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The radical pair mechanism of biological effects on hypomagnetic fields and one method to verify it

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Abstract

The biological effects due to a hypomagnetic field (HMF) is a very important subject not only for aerospace traveling and space station living but also for some magnetic shielding conditions on the ground just like the underground bunkers and etc. However, to my knowledge, the mechanisms which can be related to the biological effects of a HMF remain unclear. In this study, I firstly summary one radical pair mechanism of biological effects on a HMF based on present researches, and then propose how to prove the radical pair mechanism's truth in biological effects on a HMF through experiments. In the way of how to prove the radical pair mechanism's truth I give the relation between the singlet yield of the radical pair and the angle describing the orientation of a HMF to the basis of the hyperfine tensor related to the electron spin and the nuclei spin is the possible one radical pair mechanism on one hand, and give the crucial method which is through that angle changed causes the biological effects in vivo or vitro to prove or disprove the mechanism on the other hand, because the biological effects of a HMF can be related with that angle, which is very easy to be controlled in experiments.

Keywords: Angle, Biological effects, Hypomagnetic field, Method, Radical pair mechanism, Verify.

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Contents

Contribution of this paper to the literature
This research contributes as an updated of the mechanism and method which might be one probable solution to solve the essential problems on biological effects of an HMF. If the truth of the mechanism is proven firstly, the mechanism of bird navigation is clear firstly also in cell level because of their relation.

1. Introduction

During the evolution process, all living organisms experienced the action of the Earth's field (geomagnetic field, GMF) which is a natural component of their environment [1]. While, Interplanetary space is a natural HMF [2].The range of a HMF is between zero and 5uT [2]. Because of the difference on intensity between GMF(-50uT) and HMF(<5uT) [2] many effects appear when animals, plants and microorganisms are in the HMF [2-15]. Because the HMF is not only a key environmental factor for aerospace traveling and space station living , and but also for some magnetic shielding conditions on the ground, just like, the underground bunkers, the inner chamber of a sub-marine, and the measurement room of magnetoencephalography (MEG) analysis, the biological effect of the HMF should be seriously considered [16]. Accumulative evidence has shown the adverse effects of a HMF [2, 3, 17]. It is necessary to evaluate the effects of HMF exposure, and to develop effective counteractive strategy against the HMF to protect the health of astronauts and workers who are exposed to occupational HMF [16]. Some studies on the mechanisms underlying the biological effects of a HMF have been carried out [3].These studies give the mechanism of the biological effects of a HMF at the cellular level [18-24],the mechanism at the molecular level [8, 25-34], the mechanism at the tissue level [35-37] ,and the physical mechanism respectively Binhi [37]; Binhi and Prato [38]; Binhi and Prato [39]. Binhi and Prato [38] proposed one universal physical mechanism of biological effects on the side of magnetic moment under the action of the HMF, but the mechanism can't give the possible molecules related to biological effects. Barnes and Greenebaum [26] suggested the radical pair mechanism of biological effects under the action of weak magnetic fields, but the intensity of the fields is about 45uT which is much bigger than a HMF. Ouyang and Li [3] gave the point [3] that the change of singlet yield in a radical pair may be one quantum mechanism of biological effects on a HMF, but it is only a simple viewpoint. So, to our knowledge, the whole radical pair mechanism which can be related to the biological effects of a HMF still has not been to be discovered completely, and the method which is to prove or disprove the mechanism also is not found. The presentation order of the contents of this paper is as followed. General radical pair model and mechanism in bird navigation is introduced in part 2; The radical pair mechanism of biological effects on a HMF is showed in part 3 ; Part 4 is how to prove the radical pair mechanism's truth in biological effects on a HMF through experiments; Part 5 is discussions of several questions on the radical pair mechanism of a HMF; and the main contents are summarized in part 6.

2. General Radical Pair Model and Mechanism in Bird Navigation

A radical can be a molecule that contains an odd number of electrons. A radical pair consists of two radicals that have been created simultaneously, usually by a chemical reaction [38]. A simple radical-pair reaction scheme used in explaining magnetoreceptor mechanism is showed in Figure 1.

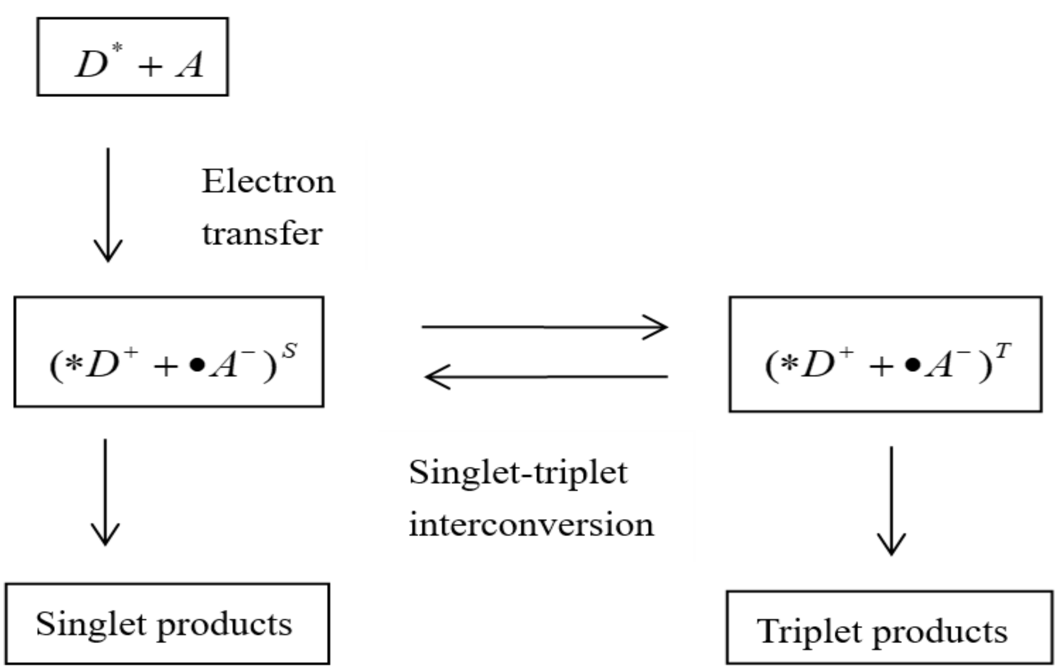

Figure 1. Reaction scheme for a radical pair reaction with magnetic field-dependent reaction products.
Note: Ritz, et al. [40].

The reaction scheme is compossed by three steps [40]. The first step is , an excited donor molecule D^* transfers an electron to an acceptor molecule A, resulting in a radical pair $*D^+ + \bullet A^-$. After the radical pair is generated in a spin-correlated state, its singlet and triplet states will be interconverted by the hyperfine interaction given corresponding situations. Singlet and triplet pairs will react to give distinct products in the final step, depleting the population of radical pairs in the step. The singlet yield ϕ_S is defined as the amount of products decaying via the singlet channel, $\phi_S = \int_0^\infty K_S P_{S(t)} dt$, $P_{S(t)} = Tr[Q_S \rho(t)]$ [40-43], here, Q_S is the singlet projection operator [41], $\rho_{(t)}$ is the density matrix and K_s is rate constant of singlet state [40].

Based on the general radical model above Xu, et al. [42] gave the following mechanism of bird navigation. The Hamiltonian of the radical pair is of the form:

$$\hat{H} = \gamma \vec{B} \bullet (\hat{S}_1 + \hat{S}_2) + \hat{S}_1 \bullet A_1 \bullet \hat{I}, \qquad (1)$$

Where γ is one constant, $\hat{S}_1$ and $\hat{S}_2$ are the spin opreator of electrons in the radical pair, A_1 is the anisotropic hyperfine tensor with a diagonal form, $\hat{I}$ is the spin operator for the nuclei, and $\vec{B}$ is the external magnetic field around the radical pair given by $\vec{B} = B_0(\sin\theta\cos\phi, \sin\theta\sin\phi, \cos\theta)$, where B_0 is the intensity of the Earth's magnetic field, θ and ϕ give its orientation to the basis of the hyperfine tensor. In the situation that rate constants of singlet state and triplet state are equal, the horizontal hyperfine coupling $A_{x1} = A_{1y} = 0$ and only considering that the vertical hyperfine coupling A_{1z} is relatively strong compared with γB_0, the singlet yield:

$$\phi_S^0(\theta) \approx \frac{1}{2} - \frac{1}{4}\sin^2\theta - \frac{\gamma^2 B_0^2}{A_{1z}^2}\left(\frac{3}{4}\sin^2\theta - \sin^4\theta\right), \qquad (2)$$

can be obtained under the influence of the geomagnetic field with the corresponding eigenvalue, here, which is equal to γB_0 [42]. When considering the horizontal hyperfine coupling $A_{1x} = A_{1y} \neq 0$, the results are similar to Equation 2 [42].

General radical pair model and mechanism in bird navigation are outlined above.When B_0 in Equation 2 is very weak, the avain compass can adopt to it to orient [42]. Can Equation 2 be applied into the non-orientation biological effects of a HMF?

3. The Radical Pair Mechanism of Biological Effects on a HMF

In Equation 2, B_0 is the intensity of the Earth's magnetic field, and θ describes its orientation to the basis of the hyperfine tensor. When B_0 is smaller than 5uT, that is to say when B_0 belongs to a HMF ,is Equation 2 still true? Prato [27] expressed the view that bird navigation should be examined as relevant to the non-orientation biological effects of weak magnetic fields. In reference Ouyang and Li [3] gave the point: Equation 2 may be one quantum mechanism of biological effects on a HMF , here, I show reasons in details: (1) when the external field is very weak, i.e., the value of B_0 is very small, Equation 2 is still a monotonous function of θ,this is consistent with the experiment that birds can adjust to a very weak field of 4 μT which is less than 10% of the geomagnetic field of 47 μT [42, 44]. Obviously, the weak field of 4 μT is in the range of HMF though the biological effects of 4 μT is of only one oriention here. (2) Equation 2 is applied in Cryptochromes in bird navigation in Xu, et al. [42], but it is fit to all potential radical pair molecules only with electrons transmission. (3)The hyperfine interaction between nuclei and electrons is general, though A_{1z} may be different in different potential radical-pair molecules, Equation 2 can be used only with A_{1z} is relatively strong compared with γB_0 .(4) Equation 2 can be used only with A_{1z} is relatively strong compared with γB_0 also shows B_0 may be very weak, even in the range of a HMF, because γ is one constant . (5) In Equation 1, $\vec{B}$ can be any static magnetic field, only $|\vec{B}| \succ 0$, and Equation 2 is derived from Equation 1, so it can be used in a HMF. Based on above reasons, we surely can propose Equation 2 as one possible quantum mechanism of the biological effects of a HMF. Equation 2 can be thought to use in explaining biological effects of a HMF, and how it can be related with HMF experiments ?

4. How to Prove the Radical Pair Mechanism's Truth in Biological Effects on a HMF through Experiments?

4.1. The General Rule

In part 2, γ is one constant in Equation 1 [42]. Because Equation 2 is based on (2), γ is one constant in Equation 2 still. In part 3, I have shown A_{1z} ,the hyperfine interaction between nuclei and electrons may be different in different potential radical-pair molecules, here , I primarily take it as certain when the molecules is determined. So from Equation 2, it can be seen that the singlet yield $\phi_S^0(\theta)$ is changed only with θ and B_0, and it can be seen that the biological effects on a HMF may be only both related θ and B_0.

In part 2 and part 3, I have shown that θ describes the orientation of B_0 to the basis of the hyperfine tensor [45]. To the axial radical pair molecules, the basis of the hyperfine tensor is the same of the axe of the molecules. In reference [40], the molecules are assumed to be oriented normal to the retina surface of birds for avian navigation. That is to say, when the birds don't moving or their orientations don't change, θ is certain on the assumation. The meaning of θ in GMF is the same as in a HMF. The meaning of θ in a HMF is described in Figure 2.

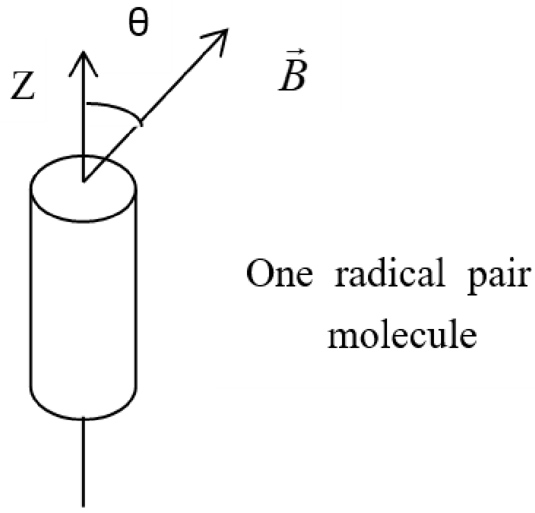

Figure 2. The meaning of θ in a HMF.

In Equation 2, θ changed by the motion of birds causes the visible effects for avian navigation when GMF $\vec{B}$ doesn't change. Based on the same assumation, in the biological effects on a HMF response experiments, θ changed can be supposed in the same way as birds in vivo if the animal is used, but in vitro or the plant is used in vivo, θ changed can be realized through the change of experimental sample's orientation or plant's orientation. Through these experiments, the truth of Equation 2 as one quantum mechanism in explaining the biological effects due to hypomagnetic fields can be proven or disproven primarily. Further studies are suggested to prove or disprove this hypothesis.

4.2. Only B_0 is Changed

When samples in vitro experiments are in geomagnetic field at first, then in HMF, B_0 is changed obviously. In the course , $\vec{B}$ is changed from GMF to a HMF, here ,and it's directions can be thought unchanged [8, 9]. If the orientation of experimental samples is kept unchanged, then θ was kept unchanged based on above assumation in 4.1 part. That is to say, in the course, only B_0 is changed. According to Equation 2, the singlet yield $\phi_S^0(\theta)$ is changed only with the change of B_0.The corresponding biological effects are only related with the change of B_0.

4.3. Both B_0 and θ are Changed

When samples in vitro experiments are in geomagnetic field at first, then in a HMF, B_0 is changed. In the course ,$|\vec{B}| = B_0$ is changed from GMF to HMF,here ,and it's directions can be thought unchanged [8, 9]. After samples are moved from GMF to a HMF, if their orientations are changed , then θ was changed based on above assumation in 4.1 part. That is to say, in the course,both B_0 and θ are changed. According to Equation 2, the singlet yield $\phi_S^0(\theta)$ is changed with the changes of both B_0 and θ.The corresponding biological effects are related with the changes of both B_0 and θ.

4.4. Only θ is Changed

When samples in vitro experiments are in a HMF at first, $\vec{B}$ can be thought unchanged [16, 18].If the orientation of experimental samples is changed, then θ was changed based on above assumation in 4.1 part. That is to say, in the course, the external magnetic field is not changed and only θ is changed. According to Equation 2, the singlet yield $\phi_S^0(\theta)$ is changed only with the change of θ.The corresponding biological effects are only related with the change of θ. This case has special use to prove the truth of Equation 2 in explain the biological effects of a HMF. At first, the samples have to be divided into same several parts in HMF, and be put in different orientations. If the samples in different orientations have different bio-response in degree, the truth of Equation 2 in HMF is proved firstly. The reason is as followed. In a HMF $B_0 < 5uT$ [2], $A_{1Z} = 500uT$ [40], $B_0 << A_{1Z}$, the last term in Equation 2 $\frac{\gamma^2 B_0^2}{A_Z^2}(\frac{3}{4}\sin^2\theta - \sin^4\theta)$ near zero, it can be obtained the singlet yield

$$\phi_S^0(\theta) \approx \frac{1}{2} - \frac{1}{4}\sin^2\theta, \quad (3)$$

Which is monotonously changed according to the change of θ. The curve between the single yield $\phi_S^0(\theta)$ and θ in Equation 2 is drawn in Figure 3.

If the relation between the biological effects of a HMF and the singlet yield $\phi_S^0(\theta)$ is line, the the relation between the biological effects and θ is just like the curve between the single yield $\phi_S^0(\theta)$ and θ in Equation 3 drawn in Figure 3. If the relation between the biological effects and the singlet yield $\phi_S^0(\theta)$ is not line, the relation between the biological effects and θ is still monotonous. Based on these, the relation between viability of mouse skeletal muscle cells in reference [18] and θ is line or monotonous.

Because , the direction of HMF is stable also and θ is changed along with the different orientation of samples, based on Equation 3 the single yield $\phi_S^0(\theta)$ is changed only with θ is changed, and different samples with the different orientation may have different effects. The change of orientation or θ can be continuous or alternating for a while. Because in order to induce biological effects or chemical reactions, $\phi_S^0(\theta)$ may be required to change continuously for a period. If the truth of Equation 3 in a HMF is proved, then the truth of Equation 2 in a HMF is done also. And to prove the truth of Equation 3 in a HMF only the orientation of the sample or θ changed is enough. The change of the orientation of the sample or θ is very easy to be controlled in experiments. That is to say, here, one primary underlying mechanism which can be related to the biological effects of a HMF directly has been to be proposed on one hand, and the method to prove or disprove the mechanism has been to be done on the other hand.

If the truth of Equation 3 or Equation 2 in a HMF is proved firstly, the truth of Equation 2 in bird navigation is proved firstly also in cell level.

When samples in vitro experiments are in geomagnetic field at first, then in a HMF, B_0 is changed obviously and θ may be changed very possibly. Here θ may be changed very possibly because when samples are moved from GMF to a HMF, their orientations to the static magnetic field $\vec{B}$ changed very possibly under the conditions that any operators don't be told the importance of keeping the orientations unchanged. Because to our known, any experiments of HMF biological effects don't be related with θ or the orientations of samples. The operators of course don't mind the change or unchange of the sample's orientation. That is to say, the reason of biological effects of a HMF experiments having done can be contributed to that both B_0 and θ are changed based on Equation 2.

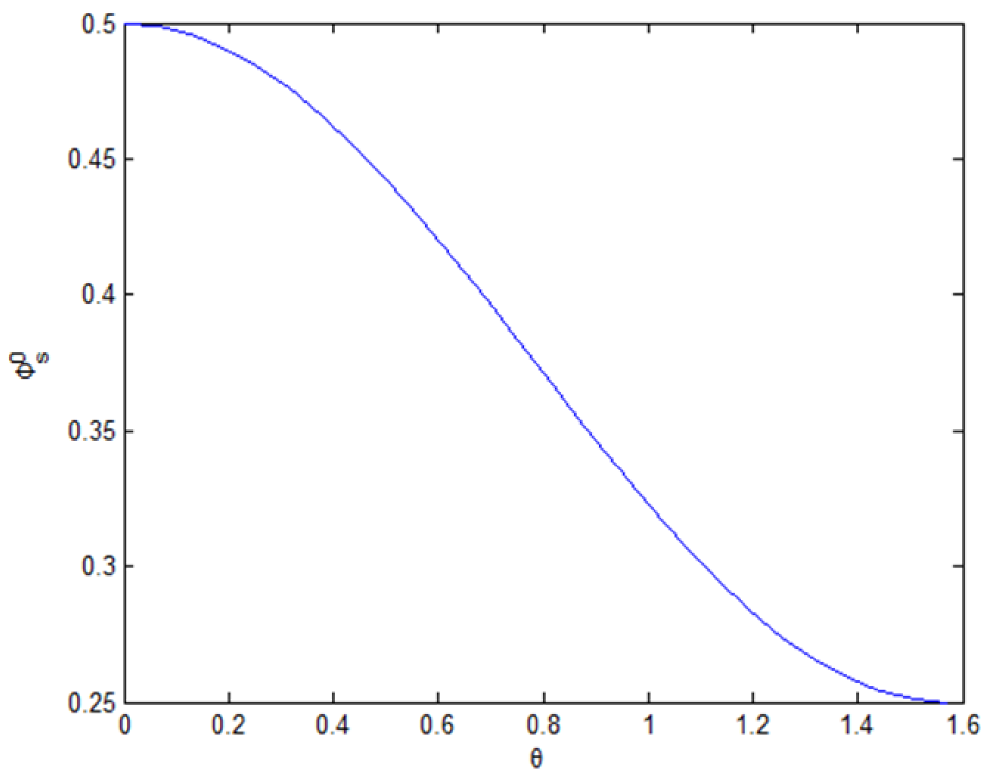

Figure 3. The curve between the single yield $\phi_S^0(\theta)$ and θ.

5. Discussion

The above radical pair mechanism of biological effects on a HMF is very simplified, but it gives the crucial method to verify the truth of it, that is to say, the effects can be related with θ, which is very easy to be controlled in experiments.

Ambient alternating fields always exist [16, 18], can they influence the biological effects on a HMF ? Above, only single nuclei radical pair model of a HMF is talked about, what's the multinuclei radical pair model of a HMF ? They will be our next research aims.

Because of the universe of Cryptochromes in organisms**,** they may be the first candidates in biological effects on HMF as putative magnetic receptor just like the role in bird navigation. Some researchers[10, 25] have suggested that. As Qin, et al. [46] show, they may compose a multimeric magneto sensing rod-like protein complex with other molecules. Zhang, et al. [16] suggests CuZn superoxide dismutase (CuZnSOD)a mediator of the HMF, and Xu, et al. [47] suggest that near-null magnetic field(or HMF) affects the distribution of auxin in Arabidopsis and results in delay of flowering in Arabidopsis. Because HMF is static field, it can be full of the whole space besides the inner part of samples. Cryptochromes may be the first response molecules, and CuZn superoxide dismutase or auxin may be the downstream one, these cases can be expanded to other radical pair molecules if there are others besides Cryptochromes.

Although radical pair mechanisms can be applied both in bird navigation on GMF and in biological effects on HMF, there are some differences in them. (1) The intensity of magnetic fields is different, one case of GMF is about

50uT, and the other case of a HMF is below 5uT. (2)The distribution of Cryptochromes ,which are their common radical pair molecules now ,is different. One case of GMF is only very rich in bird's eyes [48], and the other case of a HMF has no special rich region.(3)The factor that causes biological effects has difference. From Equation 2,we can see B_0 and θ all can cause biological effects on GMF, though the last term of Equation 2 which is $\frac{\gamma^2 B_0^2}{A_{1Z}^2}(\frac{3}{4}\sin^2\theta - \sin^4\theta)$ may be very small. Because on the case of a HMF, $B_0 < 5uT$ [2], it is about 50uT on the case of GMF, B_0 of a HMF is very much smaller than that of GMF, $\frac{\gamma^2 B_0^2}{A_{1Z}^2}(\frac{3}{4}\sin^2\theta - \sin^4\theta)$ is much smaller than that of GMF, and Equation 3 is the key mechanism in biological effects on a HMF. That is to say, θ is the key factor that can cause biological effects on a HMF.

Although some mechanisms of bird navigation which is in the center of cryptochrome as one potential magnetoreceptor have been proposed and some experiments have been done [49-51], whether magnetic sensing exists or not, is still one of the most controversial issues of animal senses [46]. It is now about 20 years since cryptochrome was first proposed as a potential radical pair magnetoreceptor, scientists are still not close to a "killer experiment" that has the power to confirm the hypothesis [52]. If the truth of Equation 3 or Equation 2 in HMF is proved firstly, the truth of Equation 2 in bird navigation is proved firstly also in cell level.

Because a HMF is one of weak magnetic fields [3], and extremely low frequency (ELF)magnetic fields from power lines belongs to weak magnetic fields too Juutilainen, et al. [53], this radical pair mechanism and method proposed in this study might be one probable solution to solve the essential problems on biological effects of the kind of magnetic field.

6. Summary

The primary underlying mechanism which can be related to the biological effects of a HMF directly is the key problem and has not been to be completely clear. I propose one whole radical pair mechanism and give the method to verify the mechanism. The above radical pair mechanism of biological effects on a HMF is very simplified, but it gives the crucial method to verify the truth of it, that is the effects can be related with θ, which is very easy to be controlled in experiments.

If the truth of Equation 3 or Equation 2 in a HMF is proved firstly, the truth of Equation 2 in bird navigation is proved firstly also in cell level.

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