Light-life interactions beyond photosynthesis

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Abstract

From 1996[1] life on Earth has, for the first time in its history, been exposed over long periods to sources of artificial light that are strictly limited to the colours that we can see. This transition has been driven by the need to conserve energy for vision indoors and at night and has been achieved using efficient white LED technology. The effects of this change were not obviously anticipated but, by breaking billions of years of evolutionary adaptation, the consequences for life are being revealed as recognisable changes in public health and the well-being of much of the biosphere. Here we review the natural and artificial light environments and explore the limited knowledge of the interactions between light and biology. The principal conclusion is that the near-infrared radiation, discovered by William and Caroline Herschel in 1800, plays an important role in respiration and metabolism. This can be regarded as a 'mirror' of photosynthesis by which certain bacteria and plants use the energy of sunlight to synthesise the carbohydrates that life uses as food.

1. Introduction

Earth's biosphere has evolved to exploit sunlight as its principal source of energy. This probably was not so when life first took hold around 3–4 billion years ago as the first steps may have taken place in the darkness of the deep ocean. There could be found warm, mineral-rich undersea vents where chemical and thermal energy was a directly available power source. However, when this early life eventually reached the surface and daylight, it adopted the energy carried by solar photons as a much richer sustainable source. The process that we now call photosynthesis — transforming light into chemical energy that could readily be used by life — was employed in the oceans by cyanobacteria and algae and, eventually, by land-based plants.

A by-product of this new energy source, which splits water into its constituent atoms, is oxygen. Until photosynthesis got going in the oceans, there was very little of this element freely available in the water or the atmosphere but was highly toxic to the life that had, until then, been in a safe anoxic environment. As oxygen was released into the oceans as a waste product, it proceeded to oxidise the metals, most notably iron, whose salts were in a soluble form. When the ocean could no longer absorb more oxygen, the gas was already entering the atmosphere where it would have cleared the hazes and enabled the first blue skies. Earth experienced these events between two and three billion years ago.

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[1] The marketing of the first white LED lighting.

As this happened, life had to adapt or die. Oxygen is a powerful but potentially dangerous fuel. Its great advantage is that it can 'burn' the sugars (carbohydrates) produced by photosynthesis in plants and bacteria and so enable a portable and accessible fuel that could be used to power animals through their fast-paced lives.

In animals, the processes of respiration and metabolism operate together as a mirror of photosynthesis by taking its products, carbohydrate + oxygen, and combining them to release some substantial fraction of the originally captured solar energy as a readily available fuel to power living cells. In this way, the animals became able to generate energy much faster than the plants could produce it by sunlight by using existing stores of food and fossil fuels (coal, oil and gas).

Knowing that the fundamental energy source for at least the near-surface life on Earth is sunlight[2], we can ask the rather fundamental question: "What effects does light have on forms of non-photosynthesising life?". Here, this question is addressed for animals although it might equally be asked for other branches of life. In this talk/article, we skip some of the obvious answers to this question, such as vision, but focus in particular on the process of energy generation, the mirror of photosynthesis.

2. The natural light environment

We start by taking a fresh look at the Earth's natural light environment. This is a necessary step for the reason that human civilisation has taken many steps to distance us from the natural state in which life has evolved over the last few billion years. Many of us now reside in a predominantly built environment where artificial light sources are used inside buildings and cover an increasing fraction of the land surface at night at an increasing level of brightness (Artificial Light at Night: State of the Science 2022, International Dark-Sky Association, https://darksky.org/app/uploads/2022/06/IDA-State-of-the-Science-2022-EN.pdf).

With a period of dark adaptation, human vision is capable of working over a range of a billion in brightness, but to experience this we have to go to special places such as well-protected and remote regions such as astronomical observatories. Figure 1 (top) shows a daytime view of the European Southern Observatory (ESO) site at Paranal in the northern Atacama desert in Chile (https://www.eso.org/public/images/archive/category/paranal/), while the lower image shows a similar view under a dark sky with no Moon above the horizon. This illustrates the factor of a billion although we would not see the lower dark sky image in colour as we would be using our sensitive, but monochromatic, rod vision under these conditions.

If you were not previously aware of the green/red airglow, you might ponder the question of its origin. It is there because the Earth is a living planet: the glowing oxygen gas in the high

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[2] There is evidence of microbial life deep underground that can release oxygen from its environment. See "Underground Cells Make 'Dark Oxygen' Without Light", Quanta magazine. https://www.quantamagazine.org/underground-cells-make-dark-oxygen-without-light-20230717/

Figure 1. Top: ESO's Paranal observatory in full sunlight, image credit: ESO/ José Francisco Salgado (josefrancisco.org); Bottom: a similar view at night with the Moon below the horizon, image credit: Y. Beletsky (LCO)/ESO. The flattened mountain-top hosts the four 8.2m aperture telescopes of the Very Large Telescope (VLT) amongst other structures. In addition to the Milky Way, the image shows the red and green airglow from oxygen gas in the upper atmosphere as it slowly releases energy captured from sunlight during the day. We can see this glow but, as our eyes rely on their sensitive, monochromatic rod receptors, we could not detect the colours. These two pictures represent the factor of a billion in brightness between full sunlight and a really dark sky. If you took the faintest star you could see with you eye at the scene of the bottom picture, you would have to go about another 10 billion times fainter to see the very faintest objects detected by the Hubble and James Webb Space Telescopes.

atmosphere is the product of photosynthesis; it is what we call a 'bio-marker'. This oxygen is excited by UV sunlight during the day and slowly releases this energy at night as predominantly green and red light. Seeing and experiencing the story a naked dark sky can tell us is a wonderful privilege that is being withdrawn from an increasing proportion of the planet's occupants. It is now relentlessly

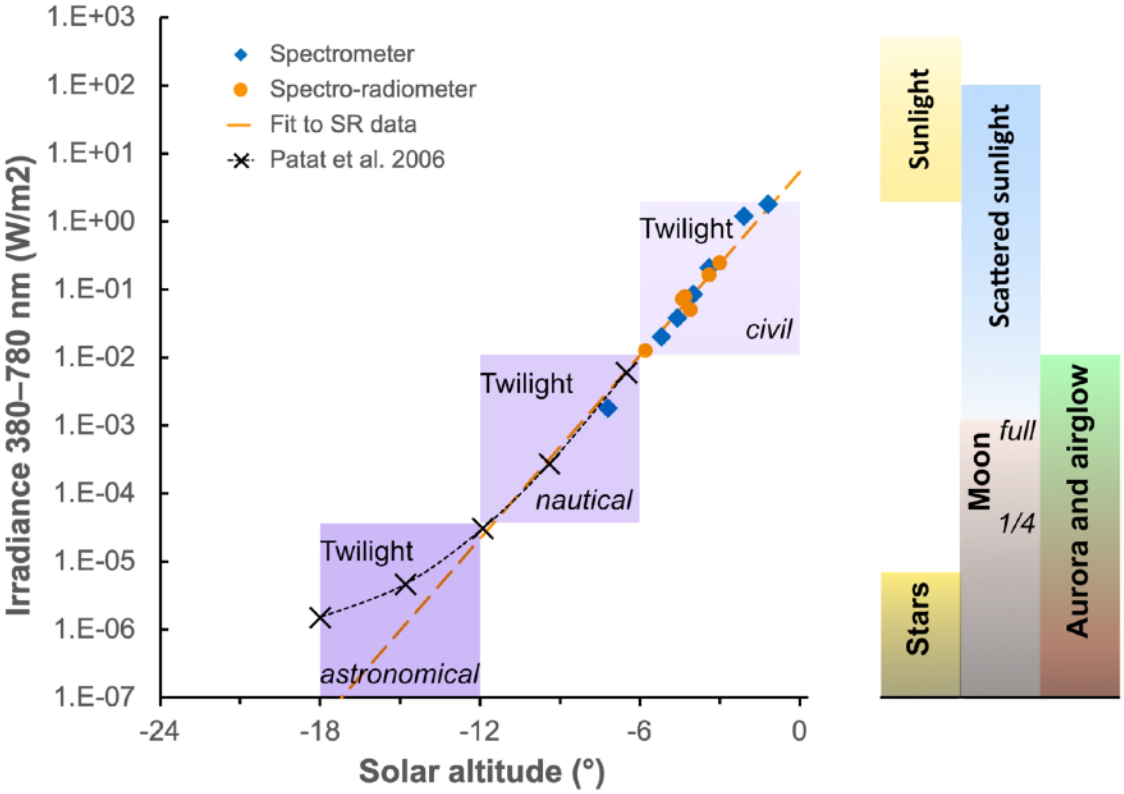

Figure 2. A map of the Earth's natural light environment. The (vertical) brightness scale, is in units of irradiance over the visible light spectrum (380 – 780nm wavelength) in units of Watts per square metre. The horizontal scale covers the twilight range produced as the Sun drops below the true horizon to the end of astronomical twilight at a solar altitude of -18° by which time it is as dark as it gets in a clear sky. The upper data points (orange circles) are from my measurements of clear sky twilights since 2018 using a Sekonic C-7000 spectro-radiometer which gives absolute spectral irradiance measurements in the visible spectrum. The blue diamond measurements are made with an Ocean Insight Maya2000Pro spectrometer which has a relative wavelength-brightness calibration that has been referred to the absolute scale of the Sekonic radiometer. The lower black "X" points use data taken from Patat et al. (2006, "UBVRI twilight sky brightness at ESO-Paranal", DOI: 10.1051/0004-6361:20064992). In this logarithmic plot referring to a moonless sky, the twilight follows a simple linear decrease with solar altitude until the starlight and airglow begin to become apparent at the beginning of astronomical twilight. Depending on atmospheric conditions, daylight covers a range of between three of four orders of magnitude while twilight extends over more than five. The coloured strips on the right illustrate the ranges of the contributors. [Note: The spectral irradiance on a surface is the radiant power falling on it from the whole hemisphere at each wavelength measured in units of, e.g, Watts/m^2/nm, The irradiance is the integral of this quantity over all or a specified range of wavelengths.] Image credit: the author.

being replaced by sources of artificial light that, while they may look superficially like sunlight, are very far from providing the broad spectrum of benefits life has evolved to require. The inadequacy of these artificial sources of 'white' light is an essential topic of this article.

Figure 2 shows a map of the major contributors of our natural light environment during the day and night. It covers the range of a billion in brightness that we have discussed above and it shows that our Sun is the dominant source of light, either directly during the day, indirectly at night by scattering from the upper atmosphere (twilight) or by reflection from the Moon. Also, electrically charged particles in the solar wind interact with the upper atmosphere over the polar regions to produce the aurorae. At the lowest brightness levels, we see the starlight from the rest of the universe, largely from our galaxy the Milky Way and also, depending on the conditions and the time of night, the airglow.

The Sun radiates over a large range of the electromagnetic spectrum from X-rays to radio wavelengths, not all of which reach Earth's surface. For our current purposes, the important region extends from the mid ultraviolet (UV-B, 280–315nm) through the the UV-A (315–400nm) and the visible spectrum — that contains most of the solar power — to the near infrared (NIR or IR-A from 750–1,400nm) and is quite likely to include part of the short-wavelength infrared (SWIR or IR-B, from 1,400–3,000nm).

Wavelengths shorter than 300nm are strongly absorbed by atmospheric ozone gas — protecting us from severe UV damage to DNA etc. — but the region between 300 and about 320nm is important for the synthesis of the hormone known as vitamin D which is made in our bodies by UB-B sunlight breaking a molecular bond in (dehydro)cholesterol in our skin. This essential hormone is difficult to make at high latitudes where the relevant UV sunlight is only available during the summer when the Sun is relatively high in the sky. From the UV-A through to the IR-A bands the atmosphere is relatively transparent but at the longer wavelengths water vapour and/or liquid begins to absorb with increasing strength into the IR-B.

Although the visible region of the spectrum contains most of the solar power, the infrared contains most of the photons of light which individually carry less energy. These photons can however interact with molecules to trigger biochemistry but, because of their lower energy, they interact in different ways to their more energetic visible and UV cousins. The latter have enough energy to move electrons around in, or remove them from, atoms and molecules and in so doing will alter the colour of the remaining light, i.e., they are coloured pigments. Perhaps the most biologically important of these are the chlorophyll in plants and the haemoglobin in the blood of many animals. The result of this propensity to strongly absorb visible light means that living tissue is largely opaque at these wavelengths: light cannot penetrate far into bodies or plants, the latter using numerous thin leaves as efficient photon collectors.

The lower energy of the infrared photons means that they can rarely move electrons around in living tissue. Instead, they can make molecules vibrate or 'ring' at certain frequencies, and molecules in different vibrational states can interact with their surroundings in different ways. At near infrared wavelengths, the photons still contain significant energy compared to what is required to make a molecule vibrate in a fundamental mode, instead they can excite a harmonic or 'overtone'. It turns out to be harder to excite these overtones and therefore living tissue is much less opaque in NIR-A than it is in the visible or UV. This leads to the existence of what is called the 'Tissue Transparency Window' or TTW (https://en.wikipedia.org/wiki/Near-infrared_window_in_biological_tissue)

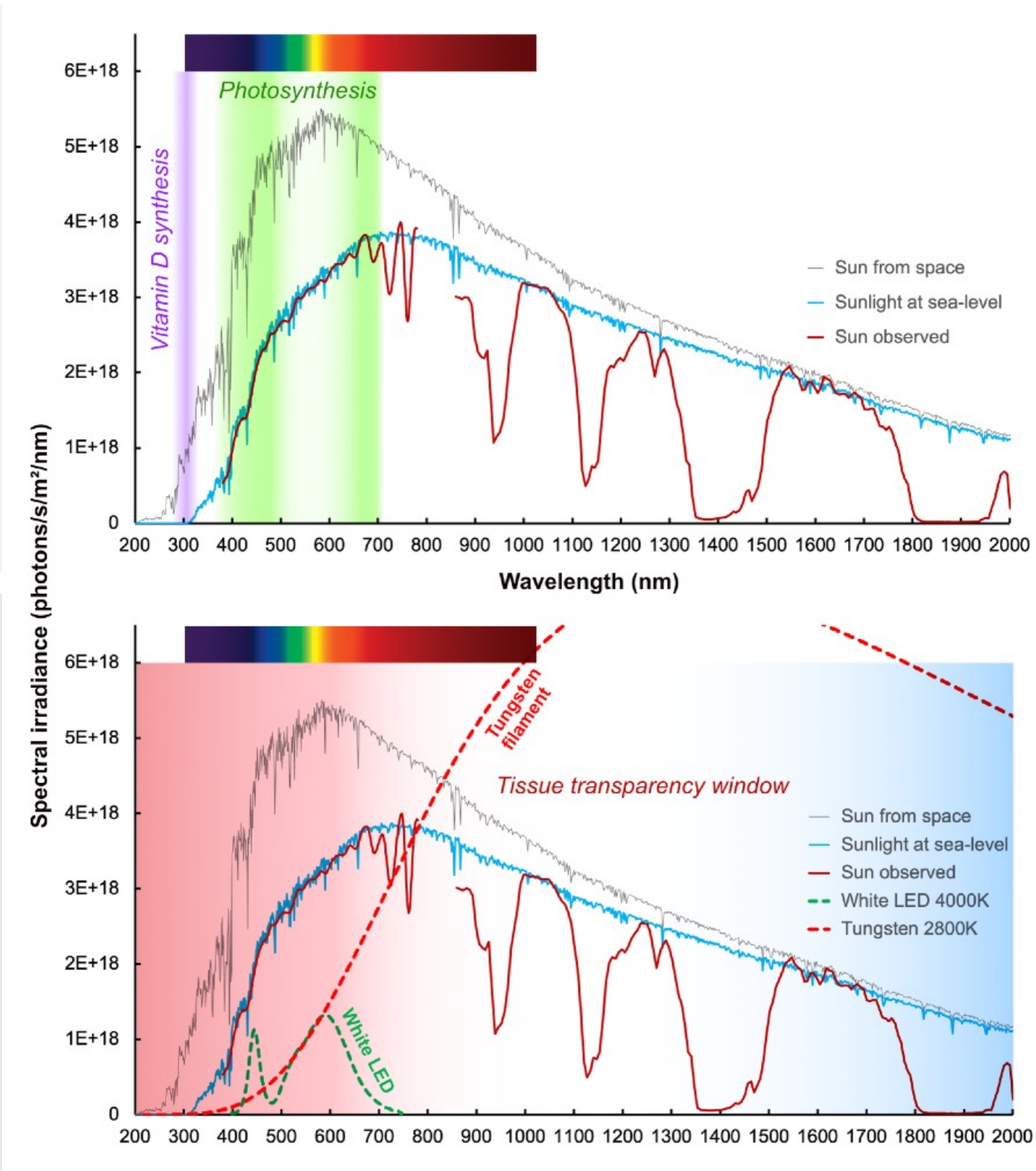

Figure 3. The spectra in these two plots show the sunlight that reaches the ground when the Sun is 30° above the horizon. The grey line is the sunlight outside the atmosphere. The blue line is the light that remains after the scattering that generates the blue sky, while the brown lines are measurements that show the atmospheric absorption produced predominantly by water vapour and oxygen on the path to ground level. The shading in the upper panel shows the narrow purple band where the UV-B sunlight can synthesise vitamin D in animal skins. The green region shows where light is absorbed for photosynthesis; this is also the spectral range where animal vision occurs. In contrast, the red and blue shading in the lower panel shows the lower and upper wavelength limits of the NIR spectrum that define the tissue transparency window (TTW) where photons can penetrate deep into living tissue. The important point to note here is that the two lamp spectra shown as dashed lines have dramatically different coverage of the NIR region: the LED emits nothing while the tungsten lamp emits most of its energy here.

where molecular absorbers are weak. This extends from around 650nm through the NIR-A band until liquid water absorbs an increasingly large fraction of the light beyond 2,000nm.

Figure 3 illustrates the spectral extent of the sunlight that reaches the ground and can interact with biology. It shows three ranges where photons interact with bio-molecules in the ways just described. The upper plot shows the UV-B band around 300nm (purple shading) where the light can synthesise vitamin D when the Sun is sufficiently high in the sky. The blue line spectrum represents the sun just 30° above the horizon and it is apparent that the incident UV radiation is too strongly absorbed by ozone to drive the synthesis, showing how difficult it is to make enough in winter at high latitudes. It is the light at longer wavelengths up to around 700nm, shaded in green, that generates chemical energy by photosynthesis. It is also in this range that animals employ coloured pigments called opsins in their visual receptor cells to enable vision.

The lower plot shows a broad band of infrared wavelengths where the the red and blue shading is used to show the transparency limits of the spectrum we have termed the TTW where the molecular absorptions are generally weak and NIR light can penetrate to significant depths in biological tissue. In addition to the solar spectrum in the figure we add two artificial light sources which are both used for providing visual illumination but have dramatically different coverage of this window. The white LED has been engineered to have maximum output in visible light to provide the best possible energy efficiency for vision. Such lamps are powered by a blue light-emitting diode which is surrounded by a mixture of phosphors that can absorb some of the blue light and re-emit it at longer wavelengths by a process called fluorescence. This generates enough green yellow and red light to give the appearance of white and the balance can be adjusted to produce shades of white between a harsh bluish colour to a softer amber glow. Confusingly the blue-white lamps have a high colour temperature (CT) rating and are termed ‘cool’ while the amber lights have a lower CT but are termed ‘warm’: this makes no physical sense but the terminology is deeply embedded. The green-dashed spectrum in the lower plot shows the clear distinction between the blue LED driver peak and the broader phosphor emission from green to red. The while LED emits essentially zero NIR radiation.

The other lamp is a now old-fashioned tungsten filament bulb that emits light from an electrically-heated tungsten filament with a temperature of between two and three thousand degrees Celsius or Kelvins (0°C = 273.15K). The reason that we have moved so comprehensively from tungsten to LED is that the former lamp emits by far the majority of its light in the infrared which is of no direct use for vision. This is seen clearly in Figure 3 as the red-dashed line which has been matched in brightness to the LED in the green/yellow where human vision is most efficient. Although we are not advocating the widespread return to the old tungsten light bulbs we are saying that the almost complete absence of NIR from the white LEDs appears to be having profoundly negative consequences for the health of the biosphere and, as seems likely, to astronauts on the International Space Station (https://doi.org/10.1016/j.cell.2020.11.002).

3. Bodies as NIR light harvesters

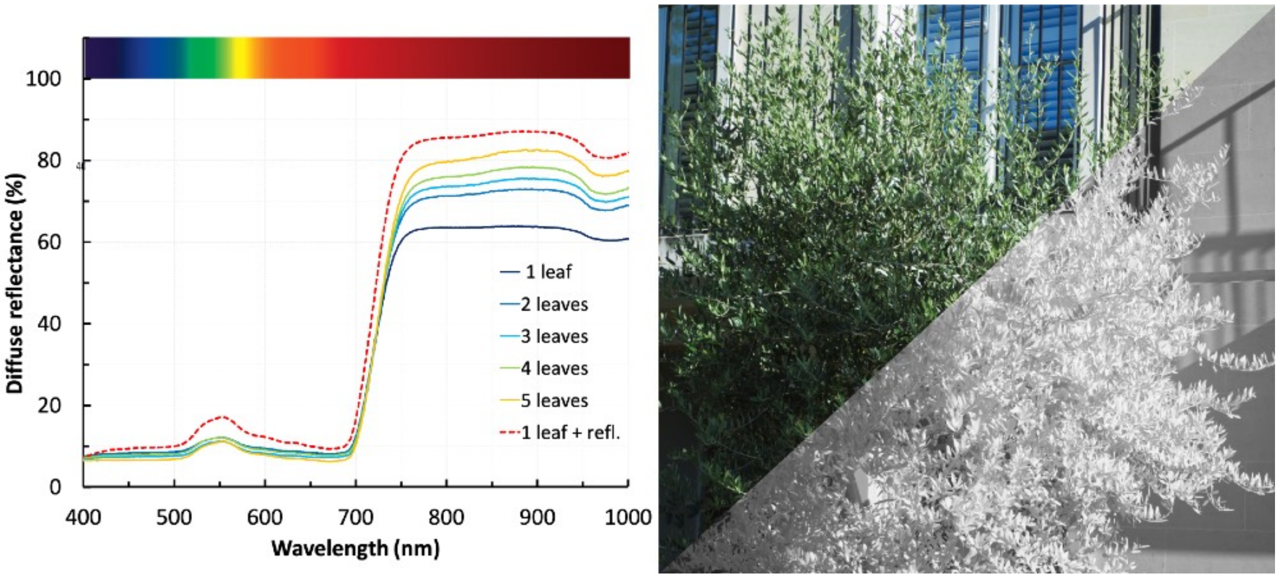

Figure 4. Leaves are not green, they are brilliant red! The plot on the left shows the diffuse reflectance of leaves from an olive tree: they appear a mid-grey-green on their upper surface and a lighter powdery-green on the lower side. The plots show the weak green reflectance at about 550nm with a very steep increase at 700nm to remarkably high values just beyond our visual range. This jump in reflectance is called the 'Chlorophyll Red Edge (CRE)' and it is a powerful spectral bio-marker in searches for life on Earth-like exoplanets. In this experiment, I used a spectrometer with an integrating sphere (see footnote [2]) to measure the diffuse reflectance from a matt surface. The lines from dark blue to orange represent measurements of 1, 2, 3, 4 and 5 leaves stacked over the entrance port of the sphere which shows that a stack of leaves form a quite effective Lambertian (diffuse) reflector between 700 and 900nm. When a single leaf is covered by an almost perfect Lambertian reflector (the material coating the inside of the integrating sphere) the reflectance approaches 90%. This is shown as the dashed red line which can be used to calculate the total absorption of the leaf at each wavelength which is very low in the NIR. The effect of this very high reflectance is shown in the two images of a sunlit olive tree combined in the right panel. The upper left is from a normal colour camera while the bottom right is from a camera that images (in B & W) above 750nm. All leaves demonstrate this effect which results in the high level of NIR illumination in the shadows of a forest understorey.

As we transition from the visible spectrum — where our experience of light interactions has been nurtured — towards the infrared, light in living tissue begins to behave very differently. We change from a situation where the photons are strongly absorbed by pigments to a regime where the photons are much more likely to be scattered than absorbed.

The effect of this change is easiest to see in plant tissue such as in a leaf. We see the leaf as green which is the result of the the absorption of blue and red light by the pigment chlorophyll and other auxiliary pigments, the engine of photosynthesis. This pigment becomes transparent longward of about 730nm and so light enters the leaf without significant absorption, allowing the photons scatter from refractive index changes at cell boundaries and other internal structures until they escape from the leaf surface. This escape benefits the plant as it cannot use the NIR light for photosynthesis and any light absorption in the NIR would simply heat the leaf and cause unnecessary water loss. Such an evolutionary advantage has ensured that leaf scattering at these wavelengths is extremely efficient, resulting the sunlit leaves appearing as bright as fresh snow in NIR photographs of vegetated landscapes. This is illustrated in Figure 4 where the photograph

Figure 5. Images of a hand/wrist with palm up and down taken with a NIR (750 – 1,000nm) camera. The back illumination is from nine 850nm LEDs shining along a 140mm tube capped by an Al foil mask to avoid light leakage around the hand. Note that the veins are seen only where they a close to the upper skin surface, notably on the back of the hand on the right, but also on the wrist of the palm-up hand on the left. The bones are not seen. The tissue and bones act as an efficient light diffuser at this wavelength and the strongest (but still weak) absorber is the de-oxygenated blood in the veins: see Figure 6 where the spectrum is obtained from the region just below the thumb: the thickest part of the hand. These are high dynamic range images from multiple exposures combined with Photomatix Pro software.

shows a sunlit olive tree imaged in visible light (upper left) and in the infrared with a camera and filter that is most sensitive at about 800nm (lower right). The plot on the left shows the diffuse reflectance of these olive tree leaves (measured with a device called an integrating sphere[3]) in the visible and NIR range.

In animal bodies, where tissue depth is generally much greater than the thickness of a plant leaf, the presence of an efficient micro/nano scale scattering matrix containing only weak absorbers allows photons to travel deep into the tissues by scattering many times They do this as a random-

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[3] A device suitable for measuring reflectance of matt surfaces: https://en.wikipedia.org/wiki/Integrating_sphere

walk until they either escape through an external surface or are absorbed. To visualise how this process works, recall walking into the departure lounge of a large airport where you are forced to follow a long, twisting path through a haze of duty-free shops. An early employment of this strategy was in Ikea stores where shoppers are led past almost every department/desk before reaching an exit even though they may be seeking just one.

There are two notable consequences of such a configuration. One is the nature of the random walk where, on average, the result of **n** scatterings will be a displacement from the starting point of √**n** times the mean distance between scatterings: the photon 'mean-free-path' which can be several mm in the NIR. For some photons to reach a depth of 3cm (the thickness of a human hand) this could require just a few 10s of scatterings. The second arises because, by scattering many times, the photons will spend more time within the tissue than they would if they travelled directly through it.

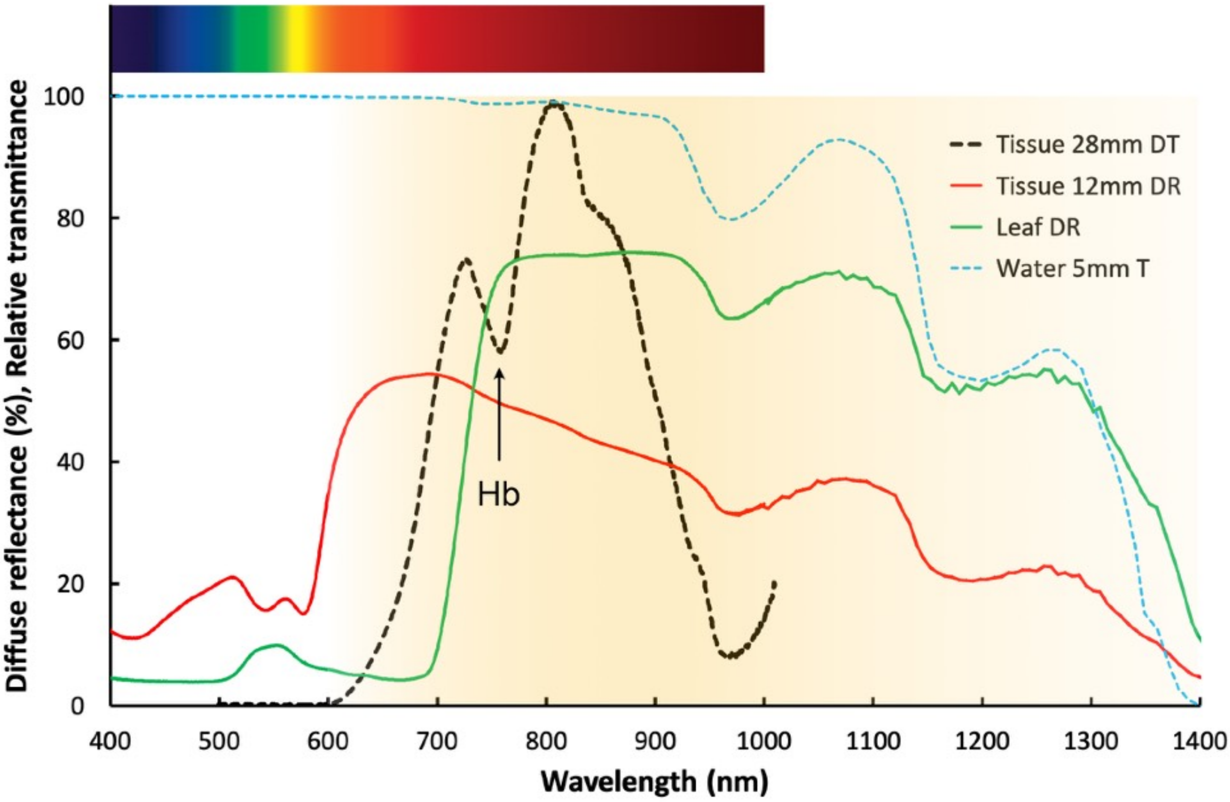

Figure 6. Diffuse reflectance (DR) spectra of plant (green line) and animal (red line) tissue covering the visible and NIR range. The transmission (T) spectrum of 5mm depth of water (blue-dashed line) is shown as a guide to the longer wavelength absorbers. The tissue transparency window (TTW) is shown here as the yellow-shaded region where it is bounded at shorter wavelengths by pigment absorption, notably by chlorophyll and haemoglobin, and at longer wavelengths by the increasing strengths of the vibrational overtone water bands. The black dashed line is a diffuse transmittance (DT) spectrum, normalised to a peak of 100% for clarity, of the thickest part of the hand illustrated in Figure 5 as described in the text. In addition to the absorption band from veinous blood (Hb), there are other absorption features in this spectrum at 675nm (on the steep short wavelength edge) and between 840 and 940nm. Most of the experiments on the effects of NIR light on mitochondrial function have been carried out in the region covered by this black-dashed spectrum.

If the absorbers are sufficiently weak, allowing a large number of scatterings, the NIR photon density within the tissue can build up to a level exceeding that in the incoming light.

The body then contains a photon gas where the individual photons scatter until they either escape from an edge or get absorbed at some distance from their entry point. This is the process that enables NIR light to diffuse into the body and interact with molecules at significant depths. The process is illustrated in Figure 5 which shows a hand illuminated from below by an array of LEDs emitting at 850nm with a bandwidth of 50nm (FWHM). The IR camera is sensitive from 750 – 1000nm. It shows that the human tissue is translucent to a depth of at least 3cm. Note that the bones cannot be seen but the veins are prominent — but relatively weak — absorbers of 750nm light by de-oxygenated haemoglobin (Hb). The scattering in the tissue diffuses the light like a frosted glass screen, and so the veins are only seen when they are close to the skin nearest the camera: on the back of the hand on the right and on the inside of the wrist on the left image. The oxygenated blood in the arteries does not exhibit the absorption at 750nm and so they, unlike the veins, are not prominent in these images. a further discussion of the optical behaviour of the human body can be found in Scott Zimmerman and Russel J. Reiter (2019, "Melatonin and the Optics of the Human Body". Melatonin Res. 2019, Vol 2 (1) 138-160; doi: 10.32794/mr11250016).

In Figure 6 we we illustrate the spectral behaviour of both plant and animal tissue in the transparency window by including diffuse reflectance measurements made in exactly the same way from a leaf and a human hand (green and red lines). Plant leaf reflectance (green) shows the sudden increase in transparency above 700nm called the CRE, and is then most strongly influenced by water absorption further into the infrared. The reflectance of human skin (red) shows the strong visible absorption of haemoglobin between 500 and 600nm and below but rapidly becomes transparent above 600nm which is why you can see red light when shining a flashlight through your fingertip. Similarly to plants, you can see the water absorption increasing into the infrared.

To look in more detail at human tissue transmission we obtained a diffuse transmission spectrum from the hand shown in Figure 5. This was done using a tungsten filament lamp, rather than the 850nm LEDs used for the photograph, to obtain broad spectral coverage in the NIR. The result is shown as the dashed black line in Figure 6. The light transmitted by 28mm of human tissue is strongly attenuated and so this spectrum has been scaled up by normalising its peak to 100% for illustration of its features. This dashed black line contains a record of the absorption of light in typical animal tissue, it is in effect a signature of animal life processes and we can use it to start disentangling the processes by which light might affect life's functions.

An obvious question to ask is: can we benefit from NIR radiation when we are wearing clothes? Figure 7 shows three pictures of a typical set of clothes that might be worn indoors or outdoors: a T-shirt, a shirt and a woollen pullover. These are shown on a hanger on the left in ambient daylight. In the central and the right frames, a lamp containing LEDs emitting red light at

Figure 7. Do you need to remove your clothes to access NIR radiation? A T-shirt, a shirt and a woollen jumper on a hanger. Left: colour image in ambient daylight; Middle: colour image backlit with with an LED lamp emitting red (660nm) and NIR (850nm) light; Right: the same as the middle image but taken with an infrared (750–1000nm) camera. This shows that the clothes (six layers in all) are nearly 100 times more transparent at 850nm than at 660nm. The answer is the NIR light penetrates normal indoor clothing quite effectively.

660nm and NIR light at 850nm is shining on the clothes. The central image is taken with a normal digital colour camera that is insensitive to the NIR, it shows the red (660nm) light that is barely penetrating the six laters of cloth. The right frame is taken with a camera that is sensitive only to NIR light above 750nm and shows the 850nm light penetrating the six layers with ease. Measurements show that the clothes transmit almost one hundred times more light at 850nm in the NIR that they do in the red at 660nm. Remember that, when wearing these clothes, you will only have three layers between your skin and the sky! Unless you are dressed for an outing in the snow and ice, sunlight is likely to give you plenty of NIR light over your entire body even though you clothes will protect you from potentially damaging UV and blue light.

4. Artificial light and public health

Life on earth has evolved in the presence of light from the Sun which shines because its radiating surface is hot, nearly 6,000°K. As we have seen, such a hot body radiates a broad spectrum of light, much of which reaches the ground. It was only in the last century that what we call ‘non-thermal’ artificial light sources were developed in the form of fluorescent tubes and, most recently, white LEDs. These artificial sources are designed to maximise the production of visible light without wasting energy on light that animals cannot see. The dominant metric for these lights is the amount of visible light emitted per unit of input power, measured as lumens/W.

The first white LED was offered for sale in 1996 and, given its very high energy efficiency for visible light, has become ubiquitous over the planet, both indoors and and outside. Since that time we have been unwittingly performing an experiment on the effects of the absence of non-visible radiation on the biosphere. These are especially acute for humans living in a predominantly built environment where many normal lifestyles include little exposure to natural daylight. During the night, it also affects animals (and plants) that are exposed to artificial white light at times where it should be dark.

What are we learning from this experiment? Even before the LED, it was apparent that the use of red and NIR light could have positive therapeutic biological effects in healing wounds and stimulating growth. The question we are addressing is whether non-visible light forms an *essential* role in the processes of life. If so, we might expect that the widespread removal of these regions of the spectrum could begin to reveal effects that were not apparent in the pre-LED era. Two properties of the white LED are particularly relevant here and are apparent in the lower panel of Figure 3: the white LED has a strong blue peak emission at around 450nm and the (thermal) tungsten filament lamp and the Sun emit vastly more infrared light above 750nm. In other words, if the LED and the thermal sources are adjusted to appear similar in brightness in the green/yellow part of the spectrum, the ratio of NIR to blue light it dramatically different in the two types of source.

Some of the results bearing on this experiment are discussed in section 6 below but, before that we introduce the the key players in the energy processing in plant and animals.

5. Chloroplasts and mitochondria

Now we see that NIR light will penetrate into plant tissue and animal bodies we come to the all-important question of how it interacts with biological processes.

In complex life — the life we can see without a microscope — the constituent cells, known as eukaryotes, contain organelles as sub-units that deal with the processing of energy. In plants, the light is captured by organelles called chloroplasts that contain antenna pigments, principally chlorophyll. The photon energy absorbed by these pigments is transferred to two ‘photosystems’ which use (broken) water and carbon dioxide to make sugars (food).

Both animals and plants contain an organelle called a mitochondrion whose job it is to combine the food with oxygen to mint the cellular energy currency called ATP (Adenosine TriPhosphate) which powers everything animals do. This process, called oxygenic respiration, can be seen as a ‘mirror’ of photosynthesis by performing the process of respiration and metabolism of food.

There is now considerable experimental evidence that red and NIR light can penetrate tissue to sufficient depths to reach many mitochondria directly. Current thinking is that the absorbed photons both increase the efficiency of oxygenic respiration, speeding up ATP synthesis, and control the levels of Reactive Oxygen Species (ROS) that the mitochondria generate when they are working hard. These two processes could be considered as lubricating and cooling the mitochondrial engine. It could be seen as a ‘mirror’ of photosynthesis by nurturing the process of respiration and metabolism of food.

It is likely that this close connection between light and mitochondrial function and the efficiency of respiration has been present throughout the history of complex cellular life. The role of both the chloroplast and the mitochondrion developed from the initial ingestion of an aerobic prokaryote which entered an endosymbiotic relationship with the host eukaryotic cell to both protect it from the dangers of oxygen exposure and to utilise it for aerobic respiration. At some stage one of these energy-enabled cells engulfed a photosynthetic prokaryote to become the specialised chloroplast. This resulted in plants that could make food from sunlight and then metabolise the food to grow its structure and animals that could eat the plants to generate enough energy to support their extravagant lifestyles.

6. Experimental evidence for light interactions

In this last section we introduce some of the experimental evidence accruing from the studies of light interacting with animals, including humans. Note that this is written in a compact style and includes relevant literature references[4].

Mitochondria regulate metabolism and the pace of ageing. They are the numerous batteries inside cells and each generates an electrical potential across a membrane used to synthesise energy in the form of ATP. They are highly dynamic and have the ability to divide or fuse in response to metabolic demand. But in age and many diseases, the energy they provide declines and they can then also generate reactive oxygen species (ROS) that drive systemic inflammation. They also have the capacity, when their membrane potential declines significantly, to signal cell death. In essence, this is the mitochondrial theory of ageing first postulated by Harman in 1954 (PMID: 23841595)

Red/NIR radiation penetrating tissue can increase mitochondrial membrane potential and ATP production and also reduce ROS. This is marked in the central nervous system (CNS) in ageing, disease and physical insult (PMID: 30219804; PMID: 28129566; PMID: 27664904; PMID: 24631333; PMID: 22595370) These cellular changes can be linked to significant improvements at the level of the organism. In simpler invertebrate systems, longer red wavelengths (670nm) significantly increase ATP production and lifespan, reducing middle-age death rates (PMID: 25788488). Aged flies show improved cognitive ability following 670nm exposure along with improved retinal function and mobility (PMID: 28917665). When these light exposures are used on bees exposed to insecticides that target mitochondrial function resulting in Parkinson-like paralysis, they provide a high degree of protection, correcting mobility deficits and preventing the death of the animal (PMID: 27846310).

The impact of red/NIR exposure is highly conserved across species and can be found with wavelengths in the range of approximately 650–1000nm (PMID: 23492552). Exposures can be as short as 3 minutes (PMID: 34819619) but efficacy is confined to limited periods of the day as mitochondrial function shifts significantly across 24h (PMID: 31554906;PMID: 35860879; PMID:

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[4] The PMID references can be accessed by pasting the prefix and the number into a search engine.

23492552). Hence, only exposures in the mornings produce improvements. This is when natural ATP production peaks along with blood glucose levels that are critical for mitochondrial function. It is likely that the initiation of these events is linked to dawn and the need for animals to increase metabolism at the start of the day.

Rodents provide a route into a wider range of disease models in which the influence of longer wavelengths can be explored. In ageing, their exposure results in very similar impacts to those of the fly, mitochondrial function and ATP production are improved in retina and brain and this results in improved retinal function (PMID: 28129566; PMID: 25788488; PMID: 24631333). However, the use of a mammal has other advantages. Longer term daily exposure over months has been found to reduce the pace of age-related cell death, consistent with the known role of mitochondria in this process. This is marked in the retina where photoreceptor loss is a key feature of ageing. Daily 670nm exposure over months reduces the pace of photoreceptor loss in mice by >20% (PMID: 31181197). Also, the use of mice allows investigations into wider changes. It had been known that exposure of longer wavelengths to specific tissues results in changes in in organs distant from the exposed region. Hence, exposure to the backs of animals can improve retinal function. Radiologists have known of this effect in cancer treatment for some time, calling it the abscopal effect ('ab' - away from, 'scopus' – target). This is where targeted radiation on a specific tumour results in the shrinkage of a separated secondary tumour that was not targeted (PMID: 37890934; PMID: 37869087; PMID: 37539054). Analysis of blood from mice exposed to 670nm light has revealed significant and complex changes in a wide range of circulating cytokines (PMID: 37478072). These are not only agents in inflammation, but also act a circulating signalling molecules and are a potential mechanism for this effect. It has been argued that in doing this, mitochondria establish and perpetuate a common rate of ageing independent of cell autonomous functions (PMID: 21215371).

Mitochondrial dysfunction results either directly or indirectly in a range of diseases of the CNS. In rodent models of many of these, there is compelling evidence that improving mitochondrial function with longer wavelengths has a positive impact on the diseases process. Consequently, efficacy has been demonstrated in physical brain damage where cell death is present (PMID: 23492552). Also this happens in Parkinson's disease where disease initiation is related to mitochondrial failure in the substantia nigra deep in the brain stem (PMID: 30625333). NIR exposure also reduces chronic inflammation in multiple sclerosis models where it is known that inflammatory cytokines drive disease (PMID: 23840675). In models of macular degeneration, mitochondrial decline has been identified as a key feature from early retinal development and again long wavelength exposure to the adult significantly reduces features of the disease (PMID: 26149919; PMID: 30705315). Rodent models of dementia are more complex as they have to be generated transgenically. However, again there is strong evidence that long wavelength exposure reduces symptoms in these transgenics (PMID: 24387311)

While there have been clear examples of the efficacy of longer wavelengths in rodent models, relatively few translational studies have been undertaken on humans or non-human primates. There are two exceptions to this. Studies on primate models of Parkinson's disease have shown marked improvements in symptoms and detailed analysis of protection at the cellular level (PMID: 28299414. ;PMID: 26456231) However, protective treatment was via light delivered through fibre optics to the substantia nigra . But given the abscopal effect non-invasive treatment in patients may be of value. Results from two small clinical trials are consistent with improvements and others are still running (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8249215/; https://pubmed.ncbi.nlm.nih.gov/34092640/).

The retina is a key target for treatment with red/NIR because it has the greatest metabolic demand and the highest concentration of mitochondria in the body. Primates suffer a >70% decline in ATP with age and humans show a marked aged decline in retinal function (PMID: 31467395; PMID: 34843576). Aspects of this decline in humans are reversed with brief 670nm light exposures. Interestingly there is a differential impact on different cone photoreceptors with larger improvements in those focused on mediating perception of shorter wavelengths (PMID: 34819619). These are known to be relatively frail, suffering more in ageing and metabolic diseases such as diabetes. They also have a smaller mitochondrial population than other cones (PMID: 31199213).

There are also significant improvements in human dark adaptation times that depend on rod photoreceptors. Full dark adaptation takes approximately 35–40 min, but this is extended in ageing. Dark adaptation is highly energy consuming as rods must increase their sensitivity to reduced luminance. These adaptation times are significantly reduced in aged subjects following 670nm exposure (PMID: 32252424).

While there is a developing understanding of the influence of red/NIR on organs and tissues and the potential mechanisms behind this, our grasp requires a greater analysis of how light operates at a systemic level. We know that mitochondria have an ability to communicate across the body and to be transferred between some cells, but not necessarily how they communicate and what are its limits. The impact of light also has wider ranging influences on health via mitochondrial influence. In insects, longer wavelengths improve mitochondrial function which increases their demand for circulating carbohydrates and so reduces their concentration (PMID: 36327250). Given that the mechanisms of light on animals are highly conserved across species, it should not be surprising that a study in progress is showing that the same happens in humans. 670nm light exposure to skin reduces serum blood sugars on a standard glucose tolerance test, and consistent with this there is an elevation in expired CO_2 that comes from increased carbohydrate consumption. The ability of light exposure to influence blood glucose levels could have profound consequences for public health.

Summary

The natural and current artificial light environments differ radically in their colour or spectral balance. As many humans spend increasing fractions of their time in built environments and the outdoors is increasingly artificially illuminated at night. many parts of the Earth's biosphere are now exposed to lighting which is very different from that under which life has evolved. The effects of this situation are most clearly revealed by the reduced performance of the mitochondria that generate cellular energy, especially in ageing life when mitochondria are increasingly frail. Red and near infrared light has the effect of increasing mitochondrial performance while its absence exposes, in addition, the negative effects of blue light. Current experimental evidence suggests some possible mechanisms that may positively drive the light-mitochondrial behaviour in this situation.

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This talk was first given to the Herschel Society in Bath, UK on the 13th October 2023. The video is available at the Bath Royal Literary and Scientific Institution (BRLSI) YouTube channel at:

https://www.youtube.com/watch?v=AST9s42LBg8&t=114s