomes on the phase-resetting of the circadian clock) (Winfree, 1980). It was shown using physiological stimuli that reproduce this type of boundary behaviour, that the model recreates these behaviours when incorporated in a Van der Pol oscillatory model of the circadian system, although further work would be needed to parameterise the combined model.

Currently, recent publications from other research groups focus only on fixed strength stimuli comparing either different durations or different stimuli strengths. It is therefore my view that the possibilities of this class of model have not been fully appreciated by the research community.

3.1.3 Publication 3: Linking the non-visual effects of light with occupational health

Publication 3 arose out of collaboration with the German Federal Institute for Occupational Safety and Health (BAuA). Representatives from six European institutions with an interest in shift work, light exposure at work and health met in Dortmund in 2018. I proposed and led an opinion paper setting out our agreed position relating to research into this area, which was published in our first-choice journal. Publication 3 explains and illustrates the need for multidisciplinary approaches to field work studies on the effects of light exposure and work patterns on health, as well as the need for a more coordinated and systematic approach to the field, as summarised in Table 3.1 (re-expressing the consensus).

Figure 2.5 sets out how circadian responses to light information regulate short-term practical outcomes, such as sleep timing. Disruption of the circadian timing mechanisms due to an inadequate light exposure profile, e.g. due to night work, is a risk factor for a range of long-term health conditions. The question of the joint impact of light exposure and work on health also has a special relevance in Europe due to the high concentration of populations at high latitudes, where shift patterns interact with seasonal changes in daylength to produce a greater range of light exposure scenarios than in other global populations closer to the equator that experience daylengths close to 12 h all year round.
<table>
<thead>
<tr>
<th>Multidisciplinary specialisations</th>
<th>Reason required, advantages</th>
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<tbody>
<tr>
<td>Shift work schedule factors</td>
<td>There is a large variety of possible shift times, durations and rotations. Epidemiological studies should address these options systematically.</td>
</tr>
<tr>
<td>Circadian responses to light</td>
<td>Models should combine field dosimetry data and chronotype to predict phase shifts etc.: For determining eye exposures to light - the basis for non-visual effects of light (NoVEL) For determining subjective time and states – the true context for circadian entrainment by light</td>
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<tr>
<td>Field dosimetry</td>
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<td>Chronotyping</td>
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<td>Sleep</td>
<td>It is considered likely that the major responses to light for long-term health relate to sleep</td>
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<tr>
<td>Biomarkers</td>
<td>Objective physiological outcomes, including endocrine function, e.g. melatonin suppression due to light at night (LAN). Convenience for field work vs accuracy</td>
</tr>
<tr>
<td>Psycho-social</td>
<td>Ecological momentary assessment (EMA) for frequent, low-bias data on cognitive performance, productivity and mental health. Personalised interventions for improved outcomes and compliance</td>
</tr>
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3.2 The optical hazards of visible light (Publications 4-6)

Artificial light is endemic in societies worldwide and is one of the most widely-used and accepted technological aspects of modern lifestyles. Expert advice should reflect strategies that balance the risks and benefits of lighting and light exposure, and be impartial between equal exposures from different lighting technologies (e.g. Publication A5). Natural light can be greatly beneficial, but sun exposure also presents risks, and it is important to consider potentially vulnerable groups (e.g. see Publication A2).

The uncertainty relating to the circadian responses to light have their counterparts in work related to the optical hazards of light exposures and lighting. Advice on some of these hazards needs further development, although for many important damage mechanisms there is expert international guidance on safe exposures published by ICNIRP (2013).

The guidelines are reviewed regularly by the international expert community. No-one denies that uncertainties exist, but these can create disproportionate misunderstandings. Other scientific reports (SCHEER, 2018; ANSES 2010, 2019), faced with the rapid advances in LED lighting have reflected public concerns, and well-meant advice may cause unnecessary concern about the safety of artificial lighting. Reviews of measured optical radiation and light emissions from new technologies and lighting can add context and reassurance.

It is plausible, however, that there may be undocumented or unproven long-term effects of light exposures; establishing causal relationships for such long-term effects is difficult. Where there are uncertainties about the risks arising from realistic exposure scenarios, then it is often helpful to suggest and investigate potential and hypothetical damage mechanisms and consider how the evidence may be collected to test these hypotheses. Practical precautions against harm might be indicated if they can be implemented consistently with existing safety measures at little extra cost.

The publications in this section are relevant for determining public facing advice covering three complementary areas of light exposures: treatment lamps; mobile phones and display screens; and general lighting. Publication 6 relates to general lighting, covering TLM and its effects (including flicker). Publications 4 and 5 cover the photochemical BLH measurements of specific sources. Publication A11 covers BLH-weighted exposure profiles from general lighting and reviews animal studies of blue-light damage from LED lights.
3.2.1 Publication 4: Efficacy and ocular safety of bright light therapy lamps

In September 2009, I joined the Health Protection Agency, having previously worked in insurance and business consultancy as an actuary. My new colleague Dr Bacynska received her PhD in laser spectroscopy that year, and had recently presented a poster on the spectral region for melatonin suppression and the emission spectra and safety of treatment lamps for Seasonal Affective Disorder (SAD lamps). It found that the emission spectra, size, shape and instructions were variable.

![Graph showing efficacy and protection ratios for SAD lamps, daylight lamps and sunrise alarm clocks](image)

Figure 3.3: Efficacy and protection ratios for the SAD lamps, daylight lamps and sunrise alarm clocks (from Publication 4), using logarithmic axes. All other things being equal, higher ratios are preferable; product performance varied widely (red and blue markers). The ratios are defined so that an equal-energy spectral distribution has a value of 1, with the following assumptions: the “circadian” treatment effect is proportional to melanopic sensitivity (an in-vivo peak sensitivity of 488 nm was used, as in Publication 7), the “phototoxic” effect is based on the BLH function $h(\lambda)$, and visibility on the photopic function, $P(\lambda)$.

Publication 4 added to and significantly developed several components of this poster. The likely action spectrum for the effect was reviewed, replacing a wavelength region with a candidate spectral weighting based on melanopsin sensitivity. The optical safety assessments were improved, and the basis of the underlying international guidance reviewed, leading to questions about its scope and suitability in SAD treatment protocols. An assessment of the flicker was added due to its potential impact on acceptance and compliance with treatment instructions. The photopic and BLH spectral weightings were
used in conjunction with the melanopsin curve (the action spectra introduced in Section 2 and Figure 1.3) to define efficacy and protection ratios, put forward as selection criteria.

I further developed the use of ratios (see Figures 3.3 & 3.4) to carry out scenario testing, for an invited presentation at the DIN Expert Forum in 2012 (DIN-Expertenforum), a symposium about light and human health in Berlin. The relative positions of all the lines and markers in Figure 3.3 depend on the assumptions selected for “circadian” and “phototoxic” sensitivity, for which there was no consensus. By varying these assumptions and redrawning Figure 3.3 each time, this presentation showed that adopting different competing action spectra models and theories for beneficial and potentially harmful effects would lead to opposite clinical decisions about the lighting to use in SAD treatment and
other health-related circadian applications (see Figure 3.4). It was following this panel that I was invited to an early evening meeting where I witnessed the DiN first contemplate abandoning the use of the Gail function for a standard.

This study links many of the publications in this portfolio (most notably Publications 1, 2, 5, 6, 7, A3, A8 and A11), as follows:

- The same melanopic action spectrum was also adopted in Publication 7 to assess the performance of a wearable device for measuring light exposures, based on a decision about the best candidate for a circadian action spectrum relating to melatonin phase shifting.
- The dynamic model in Publication 2, was based on using this melanopic action spectrum for the dosimetry of naturalistic human exposures (i.e. those broadly related to field studies rather than laboratory protocols).
- Publication 1 based the standard melanopic values (Publication A8) on this melanopic model with revisions to the lens model which I developed with two of the authors (see Publication A3 for details).
- The approach to flicker in Publication 6 arises out of methods I developed during this project, and reuses the relevant data.
- I had first made estimates of the photochemical dose allowing for sub-additivity in this publication (4), and such assessments also relate to Publication 5, in which we refuted many repeated claims about LED lighting and the health effects of blue light.
- Publication A11 explores the relevance of long-term exposures to photochemical damage, which I also discussed in more depth during the DiN presentation.

3.2.2 Publication 5: Low-energy light bulbs, computers, tablets and the blue light hazard
Publication 5 investigated devices with display screens, and new low-energy technologies that have been introduced into general lighting. The exposures from these are generally much lower than the safety thresholds relating to the BLH (see Figure 3.5). It was shown that the maximum output from the screens on the market are all orders of magnitude lower than the indirect emission from the blue sky in summer or winter, and that lighting technologies do not have significantly greater BLH-weighted components than previous lighting technologies.

These two points are, of course, statements of the obvious – even the highest contrast screens are difficult to read in outdoor daylight, and lighting commonly selected by
consumers based on appearance have the same correlated colour temperature, and hence have very similar BLH weightings. However, Publication 5 is motivated as a response to misleading scientific reports and press stories suggesting that LEDs contain greater amounts of more harmful blue light. The light measurements are carried out with traceably-calibrated laboratory measurement equipment.

![Maximum output of screens (% of thresholds)](image)

Figure 3.5: Demonstrating the blue-light safety of viewing LED-screen-based devices, as assessed in Publication 5. At maximum output, all the screens were well below both the ICNIRP rule of thumb and its BLH safety threshold, so even staring directly at them for several hours presents no risk of retinal damage: exceeding 100% of the rule of thumb for white light sources is intended to be a trigger level for carrying out a BLH assessment, and even exceeding the BLH safety threshold in this assessment does not automatically imply photochemical damage to the retina; would result from continuous staring, as the threshold is set at approximately 10% of the level which on average begins to cause retinal damage.

It is worth noting that some reports looking at blue-light exposure are not motivated by a fear of new LED technology. There is an unproven hypothesis that long-term exposure to blue light is associated with, or may even cause, age-related macular degeneration (AMD). The AMD hypothesis has not yet been demonstrated (i.e. no association), and although some epidemiological studies investigating this question have been completed, interpretation is complicated by the long-term nature of the proposed effect, and the difficulty in establishing a suitable measure for lifetime exposure. This therefore develops themes from Publication 4, which considered these long-term effects, and the DIN presentation which trialled other candidate action spectra for these long-term effects, as such long-term effects may not necessarily be from BLH-weighted exposures to light.
3.2.3 Publication 6: Can the Adverse Health Effects of Flicker from LEDs and Other Artificial Lighting Be Prevented?

During the flicker assessments in Publication 4, I began to develop a method for analysing temporal light modulation (TLM), which was consistent with observed health effects from general lighting exhibiting TLM at frequencies not causing the visible temporal light artefacts (TLA) known as flicker. The paper investigated the possibility of persistent exposure to flicker, but at subliminal levels, mediating these health effect; although flicker is classed as a visible TLA, the downstream health effects would not be exclusively TLA.

There was good reason to think that the response mechanism that leads to phase-locking of retinal photoreceptors to TLM is not restricted to when TLA can be seen. Other research groups had focussed on the possible connection between the stroboscopic effect and the phantom array (both visible TLA) with some of the unexplained effects. The phantom array relies on saccades which occur continually, and high contrast stimuli. Reading speed is reduced with TLM even when no TLA are visible, but if persistent at subliminal levels the phantom array mechanism, caused by the saccadic scanning motion of the eye during reading, may be account for reduced reading speed, and by analogy other health effects.

![Image](image.png)

Figure 3.6: Examples of unsmoothed (left) and smoothed (right) TLM from an incandescent light bulb (INC, blue), a compact fluorescent lamp (CFL, turquoise) and an LED (red), from Publication 6. The modulation depth of the unsmoothed TLM is often quoted as PF, but is independent of frequency unlike human photoreception and vision. Publication 6 introduced PPF = % modulation depth of the smoothed TLM. Unlike Fourier metrics such as SVM, PPF also adjusts for the relative phases of frequency components, producing an asymmetric response to duty cycle, similar to the human eye. Percent Flicker (PF), Physiological Percent Flicker (PPF), Stroboscopic Visibility Measure (SVM).

Subliminal flicker responses are not proven to be the cause of health effects. However, it seems unlikely the subliminal stroboscopic effect is relevant to the known health effects arising in offices and classrooms. The possibility of unwanted phantom array responses at
a subliminal level is considerably more plausible for the reasons already given. Even if the phantom array is capable of mediating health and performance effects, subliminal flicker effects may also be a contributing factor.

The paper used a simple mathematical smoothing technique to create a first-order model of the response time of cones. The Percent Flicker formula was applied to the smoothed time-series (see Figure 3.6), to create a new metric (measures used to quantify different aspects of lighting performance), Physiological Percent Flicker (PPF). PPF has a dependency on waveform shape with strong similarities to TLA (waveform shape is determined by the relative frequency, phase and amplitude of all the TLM’s harmonics, or Fourier components), and its frequency response mirrors the experimental data on TLA in the high-frequency range of interest for the regulation of TLM.

The paper applied this metric to a range of different lights that had been measured for a report on Human Responses to Light Based on LED Lighting Solutions (Publication A5), as well as the data collected in Publication 4 on SAD lamps. It showed that the metric corresponded at a given frequency with a popular existing metric, Flicker Index, that assesses the waveform shape, but is independent of frequency (unlike the TLA it tries to predict).
3.3 CCD array and dosimeter performance for field measurement (Publications 7-11)

As outlined in Section 3.1, it is important for studies to collect 24-hour exposure data based on NV spectral weighting functions and the eyes’ directional and dynamic optical response characteristics. The publications in this section concern the performance and practical convenience of wearable and portable spectral measurement instruments that can be used to collect such data. In Publication A4 I recommended the high level “dosimetry chain” of standards and practices that will be needed to achieve high quality dosimetry in field studies, to ensure data are truly comparable between studies:

- shared standard measurement quantities (as established in Publication A8, based on the proposals from Publication 1);
- assessment methods to quantify the performance of dosimetry equipment, the main topic of three publications in this section;
- information concerning the relationship between data collected at the measurement position (i.e. where the dosimeter is worn) and light entering the eyes; and
- validated models that relate time-series data to human physiological responses, (such as the model proposed in Publication 2).

The assessment methods and performance “metrics” (measures used to quantify different aspects of instrument performance) must be reproducible and meaningful for as wide a range of practical applications as possible, conveying the quantitative impact or expected average impact on the final measurements.

Some metrics are less useful than others. For instance, spectral correction factors rely on exposures being caused by a known spectrum of light, but outside of experimentally-controlled scenarios human exposure to light includes multiple simultaneous direct, reflected and transmitted sources. Daylight is continuously variable in spectrum as well as intensity, and dynamic lighting used in experimental interventions may be designed to vary the spectrum of an artificial light with several degrees of freedom, each of which would need to be independently measured in the exposure.

Improved understanding of device performance can also lead to better metrological practice. The standard field practice guidance for CCD array spectrometers mandated contemporaneous measurement of dark current (Seckmeyer, 2010), and stabilisation of board temperature to within 0.1°C was normal practice (Blumthaler et al., 2013).
Publication 8 addressed this guidance, and found that it could be simplified. Publication 9 gives details of a reproducible practical performance assessment method for determining array linearity characteristics, which has informed subsequent practice in applied studies (see Table 3.2).

Publications 7 and 10 detail the development of several performance assessment methods and metrics for wearable devices for use in NV response studies. Existing methods are optimised, and new methods are introduced making use of existing performance assessment data and adding to existing protocols and set-ups. Publication 11 makes use of one of these advances to develop a sensor with an optimised spectral sensitivity.

3.3.1 Publication 7: Performance assessment of commercial circadian personal exposure devices

Sleep research has a history of employing wearable actimeters, often worn as wrist watches, to monitor physical activity and sleep. Following the discovery that nocturnal light suppresses melatonin and disrupts sleep, manufacturers incorporated light sensors into many new models, and these actimeters also became dosimeters. Other physiological

![Graph showing spectral response of sensors.](image)

Figure 3.7: The optimised linear combination of the blue and green sensors ("Mean") of the Actiwatch Spectrum ("AWS") best matching the in-vivo melanopsin sensitivity function ("Melanopsin"), plus the standard deviation ("SD") and coefficient of variation ("SD / mean") of the optimised spectral responses of the 16 assessed AWSs (from Publication 7). Note that the spectral match is worse below around 440 nm, which could lead to modest overestimates in daylight conditions, but would be expected to have little impact under most artificial lighting. Some human non-visual response data has also suggested additional sensitivity in this region.
research fields, e.g. sports performance, began to use these sleep research devices, or had
developed equivalent devices. From this point actimeter/dosimeter devices will be referred
to as “wearable devices” or dosimeters, as actimetry is not of direct interest to optical
performance.

Publication 7 investigated the spectral, directional and dynamic performance of 16
wearable dosimeters of the same model, called the Actiwatch Spectrum (“AWS”, Philips
Respironics, model discontinued), that contains three optical sensors, with distinct
broadband spectral sensitivities within the visible wavelength range. Originally presented
at a workshop at the CIE 2011 Quadrennial Session, in the form of a conference paper and
oral presentation, the invited final article (i.e. Publication 7) gives quantitative assessments
of the sensitivity of the three sensors and the composite “white” illuminance channel
across the dynamic range, 2π field-of-view, and visible spectral range, and each is
illustrated with charts. For the dynamic performance, the non-linearity factors were given
at six light intensities. The standard cosine mismatch metric \( f_2 \) was selected for assessing
the directional response required for irradiance measurement (see Figure 3.8).

![Figure 3.8](image)

Figure 3.8: The directional match of the AWS across two axes vs the idealised cosine
response, used as a proxy for the directional response of the human eye (from Publication
7). The AWS directional mismatches (see Definitions), and similar mismatches in dosimeter
position relative to the eye, may be more significant than the AWS spectral mismatches.
Publication 7 recommended that the AWS should be worn with the directional mismatches
aligned to the selective directional response characteristics of the eyes.

For spectral sensitivity assessments, the peak wavelength and full-width half-maximum
wavelength range were determined. Two more sophisticated assessments were
developed. The first looked at batch variation within the 16 devices, based on the
wavelength range over which all the responses agreed to within a coefficient of variation
of 20%. The second looked at the optimal linear combination of the three sensors to match
the melanopic sensitivity curve (see Figure 3.7), based on five human studies on NV action spectra.

Publication 7 was the first known independent performance assessment investigating the suitability of dosimeters for NV research since the 1998 discovery of melanopsin. Manufacturers and research groups had published performance data in the form of specifications of variable quality for other devices, and there were even two papers, but these could not be independently verified prior to purchase and did not consider the importance of the melanopic action spectrum.

3.3.2 Publication 8: Effects of ambient temperature on the performance of CCD array spectroradiometers and practical implications for field measurements

In Publication 8, the influence of ambient temperatures on a small sample (6 models) of miniature CCD array spectrometers, suitable for photobiological field measurements, was studied. The devices were housed in an environmental chamber, and exposed to temperatures of between 5°C and 40°C, while being exposed to a stable light via an optical fibre from sources outside the chamber. The temperature range reflects possible outdoor conditions, for example relating to spectral solar monitoring applications. One advantage of such devices for solar monitoring is the short integration times achievable when compared with scanning instruments that typically acquire spectra over a few minutes.

The analysis looked at the change in board temperature, wavelength position, slit function, dark current, including noise, and sensitivity, and how the performance varies over time following introduction to a new stable ambient temperature. Integration times were also varied, to determine their interaction with temperatures on dark current and sensitivity.

Figure 3.9: Performance measures for a TEC cooled spectrometers (QE650D00, Ocean Optics, Dunedin, Florida, USA). Sensitivity variations (left) compared to the laboratory operating temperature of 22°C, and slit function distortion (right) due to the impact of ambient temperature on the diffraction grating performance (from Publication 8).
Two of the models tested included Thermoelectric Cooling (TEC) of the array. TEC models are designed to stabilise performance at different ambient temperatures, which brings both benefits and drawbacks. In one model, data are provided on the cooled array temperature and the target TEC temperature can be specified or cooling turned off. TEC settings impact various performance aspects differently, hence it was important to assess the full range of behaviours. Figure 3.9 confirms ambient temperature may still affect performance, even for a TEC model.

Prior to this study, expert opinion specified that reproducible data could only be collected in stable ambient temperatures within approximately 0.1°C (Blumthaler et al., 2013). For the devices tested, the data showed how board temperature lags ambient temperature and confirmed that changes in sensitivity were negligible for changes in instrument temperature within approximately 2°C, findings with important practical advantages. It not only shows that CCD arrays can be used in less stable ambient temperatures but that, with appropriate characterisation, temperature correction of sensitivity can be applied for a broad range of ambient temperatures in field measurements, thereby removing the requirement for controlled environmental temperatures.

Figure 3.10: The dark signal (or current) performance for a selected uncooled spectrometer (HR4000, also Ocean Optics) (from Publication 8). The effect by wavelength of integration time at low temperatures (5°C, left), and the variation in SD across the array of dark signal due to ambient temperature and integration time (right). Reduced counts below 550 nm were only observed with low integration times at low temperatures (e.g. 5°C). For most spectrometers, the dark signal SD is greater for longer integration times and higher temperatures (and consequently reduces the usable well-depths), but for the HR4000, uniquely amongst the spectrometers studied, this behaviour is limited by a temperature-related threshold for the dark current SD which is lower at higher ambient temperatures.

Similarly, expert guidance called for contemporaneous measurements of the array dark current with each measurement (Seckmeyer, 2010), due to changes in the combination of temperature and integration time. Figure 3.10 illustrates why this may be reasonable (see
the wavelength dependence in the left-hand chart), but this somewhat undesirable performance was found to be unique amongst the spectrometers tested and only observed at low temperatures.

### 3.3.3 Publication 9: Dynamic response of CCD array spectroradiometers

Publication 9 detailed a method for rapid characterisation of non-linearities in CCD array spectrometers with an FEL lamp, and illustrated its use for four instruments. Non-linearities limit the usable well-depth or require linear correction factors, simultaneously reducing the effective usable well-depth. The non-linearities found were only of the saturation type, reducing marginal pixel sensitivities as the counts in the pixels approached the maximum.

Table 3.2: Formulae for CCD linear corrections and related uncertainties. The corrections are based directly on raw signal counts, \( r(t) \), provided the results of correction formula are independent of changes to the integration times, as confirmed in Publication 9 for the spectrometers tested. The process was further simplified as no lower linear thresholds for \( r(t) \) were observed. Includes formulae reproduced from Publication 9.

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counts per second, ( cps )</td>
<td>( cps = (r - d)/t ), where</td>
</tr>
<tr>
<td></td>
<td>( t = ) integration time (in seconds),</td>
</tr>
<tr>
<td></td>
<td>( r = ) raw signal, and</td>
</tr>
<tr>
<td></td>
<td>( d = ) dark signal</td>
</tr>
<tr>
<td>Linear correction factor, ( LCF )</td>
<td>( LCF(r) = \frac{cps_1}{cps_2(r)} ), where</td>
</tr>
<tr>
<td></td>
<td>( cps_1 ) is based on a linear measurement, such that</td>
</tr>
<tr>
<td></td>
<td>lower linear threshold (&lt; r &lt; ) upper linear threshold,</td>
</tr>
<tr>
<td></td>
<td>and ( cps_2(r) ) on measurements that cover the full usable well-depth,</td>
</tr>
<tr>
<td></td>
<td>such that ( r &gt; d ). Corrected counts per second, ( cps' = LCF(r) \cdot (r - d)/t ).</td>
</tr>
<tr>
<td>Uncertainty, ( \delta )</td>
<td>( \delta(r) = \frac{(t/2; s_2^2) \cdot \sqrt{2 \cdot \delta^2 (d_1^2 + s_1^2) + \delta^2 (d_2^2 + s_2^2)}}{t} ), where</td>
</tr>
<tr>
<td></td>
<td>( \delta d = \delta d(t) = ) dark signal SD across the array, and</td>
</tr>
<tr>
<td></td>
<td>indices ( i = 1 ) or ( 2 ), refer to the linear and full well-</td>
</tr>
<tr>
<td></td>
<td>depth measurements for ( cps_1 ) and ( cps_2 ), respectively.</td>
</tr>
</tbody>
</table>
Performance varied between the instruments, with one array exhibiting non-linearities of up to 20% following a broad region of linear response, compared to others with lower non-linearities impacting on a greater proportion of usable well-depth.

Data from one instrument was used to illustrate that, for a given level of counts, non-linearities were independent of integration time, and used to derive linear correction factors and associated uncertainties inherent in the method. The data for this instrument and one other confirmed that the non-linearities were unrelated to ambient temperature. The paper discussed the order and priorities for routine corrections of measurements with CCD arrays, noting that non-linearity corrections are based on well-depth only, and that where both are required these corrections must be applied before stray light corrections.

Together with Publication 8, these papers cover the largest sources of error in typical field measurements due to the performance of CCD array spectrometers. It is also important data showing that more sophisticated analyses and correction methods for the stray light properties of these devices rely on selecting only linear response data under well-characterised and stable temperature conditions, and quantifying when, for convenience, such devices may be used in less technically demanding optical laboratory measurements under environmental control.

3.3.4 Publication 10: Optical performance characterization of light-logging actigraphy dosimeters

Following Publication 1, setting out the five spectral sensitivities of the NV system, there was a need to assess dosimeters used in NV research of neurophysiological responses to light, including circadian rhythm responses. This enabled previous work to be contextualised in the measurement framework recommended by Publication 1, and supported device selection decisions for future work. The range of suitable wearable devices and their performance was diverse.

Publication 10 systematically reviewed all the devices that were available, based on previously purchased devices and free loans of devices directly from manufacturers and relevant research groups. Where the devices were not available, sufficiently detailed published specifications on the optical components were requested and found using internet search methods, which were interpreted to facilitate wider quantitative comparisons. Figure 3.11 summarises the results for the available devices (adapted).
Figure 3.11: Optical performance characterisations of selected wearable devices (dosimeters and light-logging actimeters) for NV research and diagnostic use (adapted from Publication 10). Figure and caption continue on facing page below. Linearity charts, above, illustrate sensor response is often non-linear at lowest light levels (blue diamonds). The GAO has no extended linear range (far left, second row). Sensor labels: Clear [ATR only], R, G and B. Device labels: ATR = Condor ActTrust; AW* = Actiwatch*; (AW2, AWL, AWS, AWSP) = (2, L, Spectrum, Spectrum Plus or Pro), respectively (AWSP, Philips Respironics); GAO = Activinsights GENiActiv Original; and MWB = CamNtech Motionwatch B.
Figure 3.11, continued. By (row, column) on this page: spectral response (1-3, 1-2), with target NV spectral responses in (1, 1); cosine response (1-3, 3); and dynamic resolution (1-3, 4). Observations: the ATR B sensor (1, 2) best matches melanopic sensitivity (1, 1); the AWSP B and R sensors exhibit negative marginal spectral sensitivity (3, 2); directional responses (1-3, 3) generally combine parallax and material properties; arrows in (1-3, 4) indicate 100 lx of equal energy light, e.g. showing the AWL and GAO resolutions are too large to measure low light levels (2, 4).
The article developed the framework for consistent generalised **spectral mismatch**, **directional mismatch** metrics, and even suggested the possibility for a similar dynamic mismatch metric. These were employed in the assessments, and proposed as the basis of a future standard for non-visual (NV) dosimeters. Mathematical inconsistencies between the existing metrics for illuminance and luminance meters were noted. They were also shown, with examples using the device performance data, to be inappropriate for generalisation in NV applications in some respects.

Theory on the use of combined channels based on more than one sensor was developed, emphasising the metrological advantages of restricting these channels to positive linear combinations. One of the tested devices illustrated why, returning zero response to some intermediate visible wavelengths. It was highlighted that a device would need to include as many spectrally distinct sensors as the NV system had spectrally distinct photoreceptor types, i.e. five, to fully characterise the exposure in the recommended system.

To investigate zero responses, the marginal response to light of a given wavelength was investigated in the presence of a tungsten halogen light, providing a smooth stable background spectral distribution. From this it was established that the electronics were arranged so that the addition of light at some wavelengths resulted in negative contributions to the output, with a minimum of zero being imposed on the overall result reported by the device.

It was established that no device had a sufficient number (five) of spectrally distinct light sensors, and the spectral assessments concentrated on individual spectral matches to the recommended sensitivities, with an emphasis on melanopic sensitivity and photopic sensitivity, the latter being spectrally close to two of the cone sensitivities. The theory was developed to show the mismatch between the five NV photoreceptors as a benchmark for interpretation of the spectral mismatches between a sensor and a given photoreceptor. The rods and ipRGCs were shown to be matched much closer than any single sensor and either of these photoreceptors. The sensitivities between the M- and L-cone types (and the photopic curve) also matched much closer than to any single sensor (with just one possible exception based on external research data).

All characterisations were illustrated by spectral, directional and dynamic response charts for the devices, with the addition of a dynamic **resolution** chart. This illustrated that the resolution in the output data from some devices were inadequate for applications at light
levels up to equivalent illuminances of 100 lx. To enable dynamic comparisons, the equivalent illuminance concept from Publication 1 was adapted to incorporate quantities based on the sensors’ own spectral sensitivities. It was noted that equivalent illuminances are amenable to linear combinations that automatically achieve the required normalisation. This contrasts with weighted irradiance combinations using the SI system, where composite action spectra must be renormalised so that the maximum is equal to 1.

The initial results of the publication also identified domsimeters for use in the study of nurses (Publications A10 and A11), adding the GeneActiv Original and CamNtech Motionwatch 8 to the existing Actiwatch Spectrum devices. It also identified the closest single sensor match to the melanopic curve in the blue sensor of the Condor ActTrust device, which formed the basis of further development work in Publication 11. All the spectral sensitivity data measured in this study were published as freely available supplemental data, and the external sources of spectral data were all provided as accessible online links. Only two of the devices could not be assessed quantitatively – magnetic access switches in one model failed to be operable during the loan, and another device was not considered further due to having a red casing that would strongly distort the spectral sensitivity away from the eye’s spectral sensitivities.

3.3.5 Publication 11: Modification of a personal dosimetry device for logging melanopic irradiance

The availability of bandpass filters to further improve the best single sensor from Publication 10 were investigated, as much of the mismatch to the melanopic function was due to unwanted levels of sensitivity to visible light outside of the range of 430 nm to 640 nm (see Figure 3.12). The manufacturer Condor, was asked to modify the ActTrust (ATR) with the selected filter. The modified model code is given, to allow independent researchers access to the device.

Based on performance tests undertaken on the resulting device, the article confirms the expected reduction in melanopic mismatch, from over 25% to approximately 17.5%, the only available mismatch below 20% of any wearable device. Similarly, there is no material impact on the dosimeters’ relatively low photopic spectral match and a slight increase in the directional mismatch to the cosine response. However, the directional III response of the eye is not considered to be perfectly cosine, and the resulting directional response may better resemble the eyes’ response relating to exposure of the peripheral retina in the
vertical axis if the sensor is angled downwards. In the horizontal axis, arguably no device studied in Publication 10 could have the adjusted directional response that would properly account for all reasonably possible eye and head movements relative to the dosimeter. Inevitably, the dynamic response is shifted for all the sensors, but the threshold of linear responses is around an equivalent illuminance of 1 lx, and the bandpass filter effectively blocks the infrared sensor (which is not directly useful to III dosimetry).

Figure 3.12: Relative spectral sensitivities of the B and G sensors for the ATR and modified ATR compared to the human eye, log scale (from Publication 11). Left, the improved spectral melanopic match of the ATR B when modified with a bandpass filter from 420 nm to 650 nm, removing short- and long-wavelength oversensitivity and out-of-range sensitivity, with a slight overcorrection below 420 nm. Right, the changed spectral photopic match of the ATR G reduces “out-of-range” sensitivity above 650 nm, and further reduces under-sensitivity just below 650 nm – at short wavelengths below 420 nm it helps to reduce both oversensitivity and out-of-range sensitivity.
4. Conclusions and suggestions for the future

4.1 Impact on public health policy

This section deals briefly with the main areas in which my portfolio contributes to understanding human non-visual response to light.

In the first section, my publications (Publication 1 in particular) have contributed towards systemisation efforts to improve the metrology and reproducibility in field research into the non-visual effects of light on health. Publication 2 has provided a testable model proposing how to measure and interpret uncontrolled personal exposures to light in field studies, and Publication 3 specifically addresses the challenges in studying work-related influences on circadian rhythms and health.

In the second section, the publications have contributed to the understanding of the potential adverse effects of exposures due to blue-light or temporal light modulation, highlighting both where public health concerns can be allayed and where optimal clinical advice is subject to uncertainty, and making a clear distinction between the two.

The third section has investigated the performance characteristics of portable spectral and wearable dosimetry equipment in measuring exposures to light in photobiology and non-visual health research, leading to much-needed improvements in practical field measurement studies that provide the evidence for public health advice and policy relating to light exposures. By way of two examples, firstly, the equivalent illuminance system I devised in Publication 1 is a vital component of the metrology system that was adopted in research and lighting practice around the world, and has now been adopted within the first international standard on non-visual light metrology, CIE S 026:2018 (Publication A8). Secondly, Publications 7, 10 and 11 have guided the growing number of public health research projects in the use and understanding of wearable dosimeters, so that the variable levels of accuracy these devices is now an important consideration in the design of exposure studies and intervention experiments in the field.

4.2 Future directions

This section deals with the possible directions of my own research and describes some of the latest trends and findings relevant to the review and to the non-visual effects of light and health.
The human photoreceptor calculation tool I constructed is widely used and supports an International Standard that can be used by future researchers and practitioners to quantify stimuli relating to ILL responses. The melanopic light drive model opens up several potential avenues of investigation into circadian disruption based on personal dosimetry, for example following the multidisciplinary advice on shift work health studies that I coordinated. One of my immediate plans will be to complete and publish the analysis of data collected on light exposures of shift working nurses in the UK and Germany for two publications, building on the work in conference papers, Publications A10 and A11.

Concerns about lighting and technology will continue, and it is important that these can be evaluated, and where appropriate, that reassurance is given based on the totality of the evidence. Public advice about the potential benefits and risks of light, and optical radiation in general, should continue to be practical and balanced, and much of this can continue to be based on my contributions in Publications 4-6. It is hoped that in the future researchers and practitioners will have access to more data and higher quality data than ever before; my contributions to characterising field measurement devices include the leading research into the performance of wearable light-logging dosimeters, and proposals for standard performance measures that may substantially improve the quality in future.

Indeed, even without dosimetry performance standards, through my own dosimeter development work, I have already modified a commercially available dosimeter optimised for collecting personal melanopic irradiance time-series. There is still a lack of data concerning the exposures of the ipRGCs collected using sensors spectrally-matched to melanopsin. Such data will be needed to determine the impact of various demographics including age, health status, occupation and geographic location. The spectral sensitivity of melanopsin has been standardised, as practically, the standard curve is likely to be adequate for predicting effects on circadian health and well-being for the great majority of people. This is plausible especially when considering the range of complex influences on behaviour, that would be expected to mask any marginal improvements from having a significant impact.

For an exposure scenario dominated by a specialised light environment, such as night shift work or bright light therapy, there might be a stronger case for a more detailed approach. Although the melanopic curve has been standardised, there remain open scientific questions. It seems sensible not to dismiss as irrelevant developments concerning
melanopsin tristability (Emanuel and Do, 2015), the dual ipRGC transduction and relaying functions (Milner & Do, 2017; Rupp et al., 2019) and the range of NV responses governed by the different targets of the ipRGC subtypes.

Evidence has shown that circadian desynchronisation and adverse health effects can occur without disruption to sleep patterns (LeGates, 2014). van Ee et al. (2016) cited these findings in support of a proposed model for the SCN acting as an engine of Bayesian inference of time-of-day. In this model, light exposure affects the timing of genetic clock markers' expression in ventral SCN neurons (encoding an exogenously-driven likelihood distribution for time of day) that combines with dorsal SCN timing (encoding an endogenously-driven prior distribution).

At present, no model predicts responses to freely varying melanopic exposure profiles. Publication 2 provided a first approximation for this exact purpose, but more sophistication will be needed to explain the different time dependencies of melatonin suppression and phase shifting. The model does not correctly predict the differences in phase shifting responses for highly controlled constant and intermittent exposure protocols, which may be relevant for studying the effects of Light At Night (LAN) from shift work, for example. The responses of the two populations of SCN neuron may be linked to the differences between acute melatonin suppression and sustained phase-shifting responses. Like Publication 2, van Ee et al. (2016) take an engineering approach, but the single oscillator is replaced with the SCN multi-oscillator inference model and there is no proposed measure of the light stimulus. Linking the exogenously-driven likelihood distribution to a light-drive model, such as the one in Publication 2, to describe what light signals produce ventral SCN entrainment most strongly, could produce testable predictions for a range of adverse health effects from uncontrolled patterns of light exposure, whilst improving the light-drive predictions for intermittent exposures.

Several groups are developing devices to measure NV exposures to light. If successfully implemented, the new devices may offer further spectral improvements over the modified ActTrust from Publication 11. However, the limiting factor of such dosimeters is not necessarily always their spectral matches, and there is a clear need to investigate unobtrusive dosimetry protocols that better allow for position, movement and/or field of vision. Another promising direction in health studies would be an interactive dosimeter, which offers advice and targets on light exposure, perhaps integrated with a commercial
step meter, that does the same for physical exercise. Again, such targets should ideally be based on a robust exposure model to allow for flexible and real-time interactions with wearers.

Dosimetry can be achieved without a wearable dosimeter, albeit with obvious reductions in accuracy. GPS can be combined with static daylight monitoring to predict UVR exposure (Corradi et al., 2019), and with added information about indoor exposures to light it may be possible to adapt these methods to NV exposures. This could include data from measurement surveys about artificial lighting and daylighting in homes, offices, schools, hospitals and many other indoor spaces. Questionnaires about time spent outdoors could also provide a great deal of baseline data on behaviour (e.g. Baczynska et al., 2019). These can be carried out in conjunction with dosimetry studies of smaller targeted groups, either relying on the natural experiment model or with light exposures interventions.

New technology and product designs may lead to new sources of optical radiation in the human environment, and currently emerging sources include LED face-masks and skin treatment lamps using visible narrowband light, and therapy involving broadband optical radiation deeper within the body, produced by the process of sonoluminescence generated from the cavitation of intravenous microbubbles, itself triggered by focussed ultrasound (Beguin et al., 2019). The responses of human skin could be modified by multiple overlapping and potentially co-dependent effects. Cosmetic, therapeutic, diagnostic and other medical uses of optical radiation are rarely subjected to the same level of regulation as novel pharmaceuticals, and such developments create a need for public and patient safety information, including independent assessments relating to the relative efficacies and potential harms.

The findings of early research into visual responses to TLM, using sinusoidal modulation, were able to predict some results relating to rectangular waves, and this might apply to LED lighting (Kelly, 1961). However, the electroretinogram (ERG) responses reported at frequencies more than a factor of two higher (Berman et al., 1991) suggest that these data were not sufficient to preclude modulated effects on retinal photoreception. Further direct investigation using rectangular waves with the duty cycles found in LEDs, based on target time-averaged luminance and realistic illuminance levels may be the quickest way to establish the limits of potential adverse effects being induced without visual responses.
5. Summaries of the publications, their context and reception

5.1 Publication 1: Measuring and using light in the melanopsin age

This publication is summarised in two parts which were published together, Part 1, a review paper and supplementary materials, and Part 2, a toolbox (interactive spreadsheet) with a written user guide that includes details of the model used throughout Publication 1.

5.1.1 Summary of Publication 1 Part 1

The review paper sets out a consensus relating to the goal of an action spectrum that mediates IIL responses in humans. The importance of light as a stimulus for health is emphasised through its regulation of the circadian system governing human physiology, metabolism and behaviour throughout the brain and body. It concentrates on the NV role of the eyes and the measurement of light, in the context of the distinction between classical understanding of visual responses and the NV system.

The therapeutic uses of light are cited to show the potential for applying this new knowledge, but it also cautions that artificial light has disrupted the evolutionary process which linked circadian rhythms to light exposure in the first place. The main thrust of the review paper is to address the outdated use of visual measures of light in studying the NV system and related health questions, by recommending that these should be replaced – heralding the "melanopsin age". The melanopsin age marks a recognition of a new viewpoint, not just about the function of the eye, but also the importance of light, the eye and melanopsin in human life and for other species; melanopsin’s photosensitivity is common to all mammalian species, with many other commonalities across even wider taxa. However, it concludes that a single action spectrum for melanopsin would not be sufficient to explain the spectral sensitivity of several NV phenomena observed in man alone.

The review paper finds that human NV action spectra are the combined result of the five different photoreceptor types in the retina that contribute to ipRGC responses. These five photoreceptors comprise the three types of cone, the rods and the ipRGCs themselves, due to the function of their intrinsic photopigment melanopsin. The consensus view put forward is that ipRGCs are responsible for all light-stimulated NV signals from the retina, and combine signals from the rods and cones with the response due to melanopsin. However, for most practical purposes, the relative contribution of each type is yet to be determined. Against the original objective to reach a consensus on the action spectrum for NV responses to light, it therefore rather sparingly concludes only that the spectral
sensitivity depends on the five spectral weighting functions relating to the five photoreceptor types, and therefore to their respective photopigments.

For each of the five human NV photoreceptors and corresponding new weighting functions denoted by \( \alpha \), a set of \( \alpha \)-opic quantities are proposed that are equivalent to, and complementary to, the photopic quantities, as a means for measuring light. The review paper (Part 1) gives just a brief overview of the spectral systems, the details being filled out in the toolbox and user guide (Part 2). The following five terms for the five channels of NV photoreception are introduced (also see 5.1.3): cyanopic, chloropic and erythropic for the cone photopigments, rhodopic for the rod photopigment, and melanopic for melanopsin in the ipRGCs.

The review notes further complexity arises in NV action spectra, due to the change in relative contribution of the photoreceptor types, for example with increasing duration of exposure to a light stimulus. This is illustrated by the pupil response to sustained illumination, that is initially most sensitive to longer-wavelength light, mediated by cone photoreceptors, but whose wavelength sensitivity shifts to shorter wavelengths, mediated by melanopsin, with increasing exposure. Without melanopsin, the pupil response is not sustained beyond a few seconds. The pupil response is used as an example of a NV response, but others include nocturnal melatonin suppression and phase shifting of circadian rhythms.

The review paper includes advice to two groups – firstly researchers, and secondly industry and regulatory authorities. Researchers are encouraged to measure and disclose light exposures using their spectra and new \( \alpha \)-opic quantities, using traceably calibrated instruments to ensure that the data are reproducible in the dimensions that relate to NV photoreception. For reusable spectral data, they are encouraged to revisit published data disclosing photopic quantities and other visually-based metrics, republishing and reanalysing the exposures using \( \alpha \)-opic quantities. Industry and regulatory authorities are warned to consider the NIF impacts of light, not to be overly reliant on visual measures of light, and to consider the risks of overgeneralising or oversimplifying specific research into NV effects, e.g. when designing the built environment and its lighting. The conflicts due to the timing of light exposure, and mixed objectives for visual and NV effects in night-shift workers and others are noted.
The review paper concludes that the recommendations are made based on the current level of knowledge (i.e. in 2014), with the intention of providing a comprehensive basis for the future, that can therefore be used whilst our understanding continues to evolve.

5.1.2 Summary of Publication 1 Part 2

The components in Part 2 are supplemental materials to the review paper (Part 1), and according to the practice of Trends in Neurosciences (TINS) all of Publication 1 was subject to peer-review at the same time.

The toolbox comprises a spreadsheet to assist users, primarily researchers, in calculating the five new α-opic quantities, either directly from spectral measurements, or from three other broadband systems (the radiometric, photometric and photon-based systems) provided the relative spectrum is known. It can therefore also be used to convert between all these different systems, and to perform conversions back into these systems from α-opic quantities, with the same proviso.

Importantly, the toolbox includes the reference action spectra for the five photoreceptor types in the NV system. These are based on the review of the peak photosensitivity of each of the five photoreceptor types in humans provided in Part 1, used together with a template for the spectral sensitivity of mammalian opsins and a model for the pre-receptor transmittance of the eye of a standardised human observer.

As well as providing instructions for using the toolbox, the user guide has four appendices describing the derivation of the α-opic system.

The first appendix sets out the mathematical approach used to calculate the α-opic quantities, including the normalisation procedure applied to the five action spectra and the value of the efficacy of NV photoreception. The toolbox and user guide are based on using alternative spectral weightings (or action spectra) to determine equivalent α-opic quantities, which are equivalent to each other and to classical photopic illuminance when the visible spectral distribution is uniform. This is both the method for normalisation, and the means of producing α-opic quantities with comparable magnitudes to the photometric system. As uniform visible spectra correspond to white light, the magnitudes are considered to also be intuitively comparable. Some comparison to previous suggestions is included, and a note that the proposals do not (at the time of writing Publication 1) have the status of an international standard.
The second appendix summarises a review of pre-receptoral transmittance and its relation to the photopic standard observer, and a modified model of pre-receptoral transmittance function used to calculate the action spectra is tabulated.

The third appendix includes a small number of definitions of the new terminology introduced by Publication 1, and some existing physical terminology used in photobiology for those using spectral measurements for the first time.

The fourth and final appendix simply provides an example spectral distribution for users to practice using as an input to the toolbox.

5.1.3 Context and reception of Publication 1 (both parts)

This review paper set out the consensus of a three-day workshop for invited representatives of the leading laboratories and research groups into human IIL responses. These individuals had extensive publication records relating to NV photobiology and human action spectra studies. I was invited to the workshop leading to Publication 1 to act as Rapporteur to the International Commission on Illumination (CIE), and was added as an author to the review paper because it was agreed I had made a genuine contribution to their work.

The consensus was not a foregone conclusion, and does not appear to have been anticipated. One reason for the conclusion reached was the candid exploration of the uncertainties facing the field, and this was a discussion in which I played a part, based on my own interest in the consequences of comparing the effects different assumptions would have on clinical decisions and public health advice.

There were previous papers investigating the contribution of different photoreceptor types, but these did not suggest new measurement systems, or new quantities being a basis for a systematic approach to disclosing light stimuli or reviewing previous research. As shown in Section 2, the literature instead was made up of competing theories, largely consisting of single action spectrum or a fully prescribed approach. The review paper therefore contains a genuinely innovative way of approaching this field as a collaborative research enterprise, as well as a decisive statement of need for further research to improve the knowledge already being used in interventions and products.

Publication 1 has achieved 397 citations in five years (76 self), which refer to the combined parts: the review and consensus in Part 1 and the toolbox-supported system of equivalent
α-opic illuminance measurements in Part 2. It is published in a high-impact journal (2018 impact factor 12.314); even so, the publication has been and is clearly a substantial net contributor to the relevant impact factors for this journal.

My contribution to Part 1, as agreed with my 13 co-authors, was 5%. Some of my co-authors said it could be higher.

In 2015, Publication 1 became the subject of CIE technical note CIE TN 003:2015 (Publication A3), which I authored, and my Publication 1 co-authors advised. This outlined the parallel set of quantities, α-opic weighted irradiances, based on the existing SI approach to action spectra (other than visual quantities of light, which have a special place in the SI system). As well as an enhanced toolbox, it also includes information about the proceedings of the 2013 workshop, the first NV system for allowing for age-related changes in pre-receptorial transmittance, and further details of the derivation of the pre-receptorial transmittance used in the review paper.

In 2018, Publication 1 became the basis for the CIE international standard CIE S 026:2018 (Publication A8) on measurement of light in relation to ipRGC-induced responses to light (IIR responses). I was a member and Secretary of the CIE joint technical committee which produced this standard. The standard includes some changes, notably the use of the standard daylight spectrum D65, rather than uniform spectral irradiance, for the reference or equivalence condition, and the switch of the rod and cone sensitivity functions to data from existing CIE publications. The standard acknowledges its debt to Publication 1 extensively, and includes instructions for converting between the Publication 1 and standardised approach. CIE has also committed to maintaining a toolbox including backward compatibility features and assigned this responsibility to me.

My contribution to Part 2, as agreed with my co-authors, was 40%. Part 2 explicitly attributes the literature review and pre-receptorial transmittance function used throughout Publication 1 to Stuart Peirson (SNP) and myself. I developed the published toolbox from a prototype introduced by SNP, with the following features and innovations:

- a choice of input methods between spectral measurements, in the radiometric or photon system, and broadband measurements, in the radiometric, photometric or photon system, the latter supported by a range of standard spectral distribution functions;
• a correction to the established literature on calculations with action spectra between the radiometric and photon system, requiring conversion formulae not widely understood or accepted previously⁵;
• a contribution together with the first author Robert Lucas (RJL) for incorporating self-screening into the opsin template, and implementing this in the toolbox;
• a review of published pre-receptoral transmittance (mentioned above); and
• a new pre-receptoral transmittance model.

The new pre-receptoral transmittance model includes several of my own contributions:

• The outer surface of the eye in vivo is the interface between the environment and the tear film, rather than the cornea as widely misreported.
• Significant largely spectrally-neutral transmission losses occur as reflection at the outer surface of the eye.
• The original photopic standard observer should be considered to have an average age of either 32 or 33, with my recommendation of 32 being adopted in Publication 1 and the international standard - 32 being a pivotal age in some important models of age-related changes to eye transmittance.

Following construction of the toolbox and user guide with SNP, some further co-authors and their research groups were instrumental in testing it, notably George Brainard (GCB) and RJL. I coordinated the correspondence and updates relating to the testing, and I continue to respond to all enquiries concerning the toolbox (and its successors at CIE). It is notable that no calculation errors have ever been discovered.

I also wrote and presented a subsequent conference paper at Kuala Lumpur based on the technical work behind Part 2, with SNP as co-author, also translated for a Russian journal (Price & Peirson, 2014).

5.2 Publication 2: On the role of exponential smoothing in circadian dosimetry
This paper analyses data from the homes of workers retired from the former National Radiological Protection Board (UK, 1970-2005) and living within 25 miles of its base in Chilton, Oxfordshire together with data collected from homes within a retirement village

⁵ This was wholly my own contribution, for which I had to win acceptance of the authors. Through my advocacy of this point in CIE, I have now seen this formal understanding of action spectra in different spectral systems published in the 9th Edition of the SI Brochure itself (BIPM, 2019, Publication A9).
in Surrey. The data were collected using dosimeters placed in regularly used rooms, measuring light entering and exiting the main window and incident on the opposite wall (or window, if applicable) at standing eye level. The purpose of the analysis was to develop a model of how appropriate temporal data could be extracted from the available lighting (artificial and daylight combined) to explain the process of entrainment based on a variety of indoor and outdoor aspects and room designs. I introduced the term architectural dosimetry, to describe the type of data being collected, and distinguish it from analogous data sets collected from solar monitoring and personal dosimetry. These were also the first uncontrolled exposure data analysed according to the melanopic spectral weighting.

The paper reviews previous models predicting human responses to arbitrary time-series of light exposure, noting that all such models predate the discovery of melanopsin, so do not allow for the time-integrative and sustained (after lights off) nature of ipRGC responses. It adopts a feed-forward feature suggested in a previous pre-melanopic model of the light-drive to the circadian oscillator (Kronauer et al., 1999). It notes that this feature has an advantage not previously recognised: by excluding feedback mechanisms, the light-drive encapsulates the concept of a measurable light dose that is independent of prior light history, and all prior-light effects are determined by the effect of the dose on state variables of the oscillator or clock system. This makes it a particularly useful tool for interpretation and administration of interventions.

Two further restrictions placed on the feed-forward process, largely guided by the likely biological requirements are: the light dose model must be continuous and retrospective (many reports use hourly averages or similar, where the value is only retrospective once an hour), and as a first iteration, it must rely on as few parameters as possible. These criteria are most efficiently met by exponential smoothing, and the analysis showed that the combination of a half-life parameter of approximate 90 min and a light dose amplitude of approximately one order of magnitude (base 10) consistently produces a smoothed exposure (or light dose) with exactly one photoperiod per day surpassing this threshold (i.e. light dose threshold = maximum light dose / 10). It is noted that exponential smoothing also has a metabolic advantage, in that the minimum amount of data relating to previous exposures is needed to iteratively update the light dose, namely the prevailing light dose itself.
To test the relevance of this artificial entrainment model to human responses to light, the smoothing parameter of the model is compared to existing duration response data for melatonin phase delay and suppression (Chang et al., 2012). It is noted that some previous models had an exponential-smoothing-like phase built in with a half-life of around 90 min, although the purpose of this parameter was not previously fully explained. Nor have other models been tested with uncontrolled exposure data (neither with personal nor architectural dosimetry). The model explains the duration response with the same statistical success as the four-parameter model fitted by the authors themselves, and the form of the exponential has the further advantages of allowing calculations based on general light exposure profiles and having a process-driven biological justification.

The illuminance response relationship for a 6.5 h exposure to light at night, for melatonin phase delay and suppression responses (Zeitzer et al., 2000), are converted into equivalent melanopic illuminance making immediate use of the proposals from Publication 1 (Lucas et al., 2014). This benchmarks the dose-response relationship against the new model and informs the analysis of the model’s melanopic dose amplitude.

Finally, the model is completed by noting that the light-drive can be used to provide important classes of circadian (periodic) variables relating to the uncontrolled light:dark exposure cycle, namely, phase definitions (e.g. time of light onset), photoperiod (e.g. time above threshold) and amplitudes (e.g. absolute and % ranges). The discussion notes the power and possibilities for using this model in future experimental and circadian modelling work. It indicates that the light-drive could be used as a proxy for the impulse response to light exposure to deconvolute the dose process from the existing phase response curve model. It also leaves it to future work to investigate which variables would be of greatest use to experimental analysis. Some examples might be hypotheses for circadian disruption (of entrainment) in the following cases: variation in phase on successive days (e.g. > 90 minutes), insufficient amplitude (e.g. range or day-on-day change in maxima), photoperiod length too long or short, and multiple photoperiods in one day.

5.2.1 Context and reception of Publication 2

Publication 2 was entirely my own work. It is published in Photochemistry and Photobiology, which is an established high-quality photobiological publication (2018 impact factor: 2.338). This paper was the first to quantitively reinterpret the illuminance response data of Zeitzer et al. (2000) in terms of melanopic sensitivity, the first to suggest
a time-series interpretation of the duration response data of Chang et al. (2012), and the
first melanopsin-based model that could be used to predict responses to unconstrained
light exposure time-series. There are five citations to date (three self).

Subsequently, it has been shown that phase shifting responses to intermittent light, unlike
melatonin suppression responses, may not follow the model predictions (Rahman et al.,
2018). Similar results had been previously shown using light flashes (e.g. see Najjar &
Zeitzer, 2016). A reinterpretation in the light of this data suggests that the model identifies
that melatonin suppression and potentially other acute response to light follow a feed-
forward mechanism, but that dosimetry for responses downstream of the master clock in
the SCN are inherently more complex. Consequently, the use of the model remains
legitimate, including to analyse the Light and Night hypothesis that concentrates on
melatonin amplitude effects (mediated by suppression), rather than circadian
misalignment effects (mediated by phase shifting).

This publication forms the basis for the analysis of exposure time-series in an ongoing
project, and has been cited by two other research teams carrying out NV dosimetry studies.

Publications 1-3 feature literature review and interpretation components, and are
intended to have an influence on thinking and practice amongst researchers. Impact factor
and citations are objective measures, but may not quantify influence directly. Other
measures should be considered, including assessing the impact of these types of
publications as a whole. Notably, the use of the several elements of the analysis introduced
in Publication 2 were central to the theme of the second (invitational) international
workshop on Circadian Neurophysiological Photoreception, which I attended in August
2019. This means I have been invited twice to participate with the leading photobiologists
in the field of human NV and circadian responses to light. Similarly, I was an invited co-
author (minor contribution, not included) on a review paper on NV responses with Mariana
Figueiro for the 50th Anniversary of the Journal Lighting Research & Technology.

5.3 Publication 3: Linking the non-visual effects of light with occupational health

The paper summarises the complexity and multidisciplinary nature of occupational health
field studies relating to non-visual (NV) and circadian responses, i.e. those due to the
influence of shift work and indoor daytime work on light exposure profiles. Many studies
may have protocols or interpretations that are oversimplified, reflecting an incomplete
understanding of one of many specialists, e.g. epidemiology, chronobiology, NV light
dosimetry, shift working variety and detail, biological assay control, and the use of psychosocial factors from either subjective or objective methods.

It calls for a systematic approach to the subject, avoiding common and known errors in the existing literature, including:

- conflating different shift timings and rotations,
- not measuring the light exposure profiles continuously over several 24 h periods,
- actigraphy not collected for long enough,
- not considering seasonality or solar phase (i.e. latitude and longitude influences vs the social clock),
- interventions designed with an incomplete knowledge of the light exposure profiles of the target population,
- not estimating subjective time or chronotype,
- not considering confounding exposures,
- reduced power and bias through non-linear and noisy biomarker results, and
- error and bias introduced through subjective questionnaires relying on subjects recalling events from many years past.

5.3.1 Context and reception of Publication 3

I was lead author for Publication 3 and my contribution, as agreed with my 11 co-authors, was 25%. Some of my co-authors said it could be higher. It is published in a high-impact journal, the International Journal of Epidemiology (2018 impact factor 7.339), which regularly includes studies of occupational health and shift work.

This publication is recent so it is difficult to establish its direct impact. However, it is expected to form an important part of the basis for a series of international scientific workshops at BAtU (Dortmund). These workshops have continued the work of the community interested in the study and use of lighting in occupational health, taking over in many respects from the discontinued DIN Expert Forum (Berlin) meetings. I also take as an endorsement of the importance of what this article says, and my leadership of this publication, that it had the agreement of a range of experienced European co-authors. Two co-authors have cited the Publication in their employer’s IPA-Journal.
5.4 Publication 4: Efficacy and ocular safety of bright light therapy lamps

The paper investigates the characteristics of treatment lamps and other related light sources in relation to treatment efficacy, flicker, potential retinal phototoxicity and visual comfort. Ways in which the efficacy and safety of these products could be compared are proposed. In particular, blue-enriched products marketed to alleviate seasonal affective disorder (a clinical condition) and the winter blues (a vaguely related subclinical self-diagnosed condition) are found to be diverse in spectral output and size and form. As well as concerns regarding both self-treatment and ineffective designs, there is concern that blue-enhanced lighting expose users’ retinas to levels of short-wavelength blue light that could be damaging to their retinal health.

A key finding from this study is that compliance using the devices could be compromised by unwanted flicker, which could cause unwanted discomfort and eye-strain. No devices with diffusers emitted UVR, and none of the devices when used as directed or within reasonable scenarios might be expected to exceed the guidelines published by ICNIRP (International Commission on Non-Ionizing Radiation Protection). However, investigating the underlying rationale and safety margins in the limits, it finds there is a risk that the guideline thresholds for retinal damage could potentially be exceeded by a small number of the devices, based on the additive effects of repeated daily use predicted from experiments in macaque monkeys.

The guideline limits contain margins for uncertainty, and are not the effect thresholds. Together with the conservative simplifying assumptions in the assessments, this lessens the significance that the combined exposures at the level assessed from use on successive days might pass the guideline thresholds. It is therefore concluded that their repeated daily use is likely to be safe, but this cannot be absolutely confirmed, also noting that there are uncertainties relating to the daily additivity of retinal phototoxicity effects and that potential long-term phototoxic effects cannot be ruled out.

The paper also publishes two ratios: one between the melanopic stimulus mediating the effects of the treatment and the blue-light hazard weighted exposures (the protection ratio) and the other between the melanopic stimulus and the visual stimulus or brightness (the efficacy ratio). It proposes that devices with high ratios are the most suitable, provided the colour of the device is tolerated by the user, and provided the device is flicker free.
5.4.1 Context and reception of Publication 4

In contrast to the publications above, Publications 4–6 are mainly intended to have influence on practice beyond the research sphere, and in addition to citations and impact factors, the response of public or certain specialist health communities should also be considered.

My contribution to Publication 4, as agreed with my co-author, was 50%. It is published in Lighting Research & Technology (LR&T), an established international journal for lighting professionals and researchers (2018 Impact Factor: 2.311) published by Chartered Institution of Building Services Engineers (CIBSE) for The Society of Light and Lighting (SLL), its sister professional body in the UK. There are nine citations to date, including two self-citations, two foreign language citations, plus a citation in the Third Edition of Human Factors in Lighting (Boyce, 2014), perhaps the bestselling text book in the field of light research, and is referred to in a recent similar research paper (Oldham et al., 2019) as a “pioneering U.K. study”.

This work has been adopted as PHE’s opinion on the safety and efficacy of home-use light treatment. We have published an invited article in the Seasonal Affective Disorder Association newsletter (autumn, 2015) based on this research, with John O’Hagan. I also advised researchers at the Royal Hospital for Neurodisability (Fulham, London), and provided measurements of their SAD lamp intervention (in 2012-13).

I was invited to present at the 6th Expert Forum, where I reanalysed the data we had collected showing the variety in the spectra of the lamps to demonstrate the difference for clinical decisions. By linking the efficacy and protection ratios to different theories and proposed action spectra for circadian and phototoxic effects, respectively, I showed how the choice of theory or favoured action spectrum would influence the decision between the spectra of the sampled treatment lamps. This illustrated the real-world implications of the uncertainty underlying these action spectra, and was probably influential in the DIN abandoning their plans to publish an empirical action spectrum as a national standard, as this decision was effectively taken in a meeting that afternoon which I attended.

5.5 Publication 5: Low-energy light bulbs, computers, tablets and the blue light hazard

This paper looks at the potential for exposures to the light from computer, tablet and mobile phone screens to damage users’ eyes, and tackles concerns in media reports
stimulated by experiments exposing rodents to powerful blue light sources. Those concerns particularly relate to LED technology, because the spectrum of LED lighting and LED display technology both typically have a pronounced peak in the blue part of the spectrum. Emissions were found to be restricted to the visible range. Within this spectral range retinal damage can occur from a photochemical process known as the BLH.

A range of different display devices are measured displaying white and blue at their maximum power. The spectral radiance is measured and compared to the spectral radiance of the indirect solar radiation measured from the blue sky, and to international safety guidelines. The spectral radiance when weighted by the action spectrum for this damage can be compared to international guidelines designed to protect against blue light damage, and the safety threshold is set conservatively, at around a tenth of the level corresponding to actual damage. In all cases the devices are found to be much less than 1% of this threshold. In addition, the devices are below 12% of the level of the blue sky measurements in both June and December. It is common experience that continuous viewing of the sky in the UK (or overseas) does not cause acute retinal damage, provided one doesn’t stare at the sun or at a point close to the sun.

Similarly, the LED panel light tested has around 1.7% of the safety threshold, and below 20% of the peak blue sky levels in the UK. The other lamps that are assessed include an incandescent lamp, one retrofit compact fluorescent lamp and two retrofit LED lamps. The luminance (rather than blue light radiance) for these lamps exceeds the level for comfortable direct viewing – essentially this is the reason we use light shades for light bulbs. However, this means that continuously staring at these lamps is unrealistic, and the blue light radiance needed to exceed the thresholds with passing inadvertent exposures is much higher than for continuous viewing; the threshold is based on a dose calculation which is a function of radiance, source size and duration. All the lamps come in below the continuous exposure threshold in any case. Interestingly, the LED lighting spectrum is not more blue-weighted than the incandescent lamp with the same correlated colour temperature – although the blue peak can be pronounced it has a narrow bandwidth which compensates for the higher peak.

In addition, a computer display switch box with three blue indicator LEDs is assessed, at a worst-case scenario distance of 100 mm for extended viewing durations. As the lights were blue, simply applying the visual comfort test is inappropriate, although each indicator LED measured exceeds this luminance limit in any case. The source also exceeds the blue light
threshold for continuous viewing, with the maximum permissible time for viewing to stay below the system of international safety thresholds of approximately 60 min. It is unlikely the box would be viewed by continuous staring at such close range for 60 min, and based on many previous device assessments, the source is not considered representative of indicator lamps. It is noted that sources that are comfortable for adults may not be comfortable for children, as the juvenile human lens transmits more blue light.

In summary, the evidence does not support claims that LED general purpose lighting or LED display screens can damage the eye.

5.5.1 Context and reception of Publication 5

My contribution to Publication 5, as agreed with my co-authors, was 33% (all three authors contributed equally). This 2016 paper was published in Nature Eye (the official journal of The Royal College of Ophthalmologists; 2018 impact factor: 2.366), has 33 citations so was clearly a substantial net contributor to the journal’s recent 2-year impact factors (no self-citations). The initial version of the paper was an invited presentation at the Cambridge Ophthalmology Symposium (2015), which that year was concerned with photobiological hazards and the NV effects of light. It continues to be a useful reference for reassurance in the dual contexts of popular concerns about blue light from LEDs and academic concerns motivated by experiments on animals, typically under unrealistic exposure conditions.

This work has been adopted as PHE’s position when discussing the evolving international consensus on the retinal safety LED lighting and screens.

5.6 Publication 6: Can the Adverse Health Effects of Flicker from LEDs and Other Artificial Lighting Be Prevented?

This paper considers the possibility of regulating modulation, or TLM, from LED lighting and other general lighting using a measure based on directly modelling the eye’s temporal response. It suggests a simple time-response model, with a half-life of 3 ms, based on the fastest response of the cones with a margin for safety that may protect against interference effects from regular eye movements known as ocular micro-tremor (OMT).

The paper notes that the modulation remaining in the time-series after applying this model can be quantified in the same way as the raw modulation, creating a metric Physiological Percent Flicker (PPF), which is the analogue of the traditional Percent Flicker metric used to categorise flicker in lighting. It reveals PPF has a strong correlation to the other widely quoted metric Flicker Index for modulation with a base frequency of around 100 Hz. As
Flicker Index is considered a good measure for waveform for such modulation, this suggests the PPF metric may be a good way to generalise this success to other frequency ranges.

The paper proposes using PPF as a tool to regulate lighting modulation, that the threshold should be set by a wider consensus, but that a threshold in the region of 1% to 3% would ensure that future lighting is at least as good as traditional lighting.

5.6.1 Context and reception of Publication 6

This sole author work was published in LEUKOS (The Journal of the Illuminating Engineering Society; 2018 impact factor 2.647) to reach a different audience to Lighting Research & Technology. LEUKOS publishes fewer papers, and was popular for articles relating to the theme of lighting metrics and standards.

This work has been adopted as PHE’s opinion on protecting against the adverse effects of TLM and flicker in lighting, with that opinion having evolved out of a long-standing position of a threshold of 10% modulation at 100 Hz based on the typical incandescent light bulb, and other converging evidence in the literature (IEEE, 2015).

With additional analysis, I have promoted the use of the PPF metric from this paper as a method for implementing the IEEE’s thresholds for low risk and no effect from light modulation in consultations on lighting standards in Europe and America. Both these standards originally proposed following an American standard NEMA77 (National Electrical Manufacturers Association – The Association of Electrical Equipment and Medical Imaging Manufacturers), which include the measures for short-term perceptibility (Pst) and stroboscopic visibility (SVM) (NEMA, 2017).

The UK’s response to the European consultation recommended that the SVM threshold was too high, and there were multiple problems with the SVM model. At the next stage of the consultation, more research on SVM has been commissioned, and a stricter threshold proposed (25% of the original threshold), largely due to the UK’s opposition. This new proposal is more in line with our concerns about the threshold at 100 Hz, but there are still concerns about using SVM as a basis for thresholds.

I was invited to present on this publication and flicker regulation at the 2019 annual Professional Lighting Summit of the Institution of Lighting Professionals, and shortly after participated in related discussions at the 2019 Quadrennial Session of the International
Commission on Illumination (CIE) in Washington DC. I am now an adviser on this specific topic for an international review.

I was also invited to provide expert evidence to the committee for the ASHRAE standard 189.1, and they are also considering a replacement for SVM to more closely follow the IEEE recommendations.

Despite this reception in the field of regulation and the lighting industry, there are curiously no citations in the literature to date (excluding conference proceedings etc. in which I have presented further information). However, only Publication 6, out of all 11 publications in my portfolio, has fewer citations to date than might be expected based on the journal impact factor, even after excluding conference proceedings.

5.7 Publication 7: Performance assessment of commercial circadian personal exposure devices

This paper investigates the performance of arguably (at the time) the most advanced available commercial research device used to measure personal light exposures, and the only such device measuring blue light. The Actiwatch Spectrum (herein AWS) is designed to be worn by participants in experiments and patients on the nondominant wrist to monitor activity levels and comes with software to analyse the sleep patterns of the wearer. In addition, it includes three solid state sensors with different spectral sensitivities (labelled as RGB or Red, Green and Blue) within the visible spectrum. The study assesses the suitability of this device to measure light exposures in respect of its potential effects on circadian rhythms.

Although the AWS is a wrist watch, it can also be attached and worn with the straps removed at several locations on the body closer to the eye. The sensitivity to light incident from different directions is considered and compared to an ideal cosine function (similar to the wide angle response of the eye, but see Figure 2.3 Panel A), and found to be restricted by parallax, particularly around one axis. Therefore, we conclude that when worn it would be sensible for the device to be turned to approximately match the restriction of the eyebrows on the exposure of the eye.

In 2010-2011, there were several competing explanations for the role the spectrum of light exposure plays in determining the effects on circadian rhythms (as discussed previously). With the guidance of a leading expert by personal correspondence, the paper considers that the photopigment melanopsin to be the most likely explanation – this explanation is
also the closest to the consensus that has emerged. The devices are therefore tested against the in-vivo spectral response of melanopsin (the sensitivity curve used in this publication is shown in Figure 2.3 Panel B), and it is found that the blue and green sensor responses could be combined linearly to give a spectral sensitivity with a bell shape that closely matches the melanopic sensitivity curve.

The paper also establishes that the device provided a linear response over a wide range of irradiance levels. Usually the eye copes with an even wider range of irradiance levels, but the range of irradiance levels over which NV effects occur is thought to be more restricted (see Publication 2 and Figure 2.3 Panel C). It shows that the linear dynamic response is more than sufficient to cover the restricted range.

5.7.1 Context and reception of Publication 7

I was lead author for Publication 7, and my contribution as agreed with my two co-authors was 60%. It is published in Lighting Research & Technology (LR&T), which is, as noted above, an established international journal for lighting professionals and researchers (2018 impact factor 2.311). It has been cited 19 times (5 self-citations).

The results were first presented at a Workshop in the 27th Quadrennial Session of the CIE in Sun City, South Africa in 2011, was one of ten conference papers invited by Lighting Research & Technology to be submitted and reviewed as a full journal paper in a special edition, and was published in this way shortly afterwards. The paper has stimulated and influenced similar work by other authors, including at the University of Copenhagen, the Lighting Research Center (Rensselaer Polytechnic Institute, USA) and at the Federal Institute of Occupational Safety and Health (BAuA, Dortmund, Germany).

This was the first paper to generalise the standard spectral matching assessment used for illuminance and luminance meters to other spectral sensitivity curves, and the first to use the equivalence method of normalising spectral sensitivity curves, which has become part of a widely cited expert consensus, Lucas et al., 2014 (Publication 1), on the measurement of light in relation to its NV effects, which directly influenced the international standard CIE S 026:2018 (Publication A8). As set out below, the assessment methods used have been developed further in Publications 10 and 11 respectively.
5.8 Publication 8: Effects of ambient temperature on the performance of CCD array spectroradiometers and practical implications for field measurements

This and the next paper concern CCD array spectrometers (Publications 8 and 9), and their performance for taking practical field measurements to assess personal exposures to optical radiation. CCD array spectrometers are typically smaller and more robust than double grating monochromators (DGMs), which are the ‘gold standard’ for accurate measurements of spectral irradiance. In addition, CCD array spectrometers are more affordable and require only short integration times, typically measured in milliseconds, to capture an entire spectrum, compared to the scanning times for DGMs of perhaps one or two minutes. These advantages mean that they are the preferred tool in many cases for field measurements.

The performance of CCD array spectrometers outside of the laboratory may be compromised when not used in a temperature-controlled environment. The optical bench of an array spectrometer includes an entrance slit, a diffraction grating, one or more mirrors and an array of solid-state pixel detectors operated by an electronic circuit board. These components and the board itself may all be affected by ambient temperature – the data showed that there are marked effects on the performance of the array and the grating.

For this reason, some spectrometers incorporate some combination of the following features: array cooling, array temperature monitoring, user control over target array temperature and board temperature monitoring.

In this study, six spectrometers from two manufacturers, including two cooled models, are studied at ambient temperatures between 5°C and 40°C, using an environmental chamber whereby temperatures could be controlled and rapidly changed. 22°C represents normal laboratory temperature and typical calibration and reference conditions.

The effect on measurements of a stable broadband light source of known spectral irradiance and a mercury pen-ray lamp with defined peaks in known wavelength positions are reported, along with timings, dark current, temperature readouts from the chamber, the CCD array and board. The source was kept at 22°C, and the light was collected in an integrating sphere from which it propagated along an optical fibre to the spectrometers within the chamber. Once the temperature was changed, these data were recorded repeatedly until the system stabilised. Operation of the array and board produces heat, so
this stability can be considered as a mixed-process equilibrium rather than true thermal equilibrium.

At each of the ambient temperatures tested it is shown that the resulting stable operating detector (array) temperatures can be predicted. For one device the array cooling system is set to be off, or to target -10°C and -20°C; when cooled, the target array temperatures are achieved only within sub-ranges of the ambient temperatures range (agreeing to the specifications for this device). For uncooled spectrometers, a simple decay-process model allows for predictions of the time taken to achieve temperature stability to within a certain tolerance after a change of temperature. Consistently with this model, a device with a greater thermal bulk is less subject to performance variations due to recent changes in temperature, but took longer to reach stable performance.

As predicted, both the cooled spectrometers are subject to minimal increases in dark current at higher temperatures. For other spectrometers, the achievable signal-to-noise ratio is compromised, particularly from 30°C upwards for exposures above a few seconds, both by the increase in dark current reducing usable well-depth by a large percentage, and by the increase in the variance within the dark current. This mostly affects applications that require a large throughput, e.g. measurements of UVR, dim light or with restricted access to the source.

Significant variations in the spectral structure of the dark current are found in one uncooled device. The spectral sensitivity and spectral dispersion of uncooled devices are affected by ambient temperature, but not always consistently between different devices. The effect of ambient temperatures of 15°C or below on the slit function, due to the image of the slit formed on the array, should be considered, even for cooled models, as this can compromise spectral resolution.

5.8.1 Context and reception of Publication 8

I was lead author for Publication 8, and my contribution as agreed with my two co-authors was 40%. This paper has eight citations (four self-citations). The Journal of Radiological Protection is a respected journal concerned with biological effects from all types of radiation (2018 impact factor: 1.327).

I contributed significantly at all stages of the study, to experimental set-up, protocol, implementation, data analysis and writing. This included the addition of an optical switch,
allowing for contemporaneous dark current measurement, useful both in the experimental
set-up and in field work, and within the analysis, the model of temperature dependence.
Presented to the international solar monitoring community and the UK medical physics
community, the practical implications of these findings are now considered within guidance
on the use of array spectrometers in hospitals and other field settings. In PHE’s own
research, the findings are step applied consistently to support measurement quality, and
in the design of new instrumentation.

5.9 Publication 9: Dynamic response of CCD array spectroradiometers
Apart from the effects of ambient temperature, another potential limitation of CCD array
performance is non-linearity of response. Exploiting the available well-depth in full
improves signal-to-noise ratios through maximising the time-integrated signal. However,
as its capacity is approached, the sensitivity of the CCD pixel reduces; the higher the total
number of counts in a pixel the greater the potential distortion.

In this study, four spectrometers are tested, and the data combined with that from the
previous study at 22°C for two of these (i.e. from Publication 8). The four devices have
different well-depths, but the non-linear effects are similar in structure, and yield as high
as a 20% understatement of the true spectral values. A threshold is identified below which
the effects of non-linearity of each device was not significant. In addition, the paper sets
out corrections for the distortions which are independent of wavelength position and
integration time. It shows them to be increasingly reliable at high counts, demonstrating
that with these corrections the full well-depth can be exploited to reduce signal-to-noise
ratios. Finally, it explains why in applying these findings, non-linearity corrections should
be applied before stray light correction, even though other articles relating to stray light
have not considered correcting for non-linearity, and despite stray light in low count
regions being related to throughput levels in high count regions.

5.9.1 Context and reception of Publication 9
This paper’s findings are often considered along with the previous paper. As with that
paper, in PHE’s own research, measurement quality has also been improved by applying
the findings, and this paper also established a protocol for assessing the performance of
new CCD array devices, and establishing the parameters for their use in minimising
experimental errors.
My contribution to Publication 9, as agreed with my co-authors, was 35%. Radiation Protection Dosimetry is another respected journal concerned with biological effects from all types of radiation (2018 impact factor: 0.831). The article has three citations (no self-citations), and this article has been a net contributor to the impact factor of the journal.

5.10 Publication 10: Optical performance characterization of light-logging actigraphy dosimeters

In this paper updated methods from Publication 7 are used to assess a range of different products used to monitor light exposures in relation to NV responses to light including circadian rhythms. Whilst these responses might be assumed to be related to the melanopic exposure dose proposed in Publication 2, to allow a more general interpretation the spectral assessments are based on both the visual and the a-opic sensitivities set out in Publication 1, including the melanopic sensitivity curve.

Seven devices were available for measurement, and for most other devices it was possible to estimate any relevant spectral sensitivity properties from details published about the photosensor components, using the component manufacturers’ specifications, along with direct data from correspondents where possible (Hubalek et al., 2010).

For the spectral characterisations, a purpose-built monochromator was assembled for assessing optical radiation dosimeters, with several bespoke features:

- a dedicated beam-monitoring system ensures the stability and reproducibility of the conditions to which the devices are exposed, and monitors for source fade;
- a laser-driven plasma source allows sufficient throughput at UV and short visible wavelengths and supports reductions to spectral bandwidths;
- the use of cylindrical lenses exploits the vertical spectral uniformity in the unmodified beam, increasing the central throughput of the output beam;
- these two increases in throughput enable the use of circular baffles to mask the output beam into sizes matched to different devices, as using the same baffles for modified calibration of the reference instrument means the beam conditions can be traceably measured, despite being smaller than the reference input optics; and
- the option of a stable background broadband beam supports the investigation of marginal spectral response to light, a new concept in assessments for this type of device.

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This last feature made it possible to assess the responses of a device with several sensors that fell to zero at some wavelengths, and to demonstrate the underlying negative contribution due to the light at some wavelengths.

For dynamic range assessments, a new approach is designed and developed to increase the throughput based on positioning the detectors at the exit of a small integrating sphere, thus achieving greater throughput than placing devices in a large enough integrating sphere. This is motivated by the increased range of throughput achieved by another group in the field (Figueiro et al., 2013), and the new approach results in the largest useful range of published dynamic response tests for these devices to date. The paper shows further limitations with some of the devices tested, not been previously published.

Mismatch functions are introduced for spectral, and directional responses, and a new test for dynamic resolution. Unlike the existing standard for illuminance meters, these are mathematically consistent and self-consistent, and adapted for predicting performance in the range of conditions relating to NV responses to light.

The spectral metrics include the use of the α-opic curves from Publication 1. It is shown that negative spectral responses would lead to distortions for any spectral mismatch metric, and for the proposed metric negative marginal spectral responses could produce mismatches of over 100%. The sensor data should be interpreted with care if there are negative marginal spectral responses, even for mismatches below 100%. Both the new metric and the standard spectral metric for illuminance meters are reported using V(λ) to allow comparisons.

The proposed directional mismatch metric is adapted from the standard cosine error metric, to ensure that the range of possible mismatches was 0% to 100%. Again, both are reported to allow comparisons.

Into the dynamic assessment, a test for dynamic resolution is introduced, thereby showing that this is often the limiting factor for the performance towards the lower end of the dynamic response requirements – i.e. some devices are unable to report differences in conditions below equivalent illuminance thresholds of up to 10 lx, when the NV responses to light may go lower. The concept of equivalent illuminance based on the sensors' own spectral sensitivities is introduced to describe the light conditions for characterising dynamic responses. This permits the use of photometric units for spectral sensitivities matching those of the sensors, allowing more intuitive descriptions of the linearity ranges.
It also leads to simplified calculations of linear coefficients for combining sensors, such as originally suggested in Publication 7 for the AWS device. Given the uncertainty about the illuminance response relationship for different NV responses to light (see Figure 2.3 Panel C), no comparable dynamic range mismatch metric is introduced, but the non-linear responses are reported over the whole range for each sensor, demonstrating clear performance differences between devices.

The spectral data for the seven measured devices are available in an online library, as a resource for circadian personal dosimetry research (its metrology and its application). As well as showing the spectral sensitivities of the device models, it allows for other spectral metrics to be calculated from the data. For the devices not measured, the paper provides references from which the spectral sensitivities could be derived and/or inferred.

Along with spectral graphs, graphical data for the directional and dynamic responses are provided in the paper. As there are no alternative published metrics to calculate here, it was felt the underlying numerical data would only distract from these results.

5.10.1 Context and reception of Publication 10

I was lead author for Publication 10, and my contribution as agreed with my two co-authors, was 70%. This publication has eight citations (three self-citations) and is a net contributor to the journal’s impact factor. JOSA A is a leading journal in the field of optics (2018 impact factor: 1.861).

To avoid repetition, more details of the impact of this paper and the next publication are given in section 5.11.1.

5.11 Publication 11: Modification of a personal dosimetry device for logging melanopic irradiance

This paper is published as a Technical Note (short journal article), as a follow-up to Publication 10, and essentially adds a modification to a dosimeter to improve its melanopic match. Following the measurements made for Publication 10, the manufacturer of one promising device was contacted – this device already had good directional and dynamic performance and the closest single sensor match to the melanopic spectral sensitivity of any device, as well as a good match to the widely used visual sensitivity curve V(\lambda). From Publication 10 data, it is noted that a specific long-pass filter would modify the spectral sensitivity, improving the melanopic match without affecting the visual sensitivity match, by reducing the oversensitivity to short wavelengths and in the near infrared region.
For 3 test devices, supplied by the manufacturer as requested, the spectral, directional and dynamic performance is reassessed, confirming that the results match expectations, and that even the visual match marginally improves. As the only other device on the market with a passable melanopic match has been withdrawn from production (the AWS, see Publication 7), this enables personal melanopic light exposures data to be gathered for studies into NV responses.

5.11.1 Context and reception of Publication 11

I was lead author for Publication 11, and my contribution as agreed with my co-author was 70%. It is published in Lighting Research & Technology (LR&T), which is, as noted above, an established international journal for lighting professionals and researchers (2018 impact factor 2.311). It has three citations to date, with two self-citations.

Considering the impact of Publication 10 and 11 as a whole:

- We were recently asked for the spectral data for this device from an independent group, implying further that they had accessed the spectral data for the other measured devices from Publication 10.
- In the second IWCNP workshop, the results of this paper were presented by an independent researcher as the main evidence in her similar argument for developing better devices for monitoring melanopic exposures (which I have in fact done in Publication 11).
- Another group that has ordered the devices developed in Publication 11, and we have provided advice to well-known international researchers on the available dosimeters, included those previously involved in the development of other similar wearables.
- I have presented initial and complete findings of this research at CIE and other International Workshops, at the Quadrennial Session and Conference in Manchester (2015), at the joint BAuA and PHE workshop in Dortmund (Price, 2016), and at an international tutorial in Eindhoven in March 2019.
- My aim is improving the technical specifications provided for these types of devices with a clear focus on improving the spectral match to the melanopic sensitivity curve over the full indoor and outdoor environmental ranges of light conditions. Following my suggestion of designing standards in this area, e.g. including in Publication 10, presented at the 2015 Manchester workshop, Publication A4 in
2013, and as first suggested by the approach taken in Publication 7, CIE have created a Reportership for performance specification standards for these devices.

- The poster I presented at CIE 2019 (Washington DC) with initial results of melanopic personal exposures of shift workers using the reanalysed performance of the AWS devices (Publication 10 following Publication 7), attracted the attention from at least three other groups interested in developing new devices. Although other features, or lower costs, can be considered interesting, I believe improving on the Publication 11 device, that I developed based on modification of an existing model will be the accepted benchmark for these devices.

At this stage, I feel I have contributed more than any other researcher to generating the current level of interest in having appropriate specifications for commercially available dosimeters. I expect the CIE process this portfolio has already been set in motion will have a wide influence on researcher device development and device manufacturing and marketing. Together with the interpretation of the data from the device set out in Publication 7 and more directly from the new melanopic device already developed in Publication 11, the potential exists to transform the quality of data available on melanopic and other NV exposures to light.
6. References


ANSES, see *Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail*


CIE, see International Commission on Illumination


EC, see European Commission


EU, see European Union


ICNIRP, see International Commission on Non-Ionizing Radiation Protection

IEEE, see Institute of Electrical and Electronics Engineers


IWBI, see International WELL Building Institute

JCGM, see Joint Committee for Guides in Metrology


*NEMA, see National Electrical Manufacturers Association*


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SCHEER, see Scientific Committee on Health, Environmental and Emerging Risks


WHO, see World Health Organization


Appendix A: Related peer-reviewed, standards and guidance publications

I have also contributed to the selected works below. Although these publications are not being assessed, brief details are provided below for context and completeness. The three application papers relate to effects of light and optical radiation that were out of scope. The listed published standards, technical notes and guidance are not subjected to blind peer-review, although they have undergone extensive and rigorous review processes.


Publications A1 and A7 concern the assessment of lighting for the colour rendering properties of its spectral distribution. Respectively, these single author papers developed and tested novel powerful spectral band methods. I am not involved with standards work on colour rendering, but the latest proposals are in line with these papers’ findings, which illustrate why previous fidelity metrics proved inadequate for assessments of LED lighting.

To Publication A2, I contributed at the design, analysis and writing stages, and introduced a model to test for annual changes in the variability of ultraviolet radiation exposure levels.

Publications A3 (sole author, with advisers) and A8 are both published by the International Commission on Illumination (CIE) and relate to Publication 1 on measuring light for its non-visual (NV) effects. Publication A3 represents the intermediate stage towards the recognition of the essential proposals of Publication 1 in an international standard in Publication A8, as CIE S 026:2018. I have been centrally involved throughout this process.

Publication A4 is a personal opinion that links the work on dosimeter performance (Publications 7, 10 and 11) and NV measurements (Publications 1-3, A1, A3 and A8) into the wider programme of carrying out reproducible field work on the NV effects of light on health.

Publication A5 is a Public Health England (PHE) report on LED lighting, commissioned by the Chartered Institution of Building Services Engineers (CIBSE) and the Society of Light and Lighting (SLL), concerning its effects on people including NV, TLM, optical hazards and colour. It links in some way to all my work, the measurement data has been often reused to illustrate PHE’s advice, and formally reanalysed in Publications 8 and A7.

Publication A6 was an invited paper for the commemorative 50th Edition of Lighting Research & Technology and was awarded the 2018 Leon-Gaster Prize for best publication
in 2018. I contributed details about assessing photodetectors and their use (see Publications 2, 7, 10, 11 and A4). It also sets out details concerning the most up to date Circadian Stimulus spectral model of Rea, Figueiro & Bullough from the Lighting Research Center (Rea et al., 2010). Due to the conflicts with the international consensus in Publication 1, I ensured that this paper referred to Circadian Stimulus as a possible model for an average response, to avoid the impression it was widely supported or could be considered exact. This paper is proving successful, but I do not consider my contribution sufficiently distinct from other publications in the portfolio to be examinable.

Publications A7 and A8 have already been described.

Through CIE, I also achieved two updates to the SI system’s definition of action spectra in Publication A9, the SI Brochure. The SI Brochure is the basis of widely used and accepted system of quantities and units for science and scientific applications. I conceived of and provided the new wording on the difference between action spectra in the radiometric system and the photon system, relevant to work in photochemistry and photobiology. The Brochure consequently recognises the validity of reporting quantities and units in the photon system, which in practical terms is the preferred system for photochemistry. I also proposed the new wording that broadens the term action spectra to include photochemical and photobiological processes that are not purely actinic, which in practice covers most of the processes for which the term is used in photobiology.

Publication A10 provided the initial results of applying the melanopic dose model from Publication 2 to study the light exposures of night and day shift workers in the UK and Germany. This project was motivated by the lack of published 24 h light exposure dosimetry data relating to shift work, particularly at latitudes relating to central and northern Europe and exacerbated by the lack of melanopic-weighted time-series. This study was selected for a collaboration between myself and the second author (at PHE and the German Federal Institution for Occupational Health and Safety “BAuA” respectively). It is planned to publish final results of the investigation soon.

This study links many of the publications in this portfolio (notably Publications 1-3, 7 and 10) as follows: Publication 7 established that logging melanopic time-series was possible with an existing device. To help select a device for this type of work, Publication 10 explored this and further systematically reviewed the performance of known wearable dosimeters relating to IIL responses, using direct measurement and characterisations of all devices
immediately available or provided on request for a loan. Publication 10 followed the recommendations of Publication 1 and assessed the spectral sensitivities in relation of all five NV photoreceptor action spectra. The melanopic time series were processed according to the model developed for predicting circadian regulation in Publication 2. The Publication 3 opinion arises out of expanding the BAuA collaboration for future projects on occupational effects on NV light exposures and health, including shift work.

Publication A11 relates to the blue-light age-related macular degeneration (AMD) hypothesis, discussed in Publications 4-5 and A5, and applies two methods to respond to published experiments exposing rodents and rodent tissues in vitro to damaging levels of light, and refute several claims about human retinal safety and AMD put forward.

Firstly, we reviewed the non-human BLH studies, noting why inter-species comparisons should be treated with caution. The rodent species are nocturnal, sleep underground during the daytime, avoid spending long periods in bright daylight and some are albinos with heightened photosensitivity. Such experiments would stress the animals, producing additional effects that might disrupt repair mechanisms. In any case, there is also a clear disconnect between effects demonstrated with short-term exposures and the long-term exposure blue-light AMD hypothesis.

Secondly, we addressed the claim of an association of modern lighting with greater blue-light exposures. The blue light data collected when studying circadian exposures of both day and night working nurses in the UK and Germany, in Publication A10, show that blue-light exposures are dominated by outdoor exposures, even in the winter data. In contrast, Publication A11 demonstrated that the rodent retinal exposure conditions exceeded those implied by the BLH safety threshold, so that equivalent human exposures cannot be reasonably expected from general lighting.
Appendix B: Definitions

action spectrum

function representing the relative spectral effectiveness of optical radiation, for a specified actinic effect, in a specified system

Note 1: The normalised action spectrum is the wavelength dependence of the inverse of the dose of monochromatic radiation required to induce a certain (biologic) response; the action spectrum is commonly normalised to 1 at the wavelength of “maximum action”, i.e. where the smallest dose suffices to induce the required effect.

Note 2: Also referred to as: actinic spectrum [defined as:] efficiency of equal intensities of monochromatic radiation for producing [a specified] phenomenon in [a specified] system as a function of wavelength

(CIE, 2011: term 17-17, alternative definition moved to note 2 for clarity)

[The scope of the term action spectrum was extended in Appendix III of the 9th edition of the SI Brochure (BIPM, 2019, Publication A9). Based on a CIE proposal to BIPM that I initiated action spectra can refer to mixed effects of transmittance, actinic and thermal effects, and realisations of action spectra are specific to the spectral system being used, e.g. action spectra take different values in the radiometric and photon based systems.]

angular mismatch

see directional mismatch

blue light hazard (BLH)

potential for a photochemically induced retinal injury resulting from optical radiation exposure at wavelengths primarily between 400 nm and 500 nm

Note 1: This damage mechanism dominates over the thermal damage mechanism for exposure durations exceeding 10 s

Note 2: The action spectrum extends into the UV-A for persons without a normal UV-A absorbing lens

(CIE, 2011: term 17-97)
charge-coupled device (array, CCD array)

electronic sensor using the principle of photo-generation of charge, that is the basis for an array of detectors or pixels (an array of such devices)

Note 1: When briefly exposed to a spectrally dispersed image of a slit in a spectroradiometer, a linear CCD array will yield a reproducible series of charges corresponding to the spectral strength of the image at each pixel.

Note 2: 2-dimensional CCD arrays are also the basis of digital photography, where the scene rather than the aperture is imaged.

(own definition)

circadian rhythm

oscillation with a period of about 24 hours

(Aschoff, 1964)

directional mismatch (angular mismatch)

1. difference between two directional response functions

Note: An example is the mismatch between the response to directional radiation of a detector and a biological photoreceptor

2. dimensionless quantity based on two directional response functions, evaluating the expected average relative error of using one to predict the result of using the other for a specified application

Note: ISO/CIE 19476:2014(E) defines directional indices with the wording “index describing the responsivity of the photometer to light incident at an angle other than normal” combined with equations for several specific applications, but this wording does not convey the mismatch between two directional response functions, and the indices are specific to photometers.

(own definition)

entrainment

coupling of a self-sustained oscillation to a Zeitgeber (forcing oscillation) with the result that, either both oscillations have the same frequency

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(synchronisation), or that the frequencies are integral multiples (frequency demultiplication); possible only within a limited range of frequencies

(Aschoff, 1964)

equivalent illuminance (equivalent luminance)

illuminance (luminance) produced by radiation conforming to a reference spectral distribution that provides an equal weighted spectral irradiance (radiance) as the test source radiation

(own definition, generalised from Publication A8, CIE, 2018: terms 3.8 and 3.9)

Note 1: Calibration factors for weighted irradiance quantities were defined using the equivalence principle for the first time in Publication 7, Price et al. (2012): “a source with uniform spectral irradiance of [x W.m⁻²] should produce an answer of [x W.m⁻²].”

Note 2: Publications 1 and A3, Lucas et al. (2014) and CIE (2015), defined a system of standard α-opic equivalent photometric quantities, explicitly including definitions for α-opic equivalent illuminance, based on the proposed α-opic spectral weighting functions and an equi-energy or uniform radiometric reference spectrum.

Note 3: Publication A8, CIE (2018), defines a system of standard α-opic equivalent photometric daylight (D65) quantities, explicitly including definitions for α-opic equivalent daylight (D65) illuminance and luminance quantities (α-opic EDI and EDL), based on the standard α-opic spectral weighting functions and a reference spectral distribution “conforming to standard daylight (D65).”

flicker

perception of visual unsteadiness induced by a light stimulus whose luminance or spectral distribution fluctuates [or oscillates] with time, for a static observer in a static environment
[Note 1: The addition to the definition “or oscillates” removes the need for the original note 1 as “periodic and non-periodic fluctuations” are simply oscillations and fluctuations, respectively.]

Note 2: Flicker is a type of temporal light artefact (TLA).

Note 3: The definition given here is different from the current definition of "flicker" in the ILV (CIE, 2011: term 17-433). It is suggested to replace the definition in the ILV in its next revision by the one given here. [By way of explanation, the wording “for a static observer in a static environment.” is contentious amongst leading experts, as the eye is subject to a range of rapid movements, even during fixation. In any case, flicker refers to a specific response to temporal light modulation (TLM) which is not due to movements of the eye or the environment.]

(CIE, 2016) [changes and comments in square brackets]

health

a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity

Note: The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition.

(WHO, 2005)

intrinsic photosensitive retinal ganglion cell (ipRGC)

retinal ganglion cell that is photosensitive by means of the photopigment melanopsin

Note 1: ipRGCs receive signals from rods and cones and hence combine the photoreceptive contributions from all five [retinal] photopigments. However, melanopsin [accounts] for the intrinsic photosensitivity of ipRGCs.

Note 2: ipRGCs are sometimes denoted as photosensitive retinal ganglion cells (pRGCs), or melanopsin-expressing retinal ganglion cells, or melanopsin-containing retinal ganglion cells.
ipRGC-influenced responses to light (IIL responses)

see non-visual

light

[optical] radiation that is considered from the point of view of its ability to
excite the human visual system

(CIE, 2011: term 17-659, 2.) [minor change in square brackets]

melanopic

relating to the human ipRGC response due to its photopigment (melanopsin)
and its characteristics in the context of ipRGC-influenced responses to light

(Publication A8; CIE, 2018: term 3.1.5) [contextual notes omitted]

non-image-forming (NIF)

see non-visual

non-visual (NV)

relating to effects mediated by retinal photoreception by the rods, cones
and ipRGCs that are largely distinct of vision, also referred to as non-image-
forming (NIF) responses and ipRGC-influenced responses to light (IIL
responses)

Note 1: CIE, 2018 (term 3.11) defines ipRGC-influenced responses to light
(IIL responses) as "light-induced responses or effects that can be elicited by
ipRGCs."

Note 2: Skin-mediated responses may be referred to as non-visual
responses, but the definition here is the primary usage.

(own definition)

resolution (dynamic resolution)

smallest change in (the magnitude of) a quantity being measured that
causes a perceptible change in the corresponding indication
spectral mismatch

1. difference between two spectral response functions or action spectra

Note: An example is the mismatch between the response to spectral radiation of a detector and a biological photoreceptor.

2. dimensionless quantity based on two spectral response functions or action spectra, evaluating the expected average relative error of using one to predict the result of using the other for a specified application.

Note: ISO/CIE 19476:2014(E) defines a general V(Δ) mismatch index, but this definition requires V(Δ) as one of the spectral response functions, and the formulation is not mathematically general, for instance including CIE standard illuminant A as a reference spectral distribution.

(Own definition)

spectral resolution (of a spectroradiometer)

see wavelength resolution (of a spectroradiometer)

spectral weighting function

see action spectrum

suprachiasmatic nucleus (SCN)

either of a pair of neuron clusters in the hypothalamus situated directly above the optic chiasma that receive photic input from the retina via the optic nerve and that regulate the body’s circadian rhythms.

(Merriam Webster, 2019)

temporal light artefact (TLA)

change in visual perception, induced by a light stimulus the luminance or spectral distribution of which fluctuates [or oscillates] with time, for a human observer in a specified environment.
Note: The change [in] visual perception is a result of comparing the visual perception of the environment lit by the modulated light to the visual perception of the same person in the same environment, when the environment is lit by non-modulated light.

[Note: The addition to the definition "or oscillates" removes the need for the original note 1 as "periodic and non-periodic fluctuations" are simply oscillations and fluctuations, respectively.]

(CIE, 2016) [minor changes in square brackets]

temporal light modulation (TLM)

fluctuation or oscillation with time of the luminance or spectral distribution of a light stimulus

Note: The term TLM refers to any such fluctuation or oscillation, regardless of whether it can be perceived. CIE has not published a definition of TLM, but uses the term in this sense.

(own definition, derived from TLA in CIE, 2016)

wavelength resolution (of a spectroradiometer)

smallest difference in wavelength [of monochromatic radiation] that can be separated (by a spectroradiometer)

Note: The average wavelength resolution across a specified range may be of interest for characterising a spectroradiometer

(own definition, cf. resolution and Avantes, 2019 "optical resolution")
[Optical resolution is too generic a term for the definition here.]
Appendix C: Excerpt from LS16 proceedings, 2018


[References to publications in the portfolio or Appendix A are added in brackets.]

*Prior to 1998, the possibility of a third class of photoreceptor in the human eye was deeply contentious, although it was known that in many mammalian species circadian rhythms could be shifted by exposure to light, with a peak sensitivity that did not match to rods or cones. At this time, the photopigment melanopsin was discovered in a species of frog, and subsequently shown to be present in a number of locations including the hypothalamus and retina. It was quickly recognised to be a candidate for the photopigment of a third mammalian photoreceptor that might be relevant in human physiology.

*Reports on the action spectra for suppression and phase shifting of secretion of melatonin at night and the regulation of vision through a non-classical pigment, in 2001 and 2002 respectively, provided strong evidence linking these effects to the wavelength region of melanopsin photoreception. Over ten years later, a wealth of evidence had established human melanopsin photoreception:

- Melanopsin is present in a subset of Retinal Ganglion Cells (RGCs), known as intrinsically-photosensitive RGCs, or ipRGCs, and renders them light sensitive
- ipRGCs are a small proportion of all RGCs, but there are as many as six subtypes
- Melanopsin photoreception in ipRGCs has characteristics that are distinct from photoreception of the rods and cones in the wavelength, temporal and spatial domains:
  - wavelength: melanopsin sensitivity is maximal at around 490 nm in vivo, between the rods and the short-wavelength cones
  - temporal: light exposure (or dose) is integrated over time, so that responses are relatively slow to react to changes in light levels
  - spatial: the dendrites of individual ipRGCs spread across relatively large regions of the retina, ipRGCs do not form sharp images
• ipRGCs receive signals from rods and cones: ipRGC-influenced responses to light combine some of the characteristics of rod and cone photoreception with melanopsin photoreception.

“In Lucas et al., 2014 [Publication 1] we considered that there is no single action spectrum to describe all non-visual, or non-image-forming, responses to light, and further that the spectral sensitivity for a given response is derived from five different types of photoreceptor, depending on several factors:

• The light amount and spectrum,
• The timing, modulation and duration of exposure, and
• The accumulated effects of the prior light history of the individual.

“The five distinct photoreceptor sensitivities include the three cone sensitivity functions (in the peripheral retina), the rod sensitivity and the intrinsic sensitivity of ipRGCs which are combined in different ways according to these variables. Theoretically, all possible spectral sensitivities can be created in this way. Lucas et al., 2014 [Publication 1] has been extensively cited and forms the basis of the International Commission on Illumination’s (CIE’s) new international standard on non-visual metrology, CIE, 2018. [Publication A8]”

“In the same year as Lucas et al., 2014 [Publication 1], I published Price, 2014 [Publication 2] setting out a model that might explain how to predict circadian responses to an arbitrary pattern of light within the context of normal duration exposures experienced by a person undergoing a single consolidated sleep and a single consolidated activity period per day. This is still the only model capable of being applied in this way to arbitrary patterns of light exposure. I have also published three circadian dosimetry performance papers, assessing the ability of wearable motion and light monitoring devices to collect the personal exposure data needed for the requirements of Lucas et al., 2014, CIE, 2018 and/or Price, 2014 [Publications 1, A8 and 2 respectively].

“Circadian responses have been shown to be primarily linked to exposure to light acting through the non-visual system. ipRGCs project via the retinohypothalamic tract (rather than the optic tract that routes RGC projections in the visual system) to the suprachiasmatic nuclei (SCN) in the hypothalamus. The SCN is an oscillator of circadian genetic expression, often described as the master clock, that can maintain stable periodic expression close to 24 hours in period in the absence of light for several days. It also mediates the timing
information that is used to synchronise and entrain numerous peripheral oscillators and
responses of the neuro-endocrine system such as the secretion of the hormone melatonin.

"The purpose of circadian rhythms is to prepare the brain and body for various activities
and states on a periodic daily basis. Disruption of circadian rhythms therefore has the
potential to cause sustained mismatches between what the individual is doing and is
expected. For instance, and important mismatch arises where extended activity occurs
during sleep-supporting states in the subjective night (night-time according to the phase of
genetic expression in the SCN and/or other oscillators) and sleep opportunities are
restricted to the subjective daytime. This occurs during shift work for instance, as the phase
of circadian rhythms can only be shifted by up to approximately 1.5 hours per day. In
addition, exposure to light during the subjective night reduces the expression of
oscillations, as well as increasing desynchronisation between oscillators (as experienced in
jet-lag). An insufficient diurnal light:dark cycle can lead to the phase of the SCN drifting over
several days, and may exacerbate affective disorders – bright light treatment in the
morning has been shown to help reduce the effects of Seasonal Affective Disorder (SAD) in
a large proportion of sufferers.

"Circadian rhythms therefore play an important role in well-being as well as the progressive
of adverse conditions for both mental and physical health. For this reason, beneficial
circadian phase shifting and entraining responses are widely regarded as the most
important of the non-visual responses to light. It is hoped that the application of the model
in Price, 2014 [Publication 2] or more sophisticated future models, if appropriate, will lead
to a better understanding of how light exposure hygiene and interventions can be used to
support the quality of life and health.

"I have also investigated the measurement of light and optical radiation in field studies,
and led authorship on three papers concerning the use of wearable devices in studies
relating to circadian rhythms, sleep and non-visual responses to light. These are recognised
as leading contributions on this topic. I have related publications, with significant
contributions, on the measurement of light in general in relation to non-visual responses
to light, including a joint paper and toolbox created following an international workshop of
leading world experts."
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