

Magnetic Field Effects on  
Radical Pair Processes in Chemistry and Biology

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Summary

Chemical and biological photoprocesses which involve reactions between paramagnetic molecules can be affected by magnetic interactions, in particular, by external magnetic fields. Examples discussed are photoinduced electron transfer reactions, the primary process in photosynthesis and other radical pair reactions. In this article we provide experimental evidence for magnetic field effects on well characterized molecular systems and explain the physical origin of these effects.

1 Introduction

Without a measuring device like a compass needle humans cannot sense magnetic fields even in the neighbourhood of strong magnets. This insensitivity to magnetic fields does not apply to all biological species. In fact, many bacteria, insects and birds can sense magnetic fields very well and use the geomagnetic field for orientation. Zoologists and neurobiologists in collaboration with physical chemists are now facing the challenge of answering where in the organism and by which mechanism magnetic fields can influence biochemical reactions.

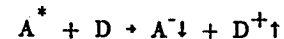
The study of possible influences of magnetic fields on chemical and biological processes with claims of rather odd effects had been long an activity of ill repute. The proponents of this activity were assumed to be unable to comprehend a simple counterargument: the strength of the

interactions of molecules with external magnetic fields are much smaller than thermal energies and, hence, on thermodynamic grounds chemical and biochemical processes cannot be influenced by magnetic fields to any measurable degree.

This argument appears to be completely valid. However, it has to be realized that a chemical reaction cannot only be affected by alterations of thermal energy barriers through external forces, but also by the perturbation of an intermediate quantum mechanical process, for which purpose interactions much weaker than thermal energies will suffice. It is necessary, however, that such an intermediate reaction step is faster than the time scale of magnetic relaxation, i.e. should not last longer than about  $10^{-6}$  s. In fact, there had been a variety of observations [1] which demonstrated through altered intensities in NMR and ESR spectra that chemical reactions can lead to products with electrons (in case of radicals) and nucleons strongly magnetically perturbed. This phenomenon known as 'Chemically Induced Dynamic Spin Polarization' opened the avenue for an understanding of magnetic field effects on chemical and biochemical reactions.

2 First Observation of a Magnetic Field Effect on a Chemical Reaction<sup>2</sup>

One of the first observations of a magnetic field effect on a well characterized 'in vitro' system was reported in Ref. 3. The reaction system, a pair of molecules A and D, is presented schematically in Fig. 1. The molecules involved in the reaction when excited by a laser flash assume the ability to transfer an electron. This light-induced electron transfer reaction is represented symbolically by



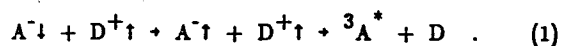
In this equation  $A^*$  represents the molecule A excited by the laser light.  $A^{-\downarrow}$  and  $D^{+\uparrow}$  are the symbols for the two molecules after the electron transfer, + and - indicating the charges. The arrows attached to A and D denote that the molecules after the electron transfer assume a magnetic moment. It is, of course, this moment which is the origin for the magnetic field effects.

Molecules which are chemically stable entail most often electrons in pairs, the pairs establishing the chemical bonds. Electrons possess magnetic moments (spins) and these attributes are the sources for the magnetic moments of molecules. In chemical bonds the magnetic moments of electrons are oriented in opposite directions and, therefore, the total magnetic moment of most stable chemical molecules vanishes. A and D are such molecules. However, by providing external energy it is possible to rotate the magnetic moments of an electron pair in a molecule, e.g. in A, into a parallel orientation. Since there are three energetically equivalent possibilities such molecular states are termed triplet. This state is represented by the symbol  $^3A^*$ .

Molecules which possess an odd number of electrons have necessarily one electron without a partner and, hence, assume a nonvanishing magnetic moment. Such molecules are often chemically aggressive and are called radicals. The molecules  $A^{\cdot-}$  and  $D^{\cdot+}$  are of this kind. The total magnetic moment of either of the molecules does not vanish, but plays a decisive role in the reaction system of Fig. 1.

Excitation by light does not directly affect the orientation of the electrons magnetic moment in molecules. Also electron transfer does not involve a reorientation of these moments. As a result the sum of the magnetic moment which vanishes for the molecular pair  $A + D$  and  $A^{\cdot-} + D^{\cdot+}$  also vanishes for the radical ion pair  $A^{\cdot-} + D^{\cdot+}$ . For this reason we have oriented the arrows denoting the magnetic moments of  $A^{\cdot-}$  and  $D^{\cdot+}$  in opposite directions.

As shown in Fig. 1 the electron transfer reaction  $A^* + D \rightarrow A^{\cdot-} + D^{\cdot+}$  is followed quickly, i.e. after about  $10^{-9}$  s, by the reverse reaction. For the backtransfer of the electron there exist two possibilities: (1) In case the magnetic moments of  $A^{\cdot-} + D^{\cdot+}$  are still oriented in opposite directions the reverse electron transfer yields the initial molecular pair  $A + D$  with vanishing magnetic moments. (2) In case the magnetic moments of  $A^{\cdot-} + D^{\cdot+}$  experience a reorientation the reverse electron transfer yields A and D with non-vanishing magnetic moments, in fact, the triplet state  $^3A^*$  mentioned above. The reorientation and reverse electron transfer is denoted by



One can consider the formation of the triplet molecule  $^3A^*$  as a chemical reaction with  $^3A^*$  as the reaction product. During the reaction the molecules carry out a Brownian motion in a solvent and are being bombarded by collisions with solvent molecules. However, these collisions have only a very small effect on the orientation of the magnetic moments of  $A^{\cdot-}$  and  $D^{\cdot+}$  such that the very faint interactions which the magnetic moments experience are not perturbed, at least not on the short time scale of the forward and backward electron transfer reaction. The faint interaction which the magnetic moments of the unpaired electrons of  $A^{\cdot-}$  and  $D^{\cdot+}$  experience involves the very small magnetic moments of the nuclear spins. This interaction is called the hyperfine interaction. Its effect is that in  $A^{\cdot-}$  as well as in  $D^{\cdot+}$  the unpaired electrons reorient their magnetic moments. This reorientation involves a precession of the magnetic moment of the unpaired electrons around an axis given essentially by the sum of the nuclear magnetic moments of the atoms constituting  $A^{\cdot-}$  and  $D^{\cdot+}$ .

An external magnetic field with strength B applied to the reaction system has an effect similar to the hyperfine interaction. The magnetic moments of the unpaired electrons interact with this field precessing around the field direction. The angular frequency of the precession increases linearly with the field strength B. The motion resulting from both the hyperfine interaction and the interaction with the external magnetic field (Zeeman interaction) is illustrated schematically in Fig. 2. This Figure shows how the magnetic moments of  $A^{\cdot-}$  and  $D^{\cdot+}$ , which are initially oriented in opposite directions, precess around the nuclear magnetic moments and an external field to assume, at least partially, a more parallel orientation. One expects then that external magnetic fields should influence the formation of triplet products  $^3A^*$  according to the reaction scheme (1) above. The observation of such effect is presented in Fig. 3. In the experimental system as shown schematically in Fig. 1 the concentration of triplet products  $^3A^*$  is found to decrease by about 15% when a magnetic field of about 100 Gauss is applied. Since the first observation of this effect in 1975 there have been numerous observations of such effects in many laboratories [4-6].

The magnetic field effect described has also given rise to new investigations and even to technical applications. For example, the precession of the magnetic moments of two radicals reacting with each

other can be employed as an internal 'clock' which allows to measure the reaction times of very fast chemical processes in liquids, e.g. of electron transfers forward or backwards. The generation of triplet products is the more likely the longer the time span between the forward and the backward electron transfer. From the observation as shown in Fig. 3 one can estimate that this time span is about  $10^{-8}$ s.

The observation and explanation of magnetic field dependent chemical reactions has already lead to a technical application, the photochemical separation of isotopes [5,7,8]. This application uses the role of the nuclear magnetic moments in radical pair reactions influenced by the reorientation of the unpaired electron magnetic moments. Materials which differ in the strength of their nuclear magnetic moments can yield the reaction product with vastly different efficiencies. Different isotopes of radicals are such materials and several laboratories have demonstrated already that radical pair reactions, as discussed here, can separate isotopes through magnetic interactions with an efficiency which is far above that of all other methods. For example, organic radicals entailing the carbon isotope  $^{13}\text{C}$ , which has a very strong interaction with the unpaired electrons magnetic moments, induce a reorientation of the radicals magnetic moments much faster the same radicals with the common carbon isotope  $^{12}\text{C}$ , which bears no hyperfine interaction. Corresponding reaction systems provided a 1000% enrichment of the isotope  $^{13}\text{C}$  over its natural abundance [5].

The magnetic field effect has also been exploited to study reactions in microcavities and on the surface of materials. A microreaction system which yields particularly strong magnetic field effects is realized by micelles made of lipid molecules [9,10]. The reaction times in micelles can be very long and, hence, magnetic field effects can be very strong. A most recent application of magnetic field effects has been to the study of the folding dynamics of polymers with paramagnetic (radicalic) end groups [11,12]. The results of these experiments are exciting because polymer folding is of such great importance in several fields of science, e.g. in biology, but also because the observations revealed that polymeric systems may be used like microcavity systems for the facilitation of some interesting chemical reactions.

### 3 Magnetic Field Effects and the Primary Process of Photosynthesis

The light-induced electron transfer reaction as in Fig. 1 constitute also the primary reaction in photosynthesis, i.e. the system which transduces the energy of sunlight into various forms of biochemical energies. The photosynthetic system for which the primary reaction and the molecular apparatus are known best is that of the photosynthetic bacterium *Rhodospseudomonas viridis*. The light-induced electron transfer in this bacterium occurs in a complex of proteins and pigments, which is located the outer membrane of the cell [13]. This complex is known as the photosynthetic reaction center. The biological pigments in the reaction center are aligned in a linear chain (with a side branch assumed to be non-functional) which connects the cytoplasmic and the extracellular side of the membrane. This chain of pigments operates exactly like a physical photodiode made of two semiconductors. Figure 4 presents schematically the chain of pigments along with their electronic states and the electron transfer pathway.

The optical excitation of the biological photodiode involves a centrally located pair of two molecules of bacteriochlorophyll. The excitation advances a negatively charged electron from an occupied electronic orbital into a higher energy unoccupied orbital; a positively charged electron hole remains in the orbital previously occupied by two electrons. The energetically excited electron jumps along a pathway of energetically descending unoccupied pigment orbitals towards the extracellular site of the reaction center while the electron hole is being transported to the cytoplasmic side. Altogether the sun light absorbed induces a transfer of an electronic charge across the bacterial membrane. This transfer is accompanied by a membrane potential which is first transformed into a proton gradient across the membrane and then utilized to drive several exothermic biochemical reactions of the cell.

Essential for the function of the photosynthetic reaction center is the high efficiency with which the primary electron transfer is achieved and the back-transfer is prevented. In order to study the molecular properties required to achieve this efficiency one has chosen to block the primary electron transfer chain in the reaction center by ionizing a ubiquinon (the first involved in the electron transfer pathway shown in Fig. 4). This

forces the electron transferred from the excited chlorophyll pair to the adjacent bacteriochlorophyll and bacteriopheophytin to return to its parent molecule.

The electron transfer of the modified reaction center just described corresponds exactly to the reaction in Fig. 1 in that the electron after the back-transfer can either occupy the original state with vanishing total magnetic moment before light excitation or the triplet state of the complex of two bacteriochlorophylls. However, in order to occupy the latter state the magnetic moments associated with the transferred electron and the electron hole left behind must be reoriented by magnetic interactions.

Spectroscopic observations of the products of the electron transfer in the modified photosynthetic reaction center revealed an expected magnetic field dependence in a field range between 0 and 400 Gauss [14,15]. Figure 4 shows a pertinent observation by Michel-Beyerle et. al. [16]. The observations showed that the magnetic field dependence of triplet formation in the photosynthetic reaction center depends sensitively on the structure of the molecular assembly. The magnetic field dependence reveals, in fact, several weak but functionally important electronic interactions between the pigment in the reaction center. The most interesting conclusion which can be drawn from the observations is that immediately after the first transfer step, which takes about  $10^{-11}$ s, the electronic interaction between the transferred electron and the hole left behind is very weak. This implies that an efficient separation of electron and hole in photosynthesis is realized already after  $10^{-11}$ s, i.e. it is this short time span in which the energy problem of photosynthetic species is solved and, thereby, of most of the remaining biological species, since they ultimately rely on the photosynthetic energy.

#### 4 A Biochemical Compass

Electron transfer (redox) processes and other reactions between pairs of radicals are involved in many parts of the metabolic pathways of biological organisms. Since these reactions can be influenced by magnetic fields they may yield an explanation of the molecular basis of the magnetic sense of higher biological species, e.g. migratory birds and

pigeons [17]. A biomagnetic compass could be realized, for example, through the biochemical reaction scheme shown in Fig. 5. In this scheme magnetic interactions as discussed above induce a reorientation of the magnetic moments of two radicals denoted by the transition  $A\downarrow + B\uparrow \rightarrow A\uparrow + B\downarrow$ . Radicals with their magnetic moments oriented in parallel should form triplet products.

The function of a compass, i.e. a dependence on the orientation of an external magnetic field, results since the hyperfine interaction between the electron and nuclear magnetic moments, in general, is anisotropic, i.e. not equally strong in the three spatial directions. In case the participating molecules are in a spatial orientation which is fixed relative to an organism, the biochemical scheme of Figure 5 can be used as a compass. This possibility is borne out by calculations, the results of which are presented in Figure 6, as well as electron transfer reactions between an organic dye and a semiconductor at the surface of the semiconducting crystal.

A biochemical compass to be utilized for the magnetic sensory organs of higher biological species has to face the difficulty that the strength of the geomagnetic field which is to be detected measures only about 0.5 Gauss. There exist many reports which indicate that magnetic sensory organs can be influenced by even weaker magnetic fields. Since the behaviour of reactions as in Fig. 1, 4 and 5 are conceptually well understood one can turn to theoretical calculations for an answer to the question if the radical pair reactions which show a dependence on the strength of magnetic fields only in the 10 Gauss to 100 Gauss range can detect also much weaker fields. The theoretical answer is yes, however, the biological apparatus must assure that the radical pair reaction can last for a long time, i.e. about  $10^{-6}$ s [18].

In calling attention to radical pair reactions for an explanation of the magnetic sensory organs in biological species we must point out that in bacterial systems a much simpler explanation has been found: bacteria with the ability to swim along the direction of the geomagnetic field can do so by virtue of magnetite crystals in their cell bodies which merely turn the swimming cell into the proper direction [19]. Since magnetite crystals are known to exist commonly in biological cells, e.g. in the skulls of migratory birds, a similar mechanism has been suggested for higher

species [20]. However, the difficulty with evoking magnetite is how the weak mechanical forces acting on cellular magnetite crystals could be detected by a neuronal system. The solution of the mechanism of the magnetosensory organ of higher organism may perhaps involve both magnetite and radical reactions.

The biochemical reaction scheme of Fig. 5 according to the results in Fig. 6 show a peculiar dependence on the field orientation: the dependence is symmetric with respect to the northern and southern directions, i.e. the system proposed cannot discern between north and south but only locate the lines of the field, including a possible inclination. This uncertainty is known to exist also for the magnetic sensory organs of migratory birds, which in order to determine north or south rely on additional information, namely a knowledge of the inclination of the geomagnetic field lines. Migratory birds in the northern hemisphere which detect lines inclined to the earth surface interpret the downwards direction as north. If one adds to the geomagnetic field in a birds cage a suitable artificial magnetic field such that the resulting field is inclined downwards in the southern direction the birds will interpret south as north [17].

Any essential progress towards the goal of understanding the magnetosensory organs of higher animals hinges on explorations of the location of the primary sensual effects. Recent electrophysiological and neuroanatomical investigations by Semm et. al. [21] indicate that as judged by electrical recordings the retina provides the primary sensual effects. The spatial organization of the rod and cone outer segments would be most suitable for a photochemical reaction with reaction partners in a spatially fixed orientation. Also the idea is most intriguing that the sensation of the geomagnetic field in birds happens actually along the visual pathway, a pathway which is well equipped to process orientational information by virtue of its highly developed neural assemblies in the brain. An answer along these lines could be formulated simply as follows: birds can literally see the magnetic field as a patterned optical shade, which is superimposed over their visual impressions, and which turns with their head movements [22].

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## FIGURE CAPTIONS

Figure 1: Cyclic electron transfer in a polar liquid: the process is induced by a ns laser flash, the concentrations of the participating compounds  $A^*$ ,  ${}^3A^*$ ,  $A^{\bullet}$  (light-excited molecule),  $A^{\bullet-}$  (radical) and  $D^{\bullet+}$  (radical) are monitored through their absorption spectra by means of a probe light; the initial electron transfer is followed by a reverse transfer either to the initial state  $A + D$  or to the triplet state  ${}^3A + D$ . The diagram indicates that the initial reaction partners  $A^{\bullet-} + D^{\bullet+}$  can separate and react with other pairs. This reaction route takes a longer time and is not magnetic field dependent.

Figure 2: Schematic illustration of the precession of the magnetic moment of the pair of radicals, a pyrene (A) and a dimethylaniline (D) molecule. Shown in the picture is the precession of the radicals magnetic moments, the orientations of the nuclear magnetic moments and the external magnetic field B.

Figure 3: Magnetic field dependence of the concentration of triplet products of the reaction schematically shown in Figure 1 involving the molecules pyrene (A), dimethylaniline (D) and the solvent methanol. (From Weller et. al. )

Figure 4: Schematic representation of the relevant molecular orbital energy levels of the constituent pigments of the photosynthetic reaction center; electronic excitation takes place at the chlorophyll - dimer in the center; (—) indicates the electron transfer processes favourable for the biological function, i.e. charge separation across the cellular membrane; (- - -) indicates processes unfavourable for this function; the structure of this molecular assembly has been provided in Ref. 13.

Figure 5: Observation of a magnetic field effect on the triplet formation in a modified photosynthetic reaction center which undergoes cyclic electron transfer (from Ref. 16).

Figure 6: Reaction scheme for a biochemical compass; a biochemical reaction produces a molecule Z, which is converted either into a molecule

X or into the radical pair  $A\downarrow + B\uparrow$ , the latter assuming initially antiparallel magnetic moments.

Figure 7: Demonstration of a biochemical compass: the concentration of triplet products formed according to the reaction scheme in Fig. 6 is dependent on the orientation with respect to an external magnetic field.

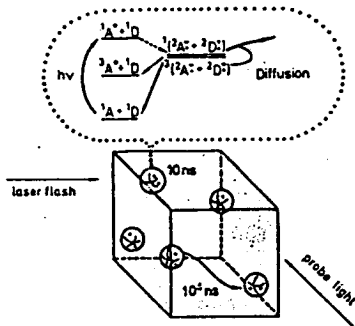


Figure 1

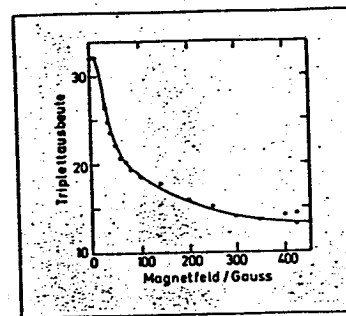


Figure 5

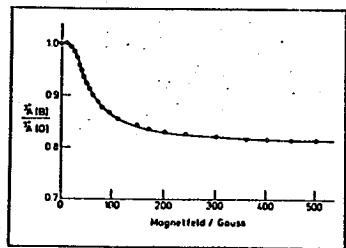
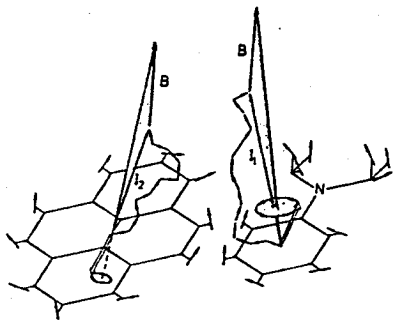


Figure 3

Figure 2

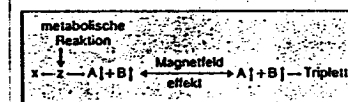


Figure 6

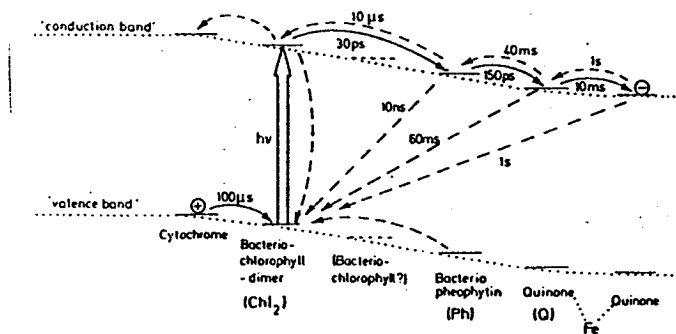


Figure 4

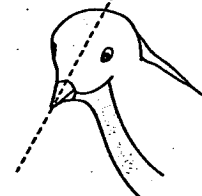
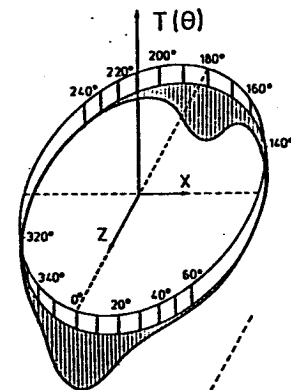


Figure 7