The Case for Symbiotic Photovoltaic Effects in the Growth of Tetrahedral Oxy-subhydride (TOSH) Structures and their Function in the Biological Exclusion Zones of Anchored Polar Solvents Including Water – Part II

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Received: January 17, 2017; Accepted: August 24, 2017; Published: December 22, 2017;
Available Online: December 22, 2017.

DOI: 10.14294/WATER.2017.5

Abstract

In Part I, five pre-existing sets of empirical data were used to propose the existence of a three dimensional geometry of negatively-charged tetra-oxysubhydride (TOSH) structures within the exclusion zones (EZs) of hydroxyl functional group anchored water, such as melting ice, rabbit muscle protein and polar solvent derived EZs adjacent to Nafion®. In the current paper we propose that TOSH-loaded EZs play a critical role in at least three key significant biological areas: a) guarding complex biomolecules, such as DNA, RNA, cytochrome c oxidase, NADPH and proteins in water, from ultraviolet and oxygen-induced free radical damage; b) regenerating oxidized protein SH functional groups (e.g. membrane proteins); and c) in regenerating glutathione from glutathione disulphide. The absorbance of photonic energy is directly involved in generating and regenerating EZs, TOSH and the copper portions of cytochrome c oxidase. TOSH can prevent premature decay of cytochrome c oxidase which suggests a previously unknown symbiotic relationship between these two systems, given that cytochrome c oxidase deficiencies are implicated in improper glucose metabolism, membrane protein malfunction and the subsequent propagation of dementia including Alzheimer's disease.

Keywords

Alzheimer's disease; cytochrome c oxidase; exclusion zones; EZ; glutathione; glutathione disulphide; infrared; light therapy; mitochondria; NADPH; Nafion®; dementia; polar solvents; protein disulphide; TOSH; trehalose; UV.

Introduction

Gerald Pollack has shown that a layer of negatively-charged water arises on the membranes of cells, distinguished by a higher pH value than what is normally found in interstitial fluids (Oehr and LeMay 2014; Pollack *et al* 2009). This gives

rise to an "exclusion zone" (EZ) water layer which has been observed to grow up to 360 ± 50 µm depending on the nature of nearby molecular anchors and ambient photonic energy inputs (Zheng and Pollack 2003; Zheng *et al* 2006). Surveying terahertz spectroscopy studies by several authors, Cameron and Fullerton maintained that EZs would likely never grow as thick in an in vivo system. They stated the probable thickness of such non-bulk water around biological molecules (e.g. protein) would be between 2-3 nm, which equates to about 7 to 10 layers of water molecules (Cameron and Fullerton 2014). Pokorný *et al.*, based on work of others including (Stebbings and Hunt 1982), describe "empty layers" measuring 5-20 nm around microtubules with the ability to exclude solutes (Pokorný *et al.* 2015). Collectively these studies imply that so-called "non-bulk" water may "jacket" all biologically-active molecules and membranes, including intracellular organelles, mitochondria, DNA and RNA. This jacketing proposition is in principle consistent with a statement made by Tsai and Hamblin (2017), citing Sommer *et al.* (2008), that "Cellular membranes are characterized by the presence of a thin (nanometer) layer of water that builds up on hydrophobic surfaces."

From an evolutionary perspective, this would suggest that the presence of such negatively-charged "water" layers growing on a wide variety of membrane surfaces as a result of photonic inputs conferred a property that likely proved vital to maintaining optimum biological function, otherwise they would have been discarded. In this paper, we explore the merits of this proposition.

Seeking to better understand how EZ water fields responded to various photonic inputs, such as wavelength, power and duration, Chai, Yoo and Pollack (2009) looked at EZ field behavior under three variant conditions: (a) artificial light over a wide range of wavelengths [e.g. from 270 to 4250 nanometers]; (b) light sources at three different power settings [i.e. 0.21, 0.34 and 1.20 mW]; and (c) several different exposure durations [i.e. 5, 10, 30 and 60 minutes] (Chai *et al.*. 2016). The fact the authors found significant EZ field growth ratios within five minutes of photonic exposure suggests organisms even with very limited exposures to light might still be able to grow EZ fields and their associated negatively-charged tetra-oxysubhydride (TOSH) structures.

As to wavelength correlations to EZ field growth, the authors found two specific wavelength regions with comparably elevated growth rates, one within the visible red light (VIS Red) region with a peak growth value at 650 nm, and another between the middle infrared (MIR) and the far infrared (FIR), namely 2600 and 3300 nm, with a peak growth value noted at 3000 nanometers. To see a summary of these results, see Table 1 below. To see the actual data plots from Chai *et al.* (2009), see *Figure 1* in the Appendix of this article.

As summarized in *Table 1*, increases in photonic inputs from different wavelengths

Wavelength Regions Sampled	Wavelengths Measured	Relative EZ Growth Rate	% Increase vs. UV
UV	270 nm	1.4	-
VIS Red	650 nm	2.2	57
Near Infrared	None	No measure taken	n/a
Middle Infrared	1750 to 3000 nm	2.0 to 2.9	43 to 107
Far Infrared	3000 to 4250 nm	1.9 to 2.9	43 to 107

Table 1: *Relative effect of light wavelength on Exclusion Zone (EZ) growth in water.*

have been shown to cause different rates of growth in EZ fields, growth we believe is tightly associated with related TOSH layer growth, which has yet to be quantified. In the case of 270 nm UV light where no net growth rate was observed, we attribute the lower relative growth rate as compared to VIS Red and Far Infrared light (FIR) to a continuous rupturing of TOSH structures on more exposed surface layers as compared to interior layer TOSH growth that would be better shielded from UV. No such TOSH structure rupturing appears to occur under VIS Red, Middle Infrared (MIR) or Far Infrared (FIR) light (Oehr and LeMay 2014; Chai *et al.* 2009). To gain a clearer perspective on where these respective wavelengths fall within the light spectrum, see *Figure 2* (source: Barolet *et al.* 2016.)

Depending on the wavelength of light involved, most drops in ambient photonic inputs generally result in concomitant drop in the charge divergent EZ fields fed by the absorption of this light. Yet this drop can hardly be described as an instantaneous phenomenon. For example, Chai *et al's* found that EZ fields remained roughly constant for about 30 minutes before they began to decrease, reaching halfway to baseline levels in about 15 minutes, and this after water had only undergone five minutes of exposure to at 1750, 2000 and 3100 nanometer infrared light (Chai *et al.* 2009, page 5). If nothing else, the foregoing suggests that both EZ fields and their associated negatively charged TOSH structures have the ability to store absorbed photon energy at least six times longer than what it took to create them.

As depicted in *Table 1*, Chai *et al.* (2009) did not examine growth behavior caused by photonic inputs between 650 nm and 1750 nm, inputs which correspond to the lower VIS Red region, all of NIR (IRA) region, and a portion of MIR (IRB) region up to 1750 nm. Although such an examination might have revealed additional peaks and valleys, interestingly, other investigators have since shown these wavelength regions to have significant biological effects, such as improving the repair of injuries to the optic nerve, the remediation of retinal neuron degeneration, traumatic brain and spinal cord injury in an *in vivo* rat model (Barolet *et al.,* 2015; Tsai and Hamblin (2017); and Beirne *et al.* IN PRESS citing Giacci *et al.* 2014).

Nonetheless, some sense of what might be transpiring within this missing NIR/MIR wavelength region can be seen in *Figure 3*. It looks at the relationship between solar photon energy irradiance and water's absorption coefficient (source: Tsai and Hamblin, 2017). Interestingly, the authors make the point that the most significant harmon-

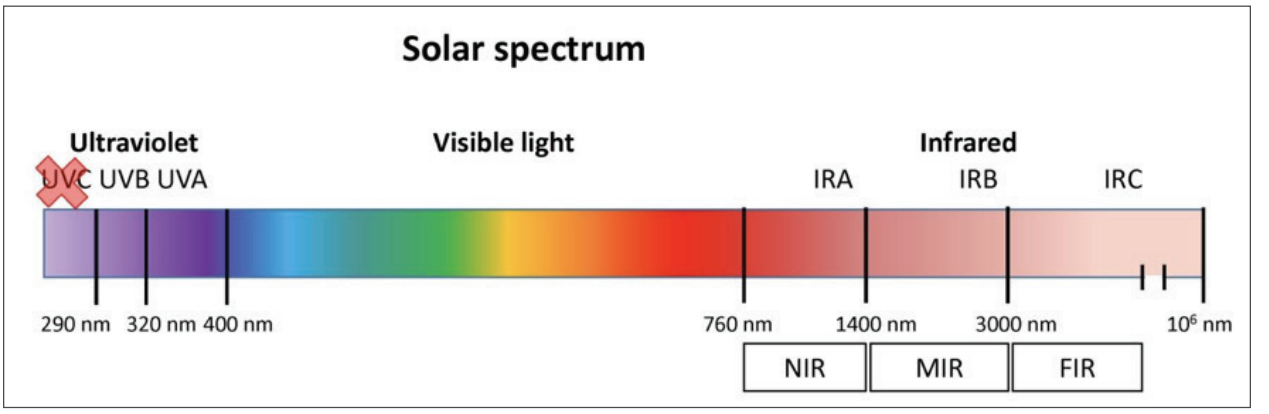


Figure 2: *Solar spectrum composition. (Red X over UVC is blocked by Earth's ozone layer. Near Infrared = NIR = IRA; Middle Infrared = MIR = IRB; Far Infrared = FIR = IRC.). [source: Barolet, Christiaens and Hamblin (2015) p. 79]*

ic resonance between the two information plots transpires between 900 and 1100 nm, while conventional water's greatest numerical photon energy absorption effects occur in the Infrared (IR) region beyond 1100 nm, although higher absorption rates might well transpire for wavelengths beyond 2300 nm, as shown here, given what Chai *et al.* (2009) found in relation to EZ field growth rates.

Although the data presented in *Figure 3* does not directly measure either EZ field or TOSH growth as such, water's increasing photon absorption efficiency as wavelengths increase appear to nonetheless mirror experimental results by Chai *et al.* (2009) in relation to EZs and their elevated growth rates, especially between 2500 and 3500 nm, wavelengths not covered in this graph. This trend is actually opposite to what the law of physics and the law of thermodynamics would normally dictate. In theory, shorter wavelengths should translate into more energy delivered in a shorter time span. But that's not what we observe when it comes to either water or TOSH. This has one especially important implication for biologically active systems relying on light to build up the antioxidant potentials offered by TOSH. It implies that creatures unable to get higher frequency shorter wavelength photons from direct sunlight under rainforest canopies, such as our own early ape ancestors, would still benefit from TOSH growth through other indirect forms of exposure to unseen photons found in longer wavelengths beyond the optical range. Such photons would be able to energetically load the ambient humid air and penetrate the dapple and shadows caused by overhanging leaves and branches.

We find it interesting this also happens to echo part of the wavelength region to which Tsai and Hamblin drew attention in Figure 3, particularly between 800 and 1300 nm, though in our view the NIR region cited appears to be somewhat closer to 900 and 1100 nm. In either case, the authors found a number of bio-molecular effects associated within this photon wavelength range. One such pertained to neural regeneration which has implications in treating Alzheimer's disease. Just two of the bio-molecules whose photon absorption profiles fall within this "sweet zone" are amyloid-β plaque proteins, which are associated with Alzheimer's disease, and the cytochrome c oxidase (CCO) protein complex, which has been implicated in reduced mitochondrial function. It too has been implicated in a

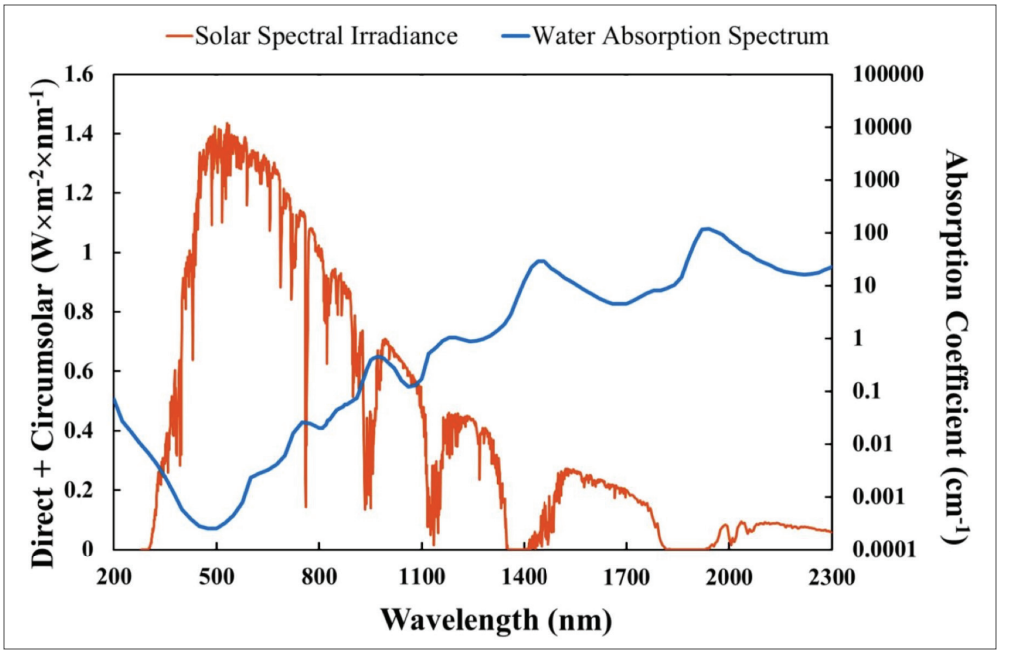


Figure 3: *Superposition of spectra of solar irradiance and water absorption. [source: Tsai and Hamblin (2017) p. 198].*

number of degenerative conditions such as Parkinson's and Alzheimer's diseases. For example, citing the work of De Taboada *et al.* (2011), Tsai and Hamblin specifically noted how pulsed doses of coherent 808 nm NIR laser light three times per week significantly reduced the numbers of amyloid-β plaque proteins in the brain, as well as the levels of this peptide in plasma and cerebrospinal fluid in a mouse model. While still citing this and another study (Wang *et al.* 2016), another wavelength, namely 810 nm NIR, was also found to induce ATP generation which is said to enhance neuronal preservation and inhibit amyloid plaque formation (Tsai and Hamblin 2017, page 203). When it came to CCO, the second study found that CCO better absorbed 810 nm light than 980 nm light by a factor of 10-100 times, a finding attributed to several of CCO's underlying light-absorbing chromophore molecules with two copper centers Cu_A and Cu_B, and two heme (iron) centers. Interestingly, in both of the specific photon absorption instances studied, it was noted that "water" also absorbed these wavelengths at low levels, suggesting that TOSH could indeed be playing a symbiotic support role in this regard. We shall explore this matter in greater detail in the next sub-section.

Despite the absence of any direct observations actually confirming the growth of EZs or TOSH under NIR (IRA) or some MIR (IRB) photon exposure, or their possible role in any of the biological effects noted above, both factors nonetheless raise the possibility that EZ fields and their associated TOSH structures could still be playing some role, however minor, in the noted biological effects. As we shall endeavor to show, we hypothesize this is in fact the case. Moreover, the current scarcity of evidence in this area also raises the possibility that some, if not most investigators examining the effects of VIS Red and various Infrared light regions on biological systems are largely unaware of TOSH, let alone EZs, and what roles they might be playing in this regard. Tsai and Hamblin appear to be among the few exceptions. Despite focusing on the effects of NIR light on biology, and the possible medical applications of such, they nonetheless recognized that EZ water was able to store electrical charges, and that said "water" was able to release up to 70% of its input energy (page 203). Interestingly, H_2O on its own is *not* a good electrical conductor, and this includes water with a relatively homogeneous mix of cations and anions (See *Web Ref. 2*, USGS). However "water" found in the interstitial fluids in our own bodies is another story. It contains various dissolved minerals (e.g. sodium, potassium, magnesium and calcium) which in their ionic, and hence electrolytic form, make interstitial fluids more than a reasonable conductor. Yet without intervening membranes to help concentrate ionic distributions to create an appreciable charge differential, it seems doubtful these fluids could on their own suddenly release up to 70% of their input energy. [For example, because there is 10,000 times more Ca^{2+} outside the average cell than inside (Seelig & Rosanoff, 2003), this helps to make its interior more electrically negative than its exterior; but during various cellular functions, calcium levels inside the cell will rise 10 to 100 fold (Ivannikov & Macleod, 2013).] On the other hand, negatively-charged TOSH structures appear to be one of the few alternative explanations that can account for a potential 70% release of stored (and presumably photonic input) energy.

Such a view would make abundant evolutionary sense. Given infrared light's general availability in the natural environment [up to 54.3% of the sun's light arrives in the form of NIR, of which 40% reaches the ground at sea level while some 14.3% of it is absorbed by water vapor in the atmosphere (Barolet *et al.* 2015)]; it seems probable that EZs and their associated TOSH structures might also be symbiotically implicated in supporting these and/or other

remedial downstream effects in living systems. However, despite Barolet *et al.*'s general assertion that very little NIR is needed to bring about remedial effects [at least in relation to promoting skin health (see page 79)], and Fitzgerald *et al.*'s (2013) claim that NIR should be able to penetrate even deep into the center of the human brain through ~7 mm of the skull and 3 mm of covering skin (page 7), serious questions have been raised by Henderson and Morries (2015) [citing their own and others' work] that NIR's ability to penetrate anything much beyond 3 mm of skin. Might this suggest NIR photons are possibly using other routes into the inner reaches of the body, such as the brain? One such route might be through respiration, given that many IR photons are absorbed by water vapor, as well as common atmospheric gases which we take in during respiration, such as oxygen and nitrogen. We hypothesize that such photonic energy could in turn be absorbed by our blood (and more specifically by the numerous π electron wave functions within hemoglobin porphyrin). This would allow inhaled photons to be distributed with ease into the deepest recesses of our bodies. Consistent with this view, Zelano *et al.* (2016) found that nasal respiration enhances fear discrimination and memory retrieval while breathing through the mouth does not. This suggests that the nasal cavity contains receptors capable of absorbing photon-charged water vapor and gases directly into tissues and the blood stream. Such a photon absorption process could, in theory at least, also make use of a quantum mechanical transfer process known as quantum tunneling to reach the inner recesses of the brain.

Bio-Anchored TOSH Structures Within EZs

At minimum, the formation of TOSH structures out of conventional bulk water requires two things: (1) molecular seed anchors; and (2) the absorption of photonic energy. We begin with the first of these. TOSH structures are able to anchor their growth off molecules such as: (a) amino or amide functional groups in protein; (b) hydroxyl; (c) the hydroxyl functional groups in the sugar phosphate portions of DNA or RNA; (d) ice in partially melted ice; and (e) sulphonic acid groups in Nafion®. As mentioned above, cell membrane proteins *in vitro* anchor the formation of water derived EZs (Zheng J and Pollack GH 2003; Zheng J *et al* 2006), rabbit muscle being a case in point. It is composed of the amino acid hydroxyl functional groups threonine, tyrosine, serine, aspartic acid and glutamic acid plus N, NH or NH_2 functional groups in arginine, histidine, lysine and proline, which account for ~35% and ~25% of typical rabbit protein weight respectively (Bivolarski *et al* 2011).

Cell membranes coated with TOSH structures should benefit from the antioxidant property these structures provide, especially in terms of preventing free radical damage (e.g. peroxidation) of unsaturated lipid bonds in cell membranes and unbridged SH functional groups in protein amino acids. These include cysteine and methionine as well as peptides such as glutathione, whose depletion has been associated with a variety of neurodegenerative diseases (Aoyama and Nakaki, 2013).

Our antioxidant proposition is based on the fact that exclusion zones (EZs) in water contain negatively-charged $(OH^-)(H_2O)_4$ structures with a tetrahedral $(OH^-)(H_2O)_3$ core and an H_4O^- sub-core (i.e. TOSH structures), and non-water polar solvent derived EZs possess analogous H_4O^- sub-cores as described by us in Part One of Oehr and LeMay (2014). Moreover, the fact that water-derived EZs *in vitro* have been seen on rabbit muscle (Zheng J and Pollack GH, 2003; and Zheng J *et al.* 2006) suggests that TOSH structures not only grow adjacent to protein structures *in vivo*, but in doing, provide an antioxidant benefit to

all hydrated biologically-active membranes more generally (Oehr and LeMay 2014, page 16). As such, we now explore the role TOSH water layers and polyol-derived EZs might be playing *in vivo* adjacent to protein and DNA anchors (e.g. deoxyribose hydroxyl anchors).

Given that TOSH-coated biological structures should possess a distinct survival advantage over biological structures lacking such a protective coating, it is easy to see why natural selection would conserve such a symbiotic relationship over time. Indeed, the fact that increasing the relative humidity of bacteria has been shown to reduce their susceptibility to UV damage appears to support this view because conventional water is largely transparent to UV light, as *Figure 4* illustrates.

It shows a typical light absorption spectrum for conventional non-EZ water [Image by Kebes. See: *Web Ref. 1*]. Note the extremely low UV absorption at 270 nm as compared to NIR light absorption. (We discuss the wider biological significance of Near Infrared light in the next sub-section of this paper.)

The fact that microscopic-sized water droplets on their own coating bacteria would simply be incapable of providing this kind of protection, while TOSH structures can, as implied earlier in *Table 1*, means that TOSH and not conventional water, is likely involved. Increasing relative humidity simply increases the feedstock for TOSH formation.

No less would be true for the jacketing of proteins DNA and RNA by TOSH/EZ, which likely occurs via hydrogen bonding to sugar-phosphates, N, NH or NH_2 or hydroxy functional groups (e.g. hydroxyl functional groups of deoxyribose in DNA, ribose in RNA, NH or OH functional groups in proteins).

Complex System Dynamics between Photons, TOSH, DNA, Glutathione and Cytochrome c Oxidase

Since the total number of possible photo-electrochemical interactions between TOSH structures and every possible biomolecule (e.g. antioxidants including vitamins) would represent an undertaking that would far exceed the scope of this paper, we have chosen to limit most of our TOSH analysis to DNA, proteins, mitochondria, cytochrome c oxidase, glutathione, NADPH and melatonin.

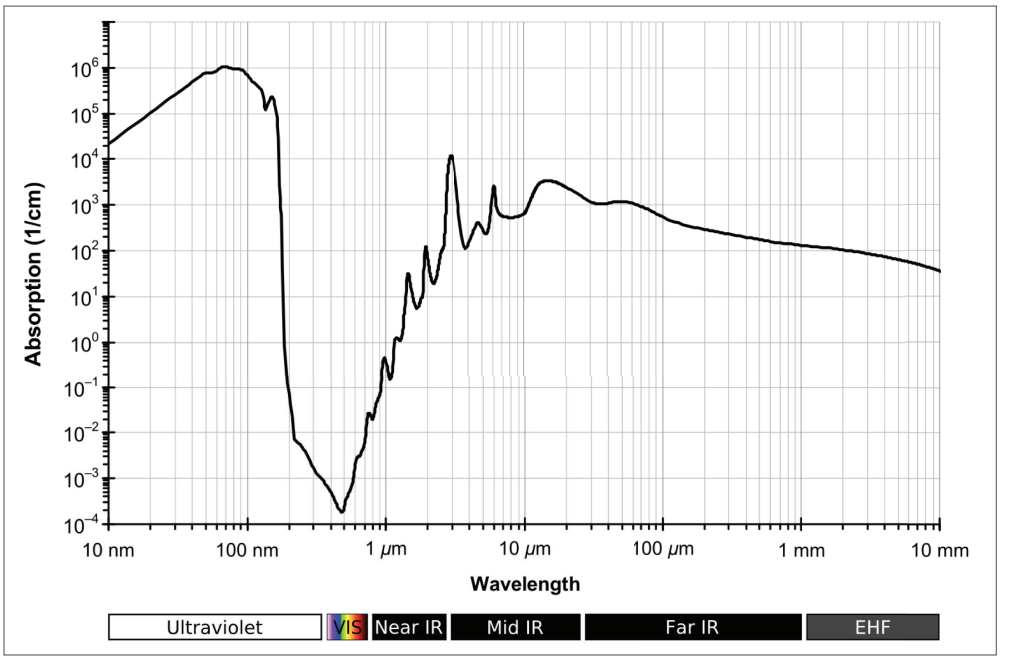


Figure 4: *Light absorption spectrum for non-EZ water.*

We begin this deeper analysis with a review of data from pre-existing DNA research in its interactions with "water." Citing others' work, Berashevich and Chakraborty (2008) stated that "DNA conductivity can increase exponentially by up to 10^6 times with rising humidity." They assert that the "interaction of the nucleobases with water molecules leads to the breaking of some of the π bonds and the appearance of unbound π electrons. These unbound electrons contribute significantly to the charge transfer at room temperature by up to 10^3 times."

Question is: What accounts for this improved conductivity? There are few apparent alternatives. Either the noted effects are the result of DNA nucleobases "downloading" electrical charge into interfacial water from ambient interstitial sources so as to create an EZ field and associated TOSH structures, or the effects are the result of a pre-existing TOSH coating that possibly grew as the result of photonic inputs in order to boost DNA conductivity. Or could there possibly be some sort of symbiotic interplay between the two? Perhaps. But to get at those answers, a number of issues must also be addressed. First off, other than skin surfaces including our eyes, is it even reasonable to assume that sufficient photonic energy is able to reach the remaining interiors of the overall estimated 37.5 trillion cells of our bodies (Eveleth, 2013), to say nothing of the 75 trillion+ DNA molecules, or the estimated 1-2 quadrillion mitochondrial DNA molecules in our bodies (Alberts *et al.* 1994) in order for TOSH layers to grow? Though we address this specific question in greater detail later in the paper, since there are reasonable scientific arguments both for and against deep tissue absorption of photons, especially longer IR wavelength photons, the best short answer we can offer at this point is to simply say maybe. Second, in the possible absence of ambient photonic energy within the inner recesses of our bodies, can TOSH structures grow off electronic rather than photonic inputs from other sources, such as negatively charged DNA bases? While this too could be possible, to our knowledge there is as yet no direct scientific evidence that can confirm this is the case. And third, what role could conventional bulk water play in regard to improved conductivity? We tackle this question first.

To be sure, the absence of water around DNA does give rise to its own set of problems. For example, decreases in DNA and RNA humidity have been found to cause significant twist angle changes to their respective ribose strand structures (Khesbak 2011; Berashevich and Chakraborty 2008; Falk 1965). In this regard Falk stated that: "At relative humidities below about 65%, DNA undergoes a transition to a disordered form." Yet, while proper DNA twist angles may help to partially account for increases or decreases in electrical resistance, the proposition that conventional water alone is responsible for improved conductivity still encounters difficulty when one considers the following. Multiple investigators have discussed how the decrease of "water" in a bio-molecular environment also increases the formation of reactive oxygen species (ROS) resulting in lipid peroxidation, denaturation of proteins and *nucleic acid damage* [italics ours] with severe consequences on overall metabolism (Morel and Barouki 1999; França *et al.* 2007; Grune *et al.* 2013). But then why should a relative decline of contiguous "water" actually generate any ROS be at all? We are of the view that such an increase in ROS is consistent with a decline in the number of TOSH layers and their associated antioxidant potentials, as was discussed in our first paper on TOSH. This better explains this phenomenon than can the relative presence of conventional water.

We attribute the growth of EZ fields in relation to the absorption of photonic inputs to a process known as photovoltaic charge divergence as evidenced by the experimental

observations noted by Chai *et al.* (2009). As water molecules absorb photonic energy, this gives rise to a dipole condition of negatively-charged TOSH "cathode" structures growing off of pre-existing seed anchors coupled with the creation of a positively-charged proton "anode" (ionic) field component at the other end of the EZ field. [While this very process was described by Pollack, Figueroa and Zhao in a paper published in 2009, they did not specifically make use of the photovoltaic term.]

Interestingly, the photovoltaic process echoes one described in Quantum Electro-Dynamics (QED) in relation to vacuum polarization, where the widely purported non-charged or net zero charged photon (a member of the boson family of wave/particles) suddenly transforms/splits into an electrically charged "virtual" electron-positron pair within the Fermion family of particles. The key behavioral difference between these two particle families is that Fermions tend to stay apart from one other, whereas bosons tend to congregate within a smaller space (von Bayer, 1988; Pauli, 1946). [The boson/Fermion distinction provides an alternative explanation to one posited by physicist Richard Feynman in relation to the counter-intuitive phenomenon known as like-likes-like, as was noted in water experiments with light by Pollack *et al.,* (2009).] What this suggests is that the underlying processes involved in the water-photon absorption photovoltaic charge divergence process is perhaps more complex than we currently imagine.

In any event, the net result of this charge divergent process is that TOSH structures effectively become rechargeable solar-powered water batteries, albeit batteries operating at the nanometer scale. When this process is examined at the picometer scale where sub-atomic electrons display various "orbital" states within various compounds, these orbital states provide at least one mechanism where the aforementioned virtual electrons can store their energy in an indeterminate state that can oscillate between classical and quantum mechanical particle-wave duality conditions, presenting conventional electro-chemical practices with a number of generally unanticipated possibilities, especially in the biological realm, where quantum effects such as superposition and non-locality were once thought non-existent. [Research showing that photosynthesis is a quantum process has effectively put a scientific end to this view (Freiberger, 2012; Collini *et al.* 2010).]

What all of the foregoing implies for biology is that while some electrons will display discrete particle-like behavior, others will display wave-like behavior. We are of the view that the former are associated with maintaining a molecule's physical structure, while the latter are more apt to be involved in sub-cellular electrical charge shunting and possibly sub-cellular structure communication as well. We also conjecture that wave state electrons are essentially synonymous with free mobility state electrons. These are also found in aromatic ring molecules where they are more generally called π electrons or p_z electrons, since they are deemed to have the ability to delocalize as a charge cloud sitting above and below the ring molecule's x-y plane as suggested in *Figure 5*.

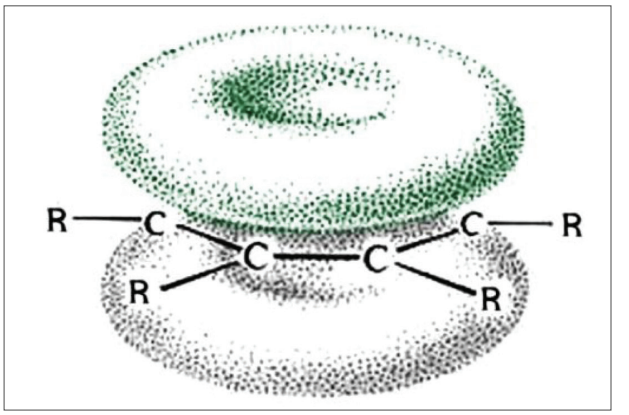


Figure 5: *Oblique view of two Z-axis delocalized electron tori clouds above and below the x-y plane of an aromatic ring molecule.*

These kinds of aromatic ring molecules are found in the four DNA bases and in at least five amino acids, namely tryptophan, histidine, tyrosine, phenylalanine and proline. This suggests that at the picometer scale, charge behavior within a molecule can become dispersed over a wider multi-molecule area. This in effect is what likely allows their associated electrical charges to be "mobile" or untethered to any immobile molecular skeletal structure and to quantumly migrate from one molecule to another.

Thus in view of the foregoing, when we turn our attention back to an increase in "DNA conductivity" in association with an increase of humidity and in the breaking of "π bonds," we can readily see how the absorption of ambient photonic energy by contiguous TOSH layers jacketing the body of DNA might come into play. While TOSH structures do not exhibit aromatic rings, the hydrogen s orbital components within the TOSH structure carry within them the potential to donate 1 mobile delocalized π electron per TOSH structure. So while Berashevich and Chakraborty (2008) were aware of the fact that an interaction between nucleobases and water lead to the breaking of some of the π bonds and the appearance of unbound π electrons, and that these unbound electrons contributed significantly to the charge transfer at room temperature by up to 10^3 times, at the time of the writing of their paper, the existence of TOSH structures was unknown to them.

This is not to imply that the energy required by DNA to accomplish π bond breakage might not have any other energy contribution mechanism available to it. One such mechanism is direct photonic absorption by DNA's base pairs and/or DNA's ribose strands, via a process known as "plasmonics" [*Web Ref. 3*]. Since the field of plasmonics represents a highly technical field of quantum study, an area beyond the scope of this paper, we shall only make minimal reference to what some of its principles imply here. Akin to the photovoltaic process, the plasmonic process converts absorbed photonic energy into an electrical current, however, it does so under very limited conditions, namely those involving a two-dimensional or "flat" carbon ring molecule, as found in graphene. This is required for photon "capture" and subsequent charge separation. As it turns out, DNA bases actually meet these special conditions. Yet while the foregoing plasmonic process is certainly a plausible contender in explaining π bond breakage, Berashevich and Chakraborty's paper only noted π bond breaks occurring in association with what they viewed as "water." In other words, moisture was specifically a part of their experimental considerations. Moreover, the plasmonic process would continue to work in the presence of photons whether or not water was present.

Since conventional water alone cannot account for the 10^3 increase in charge transfer to, from or within DNA suggests that more than proximal "water" was likely involved. Of course the fact that any ambient water molecules having surface contact with a protein membrane or sugar (i.e. the ribose backbone in this case) could serve as a molecular anchor to TOSH growth, provides a necessary condition for TOSH's "untethered" mobile π electrons. So while both the photovoltaic and plasmonic processes are able to convert net zero-charged photons into charge-divergent electrical current, in this specific case, it seems more likely that the breaking of π bonds is the result of ambient photon absorption by proximal intracellular water, and/or is possibly the result of ambient mobile electrons flowing out of DNA itself into inter-facial TOSH structures already coating DNA. In either absorption case, TOSH structures are likely involved.

Again, from an evolutionary perspective, this makes eminent sense. Over the course of billions of years, many bio-molecules "on evolutionary trial" would at some point or

another have had to contend with exposure to solar radiation ranging from the far infrared to the ultraviolet. Among these was certainly DNA. Thus DNA's evolution would have been repeatedly assaulted and tempered by the presence of light. Indeed, today's DNA and its maximum absorption spectra between 260 to 265 nm which falls within the UV region, may well be a by-product of this evolutionary history. According to Beggs, "The biological impact of UV radiation is primarily due to the absorption of photons by nucleic acids." (Beggs 2006).

Because water was also very much a part of the evolutionary equation here on Earth, the course of DNA's adaptations would also come to reflect water's mediating effects. With this in mind, we were interested to learn that dry DNA apparently absorbs UV at the slightly longer, if not slightly "safer" wavelength of 270 nm (Omerzu *et al* 2007). Yet as we've seen, dry DNA comes with a number of significant downsides, one being twist angle deformation and a significant decrease in its electrical conductivity (Khesbak 2011; Berashevich and Chakraborty 2008; Falk 1965). Remarkably, 270 nm also happens to be the maximum absorbance wavelength of EZs (Omerzu *et al* 2007). While 270 nm light doesn't represent the optimal wavelength for either EZ field or TOSH growth, as *Table 1* illustrates, what it does suggest is that TOSH structures can in some instances shield DNA from the potential deleterious impacts of 270 nm UV light.

To this point, we have devoted much of our attention to the role photon absorption plays in the growth of TOSH and how it might impact DNA function without mentioning another important element in this overall complex system equation, the sun. Given that the sun is the source of a wide wavelength range of the ambient photons to have impacted life throughout the course of evolution, it is to this part of the story that we now turn our attention.

The general proposition that other critical bio-molecules also made use of energy from photonic inputs has become evident in our review of research by other authors. As we discussed earlier, cytochrome c oxidase is one such critical bio-molecule, one necessary for glucose metabolism in mitochondria. Another is glutathione. As we came to learn in our review, VIS Red and NIR wavelengths of 655 nm and 835 nm have been shown to help regenerate cytochrome c oxidase and both wavelengths are necessary in mitochondrial glucose metabolism (Mason et al 2009, 2014). Sunlight is the only commonly and readily available source of high amplitude VIS Red or NIR light (e.g. 620 to 1400 nm) as shown in *Figure 3*, the highest NIR (IRA) irradiance amplitude is 35 mW cm^{-2} with a mean of 20 mW cm^{-2} (Barolet *et al.* 2015, Figure 7: p. 83). Here the implications are wider than TOSH regeneration alone. They extend to a variety of other key antioxidant bio-molecules and hence to human health more generally. Indeed, because NIR light deprivation appears to be associated with the incidence rate of dementia, we consider the relationship of infrared light to two such bio-molecules and their relationship with TOSH next.

In recent years, a number of authors have begun to document the effects and in some instances, the health benefits associated with exposure to VIS Red, NIR, MIR and FIR, and the reasons are fairly straightforward: As compared to UV radiation, which tends to ionize matter and damage tissue because of its high-energy photons, VIS Red and IR wavelengths do not.

Generally speaking, and as alluded to earlier, VIS Red and NIR wavelengths have been shown to: (a) bestow remedial effects in living systems impacted by oxidative stress; (b) ameliorate some aspects of coronary/artery disease; and (c) restore a significant measure of function in people suffering from Alzheimer's disease and Parkinson's disease (Sutkowsky *et al.* 2014; Enwemaka

2004; Quirk *et al.* 2012; Darlot *et al.* 2016; Beirne *et al.* IN PRESS citing others).

For example, and further to sub-paragraph (c) above, Darlot *et al.* 2016 tested 670 nm VIS Red light delivered via optical fibre to the midbrain of a macaque over a period of 5-7 days in a neurotoxin-induced monkey model of Parkinson's Disease. Reporting on Darlot *et al.*'s findings, Beirne *et al.* stated there was "a reduction in clinically-assessed behavioural impairment… as well as neuroprotection to the dopaminergic neurons of the substantia nigra… [with] no major adverse effects… observed following surgical implantation of the optical fibre."

Beirne *et al.* (IN PRESS) also assert the potential benefits of using VIS Red and NIR in the treatment of age-related macular degeneration (AMD) and retinal degeneration. Yet scientific opinion about how this comes about varies. Beirne *et al.* posit a number of reasonable possibilities, such as improvements to neuronal mitochondrial function, increased blood flow to neural tissue [presumably via glial cells], upregulation of cell survival mediators, and the restoration of normal microglial function. However, because all of the foregoing explanations tend to focus on meso-scale levels of explication and analysis, the potential role of EZs or nanostructured forms of water (and thus TOSH) being in the mix are seldom, if ever mentioned in these aforementioned studies. Among the exceptions are Tsai & Hamblin, 2017; and Passarella & Karu, 2014; hence our case for TOSH in this instance.

In this regard, it is our contention that the near ubiquitous presence of TOSH coatings on most if not virtually all of the biomolecules that the authors we reviewed discussed, suggests some measure of TOSH involvement. Here we are specifically referring to TOSH's ability to either spare critical antioxidants such as glutathione, cytochrome c oxidase, melatonin, and nicotinamide adenine dinucleotide (NADPH), or its ability to directly quench reactive oxygen species (ROS) or reactive nitrogen species (RNS) produced during normal metabolic processes; or its ability to actually regenerate glutathione. We consider TOSH's electrochemical properties in relation to free radicals and antioxidants next.

Glutathione (GSH) is a potent antioxidant also involved in cell signaling, protein function, gene expression, as well as cell proliferation and differentiation in the brain. Mitochondria contain a distinct pool of GSH but do not possess the enzymes necessary for its biosynthesis (Cooper 1998). Yet GSH is considered to be the most important, if not prevalent intracellular non-protein thiol/sulfhydryl compound in mammalian cells (Bains and Shaw 1998). A key role for GSH is as a free radical scavenger against the hydroxyl radical. This role is crucial, as there are no known enzymatic defenses against hydroxyl radicals (Aoyama and Nakaki, 2013, page 21026).

Nowhere is its role likely more important than in Alzheimer's Disease. While the network of causal factors behind this form of dementia is still the subject of great debate in the scientific community, one of the more promising explanatory candidates is the mitochondrial dysfunction hypothesis (Johnstone *et al.*, 2016, citing several authors). It proposes "that mitochondrial dysfunction is a major contributor to… neuronal death. [If] …the organelles responsible for fueling cell function [become damaged, their ability to provide] ATP (adenosine triphosphate)… would be reduced… [thereby leading] to an increase in toxic reactive oxygen species, generating oxidative stress and subsequent neuronal death, as observed in Alzheimer's disease." Because the availability of glutathione (GSH) within mitochondria is now considered key to providing protection against the oxidative and neurotoxic effects oligomeric amyloid beta (Aβ) plaques (Mandal *et al.* 2016), what role can TOSH structures play in this regard?

Because the inner mitochondrial membrane has a protein/lipid ratio similar to rabbit muscle [*Web Ref. 5*], (Pla *et al* 2004), it should therefore have the ability to not only grow TOSH structures, but to benefit from their anti-oxidant protective coating as well. This speculation stands up to the following electrochemical analysis. Typically, the outer portion of the inner mitochondrial membrane has a pH of 6.88±0.09 (Porcelli *et al* 2005). Restoration of GSH from GSSG (oxidized glutathione) at a mitochondrial membrane can be estimated from the following Schafer and Buettner equation, where E_o = +180 mV and concentrations in square brackets expressed as molarities are typically 0.0083 and 0.00047 for GSH and GSSG respectively in intracellular fluid (Wahllander et al 1979; Schafer and Buettner 2001):

$$E_{pH6.8\ mV} = -59.1/2*LOG([GSH]^2/([GSSG][H^+]^2) +180\ mV \quad (1)$$

$$E_{pH6.8\ mV} = -59.1/2*LOG([0.0083]^2/([0.00047][1.32E\text{-}07]^2) +180\ mV \quad (2)$$

$$E_{pH6.8\ mV} = -202\ mV \quad (3)$$

The electrical potential for H_4O^- contained in $OH^-(HOH)_4$ in a water exclusion zone was suggested as -208±11 mV which matches experimental data (Oehr KH and LeMay P 2014). This potential is sufficient to regenerate GSH from GSSG non-enzymatically at the surface of a mitochondrial inner membrane as follows:

$$OH^-(HOH)_4 + H^+ + GSSG = GS\text{-}OH(HOH)_4 + GSH \quad (4)$$

or

$$H_4O^- + GSSG + H^+ = GS(H_4O) + GSH \quad (5)$$

Infrared light has also been shown to interact with mitochondrial inner membranes. It is documented that infrared light at 730 to 850 nm, and especially 830 nm, stimulates the regeneration of a “first copper portion” of mitochondrial inner membrane cytochrome c oxidase (“CSR1”), which has a potential of -225 mV (Tsudzuki and Wilson 1971). Red light at 655 nm interacts with a “second copper portion” of cytochrome c oxidase (“CSR2”) at a potential of -218±5 mV (Mason *et al* 2009). These potentials are sufficient to regenerate GSH from GSSG, or TOSH (H_4O^-) from spent TOSH (H_4O). It is possible that TOSH could regenerate CSR2. GSH in cytosol would come in contact with the TOSH (H_4O^-) coating the inner mitochondrial membrane ahead of either copper portions of cytochrome c oxidase unless the TOSH coating was discontinuous (i.e. had bare spots). Further, if either of the reduced copper portions of CSR react with spent TOSH to form the oxidized copper portions of cytochrome c oxidase (“CSO1 and/or CSO2”) the regeneration of inner TOSH and glutathione could occur as follows:

$$CSR1 \text{ or } CSR2 = CSO1 \text{ or } CSO2 + e^- \quad (6)$$

$$CSR1 \text{ or } CSR2 + GS(H_4O) = GS + H_4O^- + CSO1 \text{ or } CSO2 + GS \quad (7)$$

$$CSR1 \text{ or } CSR2 + GS + H^+ = GSH + H_4O^- + CSO1 \text{ or } CSO2 \quad (8)$$

TOSH regeneration of CSR2 from CSO2 could occur as follows:

$$CSO2 + OH^-(HOH)_4 = CSR2 + OH(HOH)_4 \quad (9)$$

It is possible that TOSH exposed to the inner mitochondrial membrane regenerates oxidized membrane protein disulphide (MSSM´) (e.g. Alzheimer's amyloid β (Aβ) plaques which are oxidized proteins) via formation of MSH and M´SH as follows:

$$OH^-(HOH)_4 + H^+ + MSSM´ = M´S\text{-}OH(HOH)_4 + MSH \quad (10)$$

and

$$CSR1 \text{ or } CSR2 + M´S\text{-}OH(HOH)_4 = CSO1 \text{ or } CSO2 + M´S + OH^-(HOH)_4 \quad (11)$$

$$CSR1 \text{ or } CSR2 + M´S + H^+ = CSO1 \text{ or } CSO2 + M´SH \quad (12)$$

Therefore, it is conceivable that water EZs and TOSH structures found on inner mitochondrial membrane surfaces (including bio-molecules within mitochondria themselves) function synergistically with the copper portion of cytochrome c oxidase, by either sparing the larger cytochrome c oxidase molecule for its own antioxidant roles, or by helping to catalyze the reduction process of CSO2 to CSR2; while the presence of VIS Red and NIR light would also help to indirectly regenerate oxidized membrane proteins, as well as antioxidants such as glutathione, necessary for the prevention of oxidative stress *in vivo*.

A similar principle applies to nicotinamide adenine dinucleotide phosphate (NADPH). For example, in Aoyama and Nakaki (2013), citing the work of many others, their extensive review article referred to the electron-donating role played by NADPH in regenerating both enzymes, as well as GSSG into GSH (see page 21025). While the electrical potential of NADPH of -320 mV exceeds that of TOSH's -208 to -219 mV, the fact that TOSH can help regenerate GSH, means that the limited supply of NADPH is not wasted, thus allowing it to protect vital protein structures from oxidation and potential misfolding. The same principle applies to melatonin. While melatonin itself is a free radical scavenger, it is important to note it cannot be regenerated via TOSH or the copper portions of cytochrome c oxidase since its -950±20 mV reduction redox potential is simply too high (Mahal *et al* 1999). Nonetheless, TOSH can still serve to protect melatonin from decay from lethal hydroxyl radicals (Pieri *et al* 1994). If true, this would contradict some currently held views on the topic. For example, according to Aoyama and Nakaki (2013), no known defense has been reported against hydroxyl radicals (page 21026). It appears that TOSH can indirectly and potentially directly destroy hydroxyl and peroxynitrite, as shown below:

Hydroxyl free radical should be destroyed indirectly by TOSH via GSH as follows:

$$2HO\bullet + 2GSH = 2H_2O + GSSG \quad (13)$$

Peroxynitrite free radical should be destroyed indirectly by TOSH via GSH as follows:

$$ONOO^- + 2GSH = GSSG + NO_2^- + H_2O \quad (14)$$

Hydroxyl free radical should be destroyed directly by TOSH as follows:

$$OH^-(HOH)_4 + H^+ + HO\bullet = OH(HOH)_4 + H_2O \quad (15)$$

Peroxynitrite free radical should be destroyed directly by TOSH as follows:

$$2OH^-(HOH)_4 + 2H^+ + ONOO^- = 2OH(HOH)_4 + H_2O + NO_2 \quad (16)$$

Yet nowhere is the TOSH mechanism of action cited in any prior articles. Indeed, in the concluding remarks of their own extensive review study, Beirne *et al.* (IN PRESS) stated: "Much evidence has been gathered in efforts to elucidate the underlying mechanism responsible for the neuroprotective effects of red/NIR light, but the mechanism remains unclear. Experimental findings suggest that there are many possible molecular and cellular effects of red/NIR light, which could all contribute to the observed neuroprotective effects, when explored separately; but when taken collectively some effects appear to contradict others."

Overall, this suggests that TOSH is likely another important variable in optimizing the functionality of various antioxidant bio-molecules levels not simply within mitochondria, but in other areas both within and outside cellular confines. As we have demonstrated, no less is the case for glutathione (GSH).

Moreover, this view not only concords with results from a variety of studies looking at VIS Red and NIR light in therapeutic contexts, but the very fact it does concord with such results reinforces the proposition that TOSH's place in the antioxidant mix is a symbiotic one. For example, it is consistent with Yeager *et al.* 2007 and Kao and Sheen 2003 and their finding that light in the 650 to 670 nm range can restore the glutathione (GSH) glutathione disulfide (GSSG) redox balance (GSH/GSSG ratio) upon toxological insult. Yet while the GSH regeneration noted in their study appears to exclusively attributed the direct absorption of these wavelengths, given what we now know about TOSH growth as relates to VIS Red and IR light, should it be? Probably not: Given TOSH's electron-donating antioxidant potential, some measure of the GSH regeneration noted by these authors is likely also being supported by an indirect process mediated by TOSH. Though we have presented sound scientific reasons to suggest the latter, until such time more direct NIR-EZ growth data is actually catalogued, this question has yet to be experimentally confirmed.

Nevertheless, to recap what we have so far presented as it relates to Alzheimer's Disease, we offer the following summary of the sequential series of relationships involved:

Alzheimer's amyloid β (Aβ) plaques = oxidized protein

As Glutathione rises, oxidized protein drops

Glutathione + oxidized protein = less oxidized protein + GSSG (oxidized glutathione)

TOSH + GSSG = oxidized TOSH + GSH (glutathione)

Therefore, TOSH or GSH destroy ROS or RNS to make oxidized TOSH (water) and/or GSSG

VIS Red + NIR photonic inputs + anchored water = TOSH

VIS Red + NIR photonic inputs + oxidized cytochrome c = reduced cytochrome c

Reduced cytochrome c + glucose generates ATP

Reduced cytochrome c + GSSG = oxidized cytochrome c + GSH

VIS Red and NIR photonic inputs indirectly regenerate GSH via cytochrome c and/or TOSH

Real World Epidemiological Comparisons

Of course because theory is one thing and its real world implications often another, especially when going from events unfolding at the nanometer scale to those unfolding at the whole body macro-scale, we decided it would be prudent to consider whether the photon-TOSH principles we outlined herein might have any measurable impact on human health, especially as it relates to dementia. We posit this not only given the likely strong relationship between VIS Red/IR photon exposure in the ambient environment and TOSH growth within people, but the relationship these principles may also have in optimizing glutathione levels, given the number of studies connecting the depletion of glutathione (and other anti-oxidants) with increases in Alzheimer's risk (e.g. Mandal *et al.*2016; Kao and Sheen, 2003; Pocernich and Butterfield, 2012).

One place such an effect might be seen is in relation to sauna use, since infrared saunas emit photons at 3000 nm or longer, wavelengths sufficient to grow EZs (Vatansever and Hamblin 2012). Yet unlike the sun, most infrared saunas now on the market do not emit light in the NIR wavelength range needed to directly regenerate the antioxidant bio-molecules we considered in this paper. This suggests that optimizing TOSH growth via MIR/FIR sauna baths may simply be insufficient in helping to regenerate more potent antioxidants. This appears to be borne out in the epidemiological evidence presented in *Table 2*. Despite Scandinavia's widespread use of saunas, Scandinavia has the highest incidence rate for dementia in Europe [*Web Ref. 9*].

Countries	Latitude Ranges	Average December Sunlight Hours	% of Population with Dementia
Norway, Sweden, Finland	~ 56ºN to ~ 70ºN	35, 26, 33	1.56, 1.71, 1.82
Belgium, Netherlands, Denmark	~ 47ºN to ~ 60ºN	35, 51, 38	1.77, 1.47, 1.53
Austria, Hungary, Czech Rep.	~ 46ºN to ~49º N	51, 49, 47	1.73, 1.50, 1.36
Romania, Bulgaria	~41.5º N to 48º N	63, 64	1.26, 1.49

Table 2: *Incidence of Dementia in Europe Versus Exposure to December Sunlight.*

To compensate for any cherry-picking effects, the above data was plotted on a scatter gram to get the line-of-best-fit relationship, as seen in *Figure 6*.

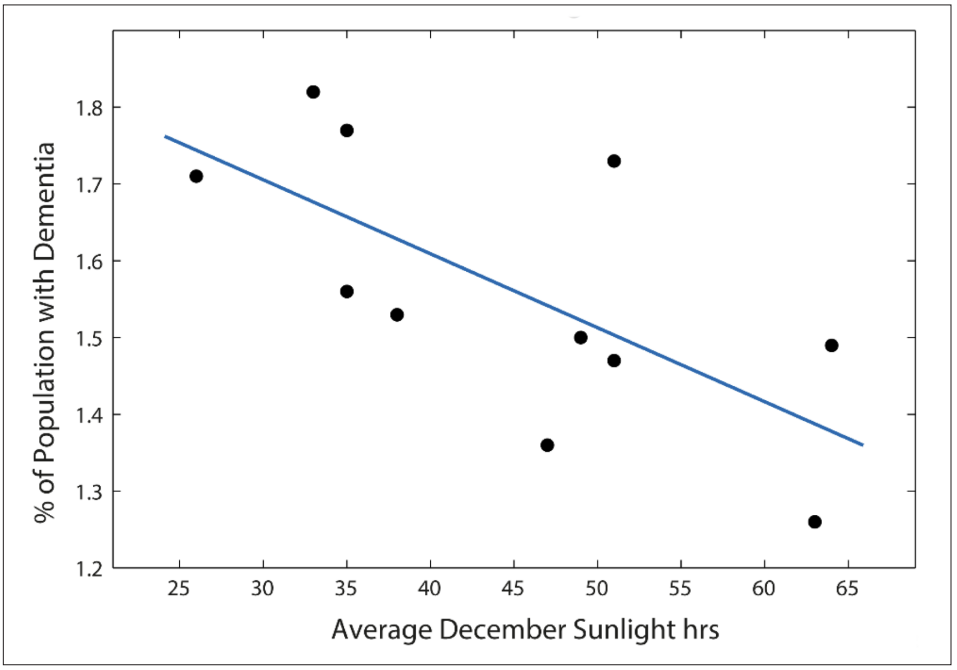


Figure 6: *Scattergram of Alzheimer's dementia incidence in eleven European countries versus December sunlight hours.*

Linear model Poly 1: f(x) = p1*x + p2
Coefficients (with 95% confidence bounds):
p1 = -0.009632 (-0.01754, -0.00172)
p2 = 1.994 (1.628, 2.36)
Goodness of fit:
SSE: 0.1685
R-square: 0.4573
Adjusted R-square: 0.397
RMSE: 0.1368
The foregoing calculations yielded **r = 0.6762**

Despite the relatively mild correlation between Alzheimer's dementia incidence with December sunlight hours [*Web Ref. 10*] which reflect this region's more northerly latitude position on the planet, the results do nonetheless suggest that a reduced presence of VIS Red and NIR light during the winter period could be exacerbating dementia rates due to a temporary decrease in cytochrome c oxidase production. Moreover, despite the theoretical likelihood that MIR/FIR saunas should help to substitute for sunshine losses during winter months to regenerate TOSH, and thus by extension boost both glutathione and one of the copper portions of cytochrome c oxidase levels (Begum *et al.* 2013), in the case of the most northerly of these countries where sauna use is more prevalent, sauna use does not seem to have much of a mitigating effect when one examines both Table 2 and the Figure 6 scattergram results. This becomes even clearer when one considers that 99% of Finland's 5.3 million people take at least one sauna bath per week. Despite this fact, the country still has the highest Alzheimer's disease rate in the world. [*Web Ref. 11*].

Since light therapy at 633 nm and 1072 nm has been shown to be of benefit in treating Alzheimer's disease (Yang *et al.* 2010; Grillo *et al.* 2013; Johnstone *et al.* 2015), and in view of the strength of the epidemiological case presented above, it would be interesting if the governments of Scandinavia undertook a number of long term research studies involving the installation of NIR/VIS Red light sources in saunas and/or at work to see what impact this might have in reducing the incidence of this disease in their populations.

Yet even though more conventional MIR/FIR saunas *may* have limited benefit in helping to regenerate glutathione and the copper portions of cytochrome c oxidase, this is not to say that saunas are generally devoid of any other health benefits. For example, after 30 minutes of aerobic exercise on a cyclo-ergometer, even after a single sauna bath, they have been shown to help retain the oxidant-antioxidant balance in the subjects tested (Sutkowy, 2014). In another study, subjects who underwent infrared sauna therapy for 15 minutes a day for two weeks experienced a significant decrease in an oxidative stress marker known as urinary 8-Epi-Prostaglandin 2α levels (Masuda *et al* 2004); and prostaglandin levels in the treatment group were about 39.5% lower than those in the non-sauna treatment group after two weeks. This reference also cited evidence that sauna therapy up-regulated mRNA and improved protein expression of arterial endothelial nitric oxide synthase in hamsters. However, the infrared wavelengths apparently involved were between 8,000 to 14,000 nm, wavelengths well beyond those examined by EZ researchers. Still, in all instances, some of the effects noted above may still be attributable to TOSH growth adjacent to biomolecules (as demonstrated by water adjacent to hydrated rabbit muscle protein). This last point remains noteworthy since many in mainstream medicine regard Alzheimer's as a protein disorder disease.

In view of the TOSH theory presented herein, and the aforementioned results above, this prompts an intriguing scientific question: Is it possible that the photons absorbed within TOSH fields retain their original wavelength signatures as virtual electrons? If so, this could fundamentally change the way we now theoretically model photochemical processes. Indeed, such a proposition might be testable by seeing what would happen if water, given a case relevant bio-molecular seed anchor condition, such as cytochrome c oxidase, was selectively exposed to 830 nm light, the wavelength known to resonate with one of cytochrome c oxidase's copper-associated complexes (i.e. CSR1). The objective would be to see whether any subsequent uptake and change in the pH level took place in the associated TOSH structure or in an oxi-

dized version of cytochrome c oxidase. If this proved to be the case, it would do more than suggest that TOSH structures are encoding and storing specific photon wavelength information. It would also suggest that they can act like wavelength-specific batteries upon which oxidized antioxidants can draw to not only regenerate themselves, but to possibly do so in quantum mechanical terms. It would also suggest that cytochrome c oxidase molecules may share the same kind of photon processing capabilities now seen in the light harvesting proteins (also known as antenna proteins) in the photosynthesis complexes of plants. These complexes have been shown to use a naturally-occurring quantum computing process to shunt photon energy to where it needs to be within ultra-short femtosecond time spans (Scholes *et al.* 2011, 2006; Collini *et al.* 2010, 2009; Freiberger, 2012). This could have much wider implications for how cellular systems as a whole might be using photonic inputs to regulate internal function.

In summary, much of the foregoing would suggest that by preventing free-radical or oxidative destruction, TOSH containing EZs could have played a key evolutionary ascendency role in the development of aerobic bio-systems. It also supports the view that early life may have arisen in areas where ultra-violet light was minimal, infrared light was plentiful, and sulphur was available for production of proteins including glutathione. Such conditions would exist near relatively shallow oceanic hydrothermal vents. As such, it would be useful to examine glutathione versus oxidized glutathione and other oxidized proteins/peptides and pH values in *in vivo* EZs as a function of location, light intensity and wavelength since growth of TOSH containing EZs generates protons.

Dimethyl Sulfoxide and Polyol Derived EZs

In a side note pertaining to EZ field formation, we felt it necessary to comment on dimethyl sulfoxide, a solvent shown to form EZs on Nafion® plus other ROH solvents including ethylene glycol and glycerol. It has been shown to prevent the structural and functional destruction of proteins, cells and tissues during freezing and thawing (Huang *et al* 1995). Although it is unclear whether much larger ROH type molecules, such as sucrose and trehalose, can sterically form EZ fields adjacent to bio-molecules in the presence or absence of water, all of these molecules have shown an ability to protect protein molecules from damage due to water desiccation. Here is a typical comment: "The survival strategy during early dehydration seems to be avoiding protein unfolding and membrane disturbances. Upon further removal of water, sugar molecules have to replace this water at hydrogen bonding sites, in order to preserve the native structure of proteins and the correct spacing between phospholipids. Trehalose is thought to replace the shell of water around macromolecules, preventing damaging effects during drying" (Liu *et al* 2005). Trehalose is thought to form a gel phase as cells dehydrate which prevents disruption of internal cell organelles, by effectively splinting them in position [*Web Ref. 12*].

Conclusions

TOSH structures in water, polyol (e.g. ethylene glycol, glycerol or trehalose) or dimethyl sulfoxide derived biochemical EZ fields can act as symbiotic regenerative donor/recipient anti-oxidants or UV radiation protectors for bio-molecule substrates including antioxidants such as glutathione (GSH), melatonin, cytochrome c oxidase and protein SH functional groups, especially membrane proteins. Partial or complete dehydration of bio-molecules causes their TOSH structures to be ruptured especially near their resonant frequency of ~270 nm. Bio-anchored TOSH containing EZ fields

can, via the photovoltaic process, be directly regenerated with hydration when exposed to UV, visible and infrared light. TOSH can also be regenerated indirectly via the copper portions of cytochrome c oxidase. Due to their ability to be seed anchored by biomolecules such as DNA, RNA, lipids, and proteins, TOSH structures are believed to be nearly ubiquitous. This allows them to play a critical role in guarding these biomolecules from ultraviolet or oxygen induced free radical damage. The ability of UV, red, NIR and FIR light to foster the formation of TOSH structures out of water and their concomitant negatively-charged "Exclusion Zones" may partially explain the therapeutic value of light therapy devices and infrared saunas, as well as the remedial benefits of infrared and red light in the treatment of various pain conditions and oxidative stress disorders such as dementia, including Alzheimer's disease. Because epidemiological evidence presented in this paper only marginally supports this view, it would be prudent if longitudinal field research involving regular exposure to infrared light during months of minimal sunlight in northern latitude countries was done to determine the extent to which the progress of these disorders can be slowed or reversed. Such knowledge would likely find application in other circumstances such as proactive light therapy treatments in at-risk populations and for those asked to take part in long-term space travel.

Other future experimental research recommendations:

1. Study the wavelength effect between 250 nm and 4250 nm and amplitude of light *in vivo* and *in vitro* on the following:

   a) growth of EZs and EZ potential (voltage) versus time in the presence and absence of GSSG and/or oxidized and reduced cytochrome c oxidase.

   b) growth of EZs and EZ potential versus ROS concentration e.g. OH• in the presence and absence of GSH or GSSG.

   c) growth of EZs and potential versus RNS concentration e.g. $ONOO^-$ in the presence and absence of GSH or GSSG.

2. Study the possibility that VIS Red and IR photons are absorbed through the nasal cavity.

3. Determine whether TOSH structures can grow in the absence of photonic inputs, but in the presence of electro-chemical inputs off of other bio-molecules, such as DNA, melatonin, NADH or cytochrome c oxidase.

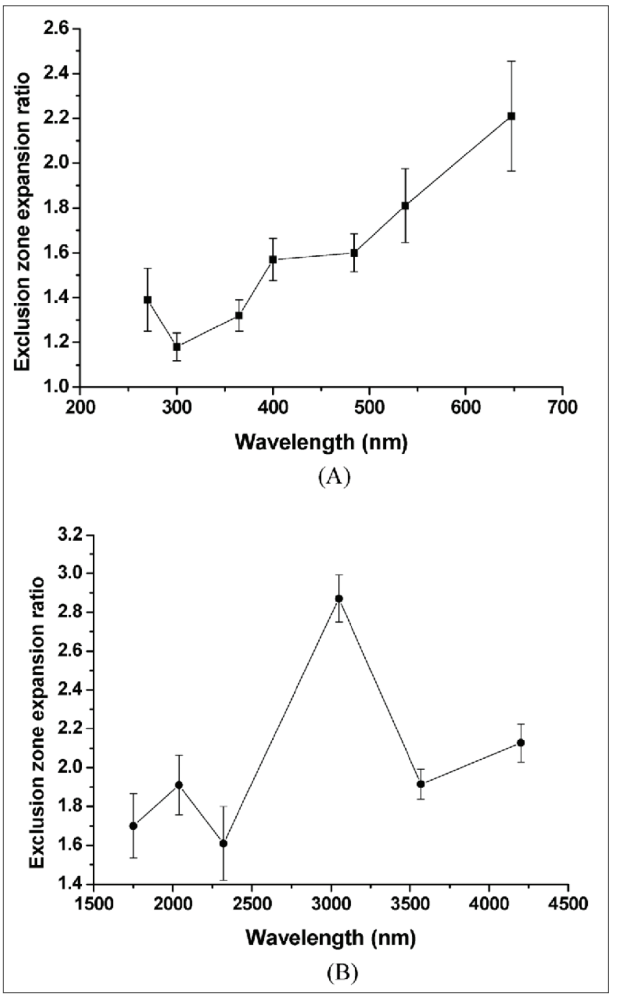
4. Determine the TOSH concentration of EZs by titration with GSSG.

5. Determine the effects of EZ/TOSH concentration on EZ viscosity.

6. Determine whether TOSH concentration of EZs is constant or dependent on variables such as pH and temperature.

7. Test TOSH/photon relationship to cytochrome c oxidase (CCO). **Step 1:** Expose water in a bio-anchor appropriate container to only 655 nm and 830 nm light, both together and separately, (as well as a range of adjacent wavelengths) for periods of five minutes to create an EZ/TOSH field. **Step 2:** Introduce oxidized versions of CCO. **Step 3:** Assess what happens to both CCO and to EZ/TOSH field size in relation to what is already known about its decay rates within 30 minutes.

Appendix



Above graphs from Chai *et al.* 2009: (A) Exclusion-zone expansion ratio under illumination for 5 minutes in the Ultra-Violet to VIS light spectrum region; (B) Exclusion-zone expansion ratio under illumination for 5 minutes in the Infrared light region of the electro-magnetic spectrum.

Acknowledgments

The authors wish to thank Carol Oehr for her careful edits and preparation of certain figures, Gerald Pollack for his encouragement in submitting this paper, and for *Figure 1* in our Appendix from Chai *et al.* 2009. The authors also wish to thank Michael R. Hamblin for his kindness in granting us permission to reproduce *Figures 2 and 3* which originally appeared in Barolet *et al.,* 2015 and Tsai & Hamblin, 2017, and by extension, also acknowledge and express our gratitude to copyright holder Ying-Ying Huang for the spectrum drawing shown under *Figure 2*; and Louise Beinhauer for providing a labeling tweak to it. Thanks also to Elsevier's Journal of Photochemistry & Photobiology, B: Biology, for granting permission to reproduce *Figure 3*. Finally, we wish to thank Felix Scholkmann for providing the data plot appearing in *Figure 6* and its associated calculations. Thanks too for the suggestions made by our referees. All proved immensely useful.

Author Contributions

Paul LeMay introduced Klaus Oehr to Gerald Pollack's concepts of EZs, helped formulate several key concepts of this paper as well as edit its contents. Oehr carried out most of the literature searches necessary to prepare the paper and wrote the chemistry equation logic. LeMay reviewed and contributed interpretations to the literature cited in relation to the subject of this paper. The authors shared in the writing of the paper.

Conflicts of Interest

The authors declare no conflicts of interest.

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