Bundesamt für Strahlenschutz

**Spotlight on EMF Research**

# Spotlight on "Radical triads, not pairs, may explain effects of hypomagnetic fields on neurogenesis" by J. Ramsay and D.R. Kattnig in PLoS Comput Biol (2022)

**Category [low frequency, theory/molecular mechanism]**

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## 1 Putting the paper into context by the BfS

The influence of magnetic fields on the spin dynamics of chemical reactions is by now one of the most prominent candidates for a biologically relevant quantum effect giving rise to mechanisms that could lead to biological effects below the currently accepted threshold values. Pairs of radicals (molecules with unpaired electrons) as reaction intermediates are capable of forming combined spin states (singlet and triplet) which are in general not eigenstates of the system and hence continuously interconvert. External magnetic fields alter the interconversion rates and consequently change spin-dependent reaction yields. This is called the radical-pair mechanism (RPM) [2-4], which is a theoretical model to explain avian magnetoreception and a model for magnetic field induced production of reactive oxygen species (ROS). Although its basic principles are well-understood, several questions remain open such as the need for long radical lifetimes to explain high magnetosensitivity, i.e. the ability to detect magnetic fields, existing in nature.

## 2 Results and conclusions from the authors perspective

The RPM and its extensions can be utilized to explain the response of biomolecular systems to external magnetic fields. Whereas in avian magnetoreception the geomagnetic field is supposed to influence photochemical reactions in light-sensitive proteins, the absence of the GMF, i.e. exposure to a hypomagnetic field showed a significant reduction of hippocampal neurogenesis and hippocampus-dependent learning in adult male mice in a recent study [5]. To explain the latter theoretically, in [6] the RPM model containing a flavin semiquinone radical (FH●) and a superoxide anion radical (O2●-), created in a singlet state (specific spin-state of the two unpaired electrons in the radical pair), was used. This system either recombines from the singlet state or releases superoxide in the triplet state (second possible state for two electron spins). Reduction of interconversion rates from singlet to triplet by changing from geomagnetic field to hypomagnetic field exposure results in more singlet states and hence less superoxide release. This is in accordance with [5], where impairment of neurogenesis was strongly correlated with a reduction of concentration of ROS. The model presented in [6] is very simple and has thus several shortcomings in reproducing the complex chemical reactions discussed in [5]. First, the redox-chemistry of flavins favors the creation of triplet-state radical pairs, which would result in the opposite effect. Second the decoherence times of radicals involving superoxide are too short to explain the sensitivity to weak magnetic fields. The present paper addresses these shortcomings. As in a previous publication [7] an extension of the RPM involving three radicals, the radical triad mechanism (R3M) is suggested: The FH●/O2●- pair is extended by a scavenging ascorbyl radical A●-, the latter stemming from ascorbic acid in neurons.

To assess the effect of a radical triad in the hypomagnetic field the reaction yield in all channels where superoxide is released is calculated. The system containing 3 radicals is modeled by the Lindblad equation (a standard method to describe quantum systems with dissipation channels). Due to the fast relaxation times of the superoxide, it is assumed that it decohers (loses its ability interact quantum mechanically with the rest of the system) infinitely fast, so that this degree of freedom can be eliminated by taking the partial trace over the subspace corresponding to this radical.

It turns out that magnetosensitivity is determined on the one hand by the FH●/A●- - recombination rate (the scavenging rate) and on the other hand by the rate by which the population of radical triads decreases. Both, protein bound and freely diffusing flavin is investigated. As a general result, it is observed that the amount of released superoxide decreases in the hypomagnetic field, compared to geomagnetic field conditions, confirming experimental observations. In certain combinations of the two rates, maxima of magnetic field effects are observed as well as unexpectedly high magnetosensitivity. Eliminating the superoxide radical by taking the partial trace reproduces the biphasic behavior of the resulting magnetic field effects known from simpler radical pair models (low- and high field effects).

The R3M correctly reproduces the experimentally observed reduction of superoxide release in hypomagnetic field compared to the geomagnetic field while eliminating several difficulties of the conventionally used RPM model. The results strengthen the role of quantum spin dynamics in explaining hypomagnetic field effects on neurogenesis and in turn the role of the geomagnetic field for redox homeostasis through magnetosensitive reactions involving ROS.

# 3 Comments by the BfS

To determine the time evolution of the spins of the radical triad system, the authors with a specific form of the time evolution equation for the spin density (the Haberkorn form). The latter is the generally accepted way to determine the probability of the system to be in a specific state. The Hilbert space of the system is the tensor product of the spin-1/2 spaces of the three radicals FH●/O2●-/A●-. Due to the comparatively fast spin relaxation of superoxide, the authors simplify the system by taking the trace over the superoxide O2●- spin space. The assumption of fast spin relaxation of superoxide is plausible comparing the relaxation rate of superoxide to the rates of the other parts of the triad system. The use of a FH●/O2●-/A●- radical triad system allows to overcome the two main difficulties of earlier RPM models: Assuming the FH●/O2●- being created in the triplet state, the reaction yield of released superoxide shows the right behavior (reduced in the hypomagnetic field). Furthermore, and conceptually important, fast spin relaxation of superoxide does not destroy magnetic field effects. The need for an additional scavenging A●- radical adds additional complexity to the mechanism and the question whether this is likely to happen is discussed extensively by the authors. It is pointed out that the abundance of ascorbic acid in neurons makes an encounter of the FH●/O2●- with A●- physiologically plausible.

The results of the paper serve as a significant step towards understanding the role of quantum spin dynamics for hypomagnetic field effects on neurogenesis and cognition. As the main point of investigation is exposure to hypomagnetic fields, there is currently no direct relevance to risk evaluation. However, understanding magnetosensitive ROS generating processes is of general importance for gaining insight into interaction mechanisms of magnetic fields with biological systems.

## References

The first reference is always the manuscript at hand and the reference in the curly braces at the end of a reference {xx} correspond to a reference in the manuscript at hand and is consistent with the manuscripts reference style.

[1] Ramsay J and Kattnig D Radical triads, not pairs, may explain effects of hypomagnetic fields on neurogenesis. PLoS Comput Biol 18(9): e1010519 2022. DOI: 10.1371/journal.pcbi.1010519.

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**Impressum**

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