A Model for Photoreceptor-Based Magnetoreception in Birds

Thorsten Ritz, Salih Adem, and Klaus Schulten
Theoretical Biophysics Group, Beckman Institute
University of Illinois at Urbana–Champaign, Urbana, IL 61801, USA

October 11, 1999

Abstract

A large variety of animals has the ability to sense the geomagnetic field and utilize it as a source of directional (compass) information. It is not known by which biophysical mechanism this magnetoreception is achieved. We investigate the possibility that magnetoreception involves radical-pair processes which are governed by anisotropic hyperfine coupling between (unpaired) electron and nuclear spins. We will show theoretically that fields of geomagnetic field strength and weaker can produce significantly different reaction yields for different alignments of the radical pairs with the magnetic field. As a model for a magnetic sensory organ we propose a system of radical pairs being (i) orientationally ordered in a molecular substrate and (ii) exhibiting changes in the reaction yields that affect the visual transduction pathway. We evaluate three-dimensional visual modulation patterns that can arise from the influence of the geomagnetic field on radical-pair systems. The variations of these patterns with orientation and field strength can furnish the magnetic compass ability of birds with the same characteristics as observed in behavioral experiments. We propose that the recently discovered photoreceptor cryptochrome is part of the magnetoreception system and suggest further studies to prove or disprove this hypothesis.

Introduction

The hypothesis that migrating birds utilize the geomagnetic field for orientation has been proposed as early as 1859 (von Middendorff, 1859). The use of a magnetic compass by migratory birds has first been demonstrated for European robins in 1966 (Wiltschko and Merkel, 1966) and, since then, in 17 further species (Wiltschko and Wiltschko, 1996). However, the biophysical mechanism of magnetoreception is still unknown. Among the theoretical models for magnetoreception mechanisms that have been proposed, the use of magnetite particles as magnetoreceptors and photoreceptor-based mechanisms involving direct magnetic effects on the visual transduction process have received the most attention. Suggestions for a magnetite-based magnetoreceptor include freely rotating single-domain magnetite particles (Kirschvink and Gould, 1981), fixed super-paramagnetic magnetite particles (Kirschvink *et al.*, 1985), or magnetite-containing liquid crystals (Edmonds, 1996). Three different hypotheses for photoreceptor-based mechanisms have been proposed. Leask (Leask, 1977) suggests a radio-frequency resonance process acting on a hypothetical triplet state of the visual pigment rhodopsin. Hong (Hong, 1977; Hong, 1995) proposed the magneto-orientation effect of rhodopsins, which occurs at field strengths of 1000 times the geomagnetic field strength due to oriented diamagnetic anisotropy, as a possible mechanism. For much weaker field strengths (10-20 times geomagnetic strength) magnetic field effects have been observed to influence radical-pair reactions in polar liquids (Schulten *et al.*, 1976) and under laboratory conditions in photosynthetic bacteria (Werner *et al.*, 1978). These studies led to the third suggestion that a radical-pair mechanism can act as a chemical sensor for magnetic compass orientation (Schulten *et al.*, 1978; Schulten, 1982; Schulten and Windemuth, 1986).

Any theoretical model has to explain the experimentally determined features of the avian magnetic compass. In a variety of studies of migratory birds including short-distance and long-distance migrants, birds of the northern as well as of the southern hemisphere, night, twilight, and day migrants (Wiltschko and Wiltschko, 1996), the magnetic compass was shown to be an inclination compass, i.e., it is sensitive to the axis but not to the polarity of the magnetic field lines. Inverting the vertical component of the field lines had the same effect as inverting the horizontal component; a reversal of both components, which means an inversion of the polarity, did not alter the bird's behavior (Wiltschko and Wiltschko, 1972).

Magnetic compass orientation has been shown to be dependent on the wavelength of the ambient light. While European robins and Australian silvereyes showed good orientation under blue light (peak at 443 nm) and green light (peak at 565 nm), they were disoriented under red light (peak at 630 nm) (Wiltschko *et al.*, 1993; Wiltschko and Wiltschko, 1995b). The high activity under red light suggests that the birds could perceive the red light, since nocturnal migrants show no activity during darkness (Gwinner, 1974). Also, all of the above wavelengths are within the visible range of passerines, in species for which the spectral sensitivity has been measured (Maier and Bowmaker, 1993). Very recent behavioral experiments show that European robins cannot orient under yellow-orange light (peak at 590 nm), although there is a significant overlap between the green light (half maximum bandwidth 550 to 583 nm), where orientation was excellent, and the yellow light (half maximum bandwidth 572 to 609 nm) without orientation (Wiltschko and Wiltschko, 1999). In the context of a vision-based magnetoreception mechanism, these findings suggest that light with an energy above a certain threshold is needed in order for the mechanism to work.

Further evidence for a light-dependent magnetoreception mechanism is given by measurements that show that neurophysiological responses depend on the presence of light and an intact retina (Semm and Demaine, 1986; Semm and Schneider, 1991). Responses to changes in the magnetic field could be recorded from two areas on the optic system, the nucleus of the basal optic root (nBOR) and the *tectum opticum*. In both areas, only one type of cell, direction-selective cells, responded to magnetic stimuli. Of these, about 60% showed increased spike frequencies, about 10% were inhibited, while the others showed no change

(Semm *et al.*, 1984; Semm and Demaine, 1986).

A third important property of the bird's magnetic compass is the limitation of its sensitivity to a narrow range of magnetic intensities. Robins captured and kept in a local magnetic field of 0.46 Gauss were able to orient only within a narrow intensity window that included 0.43 and 0.54 Gauss, but were disoriented for 0.16, 0.34, 0.6, 0.81 and 1.5 Gauss (Wiltschko and Wiltschko, 1972; Wiltschko, 1978).

In this article, we will follow the suggestion of (Schulten *et al.*, 1978; Schulten, 1982; Schulten and Windemuth, 1986) and investigate the radical-pair mechanism as a possible theoretical model for a magnetic compass. We will present a theoretical framework for a vision-based magnetoreception mechanism that connects the molecular and quantum properties of radical-pair processes with the behavioral responses of a bird. The major challenges in doing so can be summarized in three questions: Can a magnetic field as weak as 0.5 Gauss produce significant effects on radical-pair processes? At which point in the visual transduction pathway could a radical-pair mechanism be involved as a magnetoreception mechanism? How do the effects on the receptor level translate into visual perception and, ultimately, the behavior of the bird?

The first question addresses the physical feasibility of magnetoreception through a radical-pair process. The energy of magnetic interaction per particle involved in radical-pair processes is much smaller than the average thermal energy per particle under ordinary conditions (i.e. temperature, pressure, etc.) where biochemical reactions take place. However, this does not necessarily imply that magnetic field effects on radical-pair reactions become undetectable, since the spin of electrons bound to biomolecules is not coupled strongly to the thermal bath. The effects of magnetic fields on the precession of electron spins is determined by the relation between strength of magnetic field, strength of hyperfine coupling, and lifetime of the radical pairs. Thermal relaxation is only one of several factors that influence the radical-pair lifetime. In this article, the effect of weak magnetic fields on an orientationally ordered system of radical pairs with anisotropic hyperfine coupling is evaluated. The main goal of this article is to provide a proof of principle that a radical-pair system can act as a geomagnetic compass system by showing that a field of the strength of 0.5 Gauss can produce effects that significantly differ for different orientations of the radical pairs. We will explain the quantum-mechanical mechanism by which effects on product yields of radical pairs are achieved for earth-strengh magnetic fields.

While the first question can be answered within the framework of quantum physics, the question of where such a radical-pair mechanism could occur in the visual pathway must be answered by biochemical or neurophysiological experiments, and suggestions have to be speculative. Recently, however, a new class of photoreceptors has been found in the eyes of mammals, which deserves consideration as a magnetoreceptor. This new class are the cryptochromes, which have been shown to be involved in the regulation of the circadian rhythm (Cashmore *et al.*, 1999). We provide arguments that suggest the possibility that cryptochromes might also be involved in magnetoreception. We hope to prompt experiments designed to prove or disprove the involvement of these hypothetical receptors.

Whatever the exact transduction mechanism, the magnetic field effects on the model substrate system can be used to evaluate, in an anthropomorphic picture, how these effects translate into a modulation of visual perception. The visual modulation patterns are a representation for the output from the magnetic compass which can be used to arrive at qualitative predictions of animal behavior. We will show that all of the above-mentioned behavioral findings emerge as properties of the model presented in this article.

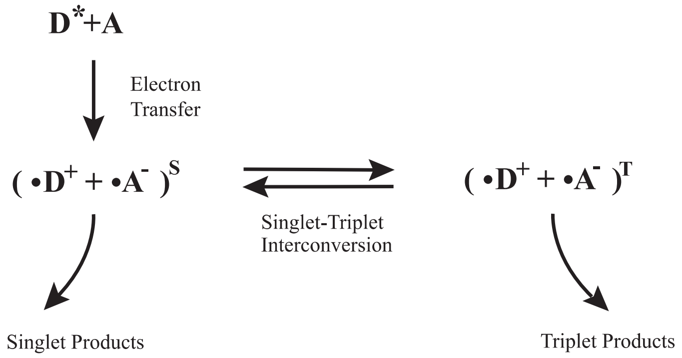

Figure 1: Reaction scheme for a radical pair reaction with magnetic field dependent reaction products. The radical pair is generated by an electron transfer from a donor molecule D to an acceptor molecule A. An external magnetic field affects interconversion between singlet and triplet states of the radical pair.

Theory

The radical-pair mechanism, by which a magnetic field alters the product yields of radical-pair reactions, is by now well established theoretically and experimentally (Salikhov *et al.*, 1984; Steiner and Ulrich, 1989). Magnetic field effects have been studied on radical-pair systems in solution (Schulten *et al.*, 1976; Werner *et al.*, 1977; Haberkorn, 1977; Schulten and Weller, 1978) and in a bacterial photosynthetic reaction center (Werner *et al.*, 1978; Haberkorn and Michel-Beyerle, 1979), see also the reviews (Hoff, 1981; Schulten, 1982; Boxer *et al.*, 1983). Changes in product yields by magnetic fields of 10–100 Gauss are well documented as reviewed in (Steiner and Ulrich, 1989). The radical-pair mechanism has been investigated also in the context of possible effects of magnetic fields on biological systems other than photosynthesis (Grissom, 1995), in particular in the context of effects on enzymatic reactions (Canfield *et al.*, 1996; Harkins and Grissom, 1994). Recently, attention in the field has focussed on the effects of weak magnetic fields on radical-pair reaction product yields (Brocklehurst and McLaughlan, 1996). An effect opposite in direction to the effects of higher magnetic field strengths has been predicted theoretically for geomagnetic field strength (Brocklehurst, 1976; Timmel *et al.*, 1998) and measured experimentally under laboratory conditions (Batchelor *et al.*, 1993).

A simple radical-pair reaction scheme, which can act as a chemical magnetoreceptor mechanism as suggested originally in (Schulten *et al.*, 1978; Schulten, 1982; Schulten and Windemuth, 1986), is depicted in Figure 1. The reaction scheme encompasses three steps. In the first step, an excited donor molecule D^* transfers an electron to an acceptor molecule A, resulting in a radical pair $D^+ + A^-$. It is crucial for the magnetic field effect that the radical pair is formed in an (electron) spin-correlated singlet or triplet state. Such a spin-correlated radical pair can be generated, for example, by photoinduced electron transfer. In this case, the transfer is induced by photoexcitation of the donor, either through direct light absorption by the donor or through light absorption by a different photoreceptor and subsequent excitation transfer to the donor. Usually, the photoexcited donor and the acceptor will be in singlet states before electron transfer, thus forming an overall singlet state. Electron transfer will then not change the spin correlation, so that the radical pair is generated in an overall singlet state.

Once the radical pair is generated in a spin-correlated state, its singlet and triplet states will be interconverted by the hyperfine interaction given that (a) exchange or dipolar couplings between the electrons are weak compared to the hyperfine couplings, and (b) the recombination reactions are slow enough to allow significant singlet-triplet conversion to take place. This singlet-triplet interconversion, representing the second step in the radical-pair reaction scheme, can be influenced by a magnetic field as detailed below.

In the final step, singlet and triplet pairs will react to give distinct products, thus depleting the population of radical pairs with respective rate constants k_S and k_T. A simple example for such a reaction is electron back-transfer from the acceptor radical to the donor radical generating a pair of molecules in either a singlet or a triplet state.

In order to evaluate the triplet yield for a radical pair, we assume that the radical pair is geometrically fixed in a substrate and generated in a singlet state. The triplet yield Φ^T is defined as the amount of products decaying via the triplet channel,

$$\Phi^T(t) = \int_0^\infty k_T T(t) dt \ , \tag{1}$$

where $T(t)$ is the fraction of radical pairs in the triplet state at any given time t and k_T is a first order reaction rate constant. $T(t)$ can be evaluated according to

$$T(t) = \mathrm{Tr}\ [Q^T \rho(t)] \ , \tag{2}$$

where $\mathrm{Tr}\ A = \sum_i A_{ii}$ and Q^T is the triplet projection operator. $\rho(t)$ is the density matrix with its time dependence governed by the stochastic Liouville equation (Kubo, 1969)

$$\dot{\rho}(t) = -\frac{i}{\hbar}[H, \rho(t)]_- - \frac{k_S}{2}[Q^S, \rho(t)]_+ - \frac{k_T}{2}[Q^T, \rho(t)]_+ \ . \tag{3}$$

Here, $[A, B]_\pm = AB \pm BA$, Q^S is the singlet projection operator, the initial condition for the density matrix is $\rho(0) = Q^S/\mathrm{Tr}\ Q^S$ since the radical pair is assumed to be initially in a singlet state, and H denotes the spin Hamiltonian of the radical pair. The three terms in Eq. 3 account, respectively, for singlet-triplet interconversion in the radical pair governed by the spin Hamiltonian H, decay of radical pairs to singlet products, and decay of radical pairs to triplet products.

If one assumes that the recombination rates are spin-independent, i.e. $k = k_S = k_T$, the spin-dependent evolution of the density matrix decouples from the first-order decay kinetics through recombination, which allows one to express the density matrix in the form

$$\rho(t) = \frac{1}{N} e^{-iHt/\hbar} Q^S e^{iHt/\hbar} e^{-kt} \ . \tag{4}$$

Here, N is the number of nuclear spin states. Insertion of Eq. 4 into Eq. 2 yields

$$T(t) = \frac{1}{N} e^{-kt} \sum_{m=1}^{4N} \sum_{n=1}^{4N} Q^T_{mn} Q^S_{mn} \cos\left[(w_m - w_n)t\right] \ , \tag{5}$$

where $\hbar w_i$ denotes the energy of the eigenstate $|i\rangle$ of the Hamiltonian H. Evaluating the integral in Eq. 1 gives the triplet yield

$$\Phi^T(t) = \frac{1}{N} \sum_{m=1}^{4N} \sum_{n=1}^{4N} Q^T_{mn} Q^S_{mn} \ \frac{k^2}{k^2 + (w_m - w_n)^2} \ . \tag{6}$$

As pointed out in (Timmel *et al.*, 1998), the effect of weak (meaning field strength is small compared to the hyperfine coupling strength) magnetic fields can be understood from the cosine term in Eq. 5. Due to the Zeeman interaction, otherwise degenerate energy levels split and cause oscillations between singlet and triplet states, thus, enhancing singlet-triplet mixing and increasing the triplet yield. This effect is opposite to the magnetic field effects for field strengths comparable to the hyperfine coupling strengths, which essentially shift the energy of triplet states with non-zero magnetic quantum numbers away from the singlet state energy and, thus, decrease singlet-triplet mixing and the triplet yield. The triplet yield for weak magnetic fields does not only depend on the strength of the applied magnetic field, but also on the ratio between the magnetic field strength and the recombination rates. In order to analyze this relation further, we choose for the sake of clarity a particular simple Hamiltonian.

For a pair of radicals $j, j = 1, 2$, each with a single electron spin S_j and a single spin-$\frac{1}{2}$ nucleus I_j, the spin Hamiltonian is

$$H(\vec{B}) = H_1(\vec{B}) + H_2(\vec{B}) \tag{7}$$

with

$$H_j(\vec{B}) = g\mu_B \vec{S}_j \cdot \left(\vec{B} + \mathbf{A}_j \vec{I}_j\right) \ . \tag{8}$$

In Eq. 8, the first term accounts for the Zeeman interaction and the second term for the hyperfine interaction. μ_B is the Bohr magneton of the electron. The g-values are chosen to be $g = 2$ for both radicals. For strong magnetic fields (larger than 1000 Gauss), singlet-triplet interconversion can occur by virtue of the different Zeeman interactions due to differences in g-values (Boxer *et al.*, 1982), but this effect can be neglected for magnetic fields smaller than 10 Gauss which we investigate here. $\mathbf{A}_j$ denotes the hyperfine coupling tensor, a 3×3 matrix.

In order for the radical pair to be sensitive to different alignments to the magnetic field, it is necessary that the hyperfine coupling tensor be anisotropic. For the sake of simplicity, we assume that the hyperfine coupling is anisotropic for only one of the radicals, i.e.,

$$\mathbf{A}_1 = \begin{pmatrix} 10 \text{ Gauss} & 0 & 0 \\ 0 & 10 \text{ Gauss} & 0 \\ 0 & 0 & 0 \end{pmatrix} , \tag{9}$$

while the hyperfine coupling tensor of the second radical is isotropic, i.e.,

$$\mathbf{A}_2 = \begin{pmatrix} 5 \text{ Gauss} & 0 & 0 \\ 0 & 5 \text{ Gauss} & 0 \\ 0 & 0 & 5 \text{ Gauss} \end{pmatrix} . \tag{10}$$

The chosen model system is a particularly simple one, crudely approximating the behavior of biological radical pairs by a radical pair with only two nuclear spins, assuming spin-independent decay kinetics, and choosing the specific hyperfine coupling tensors given above. The simple model serves mainly to demonstrate how the interplay between hyperfine coupling strength, magnetic field strength, and recombination times, as well as the alignment of the radical pairs with respect to the magnetic field, affects the magnitude of magnetic field effects. We will discuss below inhowfar the simplifications will affect the predictions made. Our interest here is to obtain qualitative results from model calculations to illustrate how magnetic compass orientation might work in birds.

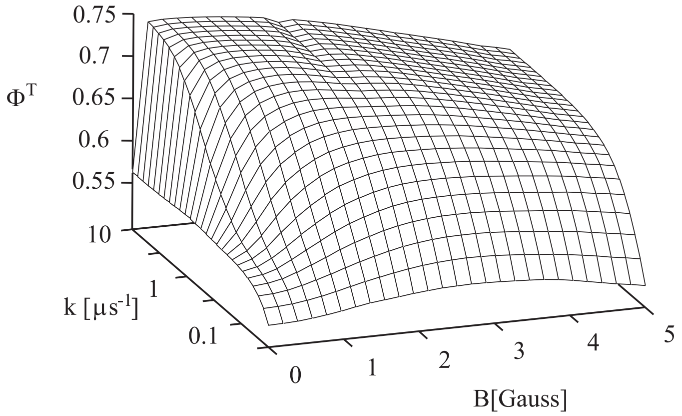

Figure 2: Dependence of triplet quantum yields Φ^T on radical-pair decay rates k and strength of an external magnetic field B. Φ^T is evaluated according to Eq. 6 for the radical pair model with anisotropic hyperfine coupling as described in Eqs. 8-10. The z-axis of the radical pair has been aligned at an angle of 68° with respect to the magnetic field vector.

Results

Magnetic Field Effects for Radical Pairs with Anisotropic Hyperfine Coupling

The role of magnetic field strength and radical-pair lifetime on the yield of triplet products of a radical-pair process with anisotropic hyperfine coupling is demonstrated in Figure . The triplet yields shown were evaluated according to Eq. 6 using the Hamiltonian with hyperfine couplings as defined in Eqs. 9, 10. The z-axis of the radical pair was aligned at an angle of 68° with the magnetic field vector, which is the angle for which an earth-strength magnetic field produces the largest triplet yield (cf. Fig.).

As can be seen from Fig. , even magnetic fields weaker than 0.5 Gauss produce a significant increase of the triplet yield which is more pronounced the slower the radical-pair decay rates are. For larger magnetic fields the effect is the opposite: the triplet yield drops slowly. This latter decrease is the magnetic field effect predicted and observed in radical-pair processes over twenty years ago as reviewed in (Steiner and Ulrich, 1989). For the purposes of magnetic compass orientation this effect is negligible since it only produces changes of a few percent over a range of 5 Gauss.

The effect of the radical-pair decay rates on triplet yields has a twofold origin. For very high decay rates ($> 10\ \mu s^{-1}$) the fast decay of the radical pair prevents efficient singlet-triplet mixing as can be seen by the decrease of the triplet yields at zero magnetic field. For such fast decays the effects of the magnetic fields become hardly detectable. For slower decays (decay rates less than $10\ \mu s^{-1}$) and large magnetic fields, the drop in triplet yields for increasing magnetic fields is essentially unaffected by the decay rates. In contrast, the effect of weak magnetic fields depends significantly on the value of the decay rate. This is demonstrated in Fig. , where the effects of weak magnetic fields are shown. The sensitivity of the radical-pair system to weak magnetic fields increases significantly with lower decay rates.

Given the significant influence of the radical-pair decay rates, one has to ask what the values of the decay rates are in biological systems. Recently, the decay rates of radical pairs have been measured in a protein environment through flash photolysis (Mohtat *et al.*, 1998), resulting in decay rates between 1

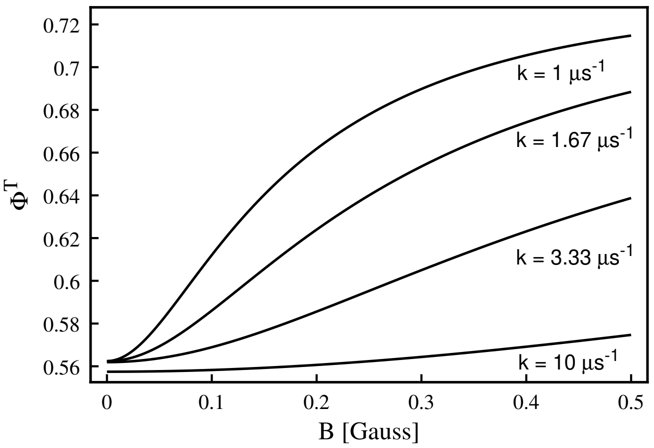

Figure 3: Triplet quantum yields Φ^T evaluated as in Fig. . The figure shows the significant influence of the radical pair decay rates on the strength of the effects of weak magnetic fields (below geomagnetic field strengh).

and 2 μs^{-1} depending on the choice of radicals and protein solutions. Though this result may not be representative, it shows that a radical-pair decay rate of 1 μs^{-1} can be achieved in biological systems. It is reasonable to assume that nature has optimized the decay rates through evolution so as to provide a maximum effect. For a decay rate of 1 μs^{-1}, the triplet yield is increased from the zero field value of 0.56 to 0.61, 0.66, 0.69, 0.71, and 0.74 for respective field strengths of 0.1, 0.2, 0.3, 0.4, and 0.5 Gauss (cf. Fig.). We will assume a decay rate of 1 μs^{-1} throughout our further calculations.

The validity of the presented results is based on the particular values chosen for the hyperfine coupling strength. It should be noted that it is the ratio between magnetic field strength and hyperfine coupling strength as well as the ratio between decay rate and hyperfine coupling strength that influences the triplet yield. If the hyperfine coupling is five times as large as the one chosen in our present description, an increase of the magnetic field strength and decay rate by a factor of five will produce the same effects.

In order to obtain directional information from the geomagnetic field it is not enough that a radical-pair reaction is influenced by a 0.5 Gauss magnetic field, but it is necessary that there is a significant difference between the effects of a 0.5 Gauss magnetic field on radical pairs with different orientations with respect to the field.

The dependence of the triplet yield on the angle θ between the z-axis of the radical pair and the magnetic field vector is shown in Fig. for the ranges 0–2.5 Gauss and 0°–90°. The symmetry of the spin dynamics does not require consideration of a wider angular range since the orientational effect is only dependent on the axis of the field, not on the direction of the field with respect to a given axis. Also, the field dependence is symmetric with respect to a change of tilt angle from θ to a value $180° - \theta$. This symmetry derives from the nearly isotropic distribution of the nuclear spins in the initial state of the radical pair.

The results show that the variation in the triplet yield can be as large as 25% for a field of 0.5 Gauss. Interestingly, the orientational variation does not increase with larger field strengths. For a field of 2.5 Gauss, the variation of the triplet yield is less than 10 %. Figure demonstrates quite dramatically that,

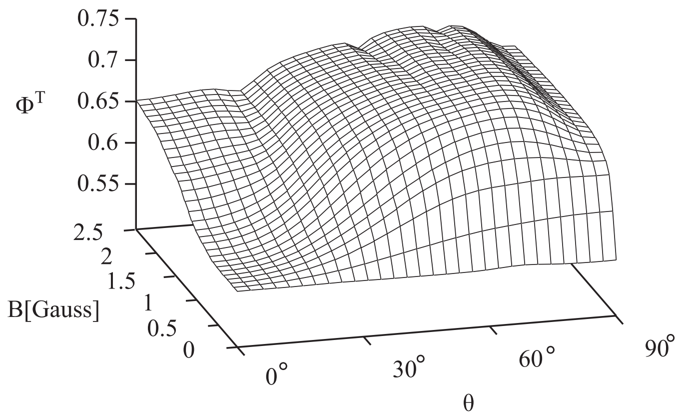

Figure 4: Triplet quantum yields evaluated for a radical pair with anisotropic hyperfine coupling. Yields are shown as a function of the angle θ between magnetic field and radical pair as well as for different field strengths.

given that the chosen parameters for hyperfine coupling and decay rates are, indeed, in a range which can be realized by biomolecular systems, the radical-pair mechanism furnishes magnetosensory capacities within a small window of the magnetic field strength. In the next section we will illustrate how an animal's visual system could exploit the chemistry of a radical-pair mechanism to yield information on the animal's orientation relative to the geomagnetic field, but we would like to stress that another sensory system, e.g., olfactory or tactile, could qualify as well.

Vision-Based Magnetic Compass

Information of the orientation of the geomagnetic field can be merged with sensory capacities of an animal if the sensory transduction pathway can be influenced by a reaction involving a radical-pair mechanism and if the molecular system involving the latter is orientationally fixed. The latter condition can be readily realized since sensory transduction involves cellular membranes which themselves often assume an ordered structure with large-scale orientational preferences in a coordinate frame defined relative to a sensory organ of the animal. A suitable example is vision, in which case the rod and cone receptor cells hold the visual pigments in membranes that are oriented tangentially to the retina of the eye.

To model the effect of a field-dependent radical-pair process on an animal's vision one needs to specify how such a process interacts with the visual pathway. For the purpose of illustration we assume that the radical-pair process affects the sensitivity of the light receptors in the eye. This modulation of sensitivity will result in a response pattern that varies over the hemisphere of the eye. We model the eye as displayed in Fig. 5 as a pinhole camera with an infinitisemal opening at O$'$. The retina is assumed to be a perfect sphere with the light receptors oriented normal to the sphere (c.f. z_1 and z_2 in Fig. 5). The eye is assumed to be cyclopean, i.e., in the center of the head. The direction of the central line connecting O and O$'$, henceforth, will be referred to as the viewing or head direction.

The unmodified signal s is represented by an integer in the range 0–255. We show how vision would be modulated if the bird was looking at a uniformly gray screen ($s = 127$) measuring $62° \times 62°$. The modified

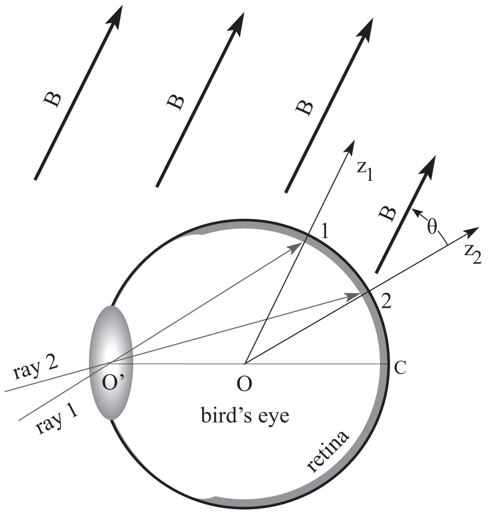

Figure 5: Eye model used for the calculation of visual modulation patterns. Rays 1,2 enter through an infinitisemal hole at O′ and are projected onto a spherical retina. The receptor molecules are assumed to be oriented normal to the retina surface (directions z_1 and z_2), thus, forming different angles with the direction of the magnetic field vector.

signal s' is determined according to a linear transduction formula

$$s'(\theta) = 127 + 255 \times [(\Phi_T(\theta) - \Phi_{gauge})M] \tag{11}$$

where Φ_{gauge} represents the triplet yield averaged over all angles and where M is an amplification factor. We have chosen $M = 4$.

The patterns which describe the modification of view for different head orientations are collected in Fig. . The numbering '0' to '180' refers to the angles of the different viewing directions with respect to the geomagnetic field vector. The modulation pattern for a bird looking parallel to the magnetic field lines ('0' in Fig.) is essentially a disk in the center of vision. We found it convenient, for the sake of illustration, to choose parameters such that the disk is darker than the surroundings. Biologically, this could correspond to a decrease of sensitivity of the receptors in this region. However, the magnetic compass would work similarly if receptor sensitivity is increased rather than decreased.

As can be seen in Fig. , the modulation pattern for a bird looking antiparallel to the magnetic field lines ('180') is identical with the pattern for parallel orientation ('0'). This shows that the radical-pair based magnetic compass is intrinsically an inclination compass. The modulation pattern does not directly differentiate geographic north and south, but provides this information through the tilt of the geomagnetic field vector relative to the horizon. On the northern hemisphere, the geomagnetic field lines point downwards in the northern direction, on the southern hemisphere they point downwards in the southern direction. Using the gravity information provided through the vestibular system, a bird can differentiate between north and south although the modulation patterns are indistinguishable. However, a problem arises at the magnetic equator, where the geomagnetic field axis lies within the horizontal plane and a bird misses the cue of geomagnetic tilt that helps to differentiate north from south.

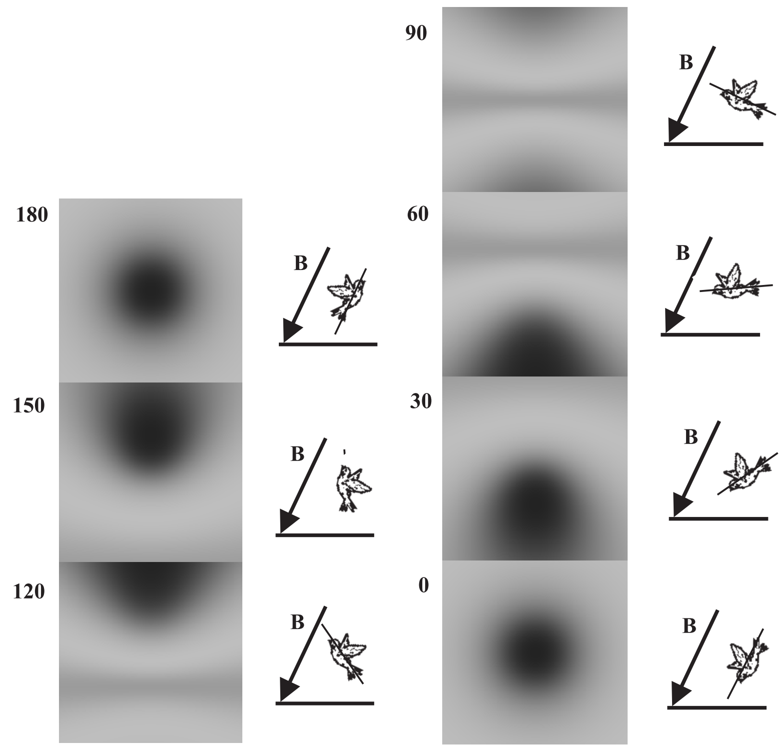

Figure 6: Visual modulation patterns through the geomagnetic field (0.5 Gauss) for a bird looking into different directions at angles 0°, 30°, 60°, 90°, 120°, 150° and 180° with the magnetic field vetor. The patterns have been evaluated assuming radical-pair receptors with anisotropic hyperfine couplings arranged in the eye model depicted in Fig. 5. The schematic illustrations next to the modulation patterns indicate the correesonding direction into which a bird would be flying at Urbana-Champaign (geomagnetic field inclination of 68°).

To exemplify the connection between the visual modulation patterns and gravity information, we illustrate in Fig. also the bird's directions corresponding to the modulation patterns for a bird flying at Urbana-Champaign, where the inclination of the geomagnetic field is about 68°. This angle has incidentally the same value as the angle θ for which an earth-strength magnetic field produces the largest effect on triplet yields (see above), but the two angles are completely unrelated.

It should be noted that the amplification factor M is chosen in such a way that the magnetic field effects become discernible to the human eye in a static picture. In life vision, much weaker amplification would suffice since a bird can detect the moving of the visual pattern induced by the geomagnetic field (noticable with head movement as discussed below) since moving patterns are visually recognized with high sensitivity. However, this sensitivity can only be illustrated through the use of a video representing an animal's vision, i.e., is beyond the static representation in these pages.

In order to understand how information on the geomagnetic field furnished through a radical-pair mechanism can be interpreted, one needs to consider how this information appears during head movement. If the bird flies parallel to the geomagnetic field vector and moves its head up, the disk will follow its eyes, however, with a reduced angular velocity. The angular velocity depends on the eye-lense geometry. In our model, the disk moves with half the angular velocity of the eye as can be readily explained on the basis of Fig. 5: the angular change of ray 1 is half that of z_1, since angle (1,O$'$,C) is half the angle (1,O,C). If the bird turns its head up and down it would 'see' a disk-like feature which follows its head movement and is only in the center of vision if the animal looks parallel or antiparallel to the geomagnetic field lines.

The same would be perceived by a bird looking parallel to the magnetic field lines and moving its head forth and back between east and west around a middle northern direction. In this case, turning towards east (west) from a northern direction would result in the disk moving towards the right (left) with half the angular velocity of the bird's movement.

The pictograms in Fig. serve as illustrations for the purpose of discussing the changes in modulation patterns if the bird moved as depicted. However, the pictograms are not representing the realistic behavioral situation, since birds always try to keep their head in a horizontal position. In order to also provide a realistic example, we show in Fig. how the modulation patterns change if a bird rotates in a plane parallel to the horizon at Urbana-Champaign. Due to the inclination angle of 68°, the rotation in this plane will produce a superposition of the two effects discussed above and, thus, result in the non-trivial changes in the modulation patterns discernible in Fig. .

The modulation patterns in Fig. and Fig. display the same symmetry that has been observed for the angular dependence of the magnetic field effects (see above). The biological effect of these symmetries is that the modulation patterns provide only axial information, but not information about the polarity of the magnetic field, in agreement with behavioral studies.

In Fig. the modulation patterns are displayed for field strengths of 0.1, 0.2, 0.5, 1.0, 2.0, and 5.0 Gauss and a bird looking parallel to the geomagnetic field vector. The different field strengths have an effect on the contrast and the shape of the modulation pattern. The contrast is strongest for fields of 0.5 and 1.0 Gauss and decreases for larger or smaller fields resulting in a hardly noticable modulation for a 0.1 Gauss field. These results are in agreement with the experimental findings that birds were able to orient only within a narrow intensity window ranging from about 30% below to about 30% above the intensity of the ambient 0.46 Gauss field in which they were kept (Wiltschko and Wiltschko, 1972).

However, the more recent experimental findings (Wiltschko, 1978) proved to be more complex: After three days of acclimatization the birds were able to orient in fields outside the normal range, e.g. 0.16 Gauss or 1.5 Gauss. In the case of acclimatization to the 1.5 Gauss fields, the birds were able to orient in both the 1.5 Gauss and the ambient 0.46 field, but not at an intermediate field strength of 0.81 Gauss. The

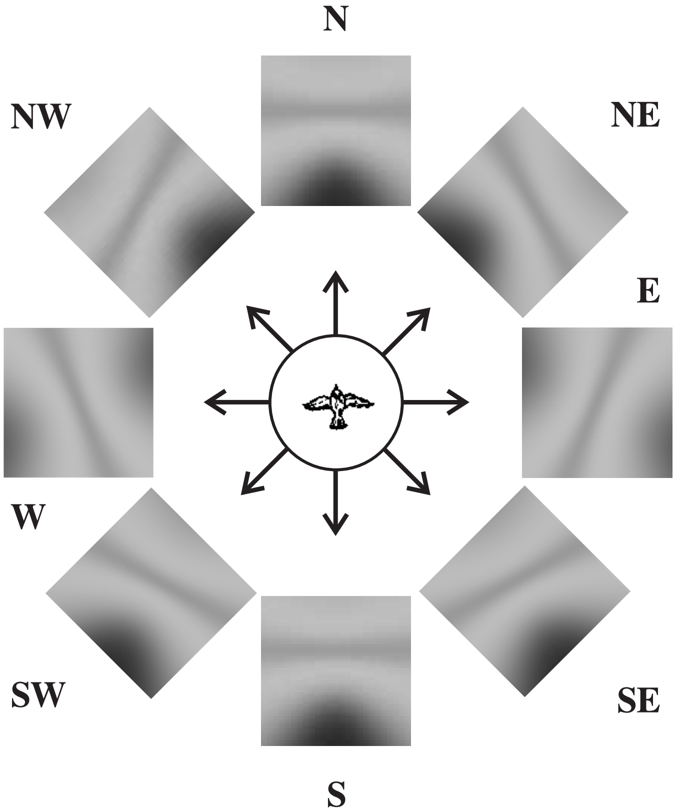

Figure 7: Visual modulation patterns through the geomagnetic field (0.5 Gauss) for a bird flying parallel to the horizon at Urbana-Champaign (geomagnetic field inclination of 68°) and looking towards N, NE, E, SE, S, SW, W, and NW. The patterns have been evaluated assuming radical-pair receptors with anisotropic hyperfine couplings arranged in the eye model depicted in Fig. 5.

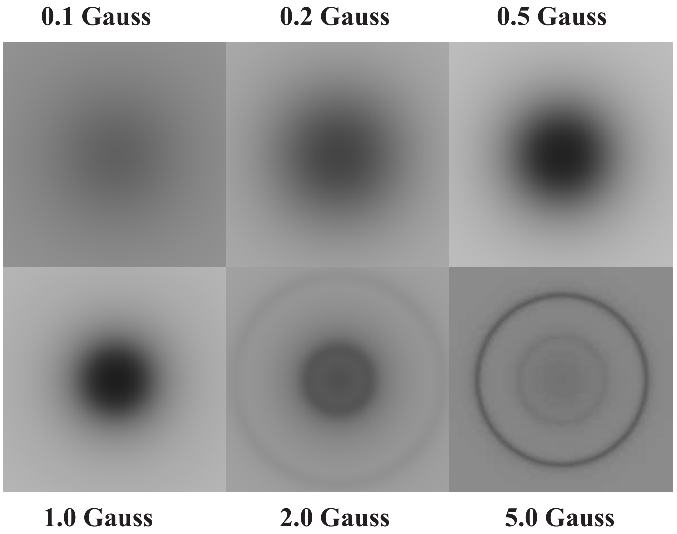

Figure 8: Visual modulation patterns through magnetic fields of 0.1, 0.2, 0.5, 1.0, 2.0, and 5.0 Gauss for a bird looking parallel to the magnetic field lines. Changes in the field strength induce changes in the contrast of the modulation pattern, e.g., the central disk feature which is clearly visible for 0.5 and 1.0 Gauss field strengths becomes less visible for lower and higher magnetic fields. In addition, also qualitative changes can be observed such as the occurence of a new ring feature for high (5 Gauss) magnetic fields.

modulation patterns in Fig. provide a possible explanation. In addition to the contrast, also the qualitative features of the modulation pattern change when the field strengths change. The central disk changes in size, being larger for smaller field strengths. For fields with much larger or smaller field strengths than the geomagnetic field, the central disk becomes less noticable. For a 5 Gauss magnetic field, a new ring-like feature is more prominent than the disk. A bird which is used to seeing the disk moving around might first be disoriented at higher fields until it becomes familiar with the new pattern. Familiarity with the new pattern would not prevent the bird from orienting with the familiar pattern generated by the geomagnetic field. A pattern at an intermediate intensity, however, might be sufficiently different from the patterns at both geomagnetic and high field intensities to be unfamiliar to the bird, thus leading to disorientation.

The modulation patterns in Figs. , , and should be considered formal, anthropomorphic representations of the bird's impression of magnetic field stimuli through an ordered photoreceptor system, and not a representation of what a bird really sees. The actual visual imaging system of a bird involving two eyes, providing nearly 360° vision with variations in sensitivity over different retina areas and a non-spherical retina geometry will result in additional variations of the modulation patterns and differences in the way this modulation information is processed. One should also keep in mind that birds may evoke other senses than vision for the purpose of magnetoreception.

Discussion

We have investigated a mechanism by which an earth-strength magnetic field can influence the product yield of a radical-pair reaction. We have shown through quantum mechanical calculations that triplet yields in a radical pair with one electron and one nuclear spin on each radical can be changed significantly, assuming anisotropic hyperfine coupling strengths and decay rates which have been realized in biological systems. Within the framework of our simple model this provides evidence that the discussed hyperfine interaction mechanism can provide magnetosensory capability for an earth-strength magnetic field.

As pointed out in the presentation of the theory, the suggested mechanism relies on the removal of degeneracies in the zero-field spin states through the influence of the external magnetic field. In real biological systems, radicals are likely to have more than one nuclear spin which interacts with the electron spin. In addition, dipolar and other electrostatic couplings exist. All of these interactions can remove the zero-field degeneracies, thus, resulting in a decrease of the magnetic field effect. Furthermore, the radical-pair lifetime of more than 100 ns, required for significant magnetic field effects to build up, is long enough so that the radical pair can lose its spin coherence through well-known spin-lattice relaxation or dephasing processes, which would again diminish field effects. These effects have not been included in the current model since their study is computationally expensive and unlikely to yield new insights beyond the ones presented without a knowledge of the molecule in question.

Despite all of these putative objections, effects of earth-strength magnetic fields have been observed under laboratory conditions in certain chemical systems, such as in pyrene + dicyanobenzene radical pairs (Batchelor *et al.*, 1993). However, the observed field effects are smaller (about 1%) than theoretically predicted. It is possible that conditions within bird tissues allow similar field effects.

The effect of weak magnetic fields on radical pairs could, in principle, have a second, alternative physical origin (Brocklehurst and McLaughlan, 1996). If the electron exchange interaction, J, between two radicals equals the energetic shift of a magnetic triplet state through an external magnetic field, crossing between the singlet state and one of the magnetic triplet states can occur. This opens an additional channel for singlet-triplet interconversion, and, consequently, leads to an increase in the triplet yield. Such increases through this so-called J-resonance mechanism have been observed for field strengths as low as 66 Gauss (Werner *et al.*, 1993). In order for a 1 Gauss magnetic field to show J-resonance, the electron exchange interaction would have to be of the order of 10^{-8} eV which might be achieved if radical pairs are fixed at an appropriate distance. An analysis of the magnitude of magnetic field effects through J-resonance is beyond the scope of this article, but we mention this mechanism for the sake of completeness.

The theoretical considerations in this article address a possible primary magnetoreception mechanism in animals, leaving the question open whether and how the primary effects will be increased through subsequent amplification processes. We predict changes in product yields of a primary radical-pair reaction of up to 25 %, but as we discussed above, the size of these changes might be reduced under realistic biological conditions because of effects not included in our model. Whether an amplification of this primary effect is then needed to provide magnetic compass information depends not only on the strength of the effect, but also on the way the primary reception process is connected to the nervous system. We like to suggest two possible ways by which the described primary reaction could be amplified. One suggestion is that a photoreceptor in the visual pathway, such as retinal, is part of the radical-pair system involved in magnetoreception. In this case the magnetic field-dependent reaction yield can directly modulate the sensitivity of a visual receptor. It is well known that the reception of a single photon by one visual receptor is sufficiently amplified to produce a significant nerve signal as reviewed e.g. in (Bialek, 1987). A modulation of the sensitivity of a single receptor through the magnetic field will thus be increased through the amplification mechanisms involved in vision. An alternative suggestion is that a neurotransmitter is part of the radical-pair system or a decay product of the radical-pair reaction. Magnetic field effects on a large number of radical pairs will then change the number of neurotransmitters and result in an increase or decrease of the signal in the nerve cell which receives the neurotransmitters. Further studies are necessary to determine the number of radical-pair receptors necessary for amplification of the primary reaction yield change in the presence of thermal and stochastic fluctuations so as to yield a sufficient signal-to-noise ratio.

Summarizing the hypotheses, suggestions, and results in this article, we can formulate the essential criteria that a candidate for a photoreceptor-based magnetoreceptor has to meet. (1) The magnetoreceptor should contain a pair of molecules capable of a radical-pair reaction influencable by weak magnetic fields. (2) The magnetoreceptor should be linked to a photoreceptor which initiates the radical-pair process upon excitation. In addition, the magnetoreceptor has to be connected to a nervous transduction chain, such as, e.g., the visual transduction chain. (3) The receptors have to be arranged in an ordered way so as to provide the orientational dependence necessary for the compass to work, i.e., their orientation should vary over a wide angular region.

Although several senses could be influenced, we have chosen vision, for the sake of illustration, to demonstrate the feasibilty of magnetic compass orientation in a model based on the above assumptions. Using a simplistic eye model, we have evaluated visual modulation patterns of such a radical-pair based magnetic compass. These patterns represent the output from the magnetic compass and can be compared directly to behavioral experiments. We have shown that a radical-pair based magnetic compass is in agreement with the observed non-polar response of the bird's inclination compass and also with the effects of field intensity on magnetic compass orientation of birds. The prediction of the necessity of light with an energy high enough to initiate a radical-pair reaction in order for magnetic compass orientation to work, has been a stimulus for experimental studies which confirmed that magnetic compass orientation requires the presence of high-energy (short wavelength) light to work without disruption. Below, we will discuss more recent experimental findings about light involvement in more detail. The radical-pair model presented in this article thus proves to be compatible with all behavioral findings about magnetic compass orientation. These results indicate that a radical-pair based magnetic compass can work in principle; the question is whether this type of mechanism is indeed used by birds for magnetic compass orientation. A definite answer to this question will require identification of the receptor molecule.

Recently, a novel class of photoreceptor molecules, cryptochromes, have been discovered in mammalian eyes. Cryptochromes are involved in the regulation of circadian rhythms (Cashmore *et al.*, 1999) for which magnetic field effects have been reported (Moore-Ede *et al.*, 1992). Cryptochromes indeed have a number of properties that suggest them as a candidate for a radical-pair based magnetoreceptor. Cryptochromes have evolved from evolutionary ancestors, the photolyases, as reviewed in (Cashmore *et al.*, 1999). Photolyases are proteins that mediate repair of defective DNA by removing harmful Pyr–Pyr dimers. Photolyases contain two cofactors, the flavin $FADH^-$ and a second chromophore. The DNA repair process is initiated by excitation of the second chromophore through 300-500 nm light and subsequent transfer of excitation to $FADH^-$. The activated $FADH^-$ then transfers an electron to the Pyr pair, thus generating a pair of a neutral FADH radical and a dimer radical anion. The $Pyr–Pyr^-$ radical is unstable and undergoes spontaneous splitting followed by electron back-transfer (Sancar, 1994). The generation of a radical pair upon light excitation is thus essential for the function of photolyases. Because of their high homology to photolyases it is likely that cryptochromes also engage in a radical-pair reaction with a yet unknown substrate.

In mice retinas, cryptochromes have been expressed in the inner nuclear layer (INL) in which they were found to be distributed rather evenly over the whole layer (Miyamoto and Sancar, 1998). In the inner nuclear layer, cryptochromes are in the vicinity of the large displaced ganglion cells which also have been found to be distributed rather evenly over the whole layer in pigeons (Fite *et al.*, 1981). The large displaced ganglion cells send axons through the inner plexiform layer and project into the nucleus of the basal optic root (nBOR), in which electrophysiological responses to magnetic stimuli have been measured (Semm and

Demaine, 1986). Thus, cryptochromes are not only a likely candidate for a radical-pair system in the eye, but furthermore provide a natural link to a particular nerve cell in agreement with experimental findings.

Moreover, cryptochromes contain light receptors, namely the flavin FADH and, as second chromophore, the blue light receptor pterin as cofactors. In photolyases the second chromophore acts as the main light absorber as can be seen from the action spectrum of DNA repair which matches exactly the absorption spectrum of the second chromophore (Sancar, 1994). If the same holds true for cryptochromes, the absorption spectrum of the second chromophore should determine in which range a cryptochrome-based magnetoreceptor is operational. A variety of photoreceptors has been found to act as second chromophores, all of which absorb in the blue and green region of the spectrum. A cryptochrome-based magnetoreceptor should thus switch off for monochromatic light with wavelengths above a threshold in the blue or green region of the spectrum. Indeed, experiments show that birds are disoriented under yellow and red light, whereas they orient under blue and green light (Wiltschko and Wiltschko, 1999).

In newt (Phillips and Borland, 1992) and fruitfly (Phillips and Sayeed, 1993) experiments, the animals have been shown to be oriented correctly for short wavelength or full spectrum light, to be oriented 90 degrees in the wrong direction for long wavelength light and to be disoriented only at an intermediate wavelength light. Recently, 90 degree shifts have been observed in birds as well for high intensities of green monochromatic light (Wiltschko *et al.*, 1999). Phillips and coworkers (Phillips and Borland, 1992; Deutschlander *et al.*, 1999a) suggested that the behavior observed in newts and fruitflies can be explained by the presence of two antagonistic magnetoreceptors with different action spectra. Such differences in the receptor sensitivity can be readily accomplished by a cryptochrome-based magnetoreceptor. For example, the magnetoreceptor for long wavelength light could have a cofactor as second chromophore which is absorbing at longer wavelengths.

Alternatively, the putative second magnetoreceptor could be excited by internal energy transfer in which case light absorption is no longer a prerequisite. Experimental findings such as the ability of fruitflies to orient in a magnetic field in complete darkness, therefore, are not *per se* a contradiction to a radical-pair based receptor mechanism. The modulation patterns presented here would then not represent changes in the visual system, but in some other nervous transduction system.

The studies in this article are, however, targeted towards understanding the magnetoreceptor which is sensitive at and dependent on the presence of short wavelength light. This magnetoreceptor is the dominant receptor for magnetic compass orientation under normal light conditions, since in experiments with different wavelengths the behavioral responses at short wavelength monochromatic light are identical to the responses at full spectrum light.

As we have pointed out repeatedly above, the presented model is a very simplified one. Its purpose is to provide a framework that connects the molecular basis of the proposed magnetoreception mechanism to the animal's behavior. The model presented thus allows a connection with existing experiments as discussed above and, more importantly, can point to new experiments. We outline several experiments that have a high potential of improving our knowledge about the biophysical mechanism of magnetoreception and hope that we can stimulate the design of such experiments.

A key hypothesis of the proposed magnetoreception mechanism is the existence of an ordered system of radical pairs linked to or including photoreceptors. Experiments that can show that a magnetic field response is dependent on a particular orientation of an animal's organ with respect to the polarisation of the ambient light might provide evidence for the proposed ordered system.

The presented model predicts qualitative changes of the magnetic compass' response with variations of the magnetic field strength by a factor two to five. Experimentally, the influence of intensity changes in magnetic compass orientation has only been studied in one animal, the european robin *Erithacus rubecula*

(Wiltschko and Wiltschko, 1972; Wiltschko, 1978). We would like to encourage similar studies with different animals to determine whether the observed intensity window, in which magnetic compass orientation is functional, is a general property of magnetic compass orientation. Assuming that such an intensity window exists, it is important to study whether animals can be trained to orient at higher or lower magnetic field intensities in order to characterize the magnetic compass of animals further.

Another crucial step in identifying the magnetoreceptor is the localization of the receptor region. In newts, it has recently been shown that extraocular photoreceptors in the pineal gland are mediating the magnetic compass response (Deutschlander *et al.*, 1999b). This breakthrough is not directly generalizable to birds, for which it has been shown that magnetic compass orientation is possible even after removal of the pineal gland (Schneider *et al.*, 1994). The third animal with a proven light-dependent magnetic compass response, the fruitfly, might be particularly well suited for investigations of the receptor region, since genetic variants lacking different photoreceptors are available.

Fruitflies are also of particular interest in regard to the involvement of cryptochromes in magnetoreception suggested in this article. A test of this hypothetical involvement is feasible since mutant strains of fruitflies lacking cryptochromes exist and a behavioral assay for the study of magnetic field effects on fruitflies has already been developed (Phillips, personal communication). If the mutant strains of fruitflies lacking cryptochromes are not able to orient in the magnetic field, unlike their wild-type counterparts, this would greatly strengthen the case for an involvement of cryptochromes in magnetoreception.

Finally, a test of the radical-pair hypothesis might be possible by applying appropriate radio frequency (1-10 MHz) AC electromagnetic fields as suggested by Phillips (personal communication). Such fields could drive transitions between singlet and triplet states of radical pairs which are separated through hyperfine couplings in the radio frequency range and, thus, disrupt singlet-triplet interconversion, resulting in changes of radical-pair based magnetoreceptor response. In contrast, magnetite is not expected to be influenced by radio frequency fields, but only by higher energy (1-10 GHz) microwave fields (Kirschvink, 1996). One problem in designing behavioral experiments is that the lack of a magnetic response due to, e.g., radio frequency AC fields, can mean that the magnetoreceptor mechanism is disrupted, but it can also mean that other nervous systems are disrupted while the magnetoreception mechanism is not affected, resulting in the same lack of behavioral response. However, if an animal exhibits different responses to magnetic fields such as, e.g., shoreward versus homing orientation in newts, and if these responses are based on different magnetoreception mechanisms as currently debated (Phillips, 1986; Wiltschko and Wiltschko, 1995a; Beason *et al.*, 1995; Beason and Semm, 1996; Munro *et al.*, 1997; Deutschlander *et al.*, 1999a), then it might be possible to disrupt just one of the two mechanisms, thus providing evidence that not the complete nervous system, but only the magnetoreception mechanism underlying the light-dependent magnetic compass is disrupted (Phillips, personal communication). Rather than being a disadvantage, the suggested existence of multiple magnetoreception mechanisms in one animal might be the key to designing behavioral experiments that allow one to distinguish between alternative hypotheses concerning the nature of the magnetoreception mechanism.

Acknowledgements

The authors would like to thank Barry Isralewitz for useful discussions and support in designing programs. We are also indebted to Prof. Wolfgang Wiltschko for comments on this article. This work has been supported by the National Institutes of Health (NIH PHS 5 P41 RR05969) and the Carver Charitable Trust.

References

Batchelor, S., C. Kay, K. McLaughlan, and I. Shkrob. 1993. Time-resolved and modulation methods in the study of the effects of magnetic fields on the yields of free radical reactions. *J. Phys. Chem.* 97:13250–13258.

Beason, R., and P. Semm. 1996. Does the avian ophthalmic nerve carry magnetic navigational information? *J. Exp. Biol.* 199:1241–1244.

Beason, R., N. Dussourd, and M. Deutschlander. 1995. Behavioural evidence for the use of magnetic material in magnetoreception by a migratory bird. *J. Exp. Biol.* 198:141–146.

Bialek, W. 1987. Physical limits to sensation and perception. *Ann. Rev. Biophys. Biophys. Chem.* 16:455–478.

Boxer, S., C. Chidsey, and M. Roelofs. 1982. Use of large magnetic fields to probe photoinduced electron-transfer reactions: An example from photosynthetic reaction centers. *J. Am. Chem. Soc.* 104:1452–1454.

Boxer, S., C. Chidsey, and M. Roelofs. 1983. Magnetic field effects on reaction rates in the solid state: An example from photosynthetic reaction centers. *Ann. Rev. Phys. Chem.* 34:389–417.

Brocklehurst, B. 1976. Spin correlation in the geminate recombination of radical ions in hydrocarbons. Part 1 – Theory of the magnetic field effect. *J. Chem. Soc. Far. Trans. II* 72:1869–1884.

Brocklehurst, B., and K. A. McLaughlan. 1996. Free radical mechanism for the effects of environmental electromagnetic fields on bioloical systems. *Int. J. Rad. Biol.* 69:3–24.

Canfield, J., R. Belford, and P. Debrunner. 1996. Calculations of earth-strength steady and oscillating magnetic field effects in coenzyme B_{12} radical pair systems. *Mol. Phys.* 89:889–930.

Cashmore, A., J. Jarillo, Y-J.Wu, and D. Liu. 1999. Cryptochromes: Blue light receptors for plants and animals. *Science* 284:760–765.

Deutschlander, M., J. Phillips, and S. Borland. 1999a. The case for light-dependent magnetic orientation in animals. *J. Exp. Biol.* 202:891–908.

Deutschlander, M., S. Borland, and J. Phillips. 1999b. Extraocular magnetic compass in newts. *Nature* 400:324–325.

Edmonds, D. 1996. A sensitive optically-detected magnetic compass for animals. *Proc. Royal Soc. B* 263:295–298.

Fite, K., M. Brecha, H. Karten, and S. Hunt. 1981. Displaced ganglion cells and the accessory optic system of pigeons. *J. Comp. Neurol.* 195:279–288.

Grissom, C. 1995. Magnetic field effects in biology: a survey of possible mechanisms with emphasis on radical-pair recombination. *Chem. Rev.* 95:3–24.

Gwinner, E. 1974. Endogenous temporal control of migratory restlessness in warblers. *Naturwiss.* 61:405.

Haberkorn, R. 1977. Theory of magnetic field modulation of radical recombination reactions I. *Chem. Phys.* 19:165–179.

Haberkorn, R., and M. Michel-Beyerle. 1979. On the mechanism of magnetic field effects in bacterial photosynthesis. *Biophys. J.* 26:489–498.

Harkins, T., and C. Grissom. 1994. Magnetic field effects on B_{12} ethanolamine ammonia lyase: Evidence for a radical mechanism. *Science* 263:958–960.

Hoff, A. 1981. Magnetic field effects on photosynthetic reactions. *Quart. Rev. Biophys.* 14:599–665.

Hong, F. T. 1995. Magnetic field effects on biomolecules, cells, and living organisms. *BioSystems* 36:187–229.

Hong, F. 1977. Phototelectric and magneto-orientation effects in pigmented biological membranes. *J. Colloid Surf. Sci.* 58:471–497.

Kirschvink, J. 1996. A possible mechanism for coupling nonthermal levels of radiation to biological systems. *Bioelectromag.* 17:242–245.

Kirschvink, J., and J. Gould. 1981. Biogenic magnetite as a basis for magnetic field detection in animals. *BioSystems* 13:181–201.

Kirschvink, J., M. Walker, S. Chang, A. Dizon, and K. Peterson. 1985. Chains of single-domain magnetite particles in chinook salmon, *Oncorhynchus tschawytscha*. *J. Comp. Physiol. A* 157:375–381.

Kubo, R. 1969. A stochastic theory of lineshape. *Adv. Chem. Phys.* 15:101–127.

Leask, M. 1977. A physicochemical mechanism for magnetic field detection by migratory birds and homing pigeons. *Nature* 267:144–145.

Maier, E., and J. Bowmaker. 1993. Colour vision in the passerine bird *Leiothrix lutea*: correlation of visual pigments absorbance and oil droplet transmission with spectral sensitivity. *J. Comp. Physiol.* 172:295–301.

Miyamoto, Y., and A. Sancar. 1998. Vitamin B_2-based blue-light photoreceptors in the retinohypothalamic tract as the photoactive pigments for setting the circadian clock in mammals. *Proc. Natl. Acad. Sci. USA* 95:6097–6102.

Mohtat, N., F. Cozens, T. Hancock-Chen, J. Scaiano, J. McLean, and J. Kim. 1998. Magnetic field effects on the behaviour of radicals in protein and DNA environment. *Photochem. Photobiol.* 67:111–118.

Moore-Ede, M., S. Campbell, and R. Reiter. 1992. Electromagnetic Fields and Circadian Rhythmicity. Birkhäuser, Boston.

Munro, U., J. Munro, J. Phillips, R. Wiltschko, and W. Wiltschko. 1997. Evidence for a magnetite-based navigational map in birds. *Naturwiss.* 84:26–28.

Phillips, J. 1986. Two magnetoreception pathways in a migratory salamander. *Science* 233:765–767.

Phillips, J., and S. Borland. 1992. Behavioral evidence for use of a light-dependent magnetoreception mechanism by a vertebrate. *Nature* 359:142–144.

Phillips, J., and O. Sayeed. 1993. Wavelength-dependent effects of light on magnetic compass orientation in *Drosophila melanogaster*. *J. Comp. Physiol. A* 172:303–308.

Salikhov, K., Y. Molin, R. Sagdeev, and A. Buchanenko. 1984. Spin Polarization and Magnetic Field Effects in Radical Reactions. Vol. 22. Budapest.

Sancar, A. 1994. Structure and function of DNA photolyase. *Biochem.* 33:2–9.

Schneider, T., H.-P. Thalau, P. Semm, and W. Wiltschko. 1994. Melatonin is crucial for the migratory orientation of pied flycatchers *Ficedula hyopoluca pallas*. *J. Exp. Biol.* 194:255–262.

Schulten, K. 1982. Magnetic field effects in chemistry and biology. *In* Festkörperprobleme. Vol. 22. J. Treusch, editor. Vieweg, Braunschweig. 61–83.

Schulten, K., C. Swenberg, and A. Weller. 1978. A Biomagnetic Sensory Mechanism Based on Magnetic Field Modulated Coherent Electron Spin Motion. *Z. Phys. Chem.* NF111:1–5.

Schulten, K., and A. Weller. 1978. Exploring fast electron transfer processes by magnetic fields. *Biophys. J.* 24:295–305.

Schulten, K., and A. Windemuth. 1986. Model for a physiological magnetic compass. *In* Biophysical Effects of Steady Magnetic Fields. Proceedings in Physics, vol. 11. G. Maret, N. Boccara, and J. Kiepenheuer, editors. Springer, Berlin. 99–106.

Schulten, K., H. Staerk, A. Weller, H.-J. Werner, and B. Nickel. 1976. Magnetic field dependence of the geminate recombination of radical ion pairs in polar solvents. *Z. Phys. Chem.* NF101:371–390.

Semm, P., and C. Demaine. 1986. Neurophysiological properties of magnetic cells in the pigeon's visual system. *J. Comp. Physiol. A* 159:619–625.

Semm, P., and T. Schneider. 1991. Magnetic responses in the central nervous system of birds. *In* Effects of atmospherical and geophysical variables in biology and medicine. H. Lieth, editor.

Semm, P., D. Nohr, C. Demaine, and W. Wiltschko. 1984. Neural basis of the magnetic compass: interaction of visual, magnetic and vestibular inputs in the pigeon's brain. *J. Comp. Physiol. A* 155:283–288.

Steiner, U., and T. Ulrich. 1989. Magnetic field effects in chemical kinetics and related phenomena. *Chem. Rev.* 89:51–147.

Timmel, C., U. Till, B. Brocklehurst, K. McLauchlan, and P. Hore. 1998. Effects of weak magnetic fields on free radical recombination reactions. *Mol. Phys.* 95:71–89.

von Middendorff, A. 1859. Die Isepiptesen Russlands. *Mem. Acad. Sci. St Petersbourg VI, Ser. Tome* 8:1–143.

Werner, H.-J., Z. Schulten, and K. Schulten. 1977. Theory of the magnetic field modulated geminate recombination of radical ion pairs in polar solvents: Application to the pyrene-N,N-dimethylaniline system. *J. Chem. Phys.* 67:646–663.

Werner, H.-J., K. Schulten, and A. Weller. 1978. Electron transfer and spin exchange contributing to the magnetic field dependence of the primary photochemical reaction of bacterial photosynthesis. *Biochim. Biophys. Acta* 502:255–268.

Werner, U., W. Kuehnle, and H. Staerk. 1993. Magnetic field dependent reaction yields from radical ion pairs linked by a partially rigid aliphatic chain. *J. Phys. Chem.* 97:9280–9287.

Wiltschko, R., and W. Wiltschko. 1995a. Magnetic orientation in animals. Springer, Berlin.

Wiltschko, W. 1978. Further analysis of the magnetic compass of migratory birds. *In* Animal migration, navigation, and homing. K. Schmidt-Koenig, and W. Keeton, editors. Springer, Berlin.

Wiltschko, W., and F. Merkel. 1966. Orientierung zugunruhiger Rotkehlchen im statischen Magnetfeld. *Verh. dt. zool. Ges.* 59:362–367.

Wiltschko, W., and R. Wiltschko. 1972. Magnetic compass of european robins. *Science* 176:62–64.

Wiltschko, W., and R. Wiltschko. 1995b. Migratory orientation of european robins is affected by the wavelength of light as well as by a magnetic pulse. *J. Comp. Physiol.* 177:363–369.

Wiltschko, W., and R. Wiltschko. 1996. Magnetic orientation in birds. *J. Exp. Biol.* 199:29–38.

Wiltschko, W., and R. Wiltschko. 1999. The effect of yellow and blue light on magnetic compass orientation in european robins, *Erithacus rubecula. J. Comp. Physiol. A* 184:295–299.

Wiltschko, W., U. Munro, H. Ford, and R. Wiltschko. 1993. Red light disrupts magnetic orientation of migratory birds. *Nature* 364:525–527.

Wiltschko, W., R. Wiltschko, and U. Munro. 1999. Light-dependent magnetoreception in birds: does directional information change with light intensity? *Naturwiss.* in press.