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# Role of radical pairs and feedback in weak radio frequency field effects on biological systems

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ABSTRACT

Radio frequency electromagnetic fields (RF) have been shown to modify the concentrations of the radical $O_2^-$, $H_2O_2$ and cancer cell growth rates at exposure levels below those that cause significant heating. Reactive oxygen species (ROS) are both signaling molecules and species that can do damage, depending on timing, location and concentrations. We briefly look at some mechanisms by which electromagnetic fields can modify the concentrations of ROS and some of the feedback and repair processes that lead to variable biological effects. Of particular interest are the role of radical pairs and their spins, which have received considerable attention recently, and the role of feedback in biological systems, to which less attention has been paid.

## 1. Introduction

There have been substantial concerns for a long time over the possible effects of radio frequency electromagnetic fields at exposure levels below those that lead to significant increases in temperature. Part of the problem has been the lack of generally accepted mechanisms by which weak fields can lead to biological responses. An additional difficulty has been that observed changes at the whole body level often stem from not only perturbations due to the RF fields but compensating changes generated by the ubiquitous biological feedback and repair processes. In general when the external environment changes, an organism responds so as to keep the biological systems operating within their normal ranges. For example an increase in core temperature in humans leads to an increase in blood flow and sweating to bring the temperature back down to within the normal range. Further complicating attempts to identity when and under what circumstances adverse or positive health effects may result from exposures to RF fields, the biological responses are dependent on current state of the system and its past history. Additionally the effects may vary in time over the course of extended exposures.

We present here some theory about one way weak magnetic fields can modify the recombination rates of radical pairs, which in turn can lead to changes in the concentrations of $O_2^-$, $H_2O_2$, and other radicals. Additionally some limited experimental data is presented showing both increases and decreases in cancer cell growth rates. The literature contains reports of many other such changes including in Usselman et al. (2016) and Chavarriaga et al. (2016). We also present some theory describing feedback mechanisms and demonstrate that the observed inconsistencies in biological responses to electromagnetic fields are of the sort that can be described through the biological systems' inherent compensatory processes, whether mediated through the radical pair or some other mechanism.

## 2. Theory

### 2.1. Radical pairs

It has been known that magnetic fields can modify chemical reaction rates for a long time. Much of this work has been reviewed at length by Steiner and Ulrich (1989), and Grissom (1995). Reviews of dynamic spin chemistry by Nagakura et al. (1999) and by Hayashi (2004) present detailed descriptions of the theory for the conversion of singlet (S) to triplet (T) states for radical pairs and the resulting changes in radical concentrations as a function of magnetic field strength, orientation, and the viscosity of the medium. Additional detailed calculations and measurements of changes in radical concentration on the applications of weak magnetic fields have been carried out by the group at Oxford (Batchelor et al., 1993; Timmel et al., 1998; Timmel and Henbest, 2004; Rodgers et al., 2007).

Briefly, radicals are defined as molecules with an unpaired spin and thus a net magnetic moment (See Fig. 1). Most molecules have an even number of electrons in the outer orbit which are paired with opposite spins. However, when these molecules split into two fragments the resulting fragments have an odd number of electrons in the outer orbit

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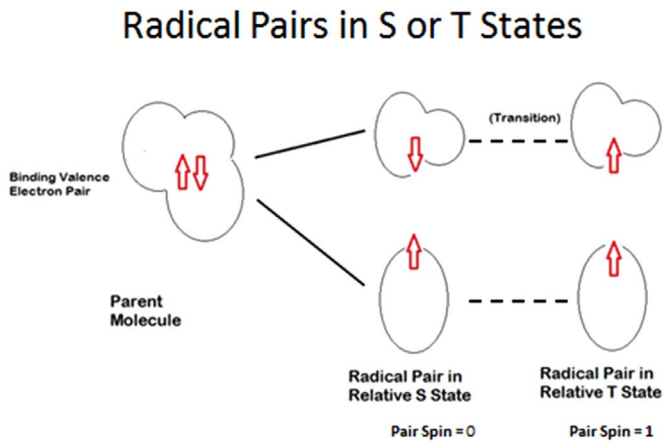


**Fig. 1.** A schematic diagram for a molecule which breaks into a pair or radicals which in turn may transition between S and T states with the spins aligned either antiparallel or parallel.

and an unpaired spin. Typically, they have different net magnetic moments. These fragments can typically recombine in $10^{-6}$ to $10^{-12}$ seconds depending on the viscosity of the medium and other parameters. A static magnetic field shifts the allowed energy states for the electrons differently in each fragment via the Zeeman Effect and changes the recombination rate. There are multiple energy levels corresponding to different electron orbits and the projections of the electron spins on the background static magnetic field (see Fig. 2) (Ramsey, 1956).

Time varying electromagnetic fields can excite transition between energy levels when $\Delta E = hf$, where $\Delta E$ is the energy separation between states, h is Planck's constant and f is the frequency of the externally applied field. These transitions in turn can change the spin populations in the fragments so that they do or do not satisfy the requirements for conservation of energy and angular moment for recombination.

As the energy separation changes with the static magnetic fields, the frequency for exciting transitions also changes. It also changes the energy match between levels in each fragment and thus the energy barrier for recombination. The net result is that we can both increase and decrease the recombination rate for the radical fragments and the concentrations of radicals such as $O_2^-$, and derivative molecules such as $H_2O_2$ with both static and time varying magnetic fields (see Fig. 3). Note that it is also possible that the concentration of the antioxidant is either increased or decreased by the magnetic field, thus leading to changes in oxidative stress and $H_2O_2$ in the opposite directions. Hence, the biological system may respond in either direction, depending on overall conditions. The forgoing approach to theoretically possible changes in radical concentrations is reviewed in much more detail in Barnes and Greenebaum (2015, 2016). Detailed calculations for resonances at RF frequencies have been carried out by Woodward et al. (2001), and it is to be noted that there are many resonances throughout the radio frequency range. Direct measurements of these resonant frequencies are often masked by the strong RF absorption by the water content of most biological materials. There are other biological processes that may be affected by the magnetic fields as well as radical pairs. The magnetic fields can act on molecules that have magnetic dipole moments, including hemoglobin, many enzymes, and cryptochromes. Much more extensive reviews of a number of other possible mechanisms by which RF fields can modify biological systems include Binhi (2002), Binhi and Prato (2017a, 2017b) and Belyaev (2015). The review of mechanisms by Engstrom (2007) has a focus on radicals.

### 2.2. Biological feedback

A second method for modifying the concentrations of radicals and other signaling molecules such as $H_2O_2$ is though biological feedback. Feedback permeates all aspects of biological systems. It is at the heart of the way radicals and other signaling molecules, as well as endogenous electrical signals operate to control essentially every process of an organism. Halliwell and Gutteridge (2015) present a book-length review of the roles of radicals in biology and medicine. Feedback also operates in many other aspects of living things (Goldstein and Kopin, 2017). Radicals and other signaling molecules, depending on their role in a particular process, the state of the system and other signals and circumstances, can serve to stimulate or to suppress a subsequent process.

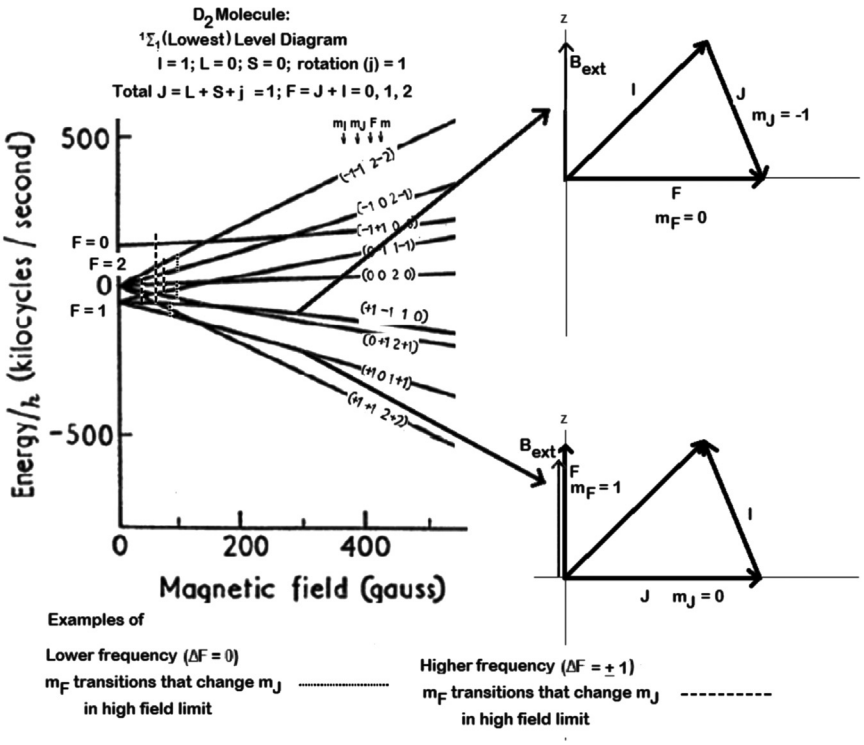


**Fig. 2.** An energy level diagram for $D_2$ showing the Zeeman Effect and a vector diagram for the sum of the nuclear and electronic magnetic moments. I is the nuclear spin quantum number, S is the electronic spin, L is the electronic orbital angular momentum, J is the total electronic angular momentum, and F = I + J is the total molecular angular momentum, applicable only at low magnetic field. The projection of each angular momentum along the direction of the applied magnetic field is given by $m_I$, $m_S$, $m_L$, etc.