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Effect of Magnetic Field on the Biological Clock through the Radical Pair Mechanism

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Abstract—There is an ongoing controversy in the literature related to the biological effects of weak, low frequency electromagnetic fields. The physical arguments and interpretation of the experimental evidence are inconsistent, where some physical arguments and experimental demonstrations tend to reject the likelihood of any effect of the fields at extremely low level. The problem arises of explaining, how the low-energy influences of weak magnetic fields can compete with the thermal and electrical noise of cells at normal temperature using the theoretical studies. The magnetoreception in animals involve radical pair mechanism. The same mechanism has been shown to be involved in the circadian rhythm synchronization in mammals. These reactions can be influenced by the weak magnetic fields. Hence, it is postulated the biological clock can be affected by weak magnetic fields and these disruptions to the rhythm can cause adverse biological effects. In this paper, likelihood of altering the biological clock via the radical pair mechanism is analyzed to simplify these studies of controversy.

Keywords—Bio-effect, biological clock, magnetoreception, radical pair mechanism, weak magnetic field.

I. Introduction

A magnetic field is produced by the moving charges, i.e. the current and the strength of the field is determined by the amount of the current flow. The main characteristics of the magnetic fields are its frequency and strength. The fields of different frequencies and strengths influence the biology in different ways. The strength of the fields depends on the power of the signal and the temperature rise in the tissues due to external fields depends on the strength. The thermal effects can occur from high power fields whereas non-thermal effects are caused from weak low power fields. Adverse biological consequences due to the thermal effects of exposure to high power magnetic fields are well understood to date. This is the foundation for the standards for limiting human exposure to such fields. Over the past few decades a controversy has arisen over possible adverse biological effects due to the exposure to low power, low frequency electromagnetic fields. Epidemiological evidence and laboratory based measurements of biological activity [1] in support of the hypothesis and proposed theoretical models [2], [3] to evaluate these evidences have been subjected to considerable criticism [4], [5].

There is a recent development of magnetoreception in animals, i.e. the ability to detect the earth's magnetic field information [6], [7]. Magnetoreception does occur in the photoreceptors where this process involves cryptochromes. These are a group of photosensitive proteins that contain flavin adenine dinucleotide (FAD) and involved in the biological rhythms of plants and animals [8]. Latest evidence indicates that the magnetoreception in birds involves a radical pair mechanism in the cryptochrome. These chemical reactions can be influenced by the weak magnetic fields [9]. Hence the ambient magnetic field affects the cryptochrome dependent response pathways. The cryptochrome1 levels were higher in the seedlings that had been grown in the magnetic field of 500 μT [10]. The cryptochrome has been shown to be involved in biological rhythm synchronization in mammals [11]. The role of cryptochromes in the rhythms suggests the possibility of the magnetic field effects on the biological clock. It is postulated that the biological clock can be affected by weak magnetic fields and these disruption to the rhythms in the longer term is believed to have significant adverse health consequences. The melatonin production is inhibited by the disruption of the circadian rhythm and this may increase the risk of developing cancer [12], [13].

The Drosophilas circadian clock is sensitive to the magnetic fields and this depends on the activation of cryptochrome and on the applied field strength [6]. The flies exposed to the static magnetic fields enhanced slowing of clock rhythms and this effect was maximal at 300 μT [11]. The magnetic fields of 50 Hz influenced the biological clock activity when the field was directed in the horizontal plane of the rat brain [14]. The biological rhythms can be shifted from the chemicals, light intensity and wavelengths [15], [16] whereas magnetoreception also depends on the intensity and wavelength of light [17]. The biological effects are caused when the radical pair process is influenced by the weak magnetic fields such that the biological rhythms are altered as shown in Fig. 1.

The possibility of altering the biological clock via the radical pair mechanism is reviewed in this paper in order to explain the influences of weak magnetic fields on the biology. First the biological rhythms and then the magnetoreception in animals are discussed. After that the key terms involved in the radical pair mechanism such as the Zeeman effect and the hyperfine interaction are explained before describe the radical pair mechanism. In the result and discussion section the influence of magnetic fields on the chemical reaction rates are explained. Finally the issues of this mechanism are raised in the conclusion.

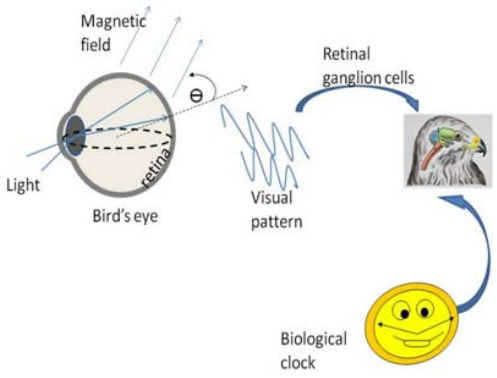

Fig. 1. The radical pair process takes place in the cryptochrome photoreceptor in the retina when it is exposed to light. Complex patterns of signals generate responses in the retina because of various orientations of radical pair with the external magnetic fields. The retinal ganglion cells collectively transmit these signals from the retina to several regions in the thalamus, hypothalamus.etc. The primary clock, which is located in the hypothalamus receives inputs from the specialized photoreceptive retinal ganglion cells, via the retinohypothalamic tract and it is responsible for controlling the circadian rhythms. Hence, altering the radical pair process by an external field will influence the biological clock.

II. Biological Rhythms

The timing and duration of biological processes is known as rhythms. These are the fundamental elements of living beings and occur in animals, plants and microbial organisms. There are several important rhythms such as the circadian rhythm, roughly a 24 hour cycle; infradian rhythms, cycles longer than a day such as reproduction cycles; ultradian rhythms, cycles shorter than 24 hours, such as cycle of growth hormone production; and gene oscillations where some genes are expressed more during certain hours of the day [18], [19]. These rhythms include the blood pressure, body temperature, hormone levels, number of immune cells in blood, sleep-wake cycle, migration, cellular regeneration and leaf movements [20]. The primary circadian "clock" in mammals and birds is located in the suprachiasmatic nucleus (SCN) of the hypothalamus where as in the microbial organisms the individual cells themselves regulate the circadian rhythms. The SCN receives information about light through the eyes. The retina of the eyes contains the photoreceptors as well as retinal ganglion cells which convert the light to electrical signals. Thus, the SCN takes the information from the retina, interprets, and passes it [7]. The peripheral oscillators, which are more or less independent circadian rhythms, are found in the lung, liver, pancreas, spleen, thymus and the skin [20].

Several genes and proteins involved in the clock regulations through the positive and negative feedback loops [20], [21]. The SCN cells in mammals contain several proteins; clock, cycle, period and cryptochrome [20]. In cyanobacteria the clock involves three major proteins; kaiA, kaiB and kaiC [22]. The rhythms generated within the organisms can be entrained by the external cues. Entrainment is the process of shifting the rhythm and these factors are light intensity, wavelength (or color) of light, temperature and certain chemicals [15], [16].

III. Magnetoreception in Animals

Most of the animals such as birds, tortoises, fish, rats, chicks, pigeons, monkeys and flies sense the earth's magnetic field [23], [24]. Birds can use the geomagnetic field as a source of navigational information. This has been explained using torque on the ferromagnetic particles and modulation of chemical reaction rates [25]. The magnetic vector provides the directional information and the magnetic intensity or inclination gives the positional information [7]. The radical pair mechanism involves in the direction finding and the positional information detection involves the iron-rich particles, such as magnetite. The photoreceptors which are capable of detecting the light and converting it to an electrical signal have been found in the eyes of mammals. The behavioral studies suggest that the photoreceptors contain a protein called cryptochrome containing FAD which involved in the magnetoreception process [7]. The birds obtain the magnetic information from the entire short-wavelength part of the spectrum. If the ambient light is of higher energy (i.e. blue, green, white) then the birds show a strong preference for a specific direction. If the ambient photons are of low energy (i.e. yellow, red), then the birds preferred direction becomes random. A very small oscillating field can disrupt the magnetic orientation behavior. The migratory birds can be disturbed by the weak radio frequency magnetic fields with the frequencies in the MHz range. The birds exposed to weak fields of frequencies from 0.1 to 10 MHz, were found to be disoriented when these fields were presented at a 24^0 or 48^0 angle, but the birds were well oriented when the same fields were presented parallel to the earth magnetic field [7], [26]. Another important property is the limitation of birds' magnetoreception to a narrow range of magnetic field intensities [17]. Some experiments demonstrate the pigeon's ability to detect differences in magnetic intensity [27].

IV. Radical Pair Mechanism

An atom or a molecule with an unpaired electron is called a radical. The electron nuclear spin motion of the radical pair is described by Hamiltonian as

$$H = \sum_k a_{1k} S_1 I_k + \sum_l a_{2l} S_2 I_l + \mu B(g_1 S_1 + g_2 S_2) - J\left(\frac{1}{2} + 2S_1 S_2\right) \quad (1)$$

where a_{1k} , a_{2l} are the hyperfine interaction constant, S_1, S_2 are the electron spins, I_k , I_l are the nuclear spins, μ is Bohr constant, B is the magnetic field, g_1, g_2 are the g-factors of two radicals and J is the exchange interaction [28]. The first two terms in the equation (1) represent the hyperfine interaction between the unpaired electron spins and the nuclear spins. The third term is the Zeeman effect which accounts the interaction between the electron spin and the magnetic field. The last term is the exchange interaction between the unpaired electron spins.

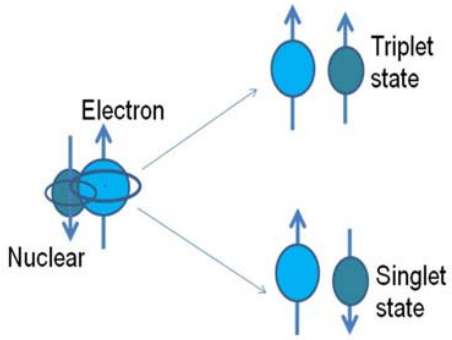

Fig. 2. The hyperfine interaction.

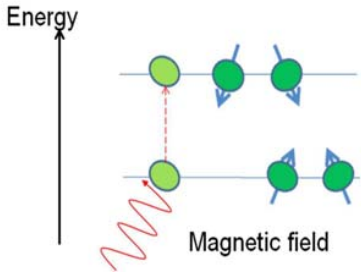

Fig. 3. The Zeeman effect in the presence of a magnetic field splits the energy levels to sub levels.

A. Hyperfine Interaction

Intra-radical coupling between the magnetic moment of an atomic nucleus and the magnetic moment of an unpaired electron is called the hyperfine interaction [29]. The electron-nuclear coupling depends on the orientation of the molecule in an external magnetic field as shown in Fig. 2 [30]. The spin state is called as singlet state (S) when the orientation of spins are anti-parallel. When the spins are aligned parallel, three triplet states (T_{-1}, T_0, T_+) are resulted [31]. The hyperfine interaction drives the interconversion of the singlet and triplet states of the radical pair and allows it to be modified by an external magnetic field [32].

B. Zeeman Effect

The molecules and the atoms exist in different energy levels. These molecules can jump from one energy level to another by absorbing or radiating energy. The frequency of the radiation is determined by the size of the jump that is the difference between the energy levels. These frequencies are called spectral lines. The splitting of a spectral line into several components in the presence of a static magnetic field (Fig. 3) is called the Zeeman effect. The distance between the Zeeman sub-levels is proportional to the magnetic field [33].

C. Exchange Interaction

The exchange interaction, J, is the interaction between the unpaired electron spins of the two radicals [34]. This interaction lifts the triplet states away from the singlet states reducing singlet-triplet interconversion. The exchange interaction decreases with the increasing pair separation. At a certain distance J becomes negligible and singlet-triplet interconversion becomes feasible. The energy difference between the singlet and the triplet state is $2J$ [35].

D. Singlet-Triplet Interconversion

A photo-excited molecule, transfers an electron to another molecule, resulting in a radical pair. The oscillations between the singlet and the triplet states at a variety of frequencies are determined by the strengths of the hyperfine interaction [31]. However, the singlet and triplet pairs will react to give distinct products, thus reducing the amount of radical pairs. The Zeeman effect due to an external field can affect the frequency of this process and hence alter the reaction rates and the products formed from the S and T radical pairs [31]. If the exchange interaction is zero ($J = 0$) and when the magnetic field strength is smaller than the hyperfine coupling strength, singlet-triplet interconversion is enhanced, thus increasing the triplet yield [36]. If the field strength is significant compared to the hyperfine interaction, the Zeeman interaction shifts the energy of the triplet states away from the singlet state energy. Due to this the numbers of triplet states which can be converted in to singlet states are reduced. Only the T_0 state is available for singlet-triplet interconversion [34]. If the J is large, singlet-triplet interconversion is not possible even at zero magnetic fields. However, at a specific magnetic field when the Zeeman energy matches the electron exchange interaction energy, the hyperfine interaction becomes feasible and singlet-triplet interconversion can be facilitated [35]. If the two radicals have different g-factors it will only induce S to T_0 spin interconversion, which is independent of hyperfine interaction. This mechanism is significant for large magnetic fields since the difference in g-factors are quite small [34].

E. Chemical Reaction Rates

A magnetic field dependent reaction scheme is shown in Fig 4 [37]. Here, the atoms or molecules subjected to the radical pair formation is taken as an light absorbed enzyme, FAD*, and amino acid Tryptophan, Trp(H). The FAD* and the Trp(H) react via the forward rate constant k_1 to form FAD* Trp(H) enzyme-acid complex. The singlet enzyme-acid complex, ^{S}[FAD$^{\bullet -}$+ Trp(H)$^{\bullet +}$], is produced through forward rate constant k_2 and singlet triplet interconversion is occurred due to the magnetic field dependent rate constant, k_{isc}. Here, ^{T}[FAD$^{\bullet -}$+ Trp(H)$^{\bullet +}$] is the triplet enzyme-acid complex. The forward reaction rate constant k_3 forms the enzyme-acid complex (FAD Trp(H))* from the singlet and triplet states. The

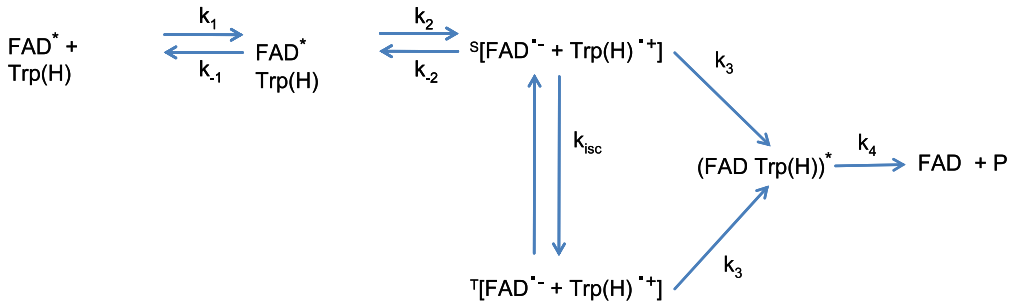

Fig. 4. A radical pair reaction. The light absorbed FAD* enzyme and Trp(H) acid react via the forward rate constant k_1 and form FAD* Trp(H) enzyme-acid complex. The singlet enzyme-acid complex, ${}^{S}[\mathrm{FAD}^{\bullet-} + \mathrm{Trp(H)}^{\bullet+}]$, is produced through the forward rate constant k_2 and singlet triplet interconversion is occurred due to the magnetic field dependent rate constant, k_{isc} . The forward reaction rate constant k_3 forms the enzyme-acid complex (FAD Trp(H))* from the singlet and the triplet states. The product P and FAD release is done via the rate constant k_4.

products P and FAD release is done via the rate constant k_4. The backward reaction rates are k_{-1} and k_{-2}. The chemical rates involved in this reaction scheme are in the microsecond to nanosecond time range [38]. The magnetic field effect is observed when $k_4 >> k_2$ [39], [40].

The magnetic field dependent rate constant for zero field ($B = 0$) is

$$k_{isc}(0) = 3\left[\frac{k_{-2}+2k_3}{\left(\frac{k_{-2}}{2}+k_3\right)^2+\left(2J+\frac{a}{2}\right)^2}\right]\left(\frac{a}{4}\right)^2 \qquad (2)$$

and for high field ($B >> A$) limit is

$$k_{isc}(B) = \left(\frac{k_{-2}+2k_3}{(\frac{k_{-2}}{2}+k_3)^2+(2J)^2)}\right) \times \left(\frac{(\Delta\omega)^2+(\frac{a}{4})^2+\gamma\left[(\Delta\omega)^2+(\frac{a}{4})^2\right]^2)}{1+\gamma\left[(\Delta\omega)^2+(\frac{a}{4})^2\right]}\right) \qquad (3)$$

where

$$\gamma = \frac{1}{k_3(k_{-2}+k_3)}\left(\frac{(k_{-2}+2k_3)^2}{(k_{-2}/2+k_3)^2+(2J)^2}\right),$$

and $\Delta\omega = \Delta g\mu B/(2\hbar)$ [39]. Here, a is the hyperfine interaction constant (rad/s), Δg is the difference between g-factors of two radical, μ is the Bohr constant, B is the magnetic field and $\hbar$ is the reduced Plank constant. When $J \approx 0$ and for the zero magnetic field and very weak magnetic fields ($B << A$), $\Delta\omega$ becomes negligible. Hence, only the hyperfine interaction drives singlet-triplet crossing between the S and T_{-1}, T_0, T_+ states. The high field limit is obtained for $B >> A$ where only S to T_0 interconversion exists. If the g-values are different, intersystem crossing between the S and the T_0 states is provided additionally to the hyperfine interaction where $\Delta\omega \approx \Delta g\mu B/(2\hbar) + \sum a_{1k}m_{1k} - \sum a_{2l}m_{2l}$ and m is the spin states of the nucleus on radicals [35].

V. Results and Discussion

The living cells are electrically noisy due to the random movements of ions and charged molecules. The average thermal energy per particle is higher than the energy of magnetic interaction per particle involved in the radical-pair processes under environmental conditions. However, the spin of electrons is weakly coupled to the thermal bath [41]. The presence of the noise does not always hinder the efficiency of an information process and the biological systems provide an efficient performance assisted by a noisy environment [32]. The lifetime of the radical pair is in microsecond range. Hence, the effects of magnetic fields are frequency independent up to few megahertz. However, experiments show the radicals can be altered by static and 50 or 60 Hz magnetic fields [42], [43]. The thermal relaxations are in the nanosecond range, thus, the question of whether the radical pair is altered by the thermal noise is still unanswered. The ratio of $k_{isc}(B)/k_{isc}(0)$ can be obtained from the equations (2) and (3). In order to consider the AC magnetic fields effect, B in $\Delta\omega$ is replaced by B = $\mathrm{B}_{DC}+ \mathrm{B}_{AC}\cos\omega_{AC}t$ where B_{DC}, B_{AC} are the strength of DC and AC magnetic fields and ω_{AC} is the frequency of AC magnetic field. The variation of this ratio with AC and DC magnetic fields is shown in Fig. 5. For higher magnetic fields ($B >> A$), the magnetic field dependent rate constant k_{isc} increases with the increasing AC and DC magnetic fields. The reaction rates are affected by the static magnetic fields than the alternating magnetic fields based on Fig. 5. For an example when $k_{isc}(B)/k_{isc}(0)$ decreases with the increasing DC magnetic field and increases after a certain DC magnetic field when $B_{AC} = 0.5$ mT, A = 1 μT, $\omega_{AC} = 0.25$ rad/s, $J = 0.05$ μT and $t = 10$ s. This is mainly due to the variation of $\Delta\omega$ with the magnetic field. When $B_{DC} < 0.4$ mT ($B >> A$), the recombination increases because of the Zeeman effect. At higher magnetic fields ($B_{DC} > 0.4$ mT) due to the Δg mechanism singlet to triplet interconversion increases. If J is significant (≈ 0.25 mT) it inhibits singlet-triplet interconversion when $\Delta\omega < 2J$. However, the effect of J is compensated by $\Delta\omega$ when $\Delta\omega > 2J$. The ratio $k_{isc}(B)/k_{isc}(0)$ changes as shown in Fig. 6 when the static magnetic field is fixed and the hyperfine interaction constant is changed. At higher hyperfine constant $A > 0.4$ mT, $k_{isc}(B)/k_{isc}(0)$ began to decreases with the increasing magnetic field and after a certain magnetic field value it again started to increase. As an example when $A = 1$ mT and B_{AC} varies from 10 mT to 30 mT where B_{DC} is fixed at 1 mT the recombination of radicals increases. This is

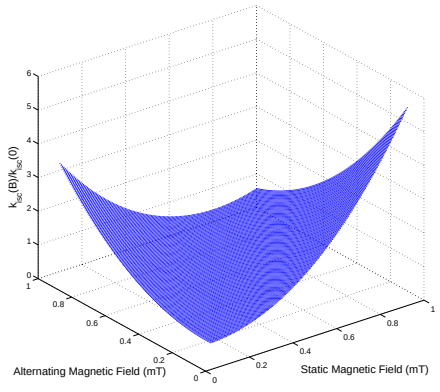

Fig. 5. The ratio of $k_{isc}(B)/k_{isc}(0)$ with AC and DC magnetic field strength. Here $k_{-2} = 1.6 \times 10^6\ s^{-1}$, $k_3 = 3.3 \times 10^6\ s^{-1}$, $\Delta g = 0.05$, $2J = 0.1\ \mu$T, $\omega_{AC} = 0.25\ rad/s$, $t = 10\ s$, $a = 10\ \mu$T.

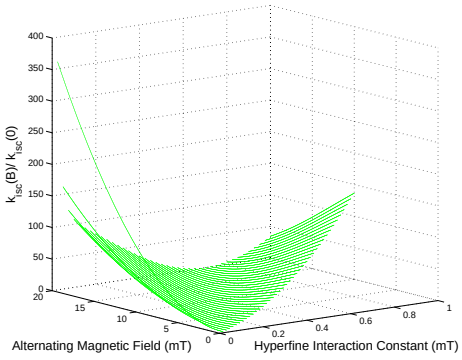

Fig. 6. The ratio of $k_{isc}(B)/k_{isc}(0)$ with AC magnetic field and hyperfine interaction constant. Here $k_{-2} = 1.6 \times 10^6\ s^{-1}$, $k_3 = 3.3 \times 10^6\ s^{-1}$, $\Delta g = 0.05$, $2J = 0.1\ \mu T$, $\omega_{AC} = 0.25\ rad/s$, $t = 10$ s, $B_{DC} = 30\ \mu$T.

due to the Zeeman splitting which occur with the increasing magnetic field where only S to T_0 interconversion exists. The radical pair recombination is reduced at the higher AC fields ($B_{AC} > 30$ mT) by increasing the magnetic field dependent reaction rate. This is because of the slightly different g-factors in the two radicals.

It is argued the external weak magnetic fields interact with biology through the radical pair mechanism because the radicals are highly reactive due to the unpaired electrons. An increase in free radical can affect various biological processes such as gene expression, release of calcium, alter spontaneous and induced DNA damage, cell growth and death [44]. Our results indicate the chemical reaction rates in the radical pair mechanism change due to the magnetic fields. These changes in reaction rates suggest the possibility of variation in the signals go to the primary and peripheral clocks which in turn alter the biological rhythms.

VI. Conclusion

The electron spins are weakly bound to the thermal bath and hence, the radical pair process can occur and the chemical reaction rates of the radical pair mechanism can be changed by the magnetic fields. Very weak magnetic fields increase the radicals when the exchange interaction is zero. Our results show that for non-zero (very weak) exchange interaction the recombination is reduced even in a high magnetic field when the g-factors in radicals are slightly different. The magnetic field dependent rate constant changes with the magnetic fields according to our results. We suggest this process can be occurred in the living organisms influencing the biological clock. Thus, the bio-effects can be arisen due to the weak magnetic fields even the magnetic fields are much higher than the hyperfine coupling strength. However, since the relaxation time of the thermal noise is in the nanosecond range, the question of whether the radical pair mechanism is altered by the thermal noise is still unanswered.

References

[1] N. A. Belova, and V. V. Lednev, "Dependence of the gravitropic response in flax stem segments on the frequency and amplitude of a weak combined magnetic field", *Biophysics*, vol. 45, pp. 1108–1111, 2000.
[2] V. V. Lednev, "Possible mechanism for the influence of weak magnetic fields on biological systems", *Bioelectromagnetics*, vol. 12, pp. 71–75, 1991.
[3] M. N. Halgamuge, C. D. Abeyrathne and P. Mendis, "Effect of Cyclotron Resonance Frequencies in Particles Due to AC and DC Electromagnetic Fields", *World Academy of Science, Engineering and Technology*, vol. 52, pp 416–419, 2009.
[4] R. K. Adair, "Constraints on biological effects of weak extremely low frequency electromagnetic fields", *Physical Review A*, vol. 43, pp. 1039–1048, 1991.
[5] M. N. Halgamuge, B. R. R. Persson, L. G. Salford, P. Mendis and J. L. Eberhardt, "Comparison between Two Models for Interactions between Electric and Magnetic Fields and Proteins in Cell Membranes", *Environmental Engineering Science*, vol 26, no. 10, pp. 1473–1480, 2009.
[6] R. J. Gegear, A. Casselman, S. Waddell, and S. M. Reppert, "Cryptochrome mediates light-dependent magnetosensitivity in Drosophila", *Nature*, vol. 454, pp. 1014–1018, 2008.
[7] W. Wiltschko, and R. Wiltschko, "Magnetoreception in birds: two receptors for two different tasks", *Journal of Ornithology*, vol. 148, pp. S61–S76, 2007.
[8] K. Maeda, K. B. Henbest, F. Cintolesi, I. Kuprov, C. T. Rodgers, P. A. Liddell et al., "Chemical compass model of avian magnetoreception", *Nature*, vol. 453, 2008.
[9] K. M. Salikhov, Y. N. Molin, R. Z. Sagdeev, and A. L. Buchachenko, "Spin polarization and magnetic effects in radical reactions", vol. 22, Hungary: Elsevier Science Publishers, 1984.
[10] M. Ahmad, P. Galland, T. Ritz, R. Wiltschko, and W. Wiltschko, "Magnetic intensity affects cryptochrome-dependent responses in Arabidopsis thaliana", *Planta*, vol. 225, pp. 615–624, 2007.
[11] T. Yoshii, M. Ahmad, and C. Helfrich-Forster, "Cryptochrome Mediates Light-Dependent Magnetosensitivity of Drosophila's Circadian Clock", *PLoS Biology*, vol. 7, no. 4, pp. 0813–0819, 2009.
[12] N. Mostafaie, E. K. llay, E. Sauerzapf, E. Bonner, S. Kriwanek, H. S. Cross, et al., "Correlated Downregulation of Estrogen Receptor Beta and the Circadian Clock Gene Per1 in Human Colorectal Cancer", *Molecular Carcinogenesis*, vol. 48, pp. 642–647, 2009.
[13] D. Velissaris, V. Karamouzos, P. Polychronopoulos, and M. Karanikolas, "Chronotypology and melatonin alterations in minimal hepatic encephalopathy", *Journal of Circadian Rhythms*, vol. 7, pp. 6, 2009.
[14] O. Hiwaki, "Influence of 50 Hz magnetic fields on circadian rhythm of the suprachiasmatic nucleus activity", Paper presented at the 20th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 1998.
[15] T. Elvitigala, J. Stckel, B. K. Ghosh, and H. B. Pakrasi, "Effect of continuous light on diurnal rhythms in Cyanothece sp. ATCC 51142". *BMC Genomics*, vol. 10, pp. 226, 2009.

[16] H. Shimada, K. Numazawa, T. Sasaki, N. Kato, and T. Ebisawa, "Introduction of tau Mutation into Cultured Rat1-R12 Cells by Gene Targeting, Using Recombinant Adeno-Associated Virus Vector". *Cell Mol Neurobiol*, 29, 699–705.
[17] E. Rieper, E. Gauger, J. J. L. Morton, S. C. Benjamin, and V. Vedral, "Quantum coherence and entanglement in the avian compass", 2009.
[18] J. Aguzzi, P. Puig, and J. B. Company, "Hydrodynamic, non-photic modulation of biorhythms in the Norway lobster Nephrops norvegicus (L.)", *Deep-Sea Research I*, vol. 56, pp. 366–373, 2009.
[19] S. Liu, Y. Cai, R. B. Sothern, Y. Guan, and P. Chan, "Chronobiological analysis of circadian patterns in transcription of seven key clock genes in six peripheral tissues in mice", *Chronobiology International*, vol. 24, no. 5, pp. 793–820, 2007.
[20] F. Weber, "Remodeling the clock: coactivators and signal transduction in the circadian clockworks", *Naturwissenschaften*, vol. 96, pp. 321–337, 2009.
[21] M. Yamato, N. Ishida, H. Iwatani, M. Yamato, H. Rakugi, and T. Ito, "Kid-1 participates in regulating ERK phosphorylation as a part of the circadian clock output in rat kidney", *Journal of Receptors and Signal Transduction*, vol. 29, no. 2, pp. 94–99, 2009.
[22] A. Mehra, C. I. Hong, M. Shi, J. J. Loros, J. C. Dunlap, and P. Ruoff, "Circadian Rhythmicity by Autocatalysis", *PLoS Computational Biology*, 2(7), 0816–0823.
[23] T. M. Fitzgerald, and P. D. Taylor, "Migratory orientation of juvenile yellow-rumped warblers (Dendroica coronata) following stopover: sources of variation and the importance of geographic origins", *Behav Ecol Sociobiol*, vol. 62, pp. 1499–1508, 2008.
[24] W. Wiltschko, and R. Wiltschko, "Magnetic Compass of European Robins", *Science*, vol. 176, pp. 62–64, 2009.
[25] P. Galland, A. Pazur, "Magnetoreception in plants", *Journal of Plant Research*, vol. 118, no. 6, pp. 371–389, 2005.
[26] T. Ritz, P. Thalau, J. B. Phillips, R. Wiltschko, and W. Wiltschko, "Resonance effects indicate a radical-pair mechanism for avian magnetic compass", *Nature*, vol. 429, 2004.
[27] C. B. Anea, M. Zhang, D. W. Stepp, G. B. Simkins, G. Reed, D. J. Fulton, et al, "Vascular Disease in Mice With a Dysfunctional Circadian Clock", *Journal of the American Heart Association*, vol. 119, pp. 1510–1517, 2009.
[28] H. J. Werner, Z. Schulten, and K. Schulten, "Theory of the magnetic field modulated geminate recombination of radical ion pairs in polar solvents : Application to the pyrene-N,N-dimethylaniline system", *The Journal of Chemical Physics*, vol. 67, no. 2, pp. 646–663, 1977.
[29] K. Schulten, "Biological effects of static and extremely low frequency magnetic fields", *BGA Schriften*, vol. 86, no. 3, pp. 133–140, 1986.
[30] T. Miura, K. Maeda, and T. Arai, "The Spin Mixing Process of a Radical Pair in Low Magnetic Field Observed by Transient Absorption Detected Nanosecond Pulsed Magnetic Field Effect", *J. Phys. Chem. A*, vol. 110, pp. 4151–4156, 2006.
[31] C. R. Timmel, and K. B. Henbest, "A Study of Spin Chemistry in Weak Magnetic Fields", *The Royal Society*, vol. 362, pp. 2573–2589, 2004.
[32] M. B. Plenio, and S. F. Huelga, "Dephasing-assisted transport: quantum networks and biomolecules", *New Journal of Physics*, vol. 10, 2008.
[33] K. Wang, and T. Ritz, "Zeeman resonances for radical-pair reactions in weak static magnetic fields", *Molecular Physics*, vol. 104, pp. 1649–1658, 2006.
[34] S. Engstrom, "Magnetic field effects on free radical reactions in biology", In: Taylor and Francis Group, LLC, 2006.
[35] I. R. Gould, N. J. Turro, and M. B. Zimmt, "Magnetic field and magnetic isotope effects on the products of organic reactions", In V. Gold and D. Bethell (Eds.), Advances In Physical Organic Chemistry (Vol. 20, pp. 1 - 51). London: Academic Press Inc Ltd, 1984.
[36] T. Ritz, S. Adem, and K. Schulten, "A Model for Photoreceptor-Based Magnetoreception in Birds", *Biophysical Journal*, vol. 78, pp. 707–718, 2000.
[37] K. B. Henbes, K. Maeda, P. J. Hore, M. Joshi, A. Bacher, R. Bittl, et al, "Magnetic-field effect on the photoactivation reaction of Escherichia coli DNA photolyase", *Proceedings of the National Academy of Sciences*, vol. 105, no. 38, pp. 14395–14399, 2008.
[38] I. A. Solovyov, and W. Greiner, "Theoretical Analysis of an Iron Mineral-Based Magnetoreceptor Model in Birds", *Biophysical Journal*, vol. 93, pp. 1493–1509, 2007.
[39] C. Eichwald, and J. Walleczek, "Model for magnetic field effects on radical pair recombination in enzyme kinetics", *Biophysical Journal*, vol. 71, pp. 623–631, 1996.
[40] C. Eichwald, and J. Walleczek, "Magnetic field perturbations as a tool for controlling enzyme-regulated and oscillatory biochemical reactions", *Biophysical Chemistry*, vol. 74, pp. 209–224, 1998.
[41] R. K. Adair, "Effects of very weak magnetic fields on radical pair reformation", *Bioelectromagnetics*, vol. 20, pp. 255–263, 1999.
[42] M. Zmyslony, E. Rajkowska, P. Mamrot, P. Politanski, & J. Jajte, "The effect of weak 50 Hz magnetic fields on the number of free oxygen radicals in rat lymphocytes in vitro", *Bioelectromagnetics*, vol. 25, pp. 607–612, 2004.
[43] F. Regoli, S. Gorbi, N. Machella, S. Tedesco, M. Benedetti, R. Bocchetti, et al, "Pro-oxidant effects of extremely low frequency electromagnetic fields in the land snail Helix aspersa", *Free Radical Biology & Medicine*, vol. 39, pp. 1620–1628, 2005.
[44] J. D. MacArthur, "Cell phones and the brain The Townsend Letter for Doctors and Patients", pp. 1–13, 2002.