The Human Eye: A Window to Health and Wellbeing

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Although world life expectancy has more than doubled over the past two centuries¹ due to advances in medicine, public health and technology,² questions could be raised as to whether or not the quality of human life can keep up with this increase in longevity. Until the last century or so, people traditionally woke up with the sunrise and went to bed shortly after sunset, possibly extending the day with candlelight, oil lamp or a fire. By the early 20th century, the use of electric lighting had become common³ and people could stay awake throughout the night. Today, postindustrial society is experiencing a proliferation of light-related disorders and diseases precisely because this technologically-based society can operate 24 hours per day in electrically illuminated indoor environments. This paper discusses lighting and light at night as possible contributors to the recent increase in chronic disease and provides recommendations for indoor environmental illumination to promote health and wellbeing for today's society.

HEALTH AND WELLNESS IN TODAY'S TECHNOLOGICAL SOCIETY

The leading causes of death for today's society have shifted from the communicable infectious diseases and epidemics of the 19th century to the chronic and age-related diseases of the new millennium.⁴ A little over a century ago the infant mortality rate in the U.S. was 20 percent. For those who survived birth, childhood mortality before age five was another 20 percent due to infectious diseases such as smallpox, measles and diphtheria.⁵ More children began to survive until adulthood largely because of the invention of vaccines in the late 19th century and the introduction of penicillin and the polio vaccine for widespread use in the mid-20th century.⁶ Today, death from chronic diseases is double that of all others combined including infant mortality, nutritional deficiencies and infectious diseases such as HIV/AIDS.⁷ It is illuminating to discover that the primary sources of death one hundred years ago were infectious diseases such as cholera, smallpox, measles, typhus, and tuberculosis, while today it is chronic diseases such as cardiovascular and

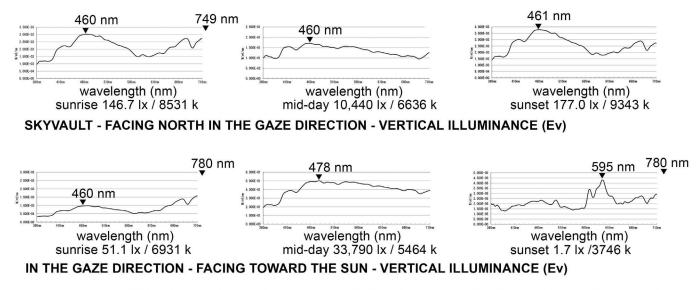
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heart disease, stroke, cancer, diabetes, and chronic respiratory disease.⁸ Nowadays, people live longer and many causes of death due to chronic disease could be delayed or avoided.

The critical difference between a chronic disease and an infectious disease is that most common chronic diseases are largely preventable by changes in lifestyle and diet.⁹ Present in many, if not all, chronic diseases is a new form of inflammation termed metaflammation,¹⁰ which is associated with lifestyle and environmental inducers¹¹ that have been linked either directly or indirectly to certain chronic diseases such as heart disease, type 2 diabetes, respiratory problems, many forms of cancer and even depression and dementia.¹² Anthropogens are the inducers of metaflammation and are a by-product of changes in the built environment due to the industrial revolution and resulting changes in lifestyle.¹³ Anthropogens incite a low level immune response to a not-immediately life-threatening situation, which builds up over time into a systemic response by the body. Although an individual might have a genetic predisposition to a certain chronic disease, early environmental influences can affect the later development of that disease.¹⁴

Recent research indicates that lighting has increasingly become a public health issue.¹⁵ These studies have shown that individuals working in natural sunlight are more productive, more effective, and happier than those who work under traditional artificial light. In addition, several studies have demonstrated a connection between environmental lighting levels and higher productivity and better performance from building occupants.¹⁶ Natural changes in daylight balance the body's circadian rhythm, which determines sleeping and eating patterns, cognitive activity, heart rate, hormone levels - in fact, virtually all physiological and behavioral parameters. Circadian phase shift and transmeridian travel have been shown to contribute to jetlag, Seasonal Affective Disorder (SAD), Delayed Sleep Phase Syndrome (DSPS), and is implicated in more various diseases and disorders, including cancer.¹⁷ Consequences due to lack of sleep is highly underrated in terms of its lifestyle risk factor for chronic disease.¹⁸ Lack of sleep is directly related to an increase in inflammatory markers¹⁹ and is associated with various chronic diseases.²⁰

Chronic disease can be affected by a mismatch between the environment one is evolutionarily and genetically programmed for and the environment one is born into or is living in.



NATURAL DAYLIGHT IN PHILADELPHIA - SUMMER NEAR THE SUMMER SOLSTICE

Figure 1: Natural Daylight in Philadelphia – Summer Near the Summer Solstice - Comparison of Wavelength, Illumination Levels and Color Temperature (source: authors).

HUMAN EVOLUTIONARY PROGRAMMING

Cultural/technological evolution is extremely rapid with many significant changes occurring within the lifetime of a single individual. Consider the technological revolution due to the internet over the past 25 years or the automobile, cinema, radio, and television over the past 100 years – technologies we cannot live without today. These are mere blips in time compared with biological evolution. The speed of cultural/technological change far outstrips most evolutionary processes. This means that humans are only partially adapted to the current environment in which they live. Also, this mismatch between biology and culture is likely to get worse as the rate of technological change increases. One aspect of our ancestors' environment – back to the origins of cellular life – is the gradual alteration of light and darkness generated by the Earth's rotation. For both design and evolutionary reasons, this environmental condition has shaped the evolution of all living systems and has profound implications for the built environment.

Biological rhythms are regular periodic variations in any biological system, such as the cardiac cycle, breathing and walking, and are a fundamental characteristic of all living processes. Rhythms are found everywhere: from cycles in biochemical rhythms, to subcellular rhythms in mitochondria and cell division cycles, to pulsatile release of hormones, sleep-wake rhythms, menstrual cycles, annual rhythms in births, etc. The human body is comprised of hundreds of rhythms with a variety of frequencies; however, the devices society uses today likely have not been designed with daily and/or seasonal rhythms in mind. Because humans have evolved oscillations, all of these cycles must be coordinated properly for the body to function optimally, which is one of the fundamental functions of rhythms – coordination of multiple activities. Just like an orchestra needs a conductor to provide temporal order to its various

instruments, the human body contains a 'conductor' – a master pacemaker or biological clock that provides temporal order to its system. This pacemaker runs at a frequency of about 1 cycle every 24.2 hours and is known as the circadian clock (located in an area of the brain called the suprachiasmatic nuclei of the hypothalamus or SCN).

The SCN help confer an internal temporal order onto the various rhythms of the human body and mind. Also, the SCN evolved to position these rhythms within the Earth's cycle of day and night so that physiological and behavioral processes occur at the appropriate times - such as activity during the day and sleep at night. Since the actual inherent rhythm of the SCN does not exactly match that of the day/night cycle (24.2 vs. 24), the SCN need to be reset every day to maintain the correct positioning. The major mechanism by which this is accomplished is through exposure to the appropriate intensities and wavelengths of light at the appropriate times, which is a light intensity that increases gradually (sunrise), then displays a powerful, sustained intensity (daylight) followed by a gradual decrease (sunset) and then a prolonged period of profound darkness (night). In addition to light intensity, there are also changes in wavelength, beginning and ending with red-vellow wavelengths bracketing periods of blue-white light and near blackness (see examples in Figure 1). For circadian systems to synchronize (a process called entrainment) to day/night cycles, they typically undergo a repeating pattern of these phase shifts which align the internal circadian clock with the external environmental cycle.

Light exposure at times other than those promoting synchronization can shift rhythms dramatically, increasing the chances of both external (mismatch between the external environment and internal rhythms) and internal desynchronization.²¹ Further, absolute intensity and duration is crucial. When the frequency expressed by the human circadian clock differs with respect to seasonal changes in photoperiod it results in alterations to daily rhythms. For example, during the summer, the period of the underlying circadian rhythm becomes longer and this is expressed

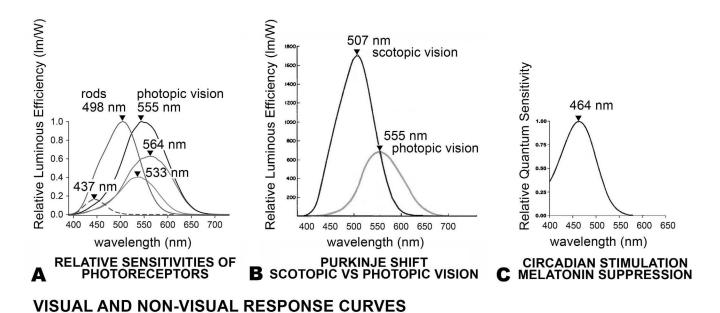


Figure 2: Visual and non-Visual Response Curves for the Human Eye (source: authors).

in a phase delay of the entrained rhythms; in winter, the opposite occurs, resulting in phase advances. These changes can trigger significant behavioral and physiological alterations, exemplified in the human condition known as Seasonal Affective Disorder (SAD).

ANATOMY OF THE VISUAL AND NON-VISUAL EYE

It is important to understand how light is perceived by the body to understand how light affects bodily rhythms. Light reaching the eye serves three major functions: object recognition (photic) vision, the internal and external synchronization of biological rhythms,²² and a direct stimulating effect on alertness and performance.²³

Human vision occurs by light entering the eye through an open and reactive pupil, passing through the lens, with the two working together to focus the light on the back of the retina at the fovea where cone cells are densely packed to provide fine visual acuity and color discrimination. Formerly identified as red, green and blue, there are three kinds of cone cells responsible for color vision: long-wavelength (L – 564 nm peak), medium-wavelength (M – 533 nm Peak) and short-wavelength (S – 437 nm peak) (Figure 2A). Color is perceived by the brain as a comparison function between the L, M and S cone cells. The cones are less dense away from the fovea where they are intermingled with the rods and together provide less precise peripheral vision. The rods are primarily responsible for peripheral vision and provide information about contrast and movement, which is why human response time is quicker when an object is seen with peripheral vision than with direct focus.

The cones are most active in medium and high light levels and function at higher photopic levels, which is at 3 candelas per square meter (cd/ m2) or higher. The rods become overwhelmed with high light levels, but at low light levels are more active than the cones are and function best at lower scotopic levels of illumination. Scotopic rod vision is sensitive starting at 0.01 cd/m2 and cone vision ceases completely once the light level drops to 0.001 cd/m2. As the general environmental brightness drops, the cones become less effective and it becomes difficult to discern fine details and colors. When moving from natural daylight to the indoor environment, or during the transition from daylight to darkness, the human eye adapts to changing illumination levels. This transition requires that the eye shift from photopic vision toward scotopic vision so that both rods and cones are contributing to visual perception. This intermediate lighting level is characteristic of most indoor environments and is called mesopic, which is considered to be between a high of 3 cd/m2 down to 0.01 cd/m2.

This change in spectral sensitivity is known as the Purkinje shift (Figure 2B). When the luminous intensity of the lighting environment begins to shift toward darkness at a lighting level of approximately 683 lumens per watt, vision begins to shift from cone vision to rod vision at the peak of the photopic response curve at around 555 nm and continues until it reaches the scotopic peak at 507 nm. Because rods are much more sensitive to light, even though illumination levels are lower at the peak of scotopic vision, the effective lighting level appears to be over twice as bright at an effective illumination level of 1700 lumens per watt. During scotopic vision, illumination brighter than a few lux saturates or blinds the rods and any light with this dark-adapted vision will appear very bright, such as a light filtering through a shaded window at night. This light may possibly alter rhythms and/or stimulate arousal, generating temporal disorder.

Rod light response peaks sharply in the blue spectrum (Figure 2A) and responds very little to red light. This leads to some interesting phenomena. If mesopic vision is desirable, for example high acuity vision at night without circadian rhythm disruption, then red-adapted vision is a solution. This can be achieved by using red light or by wearing red goggles.²⁴ This way the cones receive enough light for high-acuity photopic vision, for example reading, without disrupting one's circadian rhythms. Similarly, red goggles can block the blue light of various electronic media. The rods are not affected by the red light because they are not sensitive to long-wavelength light. However, vision will have very little color

CONES

RODS

6 million cells function well in daylight contain three types of photosensitive pigments for color responsible for color discrimination densely packed in the fovea high visual acuity and spatial resolution

RETINAL GANGLION CELLS

2.4-3 million cells conveys visual signals to the optic nerve contribute to vision stimulate pupillary light reflex

ipRGCs

1-3% of retinal ganglion cells contain the photopigment melanopsin sensitive to blue light non-image forming functions melatonin production 120 million cells function in low light contain one type of photosensitive pigment in the blue spectrum confer achromatic vision intermingled with cones in the retina good for peripheral vision, contrast and movement

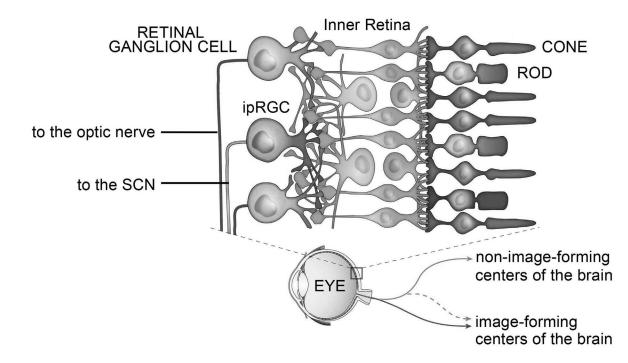


Figure 3: Anatomy of the Human Eye: Light in Layers. (Adapted by permission from Macmillan Publishers Ltd: *NATURE* (Corie Lok, "Seeing Without Seeing," 469/7330, pp. 284-285), copyright (2011).

contrast and the visual environment will appear in shades of grey, blue becomes black and yellow objects will seem to disappear. Even dim light at night without a red filter is not desirable. Since rod vision is shifted toward the blue spectrum, this may be why even a little bit of light could still transmit non-visual information as action spectra for melatonin suppression.

There is a third type of photoreceptor called the retinal ganglion cell located in the inner retina that relays signals from the rods and the cones to the brain (Figure 3). Visual information to these cells stimulate pupillary light reflex and non-visual photoneural responses (circadian, neuroendocrine, and neurobehavioral regulation) with some additional input from the rods and cones. A small subset (~1-3%) of these cells is called the intrinsically photosensitive Retinal Ganglion Cells (ipRGCs), which has an absorption peak at approximately 480 nm.²⁵ As it turns out, there are two pathways for light to take on its way to being processed by the brain. Visual information can be taken by the optic nerve to be processed by the image-forming centers of the brain in the visual cortex. Or, non-visual information can be transmitted via another pathway to the suprachiasmatic nuclei (SCN), which relay signals throughout the nervous system to provide information regarding time of day and ambient levels of light and darkness. The pineal gland receives these non-visual signals from the SCN and, in turn, regulates its production and secretion of the hormone melatonin. Melatonin production is greatest at night and lowest during the day for optimal circadian function. Its production is suppressed by blue-shifted white light²⁶ with a peak at around 464nm (Figure 2C),²⁷ close to both the 480 nm ipRGC peak and the 498nm rod peak.

BIOLOGICAL RHYTHMS

Biological rhythms are key elements controlling physiological activities. Operating at various frequencies, these rhythms must be coordinated to achieve optimum health and wellbeing. Due to the impact and predictability of the day/night cycle, evolution has equipped all eukaryotic organisms – including humans – with powerful circadian clocks that serve to both regulate these internal rhythms and align them with the geophysical cycle of day and night. Although multifaceted, the most effective means of attaining this alignment (entraining) is through the appropriate applications of light and darkness through the eyes.

Two major implications of these observations are: 1) Inappropriate application of light or darkness will disrupt internal rhythms and temporal order and 2) Such disruptions will be detrimental to human health, wellbeing and productivity.

Although it is impossible to cover all the data currently available, accidental human experiments involving shift work and travel across time zones confirmed through specific animal experimentation, have conclusively demonstrated that disrupting circadian rhythms and internal temporal order negatively impacts both behavior and physiology.²⁸ Some of these adverse effects include an increased risk for cancer,²⁹ changes in brain function,³⁰ insulin resistance and obesity,³¹ and greater incidents of cardiovascular disease³² – all diseases identified by the World Health Organization as chronic diseases. These effects are heightened with special needs populations whose physiological systems are already under more pronounced stresses such as children with autism spectrum disorder, older adults with dementia and homeless individuals. In short, poor temporal hygiene generated by disrupting circadian rhythms leads to poor health outcomes and a decrease in the quality of human life. One of the primary means of disrupting human circadian rhythms is an irregular schedule enabled by inappropriate artificial lighting.

CHRONOBIOENGINEERING THE INDOOR ENVIRONMENT

Chronobioengineering uses knowledge gleaned from the natural world out of which humans evolved to guide design of the built world into which humans find themselves living today. To date, the vast majority of design considerations and regulations concerning lighting have focused on traditional object recognition. Today, it is no longer possible to dismiss the adverse health consequences of disruptive electric lighting and structures that fail to support temporal hygiene. However, it may be possible to illuminate the indoors to promote temporal health without abandoning the flexibility 24-hour light provides. The retina and SCN cannot distinguish between artificial and natural light if the light is of similar wavelength and intensity. This represents both a disadvantage and advantage: a disadvantage if lighting is designed without considering the effects of natural daylight, but an advantage if indoor lighting is designed with the knowledge of how light impacts the circadian system.

In terms of timing, both mathematical models of biological rhythms and experimental observations of circadian rhythms in organisms indicate that a gradual onset and offset of light intensity will generate a far more powerful and sustained synchronization than light pulses or even a typical square wave approach. A typical square wave lighting system (such as turning lights on at 6 am and off again at 6 pm generating a

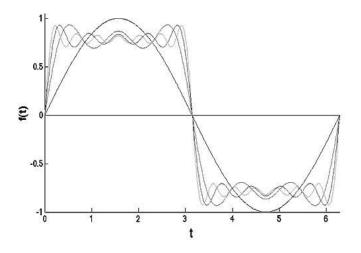


Figure 4: Fourier series for a square waveform. Shown here is a single sine wave (the fundamental) and then the sum of successive odd harmonics (i.e., sine waves with odd multiples of the frequency of the fundamental sine wave) showing how the sum approaches a square wave as more frequencies are summed up (From: Chapter 6 – *The Circle Game: Mathematics, Models and Rhythms* by Dr. Bahrad Sokhansanj in McEachron, *Chronobioengineering*, Volume 1 (Morgan and Claypool, Publishers, 2012)).

LD 12/12 cycle) is not optimal for entrainment of circadian rhythms. The signals generated by such a LD (light/dark) cycle are perceived by the circadian clock not as a single timing signal but rather as a mixture of many sine and cosine waveforms (consider the Fourier analysis of a square wave pattern in Figure 4). These conflicting signals reduce the efficacy of the LD cycle as a synchronizing agent.³³ A more appropriate sinusoidal light intensity waveform with suitable wavelengths represents the most powerful approach that can be practically implemented. This means a gradual onset/offset lighting environment that changes wavelength and intensity similarly to the rising and setting sun with sustained light intensity throughout the day like the lighting environment from which humans evolved. Light intensity varies dramatically throughout the day, drastically changing in intensity (Figure 1) when measured in the "gaze direction" or vertical illuminance (E). How light is measured, or the direction the light meter is pointing,³⁴ is crucial. In lighting design, light is characteristically measured by horizontal illumance (E,), which is facing upwards. Designers need to consider that people rarely stare up at the ceiling when in a space unless they are in a hospital bed or a dentist's chair, which is when human interaction with a light source is a critically important design consideration.

In terms of perception, designers can take advantage of the different absorption spectra of photoreception involving circadian and photic vision. If current studies by Drexel University's dLUX light lab are confirmed, then dimmer red light will allow for activities during the dark phase of lighting while having little or no impact on the circadian system.³⁵ Therefore, absolute darkness may not be needed to avoid circadian disruption, support for the notion of circadian design in lighting systems for temporal health.

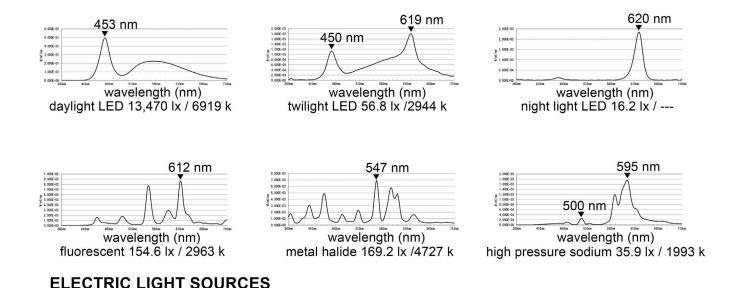


Figure 5: Various Electric Light Sources: Comparison of Wavelength, Illumination Levels and Color Temperature (source: authors)..

Human vision is normally better with daylight than electric lighting. This is largely due to the higher intensity of natural daylight and its better color rendering index, two properties of light that electric lighting seeks to emulate. Even though people tend to prefer the light levels of natural daylight, especially as provided by the midday sun, they do not always adjust their indoor lighting environment to follow the natural variation of daylight³⁶ in its diurnal change from the rising sun to the midday sun to the setting sun.

INDOOR ENVIRONMENTAL ILLUMINATION

Natural daylight is the best way to illuminate the indoors. Daylight is that portion of the electromagnetic spectrum which can be perceived by the human eye and processed as visual and non-visual information. Natural daylight ranges from 380 nm (nanometers) to about 780 nm. Infrared (IR) radiation has longer wavelengths (780-1000 nm) and is perceived by humans as heat. Ultraviolet (UV) radiation has shorter wavelengths below 400 nm and is divided into UV-A (315-400nm), UV-B (280-315 nm) and UV-C (200-280 nm).³⁷ Curiously, Solar UV-B radiation (280-315 nm) is an initiator of Vitamin D3 production in the human skin,³⁸ which makes exposure to natural light a double-edged sword. Overexposure to ultraviolet radiation from sunlight is a major determinant for several forms of skin disorders including melanoma and other forms of skin cancer, as well as photoaging.³⁹ Underexposure to sunlight can lead to deficiencies in vitamin D, which increases the risk for heart disease,⁴⁰ type 2 diabetes,⁴¹ rickets,⁴² and osteoporosis, and may contribute to depression⁴³ – all chronic diseases. On the other hand, research has shown that individuals working in natural sunlight are more productive, more effective, and happier than those who work under traditional artificial light.44

Research and policy decisions confirm that lighting has increasingly become a public health issue.⁴⁵ In June 2012 at the American Medical Association (AMA) annual meeting in Chicago, the House of Delegates of the AMA declared that light at night results in adverse health outcomes. Furthermore, the Council on Science and Public Health recognized that exposure to excessive light at night, including extended use of various electronic media, can disrupt sleep or exacerbate sleep disorders. The Council on Science and Public Health recommended that the AMA support the need for developing and implementing environmental lighting technologies at home and at work that minimize circadian disruption, while maintaining visual efficiency.⁴⁶ Adverse light effects can be minimized by using natural daylight or daylight-matching electric light during the day.

It is relatively easy to maximize the use of natural daylight when designing for health and wellness in the indoor environment. For building design, use large areas of north-facing glass and ample windows with sun control devices on the other three façades to shade the glass from radiant heat while redirecting natural daylight deep into the building interior. For interior design, use natural illumination together with electric lighting to provide ambient light while controlling glare. Passive environmental design using natural daylight for buildings is relatively old technology that precedes the Roman atrium. For electric lighting, a paradigm shift has occurred in the lighting industry over the past decade from the use of electric-filament or gas lamps for illumination to the light-emitting diode (LED) lamp, or the integrated LED luminaire with no lamp at all but LEDs integrated within the fixture.⁴⁷

The unique characteristics of LEDs include: compact size, long life and ease of maintenance, resistance to breakage and vibration, good performance in cold temperatures, lack of infrared or ultraviolet emissions, instant-on performance, color control, reduced flicker, and the ability to be dimmed. RGB (red, green, blue) LED sources have a higher theoretical maximum efficiency, potentially longer life, and allow for dynamic control of color and intensity.⁴⁸ LED lighting can be controlled and dimmed to maintain uniform lighting levels from the bright areas adjacent to daylit exterior walls to the dim areas located near the building core. Compared with either electric filament or gas lamps, LEDs can most closely match the full spectrum of natural daylight in color and intensity (Figure 5), can be tuned to mimic the rising, setting and noontime sun, and can provide red light at night. In addition, the LED waveform has continuous variability like natural daylight while the waveform of gas lamps is jagged and discontinuous – colors of the various peaks may sum to equal white in color temperature (Kelvin), but there are gaps in the spectrum. The continuous waveform is likely why human vision is more comfortable with daylight than gas-lamp lighting. Continuity of the LED waveform holds the promise of more closely matching the comfort of natural daylight (compare the peak for melatonin suppression in Figure 2C and the peaks for daylight in Figure 1 with the peaks for the daylight-matching LEDs in Figure 5).

Depending on jurisdiction, various codes govern the required illuminances for indoor lighting at the local, state and national levels. In addition, the Illuminating Engineering Society provides recommended practices for various user groups. What these guidelines do not take into consideration is the changing physiology of the aging human body or special needs populations. For example, aging decreases pupil area and reduces crystalline lens light transmission thereby blocking blue light, which results in progressive loss of circadian photoreception. The amount of light reaching the human retina decreases about 1 percent per year. This means that if a 10-year-old person's retina receives 100 percent of available environmental light, then the 90-year-old adult retina receives only 10 percent of that available light. This drastically limits the older adult's circadian system from receiving the light it needs for photoentrainment⁴⁹ and is likely why studies recommend blue-shifted light of 6500k with lighting levels as high as 2500 lux for older adults.⁵⁰ Thus, for improved health and wellbeing it is also imperative to consider lighting levels with respect to age when designing the indoor lighting environment.

CONCLUSION

For optimal health and wellbeing in interior architecture, it is important for designers to consider indoor lighting as environmental illumination with wavelength, intensity and color temperature that takes the intended occupant's biological rhythms, age and special needs into consideration.

ACKNOWLEDGEMENTS

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ENDNOTES

- 1. J. Riley, *Rising Life Expectancy: A Global History* (Cambridge: Cambridge University Press, 2001): 243.
- 2. Jim Oeppen and James W.Vaupel, "Broken Limits to Life Expectancy," *Science* 296 (10 May 2002), 1029-1030.
- 3. Ernest Freebert, *The Age of Edison: Electric Light and the Invention of Modern America* (New York: The Penguin Group, 2014).
- J. W. Sanders, G. S. Fuhrer, M. D. Johnson, and M. S. Riddle, "The epidemiological transition: the current status of infectious diseases in the developed world versus the developing world," *Science Progress*, 91/1 (2008): 1–38.
- Alexandra Minna Stern and Howard Markel, "The History of Vaccines and Immunization: Familiar Patterns, New Challenges," *Health Affairs* 24/3 (May/Jun 2005): 611-21.

- A. Hinman, "Landmark perspective: Mass vaccination against polio," JAMA 251/22 (1984): 2994–6.
- World Health Organization, http://www.who.int/chp/chronic_disease_report/part2_ch1/en/index1.html, accessed July 11, 2016.
- World Health Organization, http://www.who.int/chp/chronic_disease_report/part2_ch1/en/index4.html, accessed July 11, 2016.
- G. Danaei et al. "The Preventable Causes of Death in the United States: Comparative Risk Assessment of Dietary, Lifestyle, and Metabolic Risk Factors" *PLoS Medicine* 6/4 (April 2009).
- G. S. Hotamisligil, "Inflammation and metabolic disorders," *Nature*, 444/7121 (2006): 860–867.
- 11. R. Medzhitov, "Origin and physiological roles of inflammation," *Nature* 454/7203 (2008): 428–435.
- 12. P. Libby, "Inflammatory mechanisms: the molecular basis of inflammation and disease," *Nutrition Reviews* 65/12 (2007): S140–S146.
- Garry Egger, "In search of a "germ theory" equivalent for chronic disease," *Preventing Chronic Disease* 9/11 (2012): 1–7.
- Garry Egger and John Dixon, "Beyond Obesity and Lifestyle: A Review of 21st Century Chronic Disease Determinants," *BioMed Research International* 2014, Article ID 731685, 12 pages, http://dx.doi.org/10.1155/2014/731685.
- S. M. Pauley, "Lighting for the human circadian clock: recent research indicates that lighting has become a public health issue," *Medical Hypotheses* 63 (2004): 588-596.
- 16. C. Fay, Daylighting and Productivity A Literature Review, Lighting Research Center, Rensselaer Polytechnic Institute, 2002, Report of Project "Cross-Cutting R&D on Adaptive Full-Spectrum Solar Energy Systems for More Efficient and Affordable Use of Solar Energy in Buildings and Hybrid Photo-Bioreactors" sponsored by U.S. Department of Energy.
- J. E. Roberts, "Therapeutic Effects of Light in Humans," *Photobiology for the 21st Century*, edited by Thomas P. Coohill and Dennis P. Valenzeno (Overland Park, Kansas: Valdenmar Publishing Company, 2001): 17-29.
- M. E. Wells and B. V. Vaughn, "Poor sleep challenging the health of a Nation," *The Neurodiagnostic Journal* 52/ 3 (2012): pp. 233–249.
- J. E. Ferrie, M. Kivim "aki, T. N. Akbaraly et al., "Associations between change in sleep duration and inflammation: findings on C-reactive protein and interleukin 6 in the Whitehall II study," *The American Journal of Epidemiology* 178/6 (2013): 956–961 and S. J. Motivala, "Sleep and inflammation: psychoneuroimmunology in the context of vascular disease," *Annals of Behavioral Medicine* 42/2 (2011): 141–152.
- 20. H. R. Colten and B. M. Altevogt, eds., *Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem* (Washington, DC: National Academies Press, 2006).
- D. L. McEachron, "disruption of internal temporal order," in Chronobioengineering: Introduction to Biological Rhythms with Applications, Volume 1 (San Francisco, CA: Morgan Claypool, 2012).
- 22. J. E. Roberts," Daylight as a Visual Stimulus," Light Congress 2008, presentation.
- F. Perrin, et. al., "Nonvisual responses to light exposure in the human brain," *Current Biology* 14 (2004): 1842-1846.
- 24. M. Ayaki, et. al., Chronobiology International 33/1 (2016): 134-139.
- David M. Berson, "Phototransduction in ganglion-cell photoreceptors". *Pflügers Archiv -European Journal of Physiology* 454/5 (2007): 849–55.
- A. J. Lewy, T. A. Wehr, F. K. Goodwin, D. A. Newsome, and S. P. Markey, "Light suppresses melatonin secretion in humans," *Science* 210/4475 (Dec 12, 1980): 1267-9.
- G. C. Brainard, J. P. Hanifin, J. M. Greeson, et al., "Action spectrum for melatonin regulation in humans: evidence for a novel circadian photoreceptor," *Journal of Neuroscience* 21/16 (Aug 15, 2001): 6405-12.
- D. L. McEachron, Chronobioengineering: Introduction to Biological Rhythms with Applications, Volume 1 (San Francisco, CA: Morgan Claypool, 2012).
- Steven S. Coughlin and Selina A. Smith, "The impact of the natural, social, built and policy environments on breast cancer," *J Environ Health Sci.* 1/3 (2015): 10.15436/2378-6841.15.020 and Daniel Guitierrez and Joshua Arbesman, "Circadian dysrhythmias, physiological aberrations and the link to skin cancer" *International Journal of Molecular Sciences* 17/621 (2016): doi:10.3390/ijms17050621.
- Ilia N. Karatsoreos, et. al., "Disruption of circadian clocks has ramifications for metabolism, brain and behavior," PNAS 108/4 (2010): 1657-1662.

- Shu-qun Shi, et. al., "Circadian disruption leads to insulin resistance and obesity," Current Biology 23 (2013): 372-381.
- Sirimon Reutrakul and Kristen L. Knutson, "Consequences of circadian disruption on cardiometabolic health," *Sleep Medicine Clinic* 10 (2015): 455-468.
- 33. Ibid., Chapter 6.
- Research in Drexel University's dLUX light lab is conducted by using the CL-500A spectrophotometer by Konica Minolta.
- E.V. Ellis. D.A. Kratzer, D.L. McEachron & E.W. Gonzalez, "Red light at night to enhance cognitive functioning for society's special needs groups," *Proceedings of the 2016 ARCC/ EAAE International Conference on Architectural Research* (Lisbon: Taylor & Francis, 2016).
- G.R. Newsham, M.B.C. Aries, S. Mancini and G. Faye, "Individual control of electric lighting in a daylit space," *Lighting Research and Technology* 40 (2008): 25–41.
- M.B.C. Aries, M.P.J. Aarts, and J. van Hoof, "Daylight and health: A review of the evidence and consequences for the built environment," *Lighting Research and Technology* 47 (2015): 6-27.
- D. J. Turnbull, A. V. Parisi and M. G. Kimlin, "Vitamin D effective ultraviolet wavelengths due to scattering in shade," J Steroid Biochem Mol Biol 96/5 (September 2005): 431-6.
- P. A. Morganroth, H.W. Lim, and C. T. Burnett, "Ultra-violet radiation and the skin: an in-depth review," *The American Journal of Lifestyle Medicine* 7/3 (2013): 168–181.
- A. Zittermann and R. Koerfer, "Vitamin D in the prevention and treatment of coronary heart disease," *Current Opinion in Clinical Nutrition and Metabolic Care* 11/6 (2008): 752–757.
- T. Mezza, G. Muscogiuri, and G. P. Sorice, "Vitamin D deficiency: a new risk factor for type 2 diabetes?" Annals of Nutrition and Metabolism 61/4 (2012): 337–348.
- T. J. Caruso and G. Fuzaylov, "Severe vitamin D deficiency—rickets," The New England Journal of Medicine 369 (2013): article 9.
- R. E. Anglin, Z. Samaan, S. D. Walter, and S. D. McDonald, "Vitamin D deficiency and depression in adults: systematic review and metaanalysis," *The British Journal of Psychiatry* 202 (2013): 100–107.
- F. Perrin, P. Pelgneux, S. Fuchs, S. Verhaeghe, S. Laureys, B. Middleton, C. Degueldre, G. Del Flore, G. Vanderwalle, E. Balteau, R. Poirrier, V. Moreau, A. Luxen, P. Maquet, and D-J. Dijk, "Nonvisual responses to light exposure in the human brain" *Current Biology* 14 (2004): 1842-1846.
- S.M. Pauley, "Lighting for the human circadian clock: recent research indicates that lighting has become a public health issue," *Medical Hypotheses* 63 (2004): 588-596.
- Blask, D., Brainard, G., Gibbons, R. Lockley, S., Stevens, R., Motta, M. 2012. Light Pollution: Adverse Health Effects of Nighttime Lighting. Action of the AMA House of Delegates 2012 Annual Meeting: Council on Science and Public Health Report 4 (A-12) 25 pages.
- E.V. Ellis. D.A. Kratzer, D.L. McEachron & E.W. Gonzalez, "EBD Using Daylight-Mimicking LEDs for Improved Health Outcomes in Older Adults at St Francis," *Proceedings of the 2014 ARCC/EAAE International Conference on Architectural Research* (Mānoa: University of Hawai'i, 2014): 275-285.
- 48. DOE 2013. http://www1.eere.energy.gov/buildings/ssl/ (accessed 01-18-2013).
- 49. P. L. Turner and M. A. Mainster, "Circadian photoreception: ageing and the eye's important role in systemic health," *British Journal of Ophthalmology* 92(2008): 1439-1444.
- J. Van Hoof, M. P. J. Aarts, C. G. Rense, and A.M. C. Schoutens, "Ambient bright light in dementia: effects on behavior and circadian rhythmicity," *Building and Environment* 44 (2009): 146-155 and M. M. Sinoo, J. van Hoof, H. S. M Kort, "Light conditions for older adults in the nursing home: Assessment of environmental illuminances and colour temperature," *Building and Environment* 46 (2011): 1917-1927.