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FACULTY OF SCIENCE
Institute for Quantum Science and Technology

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Could quantum entanglement play a role in the brain?

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Entanglement

A unique **quantum** physical property that allows two or more particles to act in a **correlated** way even when they are separated in space.

These quantum correlations can not be explained in classical terms (**Bell's theorem**).

An entangled quantum system should be thought of as **one coherent whole**, even if it contains many particles.

What would entanglement in the brain accomplish?

- **Quantum information processing?** Nature might also have found a way to harness quantum advantage in computing or communication complexity
- **Binding problem** of consciousness – How does unified yet complex conscious experience arise from dynamics of many neurons (or molecules)? For **entangled** systems, the whole is more than the sum of its parts in a well-defined physical and mathematical sense.

C. Simon, arXiv:1809.03490, J. Consc. Stud. 26, 204 (2019)

Photons and spins would be natural choices

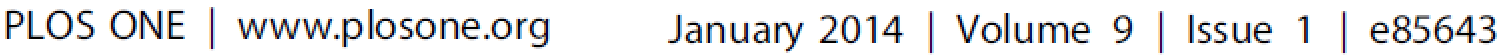
- What ingredients might nature use to implement quantum functionalities in the brain? **Quantum technology** can provide hints.
- **Photons** are ideal for sending quantum information over macroscopic distances
- **Spins** can serve as quantum processors and memories even in condensed matter systems at room temperature.

C. Simon, arXiv:1809.03490, J. Consc. Stud. 26, 204 (2019)

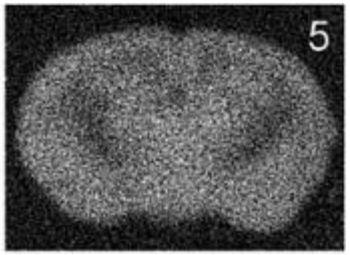
Photons in the brain

Spatiotemporal Imaging of Glutamate-Induced Biophotonic Activities and Transmission in Neural Circuits

Rendong Tang[1,2], Jiapei Dai[1,2,3]*



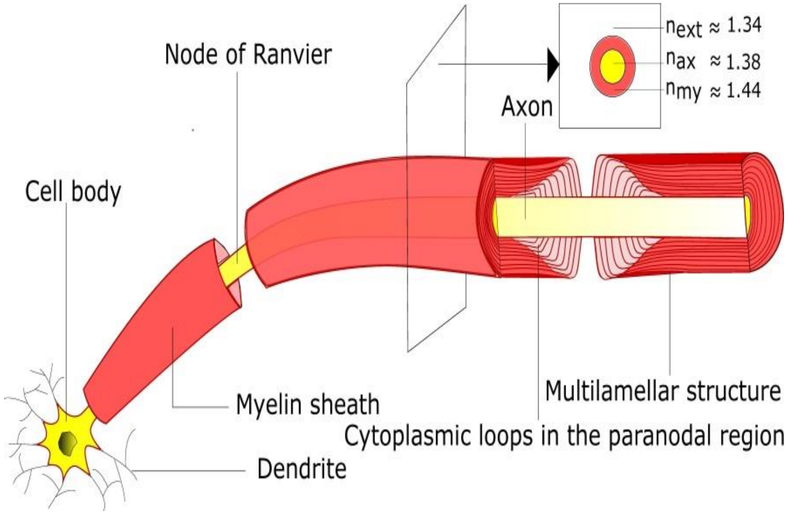
PLOS ONE | www.plosone.org January 2014 | Volume 9 | Issue 1 | e85643



- **Reactive oxygen species** in mitochondria are one likely source
- Could these photons be used for **communication**?
- Potential single-photon detectors exist in the brain, e.g. **opsins**
- My focus is on **quantum** communication, but even classical communication via light would be very interesting!

Could axons serve as waveguides?

- **Refractive index** of axon is higher than that of surrounding liquid, and refractive index of myelin sheath is higher still – so light guidance is possible.



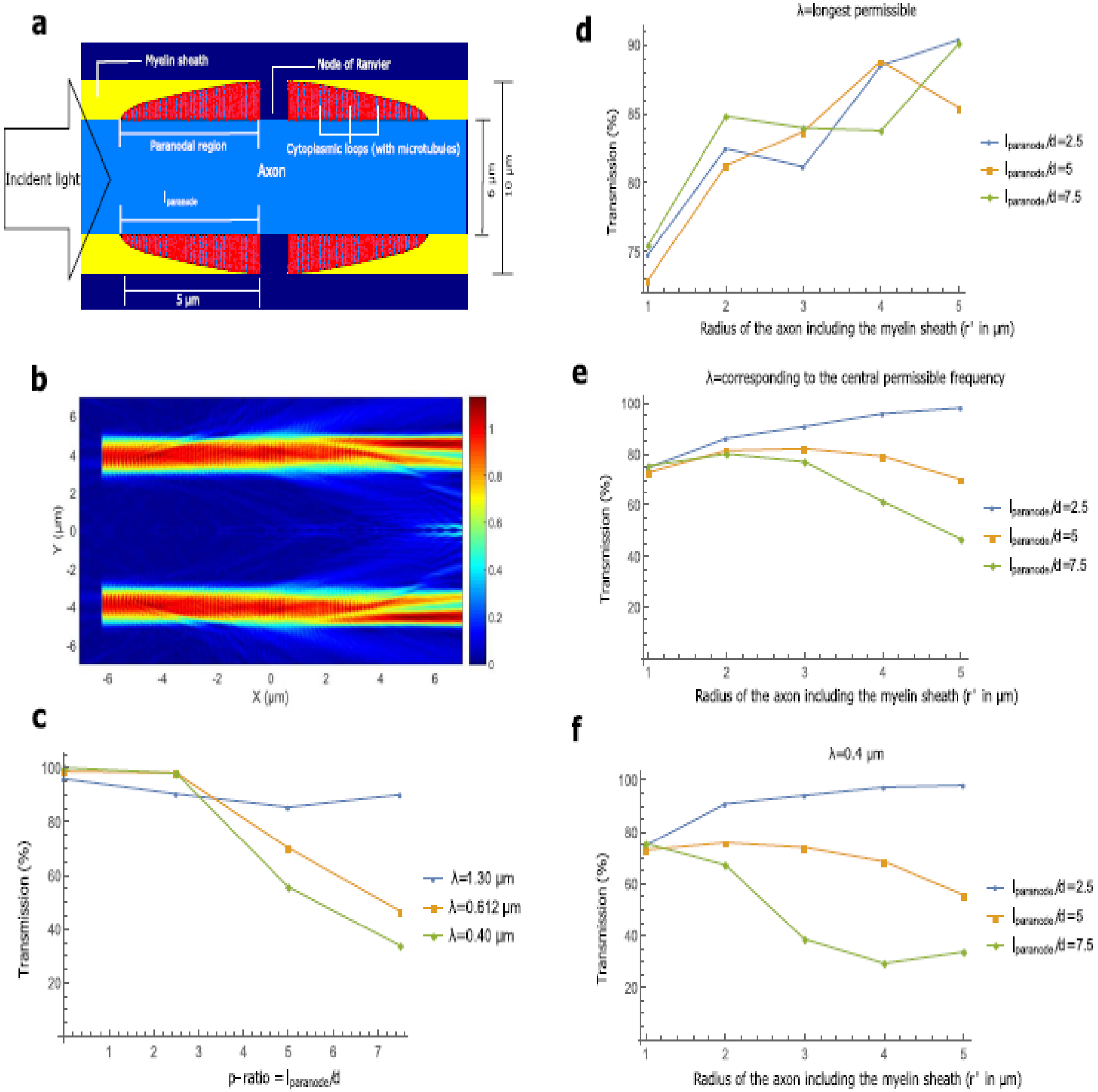
- But could it be a good **photonic waveguide** despite the many '**imperfections**'? Our detailed theoretical modeling suggests it could!

Kumar, Boone, Tuszynski, Barclay, Simon,
Scientific Reports 6, 36508 (2016)

Transmission through paranodal region

Made detailed model for **Ranvier node** and surrounding region.

Transmission can be very high despite interruption in myelin sheath, presence of scatterers.

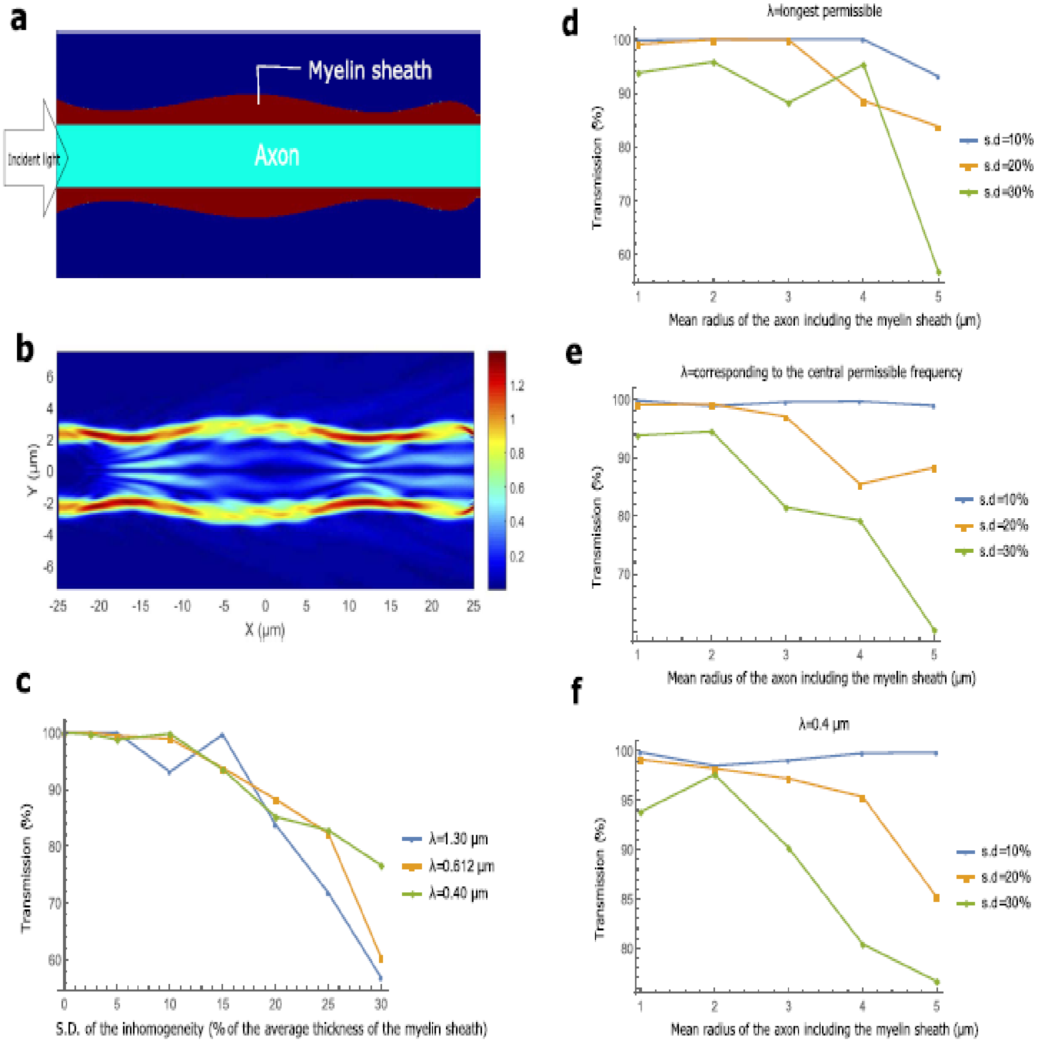


Kumar, Boone, Tuszynski, Barclay, Simon, Scientific Reports 6, 36508 (2016)

Varying cross-sectional area

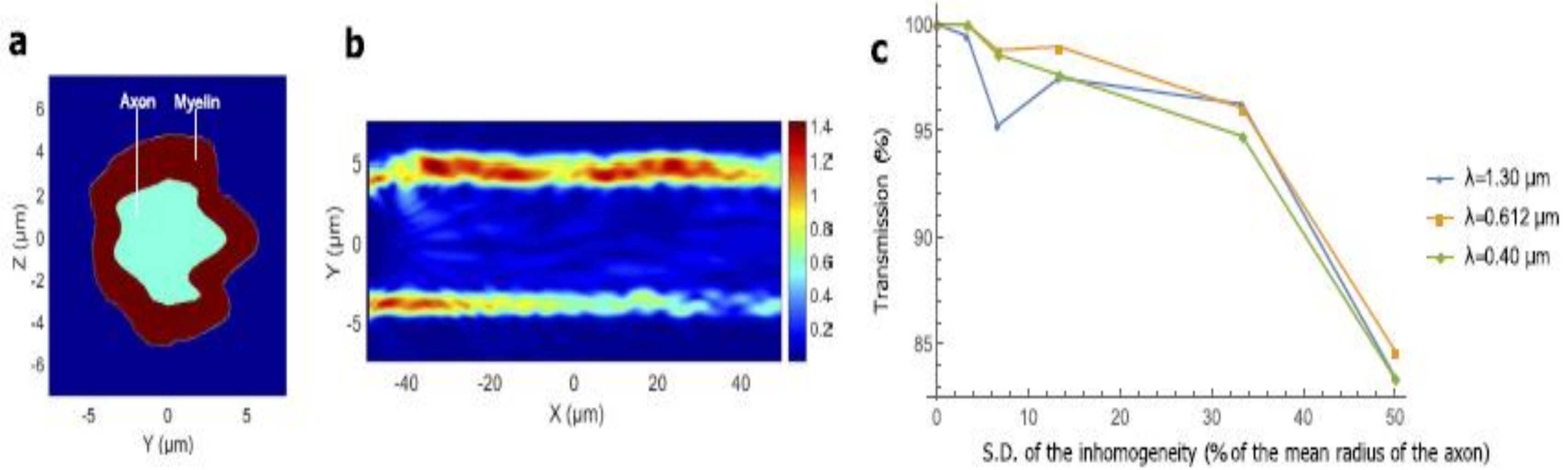
Cross-sectional area varies for realistic axons.

Transmission can be high nevertheless.



Kumar, Boone, Tuszynski, Barclay, Simon, Scientific Reports 6, 36508 (2016)

Non-circular cross-section



Transmission can be high also for non-circular cross-section.

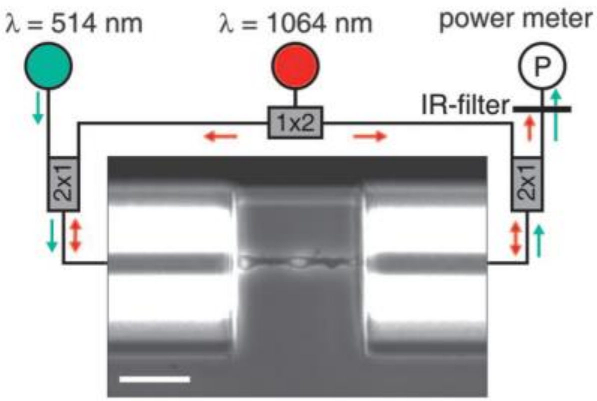
Also looked at bends, cross-talk between axons, absorption.

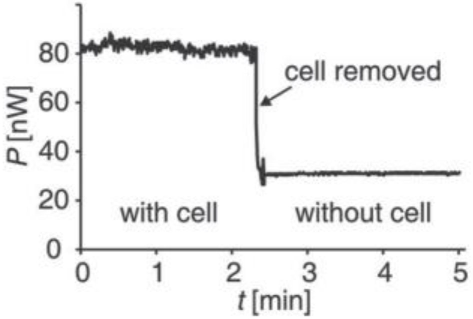
Kumar, Boone, Tuszynski, Barclay, Simon,
Scientific Reports 6, 36508 (2016)

Estimates for achievable range and rates

- High transmission (a few % to almost 100%) for distances in the **mm to cm range**, at least for certain axons.
- A **billion** photons emitted per second throughout the brain.
- Could transmit a lot of information or entanglement.
- **Bandwidth of consciousness** is probably in the range 100-100,000 bits/second (psychophysics estimates based on reading, sensor design)

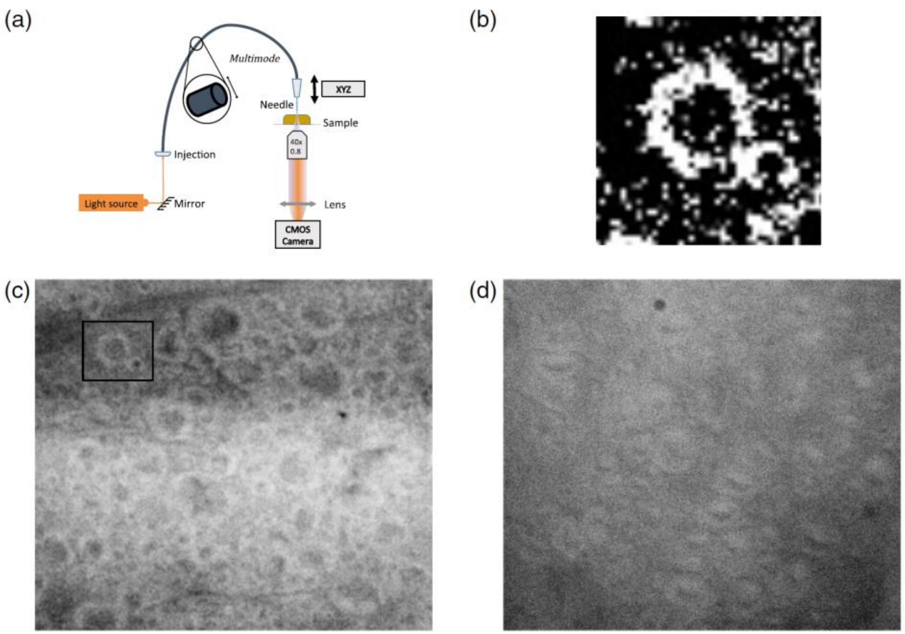
Experimental evidence for light guidance





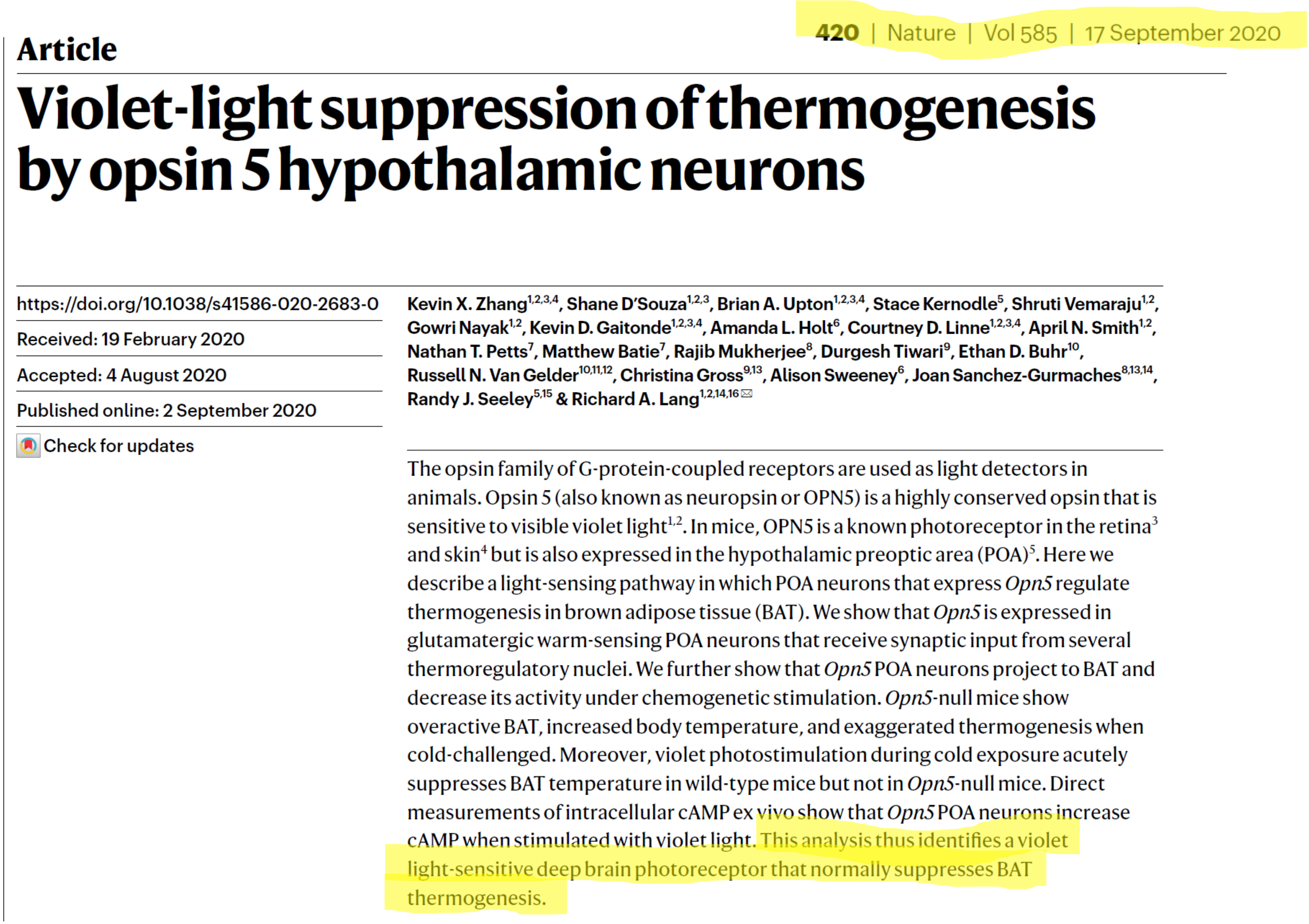
Franze, K. *et al.* **Müller cells are living optical fibers in the vertebrate retina**. *Proc. Natl. Acad. Sci. USA* **104**, 8287–8292 (2007).

Müller cells are glia cells, the type of cells that **myelin** is made of.



Observation of **anisotropic light scattering from axons**: DePaoli et al., Neurophoton. 7, 015011 (2020).

Direct tests of light guidance for axons would still be welcome!



420 | Nature | Vol 585 | 17 September 2020

Article

Violet-light suppression of thermogenesis by opsin 5 hypothalamic neurons

https://doi.org/10.1038/s41586-020-2683-0

Received: 19 February 2020

Accepted: 4 August 2020

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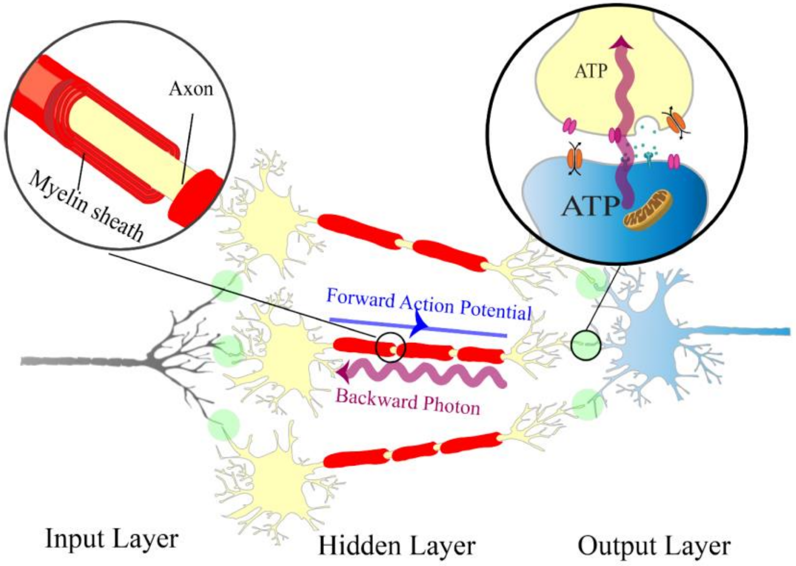
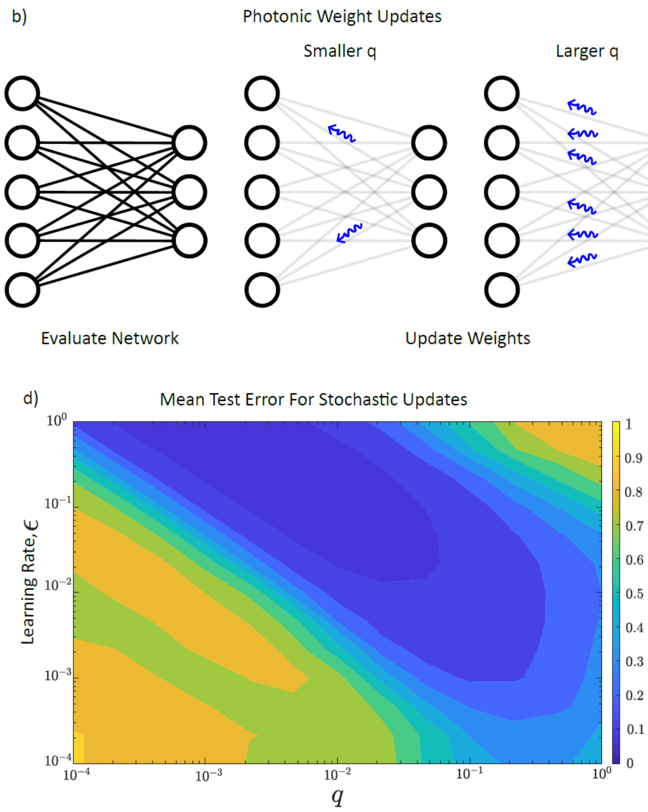
The opsin family of G-protein-coupled receptors are used as light detectors in animals. Opsin 5 (also known as neuropsin or OPN5) is a highly conserved opsin that is sensitive to visible violet light[1,2]. In mice, OPN5 is a known photoreceptor in the retina[3] and skin[4] but is also expressed in the hypothalamic preoptic area (POA)[5]. Here we describe a light-sensing pathway in which POA neurons that express *Opn5* regulate thermogenesis in brown adipose tissue (BAT). We show that *Opn5* is expressed in glutamatergic warm-sensing POA neurons that receive synaptic input from several thermoregulatory nuclei. We further show that *Opn5* POA neurons project to BAT and decrease its activity under chemogenetic stimulation. *Opn5*-null mice show overactive BAT, increased body temperature, and exaggerated thermogenesis when cold-challenged. Moreover, violet photostimulation during cold exposure acutely suppresses BAT temperature in wild-type mice but not in *Opn5*-null mice. Direct measurements of intracellular cAMP ex vivo show that *Opn5* POA neurons increase cAMP when stimulated with violet light. This analysis thus identifies a violet light-sensitive deep brain photoreceptor that normally suppresses BAT thermogenesis.

Photons might enable learning in the brain by stochastic backpropagation





Photons can travel backwards along axons.

Good learning performance with stochastic signals.

Still works for limited bit content and in presence of noise.

Zarkeshian, Kergan, Ghobadi, Nicola, Simon, arXiv:2203.11135

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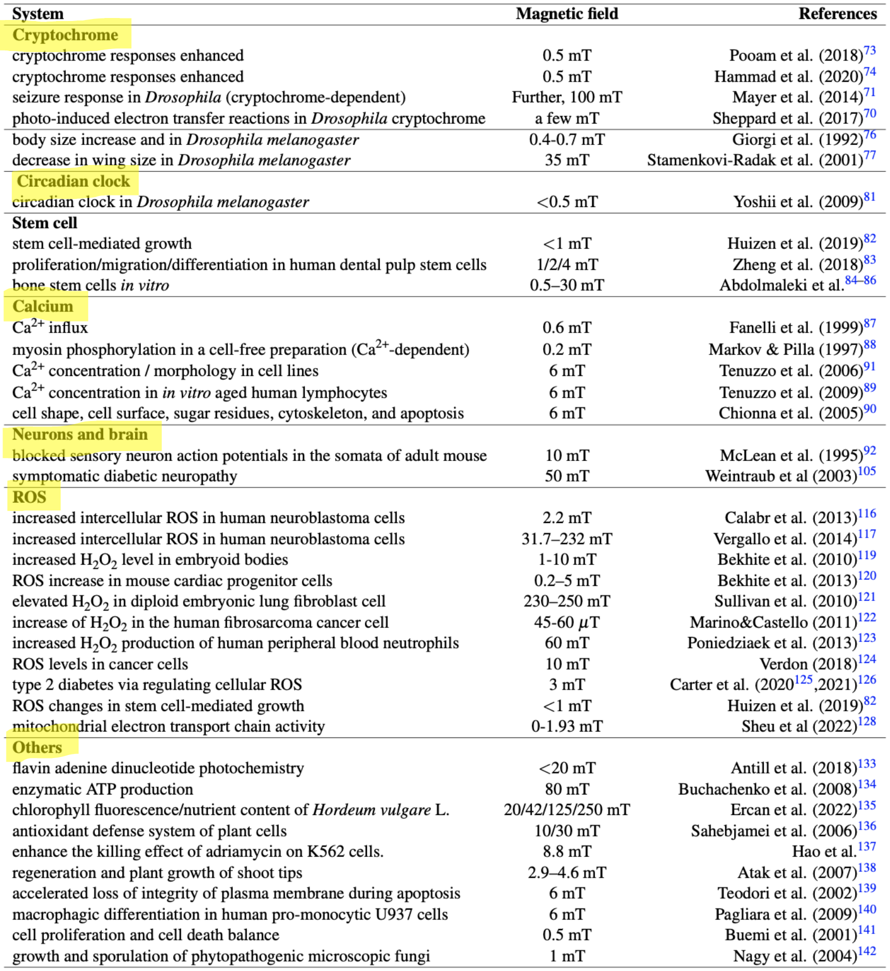
C. Simon, arXiv:1809.03490, J. Consc. Stud. 26, 204 (2019)

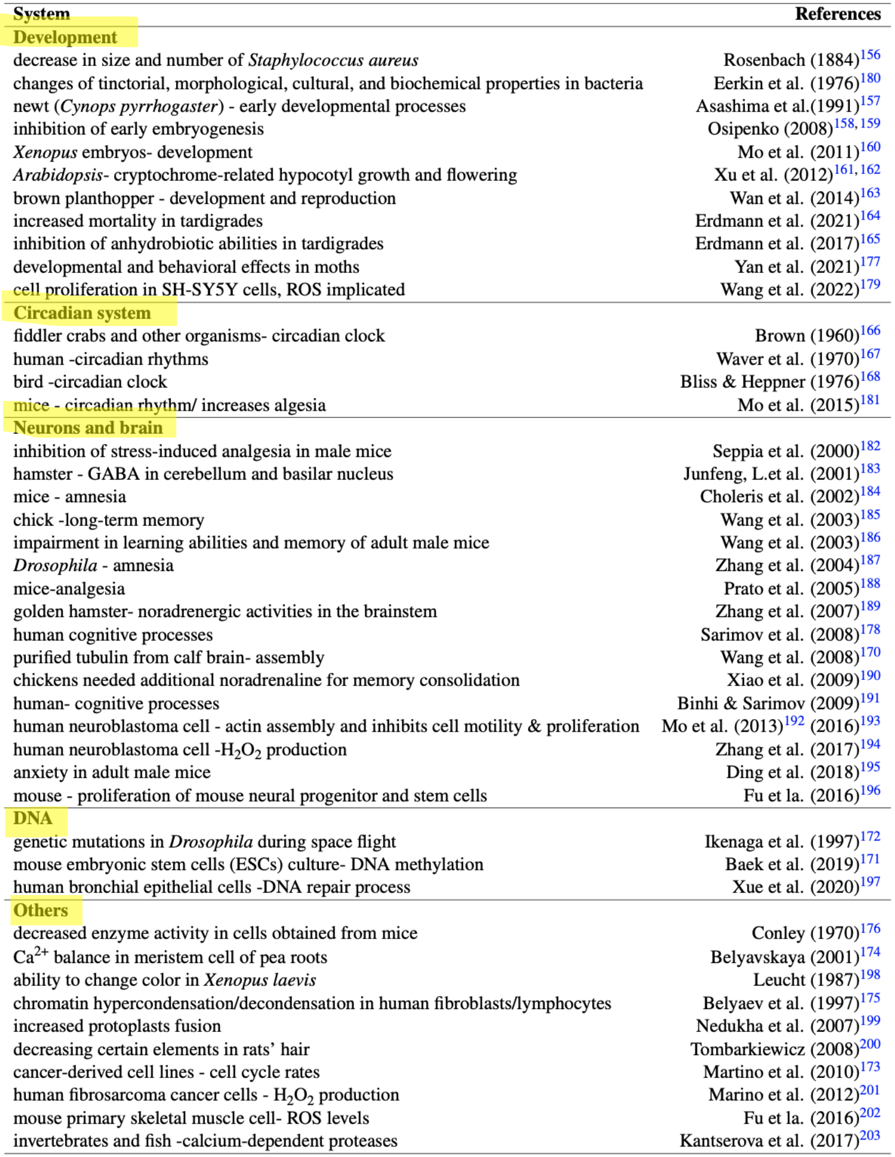
Weak Magnetic field and isotope effects in biology

Table 1. Static magnetic field effects on different biological functions.



System	Magnetic field	References
Cryptochrome		
cryptochrome responses enhanced	0.5 mT	Pooam et al. (2018)[73]
cryptochrome responses enhanced	0.5 mT	Hammad et al. (2020)[74]
seizure response in *Drosophila* (cryptochrome-dependent)	Further, 100 mT	Mayer et al. (2014)[71]
photo-induced electron transfer reactions in *Drosophila* cryptochrome	a few mT	Sheppard et al. (2017)[70]
body size increase and in *Drosophila melanogaster*	0.4-0.7 mT	Giorgi et al. (1992)[76]
decrease in wing size in *Drosophila melanogaster*	35 mT	Stamenkovi-Radak et al. (2001)[77]
Circadian clock		
circadian clock in *Drosophila melanogaster*	<0.5 mT	Yoshii et al. (2009)[81]
Stem cell		
stem cell-mediated growth	<1 mT	Huizen et al. (2019)[82]
proliferation/migration/differentiation in human dental pulp stem cells	1/2/4 mT	Zheng et al. (2018)[83]
bone stem cells *in vitro*	0.5–30 mT	Abdolmaleki et al.[84–86]
Calcium		
Ca^{2+} influx	0.6 mT	Fanelli et al. (1999)[87]
myosin phosphorylation in a cell-free preparation (Ca^{2+}-dependent)	0.2 mT	Markov & Pilla (1997)[88]
Ca^{2+} concentration / morphology in cell lines	6 mT	Tenuzzo et al. (2006)[91]
Ca^{2+} concentration in *in vitro* aged human lymphocytes	6 mT	Tenuzzo et al. (2009)[89]
cell shape, cell surface, sugar residues, cytoskeleton, and apoptosis	6 mT	Chionna et al. (2005)[90]
Neurons and brain		
blocked sensory neuron action potentials in the somata of adult mouse	10 mT	McLean et al. (1995)[92]
symptomatic diabetic neuropathy	50 mT	Weintraub et al (2003)[105]
ROS		
increased intercellular ROS in human neuroblastoma cells	2.2 mT	Calabr et al. (2013)[116]
increased intercellular ROS in human neuroblastoma cells	31.7–232 mT	Vergallo et al. (2014)[117]
increased H_2O_2 level in embryoid bodies	1-10 mT	Bekhite et al. (2010)[119]
ROS increase in mouse cardiac progenitor cells	0.2–5 mT	Bekhite et al. (2013)[120]
elevated H_2O_2 in diploid embryonic lung fibroblast cell	230–250 mT	Sullivan et al. (2010)[121]
increase of H_2O_2 in the human fibrosarcoma cancer cell	45-60 μT	Marino&Castello (2011)[122]
increased H_2O_2 production of human peripheral blood neutrophils	60 mT	Poniedziaek et al. (2013)[123]
ROS levels in cancer cells	10 mT	Verdon (2018)[124]
type 2 diabetes via regulating cellular ROS	3 mT	Carter et al. (2020[125],2021)[126]
ROS changes in stem cell-mediated growth	<1 mT	Huizen et al. (2019)[82]
mitochondrial electron transport chain activity	0-1.93 mT	Sheu et al (2022)[128]
Others		
flavin adenine dinucleotide photochemistry	<20 mT	Antill et al. (2018)[133]
enzymatic ATP production	80 mT	Buchachenko et al. (2008)[134]
chlorophyll fluorescence/nutrient content of *Hordeum vulgare* L.	20/42/125/250 mT	Ercan et al. (2022)[135]
antioxidant defense system of plant cells	10/30 mT	Sahebjamei et al. (2006)[136]
enhance the killing effect of adriamycin on K562 cells.	8.8 mT	Hao et al.[137]
regeneration and plant growth of shoot tips	2.9–4.6 mT	Atak et al. (2007)[138]
accelerated loss of integrity of plasma membrane during apoptosis	6 mT	Teodori et al. (2002)[139]
macrophagic differentiation in human pro-monocytic U937 cells	6 mT	Pagliara et al. (2009)[140]
cell proliferation and cell death balance	0.5 mT	Buemi et al. (2001)[141]
growth and sporulation of phytopathogenic microscopic fungi	1 mT	Nagy et al. (2004)[142]

Table 2. Hypomagnetic field effects on different biological functions.



System	References
Development	
decrease in size and number of *Staphylococcus aureus*	Rosenbach (1884)[156]
changes of tinctorial, morphological, cultural, and biochemical properties in bacteria	Eerkin et al. (1976)[180]
newt (*Cynops pyrrhogaster*) - early developmental processes	Asashima et al.(1991)[157]
inhibition of early embryogenesis	Osipenko (2008)[158, 159]
Xenopus embryos- development	Mo et al. (2011)[160]
Arabidopsis- cryptochrome-related hypocotyl growth and flowering	Xu et al. (2012)[161, 162]
brown planthopper - development and reproduction	Wan et al. (2014)[163]
increased mortality in tardigrades	Erdmann et al. (2021)[164]
inhibition of anhydrobiotic abilities in tardigrades	Erdmann et al. (2017)[165]
developmental and behavioral effects in moths	Yan et al. (2021)[177]
cell proliferation in SH-SY5Y cells, ROS implicated	Wang et al. (2022)[179]
Circadian system	
fiddler crabs and other organisms- circadian clock	Brown (1960)[166]
human -circadian rhythms	Waver et al. (1970)[167]
bird -circadian clock	Bliss & Heppner (1976)[168]
mice - circadian rhythm/ increases algesia	Mo et al. (2015)[181]
Neurons and brain	
inhibition of stress-induced analgesia in male mice	Seppia et al. (2000)[182]
hamster - GABA in cerebellum and basilar nucleus	Junfeng, L.et al. (2001)[183]
mice - amnesia	Choleris et al. (2002)[184]
chick -long-term memory	Wang et al. (2003)[185]
impairment in learning abilities and memory of adult male mice	Wang et al. (2003)[186]
Drosophila - amnesia	Zhang et al. (2004)[187]
mice-analgesia	Prato et al. (2005)[188]
golden hamster- noradrenergic activities in the brainstem	Zhang et al. (2007)[189]
human cognitive processes	Sarimov et al. (2008)[178]
purified tubulin from calf brain- assembly	Wang et al. (2008)[170]
chickens needed additional noradrenaline for memory consolidation	Xiao et al. (2009)[190]
human- cognitive processes	Binhi & Sarimov (2009)[191]
human neuroblastoma cell - actin assembly and inhibits cell motility & proliferation	Mo et al. (2013)[192] (2016)[193]
human neuroblastoma cell -H_2O_2 production	Zhang et al. (2017)[194]
anxiety in adult male mice	Ding et al. (2018)[195]
mouse - proliferation of mouse neural progenitor and stem cells	Fu et la. (2016)[196]
DNA	
genetic mutations in *Drosophila* during space flight	Ikenaga et al. (1997)[172]
mouse embryonic stem cells (ESCs) culture- DNA methylation	Baek et al. (2019)[171]
human bronchial epithelial cells -DNA repair process	Xue et al. (2020)[197]
Others	
decreased enzyme activity in cells obtained from mice	Conley (1970)[176]
Ca^{2+} balance in meristem cell of pea roots	Belyavskaya (2001)[174]
ability to change color in *Xenopus laevis*	Leucht (1987)[198]
chromatin hypercondensation/decondensation in human fibroblasts/lymphocytes	Belyaev et al. (1997)[175]
increased protoplasts fusion	Nedukha et al. (2007)[199]
decreasing certain elements in rats' hair	Tombarkiewicz (2008)[200]
cancer-derived cell lines - cell cycle rates	Martino et al. (2010)[173]
human fibrosarcoma cancer cells - H_2O_2 production	Marino et al. (2012)[201]
mouse primary skeletal muscle cell- ROS levels	Fu et la. (2016)[202]
invertebrates and fish -calcium-dependent proteases	Kantserova et al. (2017)[203]

Zadeh-Haghighi & Simon. *arXiv:2204.09147* (2022).
Journal of Royal Society Interface
https://doi.org/10.1098/rsif.2022.0325

Weak Magnetic field and isotope effects in biology

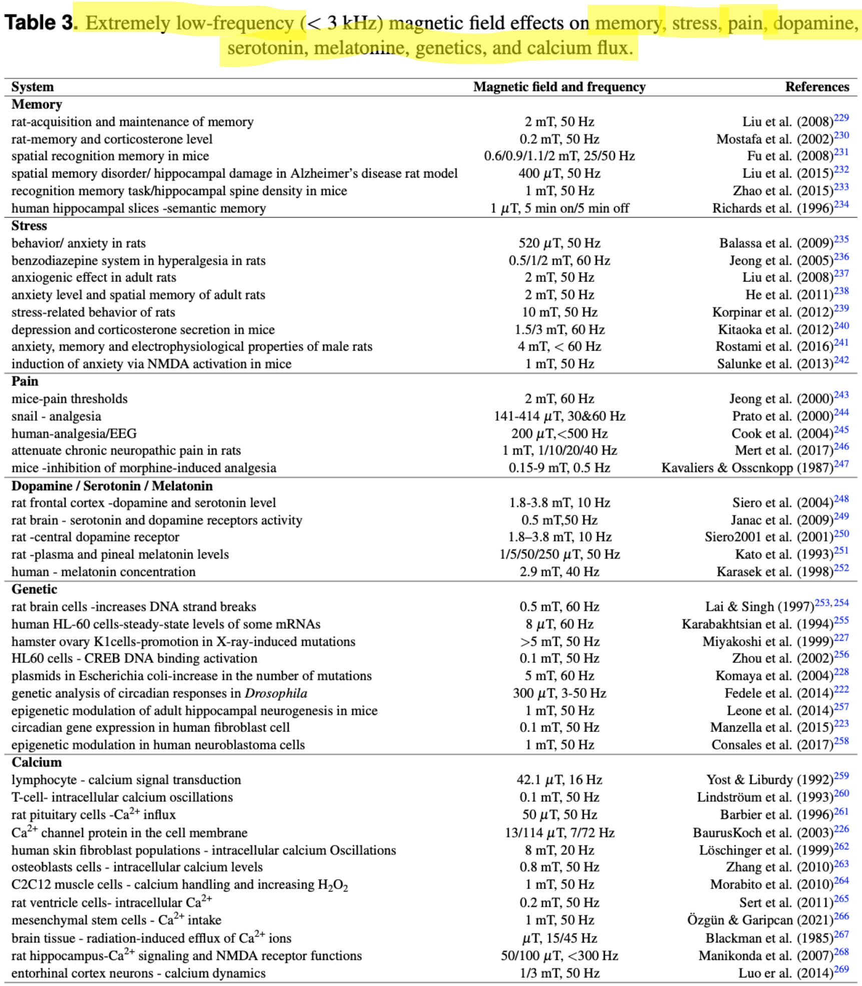


Table 3. Extremely low-frequency (< 3 kHz) magnetic field effects on memory, stress, pain, dopamine, serotonin, melatonine, genetics, and calcium flux.

System	Magnetic field and frequency	References
Memory		
rat-acquisition and maintenance of memory	2 mT, 50 Hz	Liu et al. (2008)[229]
rat-memory and corticosterone level	0.2 mT, 50 Hz	Mostafa et al. (2002)[230]
spatial recognition memory in mice	0.6/0.9/1.1/2 mT, 25/50 Hz	Fu et al. (2008)[231]
spatial memory disorder/ hippocampal damage in Alzheimer's disease rat model	400 μT, 50 Hz	Liu et al. (2015)[232]
recognition memory task/hippocampal spine density in mice	1 mT, 50 Hz	Zhao et al. (2015)[233]
human hippocampal slices -semantic memory	1 μT, 5 min on/5 min off	Richards et al. (1996)[234]
Stress		
behavior/ anxiety in rats	520 μT, 50 Hz	Balassa et al. (2009)[235]
benzodiazepine system in hyperalgesia in rats	0.5/1/2 mT, 60 Hz	Jeong et al. (2005)[236]
anxiogenic effect in adult rats	2 mT, 50 Hz	Liu et al. (2008)[237]
anxiety level and spatial memory of adult rats	2 mT, 50 Hz	He et al. (2011)[238]
stress-related behavior of rats	10 mT, 50 Hz	Korpinar et al. (2012)[239]
depression and corticosterone secretion in mice	1.5/3 mT, 60 Hz	Kitaoka et al. (2012)[240]
anxiety, memory and electrophysiological properties of male rats	4 mT, < 60 Hz	Rostami et al. (2016)[241]
induction of anxiety via NMDA activation in mice	1 mT, 50 Hz	Salunke et al. (2013)[242]
Pain		
mice-pain thresholds	2 mT, 60 Hz	Jeong et al. (2000)[243]
snail - analgesia	141-414 μT, 30&60 Hz	Prato et al. (2000)[244]
human-analgesia/EEG	200 μT,<500 Hz	Cook et al. (2004)[245]
attenuate chronic neuropathic pain in rats	1 mT, 1/10/20/40 Hz	Mert et al. (2017)[246]
mice -inhibition of morphine-induced analgesia	0.15-9 mT, 0.5 Hz	Kavaliers & Osscnkopp (1987)[247]
Dopamine / Serotonin / Melatonin		
rat frontal cortex -dopamine and serotonin level	1.8-3.8 mT, 10 Hz	Siero et al. (2004)[248]
rat brain - serotonin and dopamine receptors activity	0.5 mT,50 Hz	Janac et al. (2009)[249]
rat -central dopamine receptor	1.8–3.8 mT, 10 Hz	Siero2001 et al. (2001)[250]
rat -plasma and pineal melatonin levels	1/5/50/250 μT, 50 Hz	Kato et al. (1993)[251]
human - melatonin concentration	2.9 mT, 40 Hz	Karasek et al. (1998)[252]
Genetic		
rat brain cells -increases DNA strand breaks	0.5 mT, 60 Hz	Lai & Singh (1997)[253,254]
human HL-60 cells-steady-state levels of some mRNAs	8 μT, 60 Hz	Karabakhtsian et al. (1994)[255]
hamster ovary K1cells-promotion in X-ray-induced mutations	>5 mT, 50 Hz	Miyakoshi et al. (1999)[227]
HL60 cells - CREB DNA binding activation	0.1 mT, 50 Hz	Zhou et al. (2002)[256]
plasmids in Escherichia coli-increase in the number of mutations	5 mT, 60 Hz	Komaya et al. (2004)[228]
genetic analysis of circadian responses in *Drosophila*	300 μT, 3-50 Hz	Fedele et al. (2014)[222]
epigenetic modulation of adult hippocampal neurogenesis in mice	1 mT, 50 Hz	Leone et al. (2014)[257]
circadian gene expression in human fibroblast cell	0.1 mT, 50 Hz	Manzella et al. (2015)[223]
epigenetic modulation in human neuroblastoma cells	1 mT, 50 Hz	Consales et al. (2017)[258]
Calcium		
lymphocyte - calcium signal transduction	42.1 μT, 16 Hz	Yost & Liburdy (1992)[259]
T-cell- intracellular calcium oscillations	0.1 mT, 50 Hz	Lindströum et al. (1993)[260]
rat pituitary cells -Ca^{2+} influx	50 μT, 50 Hz	Barbier et al. (1996)[261]
Ca^{2+} channel protein in the cell membrane	13/114 μT, 7/72 Hz	BaurusKoch et al. (2003)[226]
human skin fibroblast populations - intracellular calcium Oscillations	8 mT, 20 Hz	Löschinger et al. (1999)[262]
osteoblasts cells - intracellular calcium levels	0.8 mT, 50 Hz	Zhang et al. (2010)[263]
C2C12 muscle cells - calcium handling and increasing H_2O_2	1 mT, 50 Hz	Morabito et al. (2010)[264]
rat ventricle cells- intracellular Ca^{2+}	0.2 mT, 50 Hz	Sert et al. (2011)[265]
mesenchymal stem cells - Ca^{2+} intake	1 mT, 50 Hz	Özgün & Garipcan (2021)[266]
brain tissue - radiation-induced efflux of Ca^{2+} ions	μT, 15/45 Hz	Blackman et al. (1985)[267]
rat hippocampus-Ca^{2+} signaling and NMDA receptor functions	50/100 μT, <300 Hz	Manikonda et al. (2007)[268]
entorhinal cortex neurons - calcium dynamics	1/3 mT, 50 Hz	Luo er al. (2014)[269]

Table 4. Extremely low-frequency (< 3 kHz) magnetic field effects on reactive oxygen species (ROS) levels.

System	Magnetic field	References
ROS		
ageing via ROS involvement in brain of mongolian gerbils	0.1/0.25/0.5 mT, 50 Hz	Selakovi et al. (2013)[270]
hippocampus mitochondria via increasing H_2O_2 in mice	8 mT, 50 Hz	Duan et al. (2013)[271]
neural differentiation/ H_2O_2 elevation in mesenchymal stem cells	1 mT, 50 Hz	Park et al. (2013)[272]
H_2O_2 production in neuroblastoma cell	2±0.2 mT, 75±2 Hz	Osera et al. (2015)[273]
pro-Parkinson's disease toxin MPP$^+$/ H_2O_2 increase in SH-SY5Y cells	1 mT, 50 Hz	Benassi et al. (2015)[274]
rat peritoneal neutrophils -oxidative burst	0.1 mT, 60 Hz	Roy et al. (1995)[275]
cortical synaptosomes of Wistar rats-oxidative stress	0.7 mT, 60 Hz	Túnez et al. (2006)[276]
pro-oxidant effects of H_2O_2 in human neuroblastoma cells	2 mT, 75 Hz	Falone et al. (2016)[277]
reducing hypoxia/inflammation damage ROS-mediated in neuron-like and microglial cells	1.5±0.2 mT, 75 Hz	Vincenzi et al. (2016)[278]
mouse brain-antioxidant defense system	1.2 mT, 60 Hz	Lee et al. (2004)[279]
rat-cortical neurons -redox and trophic response/ reducing ROS	1 mT, 50 Hz	DiLoreto et al. (2009)[280]
human monocytes-cell activating capacity/ROS modulation	1 mT, 50 Hz	Lupke et al. (2004)[281]
HL-60 leukemia cells- proliferation / DNA damage implicating ROS	1 mT, 50 Hz	Wolf et al. (2005)[282]
human monocytes-alteration of 986 genes/ modulating ROS	1 mT, 50 Hz	Lupke et al. (2006)[283]
prostate cancer cells -apoptosis through ROS	0.2 mT, 60 Hz	Koh et al. (2008)[284]
K562 cells -$O_2^{\bullet-}$ formation and HSP70 induction	0.025–0.1 mT, 50 Hz	Mannerling et al. (2010)[285]
K562 Cells -differentiation via increasing $O_2^{\bullet-}$ production	5 mT, 50 Hz	AySe et al. (2010)[286]
K562 leukemia cell -number of apoptotic cells via increasing $O_2^{\bullet-}$ production	1 mT, 50 Hz	Garip & Akan (2010)[287]
PC12 cells -H_2O_2 increase	1 mT, 50 Hz	Morabito et al. (2010)[288]
carcinoma cells - cisplatin via increasing H_2O_2	1 mT, 50 Hz	Bułdak et al. (2012)[289]
human carcinoma cells -morphology and biochemistry implicating ROS	0.1 mT, 100&217 Hz	Sadeghipour et al. (2012)[290]
rats- DNA strand breaks in brain cells by modulating ROS	0.1–0.5 mT, 60 Hz	Lai & Singh(2004)[291]
cardiomyocytes-injury treatment implicating ROS	4.5 mT, 15 Hz	Ma et al. (2013)[292]
genomic instability/oxidative processes in human neuroblastoma cells	100μT, 50 Hz	Luukkonen et al. (2014)[293]
expression of NOS and $O_2^{\bullet-}$ in human SH-SY5Y cells	1 mT, 50 Hz	Reale et al. (2014)[294]
ROS-related autophagy in mouse embryonic fibroblasts	2 mT, 50 Hz	Chen et al. (2014)[295]
healing via reducing ROS production in artificial skin wounds	< 40 μT, 100 Hz	Ferroni et al. (2015)[296]
apoptosis via oxidative stress in human osteosarcoma cells	1mT, 50 Hz	Yang et al. (2015)[297]
increase $O_2^{\bullet-}$ in erythro-leukemic cells	1 mT, 50 Hz	Patruno et al. (2015)[298]
Genomic instability/ H_2O_2 increase in SH-SY5Y cells	100 μT, 50 Hz	Kesari et al. (2015)[299]
Nox-produced ROS in hAECs	0.4 mT, 50 Hz	Feng et al. (2016)[300]
mitochondrial permeability via increasing H_2O_2 in human aortic endothelial cells	0.4 mT, 50 Hz	Feng et al. (2016)[301]
apoptotic via mitochondrial $O_2^{\bullet-}$ release in human aortic endothelial cells	0.4 mT, 50 Hz	Feng et al. (2016)[302]
antioxidant activity implicating H_2O_2 in human keratinocyte cells	25-200 μT, 1-50 Hz	Calcabrini et al. (2016)[303]
antioxidative defense mechanisms via ROS in human osteoblasts	2-282 μT, 16 Hz,	Ehnert et al. (2017)[304]
astrocytic differentiation implicating ROS in human bone stem cells	1 mT, 50 Hz	Jeong et al. (2017)[305]
reduce mitochondrial $O_2^{\bullet-}$ production in human neuroblastoma cells	100 μT, 50 Hz	Höytö et al. (2017)[306]
ROS production in human cryptochrome	1.8 mT, <100 Hz	Sherrard et al. (2018)[219]
proliferation by decreasing intracellular ROS levels in human cells	10 mT, 60 Hz	Song et al. (2018)[307]
cytotoxic effect in by raising intracellular ROS in human GBM cells	1–58 mT, 350 Hz	Helekar et al. (2021)[308]

Zadeh-Haghighi & Simon. *arXiv:2204.09147* (2022). *Journal of Royal Society Interface*. **https://doi.org/10.1098/rsif.2022.0325**

Weak Magnetic field and isotope effects in biology

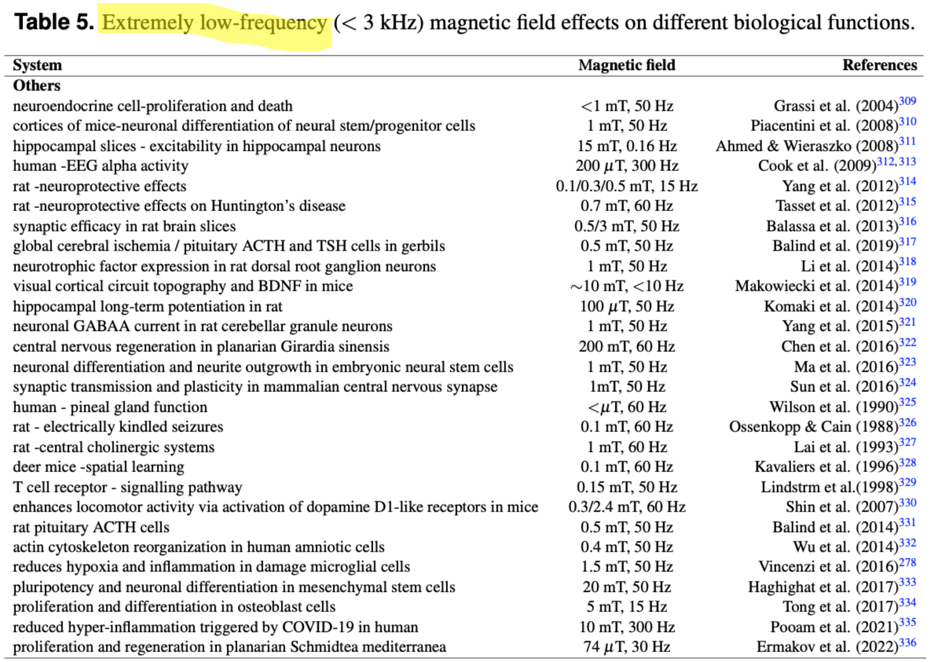


Table 5. Extremely low-frequency (< 3 kHz) magnetic field effects on different biological functions.

System	Magnetic field	References
Others		
neuroendocrine cell-proliferation and death	<1 mT, 50 Hz	Grassi et al. (2004)[309]
cortices of mice-neuronal differentiation of neural stem/progenitor cells	1 mT, 50 Hz	Piacentini et al. (2008)[310]
hippocampal slices - excitability in hippocampal neurons	15 mT, 0.16 Hz	Ahmed & Wieraszko (2008)[311]
human -EEG alpha activity	200 μT, 300 Hz	Cook et al. (2009)[312,313]
rat -neuroprotective effects	0.1/0.3/0.5 mT, 15 Hz	Yang et al. (2012)[314]
rat -neuroprotective effects on Huntington's disease	0.7 mT, 60 Hz	Tasset et al. (2012)[315]
synaptic efficacy in rat brain slices	0.5/3 mT, 50 Hz	Balassa et al. (2013)[316]
global cerebral ischemia / pituitary ACTH and TSH cells in gerbils	0.5 mT, 50 Hz	Balind et al. (2019)[317]
neurotrophic factor expression in rat dorsal root ganglion neurons	1 mT, 50 Hz	Li et al. (2014)[318]
visual cortical circuit topography and BDNF in mice	~10 mT, <10 Hz	Makowiecki et al. (2014)[319]
hippocampal long-term potentiation in rat	100 μT, 50 Hz	Komaki et al. (2014)[320]
neuronal GABAA current in rat cerebellar granule neurons	1 mT, 50 Hz	Yang et al. (2015)[321]
central nervous regeneration in planarian Girardia sinensis	200 mT, 60 Hz	Chen et al. (2016)[322]
neuronal differentiation and neurite outgrowth in embryonic neural stem cells	1 mT, 50 Hz	Ma et al. (2016)[323]
synaptic transmission and plasticity in mammalian central nervous synapse	1mT, 50 Hz	Sun et al. (2016)[324]
human - pineal gland function	<μT, 60 Hz	Wilson et al. (1990)[325]
rat - electrically kindled seizures	0.1 mT, 60 Hz	Ossenkopp & Cain (1988)[326]
rat -central cholinergic systems	1 mT, 60 Hz	Lai et al. (1993)[327]
deer mice -spatial learning	0.1 mT, 60 Hz	Kavaliers et al. (1996)[328]
T cell receptor - signalling pathway	0.15 mT, 50 Hz	Lindstrm et al.(1998)[329]
enhances locomotor activity via activation of dopamine D1-like receptors in mice	0.3/2.4 mT, 60 Hz	Shin et al. (2007)[330]
rat pituitary ACTH cells	0.5 mT, 50 Hz	Balind et al. (2014)[331]
actin cytoskeleton reorganization in human amniotic cells	0.4 mT, 50 Hz	Wu et al. (2014)[332]
reduces hypoxia and inflammation in damage microglial cells	1.5 mT, 50 Hz	Vincenzi et al. (2016)[278]
pluripotency and neuronal differentiation in mesenchymal stem cells	20 mT, 50 Hz	Haghighat et al. (2017)[333]
proliferation and differentiation in osteoblast cells	5 mT, 15 Hz	Tong et al. (2017)[334]
reduced hyper-inflammation triggered by COVID-19 in human	10 mT, 300 Hz	Pooam et al. (2021)[335]
proliferation and regeneration in planarian Schmidtea mediterranea	74 μT, 30 Hz	Ermakov et al. (2022)[336]

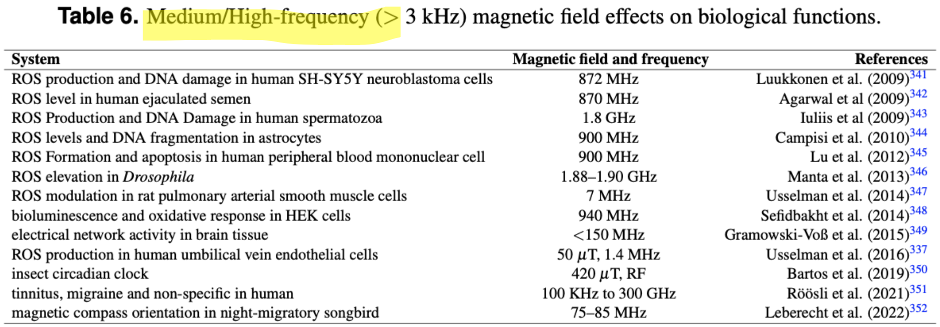


Table 6. Medium/High-frequency (> 3 kHz) magnetic field effects on biological functions.

System	Magnetic field and frequency	References
ROS production and DNA damage in human SH-SY5Y neuroblastoma cells	872 MHz	Luukkonen et al. (2009)[341]
ROS level in human ejaculated semen	870 MHz	Agarwal et al (2009)[342]
ROS Production and DNA Damage in human spermatozoa	1.8 GHz	Iuliis et al (2009)[343]
ROS levels and DNA fragmentation in astrocytes	900 MHz	Campisi et al. (2010)[344]
ROS Formation and apoptosis in human peripheral blood mononuclear cell	900 MHz	Lu et al. (2012)[345]
ROS elevation in *Drosophila*	1.88–1.90 GHz	Manta et al. (2013)[346]
ROS modulation in rat pulmonary arterial smooth muscle cells	7 MHz	Usselman et al. (2014)[347]
bioluminescence and oxidative response in HEK cells	940 MHz	Sefidbakht et al. (2014)[348]
electrical network activity in brain tissue	<150 MHz	Gramowski-Voß et al. (2015)[349]
ROS production in human umbilical vein endothelial cells	50 μT, 1.4 MHz	Usselman et al. (2016)[337]
insect circadian clock	420 μT, RF	Bartos et al. (2019)[350]
tinnitus, migraine and non-specific in human	100 KHz to 300 GHz	Röösli et al. (2021)[351]
magnetic compass orientation in night-migratory songbird	75–85 MHz	Leberecht et al. (2022)[352]

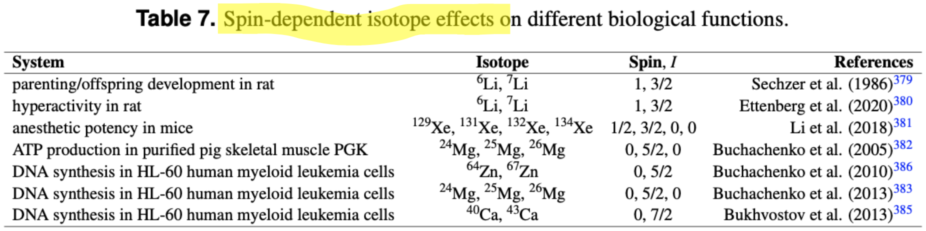


Table 7. Spin-dependent isotope effects on different biological functions.

System	Isotope	Spin, *I*	References
parenting/offspring development in rat	^{6}Li, ^{7}Li	1, 3/2	Sechzer et al. (1986)[379]
hyperactivity in rat	^{6}Li, ^{7}Li	1, 3/2	Ettenberg et al. (2020)[380]
anesthetic potency in mice	^{129}Xe, ^{131}Xe, ^{132}Xe, ^{134}Xe	1/2, 3/2, 0, 0	Li et al. (2018)[381]
ATP production in purified pig skeletal muscle PGK	^{24}Mg, ^{25}Mg, ^{26}Mg	0, 5/2, 0	Buchachenko et al. (2005)[382]
DNA synthesis in HL-60 human myeloid leukemia cells	^{64}Zn, ^{67}Zn	0, 5/2	Buchachenko et al. (2010)[386]
DNA synthesis in HL-60 human myeloid leukemia cells	^{24}Mg, ^{25}Mg, ^{26}Mg	0, 5/2, 0	Buchachenko et al. (2013)[383]
DNA synthesis in HL-60 human myeloid leukemia cells	^{40}Ca, ^{43}Ca	0, 7/2	Bukhvostov et al. (2013)[385]

Zadeh-Haghighi & Simon. *arXiv:2204.09147* (2022).
Journal of Royal Society Interface.
https://doi.org/10.1098/rsif.2022.0325

Radical pair mechanism

Certain chemical reaction yields are affected by exposure to magnetic fields.

Magnetic energies millions of times lower than thermal energies.

Radicals; transient molecules; molecules with an odd number of electrons in the outer shell.

Created by electron transfer from one molecule to another or by breaking a chemical bond.

Spatially separated and spin correlated (typically singlet or triplet).

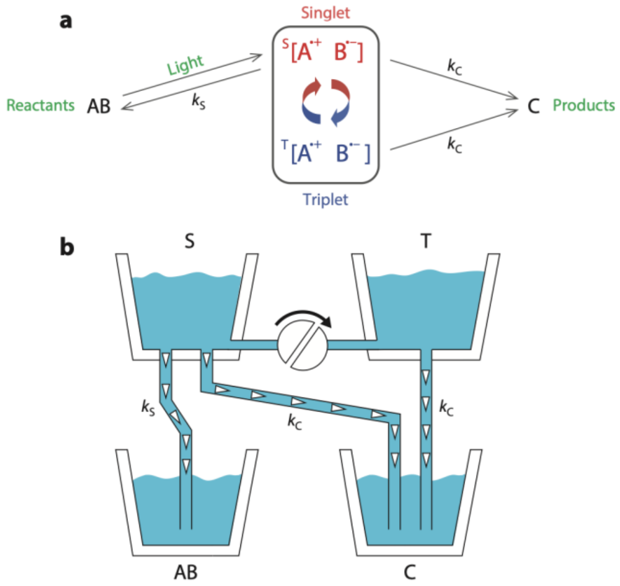
Steiner & Ulrich, *Chem. Rev.* **89**, 51 (1989). Hore & Mouritsen, *Ann. Rev. Biophys.* **299**, 45 (2016).

Radical pair mechanism

Hamiltonian: Zeeman (electrons and external magnetic field), hyperfine (electron-nucleus), dipolar and exchange (electron-electron).

Spin state of the radical pair undergoes singlet-triplet interconversion.

Spin state determines chemical reaction products.



Hore & Mouritsen, *Ann. Rev. Biophys.* **299**, 45 (2016).

Radical pairs in biology

Cryptochrome-based radical pairs

- Avian magnetoreception: cryptochrome: flavin adenine dinucleotide (FAD) and tryptophan (Trp) [$FAD^{\cdot -}$ …$Trp^{\cdot +}$], and FADH and superoxide [$FADH^{\bullet}$ … $O_2^{\cdot -}$].

  Player & Hore, *J. Chem. Phys.*, **151**, 225101 (2019).

- Cryptochrome is also implicated in axon growth response to TMS.

  Dufor et al. *Sci. Adv.*, **V5**, eavv9847 (2019).

Beyond cryptochrome-based radical pairs

- Trafficking of the RP is more important than the specific nature of the RP; magnetosensitivity is likely to be a widespread property of cells.

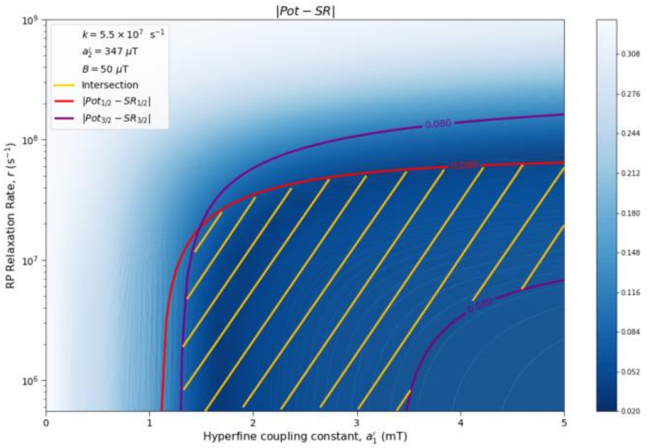
- Other, non-photochemical RPs, may contribute to magnetoreception, which is consistent with magnetoreception in darkness.

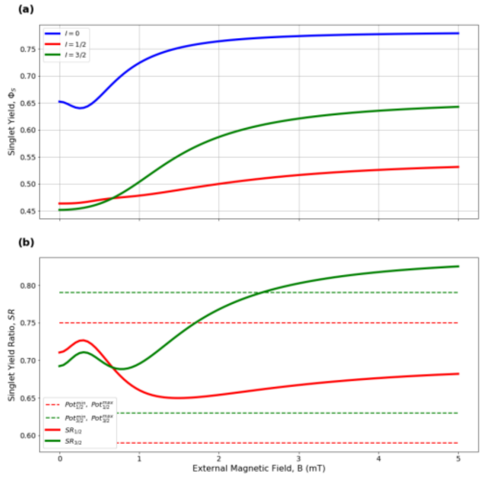
  Bradlaugh et al., *preprint* bioRxiv 2021.10.29.466426v1 (2021).

- Trp, Tyr, histidine (His), and proline (Pro).

Xenon anesthesia

- Anesthesia provides an important window on consciousness, but many open questions.
- Recent experiments on xenon anesthesia implicate electron and nuclear spins (electron spin resonance with fruitflies, isotope effects for mice).
- Our **radical pair model** can explain the observed nuclear spin-dependent isotope effects quantitatively (and the electron spin resonance effects qualitatively)

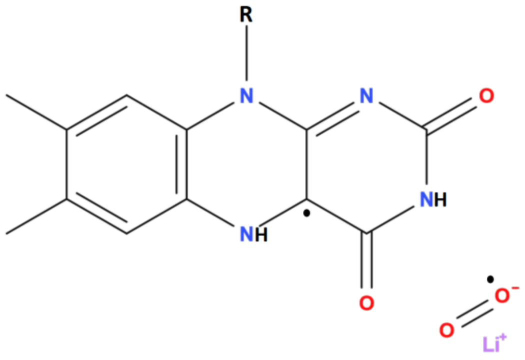


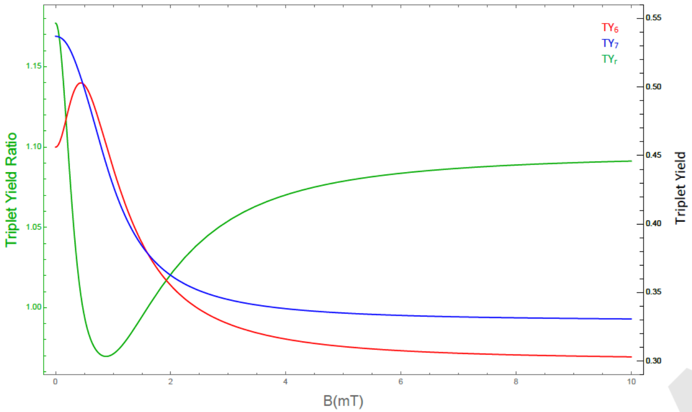


We predict **magnetic field effects** on anesthetic potency that can be tested experimentally.

J. Smith, H. Zadeh-Haghighi, D. Salahub, C. Simon, *Scientific Reports* **11**, 6287 (2021)

Lithium effects on mania





Reproduces isotope effects for hyperactivity in rats

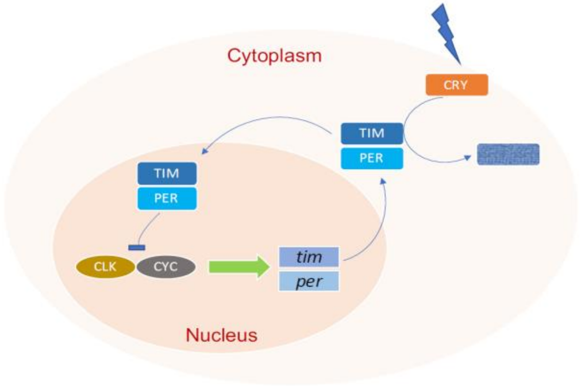
Alternative explanation to Posner molecules

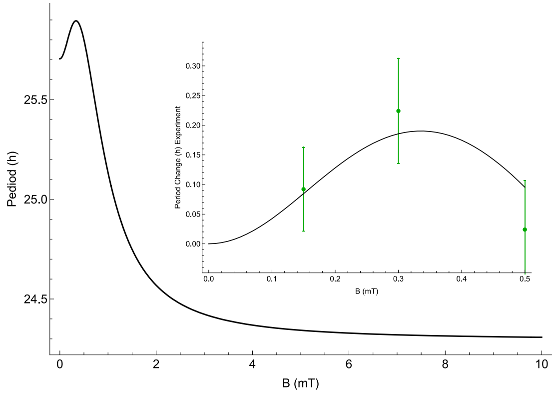
Predicts **magnetic field effects**

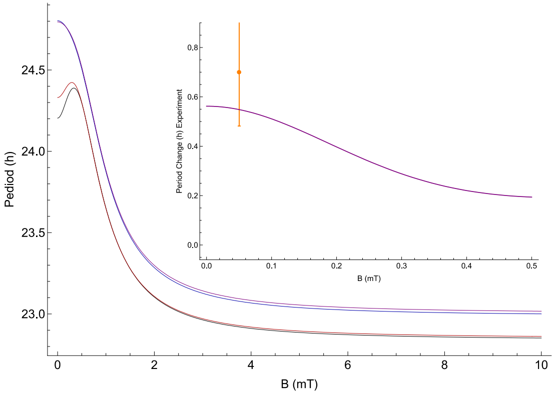
Another piece of evidence that entanglement may be important for the brain

Zadeh-Haghighi and Simon, *Scientific Reports* **11**, 12121 (2021)

Drosophila's circadian clock







Chemical oscillator model of the circadian clock (mRNA, protein)

CRY radical pair dynamics modifies a key rate – changes clock period

Our model reproduces experimental observations.

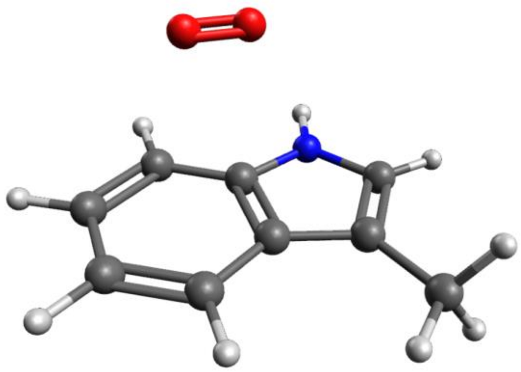
We predict a **shortening of the period at higher fields**, as well as lithium isotope effects.

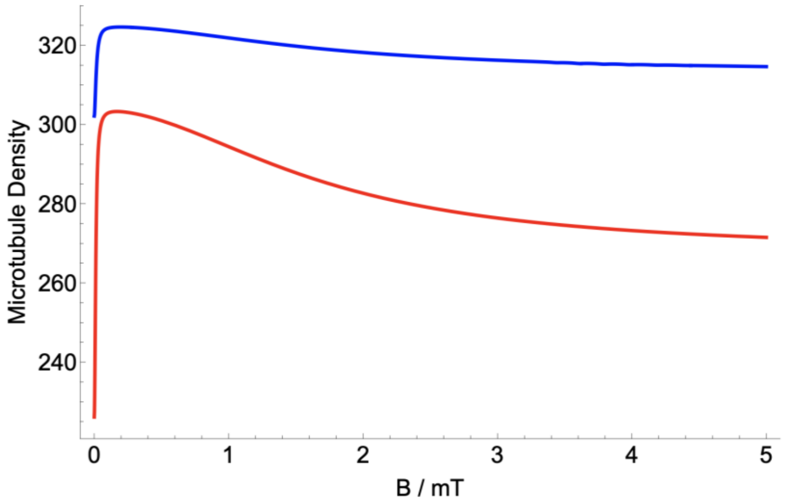
H. Zadeh-Haghighi and C. Simon, *Scientific Reports* **12**, 269 (2022)

Hypomagnetic field effects on microtubule reorganization

Shielding geomagnetic field causes disorders in microtubule assembly.

Combining radical pair model (based on **tryptophan-superoxide**) and simple model of microtubule assembly can explain experimental results.

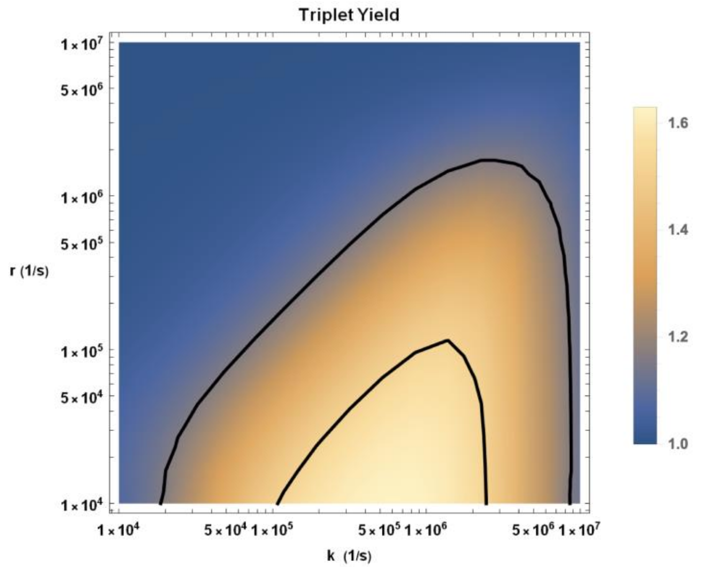




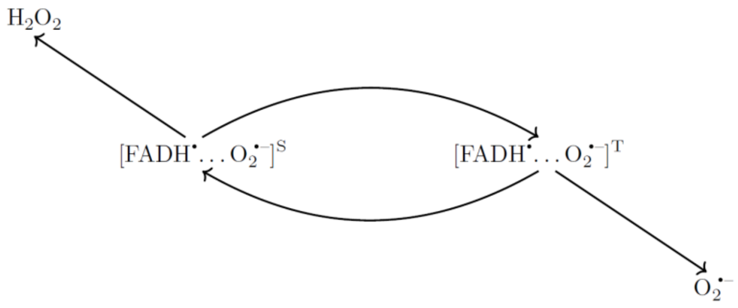
Our model predicts small effects at higher fields and zinc isotope effects.

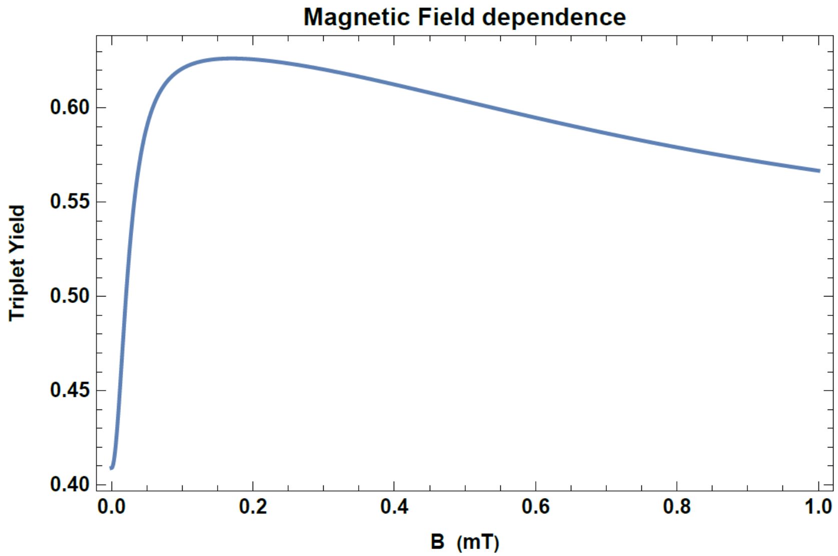
Zadeh-Haghighi & Simon. *Sci. Rep.* ***12**, 6109* (2022).

Hypomagnetic fields and hippocampal neurogenesis



Triplet yield ratio (GMF to HMF) for singlet-born RP in the $k - r$





Singlet-born radical pair can explain why shielding the geomagnetic field causes a decrease in **superoxide**. Size of the effect is comparable to observed change in neurogenesis.

Rishabh, Zadeh-Haghighi, Salahub & Simon. *PLOS Comput. Biol* 18(6):e1010198 (2022).

Experimental collaborations

- Biophotons: imaging, spectroscopy, magnetic field effects (D. Oblak, V. Salari, S. MacFarlane, G. Bertolesi, UCalgary; D. England, U. Iqbal, M. Moreno, J. Tauskela, NRC Ottawa)
- Magnetic field effects on stem cells in planaria (W. Beane, WMU)
- Magnetic field effects on circadian clock (S. MacFarlane, G. Bertolesi, UCalgary)
- Isotope effects and magnetic field effects on microtubule assembly (T. Craddock, NSU)
- Biophotons and magnetic field effects (N. Murugan, Algoma U/WLU)

Conclusions and Outlook

- **Photons guided by axons** could enable classical as well as **quantum communication** in the brain

  Kumar, Boone, Tuszynski, Barclay, Simon, Scientific Reports 6, 36508 (2016)

  Zarkeshian, Kergan, Ghobadi, Nicola, Simon, arXiv:2203.11135 (2022)

- The **entanglement of electron spins in radical pairs** may be what is disturbed by **anesthetics.** A similar mechanism may underlie isotope effects for **lithium** treatment of **mania**, and magnetic field effects on the **circadian clock**, on **microtubules**, on **neurogenesis,** and possibly many other biological phenomena.

  Smith, Zadeh Haghighi, Salahub, Simon, Scientific Reports 11, 6287 (2021)

  Zadeh-Haghighi & Simon, Scientific Reports 11, 12121 (2021)

  Zadeh-Haghighi & Simon, Scientific Reports 12, 269 (2022)

  Zadeh-Haghighi & Simon, Scientific Reports 12, 6109 (2022)

  Rishabh, Zadeh-Haghighi, Salahub, Simon, PLoS Comp Bio 18, e1010198 (2022)

  Zadeh-Haghighi & Simon, J. Roy. Soc. Interface https://doi.org/10.1098/rsif.2022.0325 (2022)

- These results are consistent with the idea that **large-scale entanglement** (e.g created via radical pair processes and distributed via photons) could be fundamental for **consciousness**

  C. Simon, arXiv:1809.03490, J. Consc. Stud. 26, 204 (2019)

Thanks to my group members, collaborators, and funders on ‘quantum neuroscience’ topics

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Wendy Beane (W Michigan U)

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