



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)

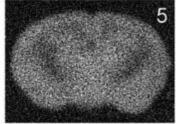
Photons and spins would be natural choices

- 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}***

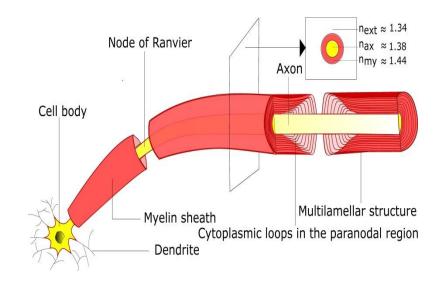


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- Reactive oxygen species in mitochondria are one likely source
- Could these photons be used for **communication**?
- Potential single-photon detectors exist in the brain, e.g. opsins
- My focus is on quantum communication, but even classical communication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

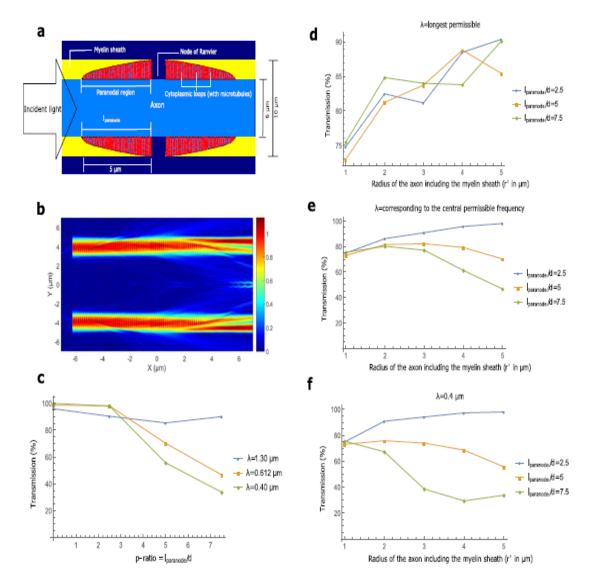
Kumar, Boone, Tuszynski, Barclay, Simon, Scientific Reports 6, 36508 (2016)

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.

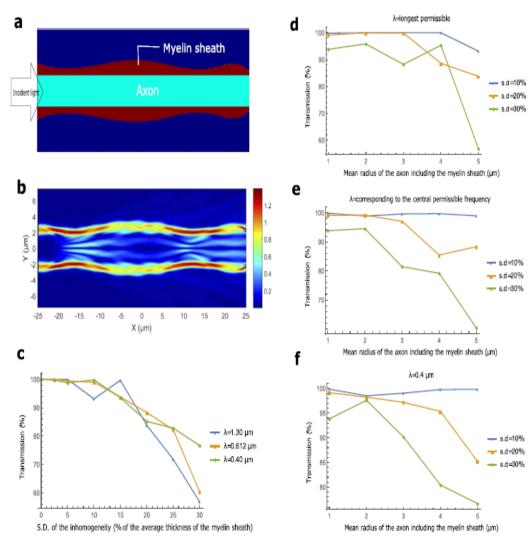
Kumar, Boone, Tuszynski, Barclay, Simon, Scientific Reports 6, 36508 (2016)



Varying cross-sectional area

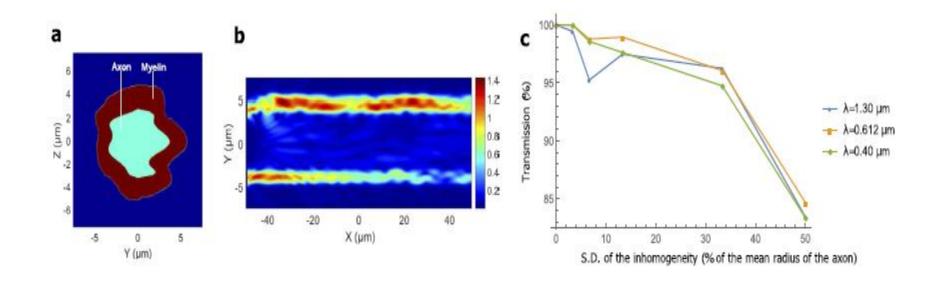
Cross-sectional area varies for realistic axons.

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.

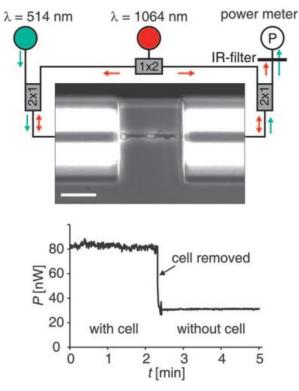
Also looked at bends, cross-talk between axons, absorption.

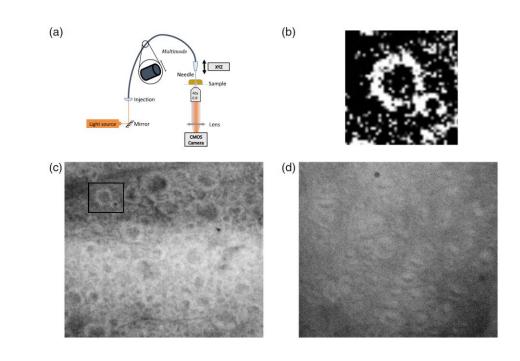
Kumar, Boone, Tuszynski, Barclay, Simon, Scientific Reports 6, 36508 (2016)

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!

Article

Violet-light suppression of thermogenesis by opsin 5 hypothalamic neurons

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

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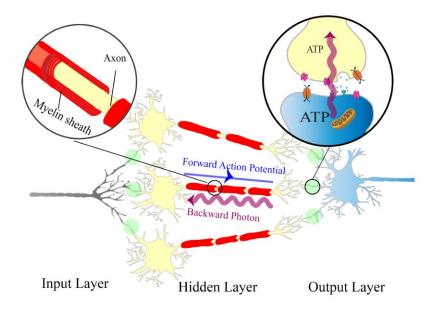
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The opsin family of G-protein-coupled receptors are used as light detectors in animals. Opsin 5 (also known as neuropsin or OPN5) is a highly conserved opsin that is sensitive to visible violet light^{1,2}. In mice, OPN5 is a known photoreceptor in the retina³ and skin⁴ 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 exvivo 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.

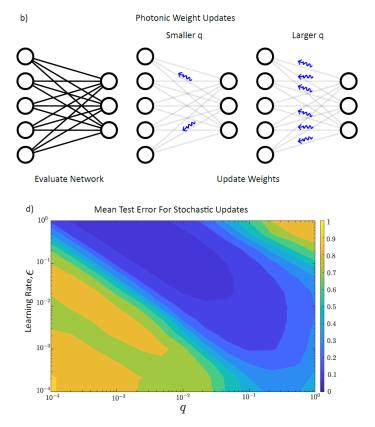
Photons might enable learning in the brain by stochastic backpropagation



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

Photons and spins would be natural choices

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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	8	
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 <i>Drosophila</i> (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 <i>Drosophila melanogaster</i>	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 <i>in vitro</i>	0.5-30 mT	Abdolmaleki et al. ^{84–86}
Calcium	010 00 111	
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 <i>in vitro</i> 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	0 111	Chionna et al. (2003)
blocked sensory neuron action potentials in the somata of adult mouse	10 mT	McLean et al. (1995) ⁹²
	50 mT	Weintraub et al $(2003)^{105}$
symptomatic diabetic neuropathy ROS	30 111	weintraub et al (2003)
increased intercellular ROS in human neuroblastoma cells	2.2 mT	Calabr et al. (2013) ¹¹⁶
		Vergallo et al. $(2013)^{117}$
increased intercellular ROS in human neuroblastoma cells	31.7–232 mT 1-10 mT	Bekhite et al. $(2014)^{119}$
increased H ₂ O ₂ level in embryoid bodies		
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 ₂ O 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		122
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

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

 Table 2. Hypomagnetic field effects on different biological functions.

System	Reference
Development	
decrease in size and number of Staphylococcus aureus	Rosenbach (1884) ¹⁵
changes of tinctorial, morphological, cultural, and biochemical properties in bacteria	Eerkin et al. (1976) ¹⁸
newt (Cynops pyrrhogaster) - early developmental processes	Asashima et al.(1991) ¹⁵
nhibition of early embryogenesis	Osipenko (2008) ^{158, 15}
Xenopus embryos- development	Mo et al. $(2011)^{10}$
Arabidopsis- cryptochrome-related hypocotyl growth and flowering	Xu et al. (2012) ^{161, 10}
prown planthopper - development and reproduction	Wan et al. (2014) ¹⁰
increased mortality in tardigrades	Erdmann et al. (2021) ¹⁰
nhibition of anhydrobiotic abilities in tardigrades	Erdmann et al. (2017) ¹
developmental and behavioral effects in moths	Yan et al. (2021) ¹
cell proliferation in SH-SY5Y cells, ROS implicated	Wang et al. (2022) ¹
Circadian system	
fiddler crabs and other organisms- circadian clock	Brown (1960) ¹⁰
numan -circadian rhythms	Waver et al. $(1970)^{1}$
bird -circadian clock	Bliss & Heppner (1976) ¹
nice - circadian rhythm/ increases algesia	Mo et al. $(2015)^{1}$
Neurons and brain	
nhibition of stress-induced analgesia in male mice	Seppia et al. (2000) ¹
hamster - GABA in cerebellum and basilar nucleus	Junfeng, L.et al. $(2001)^{1}$
nice - amnesia	Choleris et al. $(2002)^1$
chick -long-term memory	Wang et al. $(2003)^{1}$
impairment in learning abilities and memory of adult male mice	Wang et al. $(2003)^{11}$
Drosophila - amnesia	Zhang et al. $(2003)^{11}$
nice-analgesia	Prato et al. $(2005)^{11}$
golden hamster- noradrenergic activities in the brainstem	Zhang et al. $(2007)^{11}$
numan cognitive processes	Sarimov et al. $(2008)^1$
purified tubulin from calf brain- assembly	Wang et al. $(2008)^1$
chickens needed additional noradrenaline for memory consolidation	Xiao et al. $(2009)^{1}$
•	Binhi & Sarimov (2009) ¹
numan- cognitive processes	Mo et al. $(2013)^{192} (2016)^1$
numan neuroblastoma cell - actin assembly and inhibits cell motility & proliferation	Zhang et al. $(2013)^{1/2}$ $(2017)^{1/2}$
numan neuroblastoma cell $-H_2O_2$ production	
anxiety in adult male mice	Ding et al. $(2018)^{11}$
nouse - proliferation of mouse neural progenitor and stem cells	Fu et la. (2016) ¹
genetic mutations in <i>Drosophila</i> during space flight	Ikenaga et al. (1997) ¹
nouse embryonic stem cells (ESCs) culture- DNA methylation	Baek et al. $(2019)^1$
numan bronchial epithelial cells -DNA repair process	Xue et al. $(2019)^{1}$
Others	Aue et al. (2020)
decreased enzyme activity in cells obtained from mice	Conley (1970) ¹
Ca^{2+} balance in meristem cell of pea roots	Belyavskaya (2001) ¹
ability to change color in <i>Xenopus laevis</i>	Leucht (1987) ¹⁹
	Belyaev et al. $(1987)^{12}$
chromatin hypercondensation/decondensation in human fibroblasts/lymphocytes	Nadukha at al. $(1997)^{-1}$
increased protoplasts fusion	Nedukha et al. $(2007)^{1}$
decreasing certain elements in rats' hair	Tombarkiewicz (2008) ²
cancer-derived cell lines - cell cycle rates	Martino et al. $(2010)^{17}$
numan fibrosarcoma cancer cells - H_2O_2 production	Marino et al. $(2012)^2$
mouse primary skeletal muscle cell- ROS levels	Fu et la. (2016) ²
nvertebrates and fish -calcium-dependent proteases	Kantserova et al. (2017) ²

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.</th>

SystemMagnetic field and frequencyReferencesMemory2 mT, 50 HzLiu et al. (2008) ²¹⁰ rat-acquisition and maintenance of memory2 mT, 50 HzLiu et al. (2008) ²¹⁰ spatial recorgition memory in mice0.60.991.1/2 mT, 2550 HzFue et al. (2005) ²¹⁰ spatial memory disorder/ hippocampal spine density in mice1 mT, 50 HzLiu et al. (2015) ²¹² recognition memory task/hippocampal spine density in mice1 mT, 50 HzEute et al. (2005) ²¹⁰ stress520 µT, 50 HzBalassa et al. (2009) ²¹³ behavior d matery in rats0.571/2 mT, 60 HzFlaess et al. (2005) ²¹³ anxicey in rats0.571/2 mT, 60 HzHe et al. (2005) ²¹³ anxicey in rats0.571/2 mT, 60 HzFlaess et al. (2005) ²¹⁴ stress-related behavior of rats1 D mT, 50 HzKinaka et al. (2012) ²¹⁰ depression and corricostrone secretion in mice1.53 mT, 60 HzReinawa et al. (2012) ²¹⁰ anxiety, memory and dectorphysicological properties of male rats1 mT, 50 HzRoute al. (2009) ²¹⁴ nucce pain thresholds2 mT, 60 HzPrinto et al. (2000) ²¹⁴ small - analgesia0.15-9 mT, 0.51 HzKanaka et al. (2009) ²¹⁴ stress-related behavior of rats1 mT, 10/20/40 HzMert et al. (2009) ²¹⁴ smale - analgesia0.15-9 mT, 0.51 HzKanalers et al. (2009) ²¹⁴ smale - analgesia0.15-9 mT, 0.51 HzSalunke et al. (2009) ²¹⁴ smale - analgesia0.15-9 mT, 0.51 HzKanalers et al. (2009) ²¹⁴ smale - analgesia0.15-9 mT, 0.51 HzKanalers et al. (2009) ²¹⁴			
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anxiety, memory and electrophysiological properties of male rats 4 mT , $\leq 60 \text{ Hz}$ 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 $141+414 \mu$ T, 30&660 Hz Prato 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 $0.15-9 \text{ mT}$, 0.5 Hz Kavaliers & Ossenkopp (1987) ²⁴⁷ Dopamine / Serotonin / Melatonin rat frontal cortex -dopamine and serotonin level $1.8-3.8 \text{ mT}$, 10 Hz Siero et al. (2004) ²⁴⁸ attenuate chronic neuropathic pain in receptor $1.8-3.8 \text{ mT}$, 10 Hz Siero et al. (2009) ²⁴⁹ rat central dopamine receptor $1.8-3.8 \text{ mT}$, 10 Hz Siero 2001 et al. (2009) ²⁴⁹ rat central dopamine receptor 2.9 mT , 40 Hz Karasek et al. (1998) ²⁵¹ Genetic rat brain - serotonin and dopamine receptor 2.9 mT , 40 Hz Karasek et al. (1998) ²⁵¹ thorman - melatonin concentration 2.9 mT , 40 Hz Karasek et al. (1998) ²⁵¹ thorman - melatonin concentration 2.9 mT , 60 Hz Karabakhisian et al. (1999) ²⁵² thorman + melatonic noncentration 0.1 mT , 50 Hz Miyakoshi et al. (2004) ²⁴⁸ plasmids in Escherichia coli-increase in the number of mutations 5 mT , 60 Hz Karabakhisian et al. (2004) ²⁵⁸ plasmids in Escherichia coli-increase in the number of mutations 5 mT , 60 Hz Karabakhisian et al. (2004) ²⁵⁸ plasmids in Escherichia coli-increase in the number of mutations 5 mT , 60 Hz Karabakhisian et al. (2014) ²²⁸ epigenetic modulation of adult hippocampla neurogenesis in mice 1 mT , 50 Hz Consales et al. (2014) ²²⁹ epigenetic modulation in human neuroblast cells 0.1 mT , 50 Hz Liongenesis an (2002) ²⁵⁸ Calcium Jmine neuroblast cells 0.1 mT , 50 Hz Liongenesis and (2017) ²⁵⁸ Calcium signal transduction $- \text{ intracellular calcium Oscillations 0.1 \text{ mT}, 50 Hz Liongenesis et al. (2017)258Cad$	stress-related behavior of rats	10 mT, 50 Hz	Korpinar et al. (2012) ²³⁹
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$\begin{array}{cccc} \mbox{mic-pain thresholds} & 2 \mbox{mic-pain thresholds} & 141444 \mbox{mic-main-gain/2004} \mbox{Hz} & Cook et al. (2000) ^{244} \\ \mbox{mura-analgesia/EEG} & 200 \mbox{\mur}_{<} < S00 \mbox{Hz} & Cook et al. (2001) ^{247} \\ \mbox{mic-inhibition of morphine-induced analgesia} & 0.159 \mbox{mic-molareshold} & 0.5 \mbox{mic-molareshold} &$	induction of anxiety via NMDA activation in mice	1 mT, 50 Hz	Salunke et al. (2013)242
snail - analgesia141-141 μ 17, 30&600 HzPrane et al. (2000) 244human-analgesi/EEG200 μ T, <500 Hz	Pain		
$\begin{split} \text{human-malgesia/EEG} & 200 \ \mu\text{T}, 2500 \ \text{Hz} & Cook et al. (2004)^{245} \\ \text{attenuate chronic neuropathic pain in rats} & 1 \ \text{mT}, 1/1020/40 \ \text{Hz} & Mert et al. (2017)^{246} \\ \text{mc}: -inhibition of morphine-induced analgesia} & 0.15-9 \ \text{mT}, 0.5 \ \text{Hz} & Kavaliers \& Ossenkopp (1987)^{247} \\ \hline \text{Dopamite / Serotonin / Melatonin} \\ \text{rat frontal cortex -dopamine and serotonin level} & 1.8-3.8 \ \text{mT}, 10 \ \text{Hz} & Siero et al. (2004)^{246} \\ \text{rat tarb taris -serotonin and dopamine receptors activity } & 0.5 \ \text{mT}, 50 \ \text{Hz} & Janac et al. (2009)^{249} \\ \text{rat -central dopamine receptor articles & 1/55/0/250 \ \mu\text{T}, 50 \ \text{Hz} & Siero 2001 \ et al. (2001)^{250} \\ \text{numan - melatonin concentration & 2.9 \ \text{mT}, 40 \ \text{Hz} & Karasek \ et al. (1993)^{252} \\ \text{Genetic } \\ \text{rat brain - seleady-state levels of some mRNAs & 8 \ \mu\text{T}, 60 \ \text{Hz} & Karasek \ et al. (1994)^{255} \\ \text{hamaster ovary K lcells-promotion in X-ray-induced mutations & 5 \ \text{mT}, 50 \ \text{Hz} & Karasekhtsian \ et al. (2004)^{248} \\ \text{plasmids in Escherichia coli-increase in the number of mutations & 5 \ \text{mT}, 50 \ \text{Hz} & Konsyn \ al. (2002)^{259} \\ \text{plasmids in Given contain and bippole main neurogenesis in mice & 1 \ \text{mT}, 50 \ \text{Hz} & Karasek \ et al. (2017)^{251} \\ \text{circadian response in Drosophila \ 300 \ \mu\text{T}, 50 \ \text{Hz} & Manzella \ et al. (2014)^{225} \\ \text{circadian gene expression in human fibroblast cell & 0.1 \ \text{mT}, 50 \ \text{Hz} & Conselles \ et al. (2017)^{251} \\ \text{Calcium} & 50 \ \mu\text{T}, 50 \ \text{Hz} & Manzella \ et al. (2017)^{251} \\ \text{Calcium scillations in human scillations \ model and mater and mutations \ mum aneuroblastoma cells \ mt, 50 \ \text{Hz} & Conselles \ et al. (2017)^{251} \\ \text{Calcium scillations in human fibroblast cell \ et al. (2017)^{251} \\ \text{Calcium scillations in human fibroblast cell \ et al. (2017)^{251} \\ \text{Calcium scillations in human fibroblast cell \ et al. (2017)^{251} \\ \text{Calcium scillations in human fibroblast cell \ et al. (2017)^{251} \\ Calcium scillations in human fibroblast cell$	mice-pain thresholds	2 mT, 60 Hz	Jeong et al. (2000) ²⁴³
$\begin{split} \text{human-malgesia/EEG} & 200 \ \mu\text{T}, 2500 \ \text{Hz} & \text{Cook et al.} (2004)^{246} \\ \text{attenuate chronic neuropathic pain in rats} & 1 \ \text{mT}, 1/1020/40 \ \text{Hz} & \text{Mert et al.} (2017)^{246} \\ \text{mc}: -inhibition of morphine-induced analgesia} & 0.15-9 \ \text{mT}, 0.5 \ \text{Hz} & \text{Kavaliers \& Ossenkopp} (1987)^{247} \\ \hline \text{Dopamite / Serotomi / Melatomi} \\ \text{rat frontal cortex -dopamine and seroton in level & 1.8-3.8 \ \text{mT}, 10 \ \text{Hz} & \text{Siero et al.} (2004)^{246} \\ \text{rat tarb taris -serotoni and dopamine receptors activity & 0.5 \ \text{mT}, 50 \ \text{Hz} & \text{Janae et al.} (2009)^{249} \\ \text{rat -central dopamine receptor attributes & 1/55/0/250 \ \mu\text{T}, 50 \ \text{Hz} & \text{Kavaliers & Cossenkopp} (1987)^{247} \\ \text{fart art pains and pincel melatonin levels & 1/55/0/250 \ \mu\text{T}, 50 \ \text{Hz} & \text{Karose et al.} (2009)^{249} \\ \text{rat -central dopamine receptor attributes & 1/55/0/250 \ \mu\text{T}, 50 \ \text{Hz} & \text{Karose et al.} (1993)^{252} \\ \text{fart brain colls-increases DNA strand breaks & 0.5 \ \text{mT}, 60 \ \text{Hz} & \text{Karasek et al.} (1993)^{252} \\ \text{human HL-60 cells-steady-state levels of some mRNAs & 8 \ \mu\text{T}, 60 \ \text{Hz} & \text{Karabakhtsian et al.} (2002)^{249} \\ \text{plasmids in Excherichia coli-increase in the number of mutations & 5 \ \text{mT}, 50 \ \text{Hz} & \text{Komaya et al.} (2004)^{248} \\ \text{genetic analysis of circadian responses in Drosophila 300 \ \mu\text{T}, 350 \ \text{Hz} & \text{Komaya et al.} (2014)^{223} \\ \text{circadian gene expression in human fibroblast cell & 0.1 \ \text{mT}, 50 \ \text{Hz} & \text{Karasel et al.} (2014)^{223} \\ \text{calcium odulation of adult hippocampal neurogenesis in mice \\ 1 \ \text{mt}, 50 \ \text{Hz} & \text{Consales et al.} (2017)^{253} \\ \text{Calcium } \\ 1 \ \text{mon skin fibroblast cell membrane \\ 1 \ \text{marks} 50 \ \mu\text{T}, 50 \ \text{Hz} & \text{Lacose et al.} (2017)^{253} \\ \text{Calcium } \\ 1 \ \text{marks} 0 \ \mu\text{T}, 50 \ \text{Hz} & \text{Lacose et al.} (2017)^{254} \\ \text{Calcium } \ \text{modulation in human neuroblastoma cells \\ 1 \ \text{mT}, 50 \ \text{Hz} & \text{Lacose et al.} (2017)^{254} \\ \text{Calcium } \ \text{modulation in human fibroblast cell membrane \\ 1 \ \text{marks}, 50 \ \mu\text{T}$	snail - analgesia	141-414 µT. 30&60 Hz	Prato et al. (2000) ²⁴⁴
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	brain tissue - radiation-induced efflux of Ca ²⁺ ions		
entorhinal cortex neurons - calcium dynamics 1/3 mT, 50 Hz Luo er al. (2014) ²⁶⁹			
	entorhinal cortex neurons - calcium dynamics	1/3 mT, 50 Hz	Luo er al. (2014) ²⁶⁹

Zadeh-Haghighi & Simon. *arXiv:2204.09147* (2022). Journal of Royal Society Interface. https://doi.org/10.1098/rsif.2022.0325
 Table 4. Extremely low-frequency (< 3 kHz) magnetic field effects on reactive oxygen species (ROS)</th>

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 ₂ O ₂ in mice	8 mT, 50 Hz	Duan et al. (2013) ²⁷¹
neural differentiation/ H2O2 elevation in mesenchymal stem cells	1 mT, 50 Hz	Park et al. (2013) ²⁷²
H ₂ O ₂ production in neuroblastoma cell	2±0.2 mT, 75±2 Hz	Osera et al. (2015) ²⁷³
pro-Parkinson's disease toxin MPP ⁺ / H ₂ O 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 ⁻ formation and HSP70 induction	0.025-0.1 mT, 50 Hz	Mannerling et al. (2010) ²⁸⁵
K562 Cells -differentiation via increasing O_2^{*-} production	5 mT, 50 Hz	AySe et al. (2010) ²⁸⁶
K562 leukemia cell -number of apoptotic cells via increasing O_2^{-} production	1 mT, 50 Hz	Garip & Akan (2010) ²⁸⁷
PC12 cells -H ₂ O 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 ⁻ 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	$< 40 \ \mu$ T, 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^{-} in erythro-leukemic cells	1 mT, 50 Hz	Patruno et al. (2015) ²⁹⁸
Genomic instability/ H ₂ O 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^{-1} 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^{-} production in human neuroblastoma cells	$100 \ \mu T$, 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. $(2021)^{308}$

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	\sim 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	$<\mu$ T, 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.

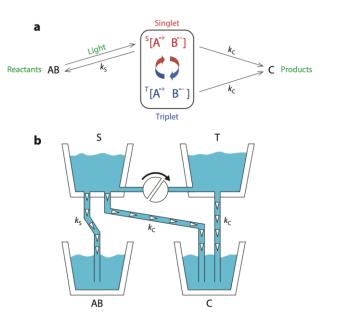
Spatially separated and spin correlated (typically singlet or triplet).

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.



19

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⁻⁻...Trp⁻⁺], and FADH and superoxide [FADH⁻...O₂⁻⁻]. 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

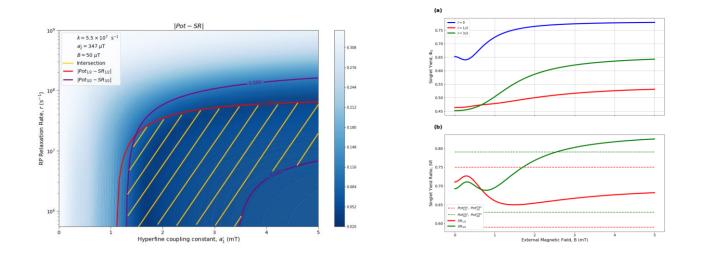
- Trafficking of the RP is more important than the specific nature of the RP; magnetosensitivity is likely to be a widespread property of cells.
- Other, non-photochemical RPs, may contribute to magnetoreception, which is consistent with magnetoreception in darkness.

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

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

Xenon anesthesia

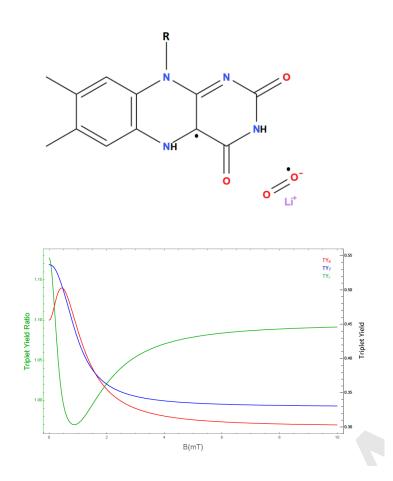
- Anesthesia provides an important window on consciousness, but many open questions.
- Recent experiments on xenon anesthesia implicate electron and nuclear spins (electron spin resonance with fruitflies, isotope effects for mice).
- Our **radical pair model** can explain the observed nuclear spin-dependent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

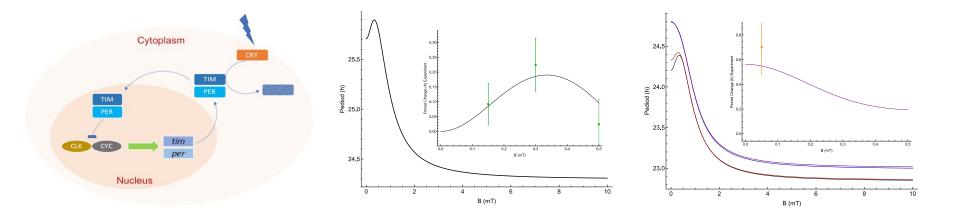
Alternative explanation to Posner molecules

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.

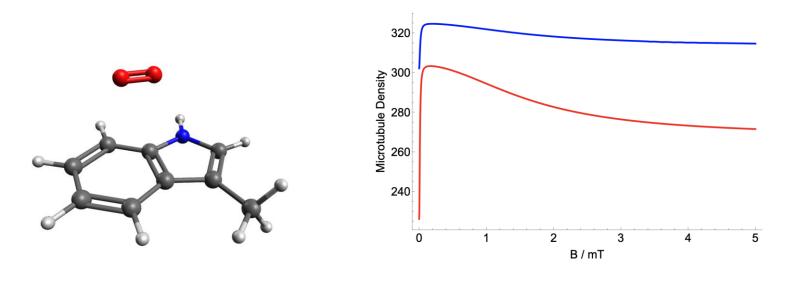
We predict a **shortening of the period at higher fields**, as well as lithium isotope effects.

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.

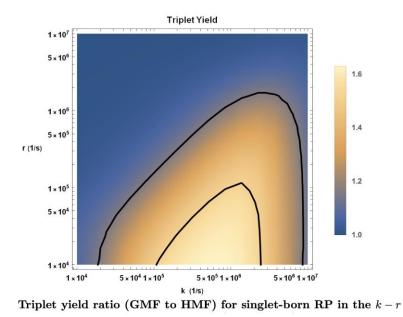
Combining radical pair model (based on **tryptophan-superoxide**) and simple model of microtubule assembly can explain experimental results.



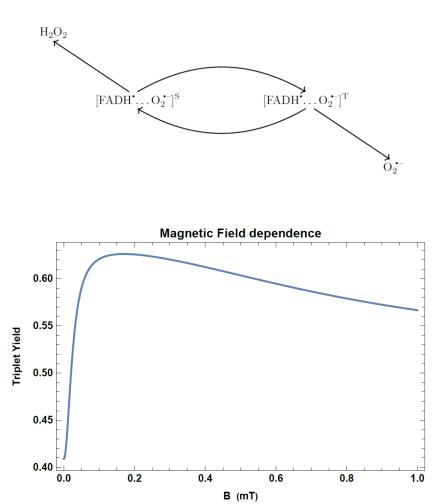
Our model predicts small effects at higher fields and zinc isotope effects.

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

Hypomagnetic fields and hippocampal neurogenesis



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 <u>https://doi.org/10.1098/rsif.2022.0325</u> (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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