

Magnetoreception and its use in bird navigation

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Recent advances have brought new insight into the physiological mechanisms that enable birds and other animals to use magnetic fields for orientation. Many birds seem to have two magnetodetection senses, one based on magnetite near the beak and one based on light-dependent radical-pair processes in the bird's eye(s). Among the most exciting recent results are: first, behavioural responses of birds experiencing oscillating magnetic fields. Second, the occurrence of putative magnetosensory molecules, the cryptochromes, in the eyes of migratory birds. Third, detection of a brain area that integrates specialised visual input at night in night-migratory songbirds. Fourth, a putative magnetosensory cluster of magnetite in the upper beak. These and other recent findings have important implications for magnetoreception; however, many crucial open questions remain.

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Introduction

Information from the Earth's magnetic field plays a key part in bird orientation, but the physiological mechanism(s) enabling birds to sense the Earth's magnetic field remain one of the most fascinating unresolved mysteries in biology. Recently, however, the search for the avian magnetoreceptor(s) and the cognitive processes integrating magnetic information into the birds' orientation system has gathered a lot of momentum, mostly because of interdisciplinary interactions among theoretical biophysicists and neuro-, molecular-, and behavioural- biologists. Here, we discuss the implications of recent findings and the crucial open questions that remain. This review focuses primarily on evidence published during the past two to five years.

The role of magnetic information in bird orientation

Magnetic information can, in principle, be useful for orientation in two different ways. The direction of the magnetic field lines can provide the reference direction for a magnetic compass [1], and changes in intensity and/or inclination angle can provide positional information in the form of magnetic 'signposts' or a full magnetic map (e.g. [2–5]).

Behavioural experiments have conclusively shown that both migratory birds (e.g. [1,6,7]) and homing pigeons [7,8] can extract compass information from the geomagnetic field. The standard experimental design for migratory birds involves testing of individual birds in a circular test cage. It has yielded highly reproducible and consistent results for long- and short- distance migrants, for juvenile birds that have never migrated before and adult birds alike. It is less clear how birds use magnetic cues during free migratory flights, where they can obtain compass and position information from many additional sources (e.g. [9,10]). There is general agreement that compass cues of a global nature such as celestial (sun, stars) and magnetic compass cues are likely to be most important for long-distance navigation, the first stage of a migratory flight [11], but the relative importance of the different cues remains controversial [12]. Very recent orientation experiments relying on the behaviour of night-migratory songbirds during natural migratory flights suggest that they primarily use a magnetic compass in midair [10]. Consequently, understanding how birds sense and process magnetic compass information seems to be one key to understanding the mechanisms enabling long-distance migratory birds to navigate successfully over thousands of kilometres.

How can birds and other animals detect magnetic information?

This seemingly straightforward question has very different meaning for different biologists. A physical biologist looks for the primary biophysical mechanism of magnetoreception, a molecular biologist seeks the molecules involved, a neurobiologist asks how magnetic information is transmitted through the nervous system and represented in the brain, and behavioural biologists typically ask whether birds can use magnetic information under specific environmental conditions. The fact that the magnetic sensory structures are still unknown despite more than 40 years of research suggests that for magnetic sensing, more than for other sensory systems, it is important to integrate these different perspectives to find the most diagnostic experiments and avoid pitfalls. Over the

years, many theories suggesting how birds can sense the Earth's magnetic field have been proposed (e.g. [13–18]). Two biophysical mechanisms have since emerged as the most promising magnetodetection candidates, namely magnetite-based magnetoreception or chemical (photo-receptor-based) magnetoreception.

Magnetite-based magnetoreception

The passive alignment of magnetotactic bacteria to the geomagnetic field is based on magnetite crystals [19], and magnetite crystals have also been found in many other animals, including birds [6]. Consequently, it has been suggested that magnetoreception is magnetite-based. However, because magnetite synthesis seems to be a common way for organisms to deposit excess iron, more evidence than the mere presence of magnetite is required. The first strong evidence supporting a role of magnetite in active magnetoreception came from salmonid fish [20]. For a detailed discussion of the theoretical background and available evidence for magnetite-based magnetoreception, see Walker *et al.* [4]. The two most exciting recent findings related to magnetite-based magnetoreception in birds are outlined below.

First, a magnetite-rich, candidate structure located in the upper beak of pigeons has been characterized at the ultra-structural level and it has been indicated that this structure is connected to nerve fibres that access the brain via the trigeminal nerve [21^{••}]. The characterization of this structure enables detailed physical modelling that could result in more accurate predictions of the effects of different magnetic fields, such as the effects on orientation performance of strong permanent magnets (e.g. [22,23]) and strong magnetic pulses intended to re-magnetize magnetite structures [24[•]].

Second, operant conditioning experiments have shown that pigeons can detect a strong (~100 000 nanoTesla) magnetic anomaly. Moreover, this ability disappears when the ophthalmic branch of the trigeminal nerve is sectioned, whereas magnetic sensing ability remains when the olfactory nerve is cut [25[•]], confirming a role of the trigeminal nerve in transmitting magnetic information from the beak to the brain [26]. Because magnetic compass orientation responses seem unaffected when the ophthalmic branch of the trigeminal nerve is blocked [26], one can speculate that the structure in the beak is involved in detecting magnetic intensities. However, in order for a magnetic 'map-sense' to work, birds must be able to detect naturally occurring local changes in magnetic field strengths that are about five orders of magnitude smaller (~10 nanoTesla) than the anomalies used by Mora *et al.* [25[•]]. Thus, it still needs to be shown whether the magnetite-based trigeminal magnetodetection system can detect biologically relevant magnetic anomalies (see e.g. [27]).

Chemical magnetoreception

Magnetic compass orientation in night-migratory birds is influenced by the availability of light with specific wavelengths [7,28–30], and appears to be strongly lateralized; as covering up the right eye of migratory birds seemed to destroy their magnetic compass orientation capabilities [31]. These findings suggest that reception of magnetic compass information is light-dependent. Furthermore, birds with their pineal gland removed can still orient magnetically [32], suggesting that the eyes (or one eye) are somehow involved in detecting magnetic compass information. But how can a bird's eye detect the direction of the Earth's magnetic field?

Photopigments can respond to light in fundamentally different ways. Photopigments such as retinal in the opsin-family of photoreceptors undergo a conformational change upon light absorption, triggering the reaction cascade underlying normal visual photoreception. Other photopigments, such as chlorophylls or flavins, use light energy to transfer electrons to nearby molecules, thereby generating a pair of molecules with unpaired electrons, a so-called radical pair. Radicals are very reactive molecules and their presence quickly leads to further reaction steps and products. Under certain conditions, magnetic fields can influence the speed or yield with which radical-pair products are formed. Effects of Earth-strength magnetic fields on radical pair reactions were suggested by Schulzen *et al.* [14] and have since been demonstrated through *in vitro* studies of pigment molecules (e.g. [33]). Ritz *et al.* [17] discuss how the observed magnetic sensitivity of radical pairs to Earth-strength magnetic fields could be harnessed in the eyes of birds to provide magnetic compass information. Crucial necessary conditions are first, the existence of photopigments that can form long living radical pairs in the eyes of birds, second, a sufficient number of photopigments fixed in the same orientation to provide directional information, and third, a link of photopigments to the visual transduction system.

Assuming a fixed orientation of the radical-forming photopigments inside the retinal cells, the magnetic field would modulate the radical-pair reaction, and thereby affect light signalling differently in different parts of the retina, leading to perception of the magnetic field as visual modulation patterns [17]. Expectations from radical-pair mediated magnetoreception are consistent with previous experimental observations, for example, the inclination-based nature of the songbird magnetic compass and the observation of a narrow functional window of the magnetic compass of European robins [1,6].

Biophysical mechanism: diagnostic tests

Being faced with two viable alternatives for the primary detection mechanism in magnetic compasses, researchers have devised tests that can indicate which of the two mechanisms is involved in magnetoreception. These tests

are necessarily of an indirect nature and typically involve the use of a disruptive stimulus that is specific to either mechanism. To test for a role of magnetite, a magnetized material, one can apply a strong pulse before a behavioural test in an attempt to re-magnetize the material, but the strong intensity of the pulse makes it difficult to exclude effects on systems other than magnetite. Recently, oscillating magnetic fields in the low radio-frequency range (1–50 MHz) have been proposed as a diagnostic test. Such fields are expected to affect radical-pair reactions and compete with the effects of the geomagnetic field, thereby influencing the ability of a radical-pair based mechanism to detect the geomagnetic field. By contrast, very weak oscillating fields are less likely to have an effect on a magnetite-based system [17,34^{••}]. One can estimate that 1–50 MHz oscillating fields will only affect (ferromagnetic) magnetite crystals as found in bacteria or fish if they are considerably stronger than the geomagnetic field.

Magnetic compass responses of European robins, *Erithacus rubecula* (a night-migrating songbird) become disorientated when they are exposed to weak (<1/50 of geomagnetic field strength), radio-frequency magnetic fields. The effects of oscillating fields depend on the alignment between the oscillating and the geomagnetic fields, as expected from theory [34^{••},35]: birds show normal magnetic compass responses only when the oscillating field is parallel to the geomagnetic field [34^{••},36]. Such effects are consistent with expectations from the radical-pair mechanism and cannot be reconciled easily with other known mechanisms. They provide strong indirect evidence that the magnetic inclination compass of night-migrating songbirds is really based on a radical pair mechanism [34^{••}].

Candidate molecules: cryptochromes and their location within the birds' retina

With evidence supporting involvement of a radical-pair mechanism, the immediate question that arises is whether a photopigment that could form the radical pair in question exists in the eyes of birds. Cryptochromes, which involve the photopigment flavin dehydrogenase (FAD), are blue-green light photoreceptors [37,38] and have been suggested as magneto-sensory candidate molecules [17]. Cryptochromes can form radical pairs upon photoexcitation [39[•]]. Photolyases, proteins with FAD co-factors and high homology to cryptochromes, form radical-pair intermediates with sufficiently long lifetimes for magnetic field effects to develop (see [40]). Cryptochromes are present in the retinae of many animals, including mouse, *Drosophila*, human, quail, and chicken, where they have been implicated in regulating the internal clock [37,38,41,42]. Recently, cryptochromes were also shown to be present in the retinae of two species of night-migratory birds: garden warblers, *Sylvia borin* [43^{••}], and European robins [44[•]].

When garden warblers perform magnetic orientation at night, cryptochrome 1a (CRY1a) is predominantly found in ganglion cells and displaced ganglion cells, but also appears in photoreceptors and in ~ 15% of the cells in the inner nuclear layer of the retina [43^{••}]. By contrast, CRY1a is virtually absent from the retina of awake non-migratory birds at night (chicken [42] and zebra finches, *Taeniopygia guttata* [43^{••}]). During the day, retinal CRY1a is found in both garden warblers and zebra finches. The clearest differences in cryptochrome expression occurred in the large displaced ganglion cells: they always contained much cryptochrome in garden warbler retinae, whereas these cells never seemed to contain cryptochrome in zebra finches [43^{••}]. The large displaced ganglion cells of pigeons project exclusively to the nucleus of the basal optic root (nBOR, [45,46]), where magnetically sensitive cells have been reported ([47] but these findings have proved difficult to replicate).

The high cryptochrome concentration in both normal and displaced ganglion cells of migrants makes them good host candidates for magnetic compass detectors. One potential problem of putative magneto-detecting cryptochromes being located in ganglion cells is how they can be fixed inside the cell, so that the expected magnetic effects on the radical-pair reaction do not cancel out. The most likely candidate structures found inside ganglion cells are cytoskeletal proteins and cytosolically embedded membranes (e.g. endoplasmic reticulum). However, because cryptochromes are also expressed in other cell types (including photoreceptors), any of these cells could harbour the putative primary magnetoreceptors. A photoreceptor location of radical-pair mediated magnetodetection would be favourable because of the many ordered structures inside photoreceptor cells well suited to provide a spatially ordered array of cryptochromes.

No matter where in the eye the primary magnetic compass sensors are located, the magnetic information must pass through the ganglion cells to reach the brain for further processing. It is therefore important that the ganglion cells seemed to be highly active (i.e. were sending information to the brain) when garden warblers performed magnetic orientation at night under very dim light [43^{••}]. By contrast, zebra finch ganglion cells seemed to be much less active at night. These results correlate well with the suggestion that cryptochromes could be involved in a magnetosensitive radical-pair reaction underlying magnetic compass orientation. Electrophysiological recordings from retinal ganglion cells should be able to prove whether the eye(s) transmit magnetic compass information to the brain.

At present, we do not know whether none, all, or only a subset of the ganglion cells transmit magnetic compass information. If all ganglion cells are involved in relaying magnetic compass information to the brain, a light-

mediated magnetic compass mechanism of night-migratory birds might be masked by normal visual processing during the day and, therefore, might only work in low light conditions. However, if only a specialized subset of ganglion cells transmit vision-mediated magnetic information to the brain, light-mediated magnetoreception could work anytime of day, because cryptochromes are found in the retinae of both migratory and non-migratory birds during the day, and species differences might be expected.

Neurobiological mapping

A different avenue for identifying areas involved in magnetoreception involves immediate early genes such as ZENK (acronym for zif268, Egr-1, NGF-1A, and Krox-24) and *c-fos* [48,49,50••]. ZENK and *c-fos* are only expressed in active cells showing neuronal activity and can, therefore, be used to investigate which brain areas are involved in a particular sensory or behavioural task [51,52]. Mouritsen *et al.* [50••] used this so-called behavioural molecular mapping technique to show that a specific cluster of regions named ‘cluster N’ in the forebrain of migratory birds is active at night and that this activity disappears when the birds’ eyes are covered. Activity in the same brain cluster is not observed in non-migratory zebra finches. These findings further support the hypothesis that magnetic compass signals are light-dependent, originate in the retina, and enter the brain as visual information. Unfortunately, some parts of the avian brain, including the nBOR and the thalamus, do not express ZENK and *c-fos* [53]. Consequently, studies using ZENK or *c-fos* cannot show whether, for example, the nBOR is active during magnetic compass orientation.

In all neurophysiological approaches it is important to realize that if the theory of Ritz *et al.* [17] of magnetic compass detection is true, magnetic fields only modulate a primary light-induced signal. When a changing or normal magnetic field is present, firing rates of some neurons would be expected to increase, whereas the firing rate of others are expected to decrease depending on the location in the retina. Even in a zero magnetic field in which no magnetic modulation takes place, we expect the light-induced primary signal to be processed in the brain as long as light is present. Therefore, the total amount of neuronal activity as reflected by immediate early gene expression in a brain region normally extracting the magnetically modulated visual patterns should be largely independent of the surrounding magnetic field conditions. Only in the presence of a magnetic field of appropriate strength, however, will this processing lead to migratory restlessness behaviour (wing whirring and jumping around in their cage) oriented in a constant magnetic compass direction.

Head scanning movements

Recently, it was observed that caged garden warblers seem to use scanning movements of the head to detect

the reference compass direction of the Earth’s magnetic field [54•]. This suggests that magnetic compass detection, similar to other sensory systems, relies on relative measures and that the primary sensory organ must be located in the head. Scanning movements of the head would provide useful information for either magnetodetection mechanism discussed.

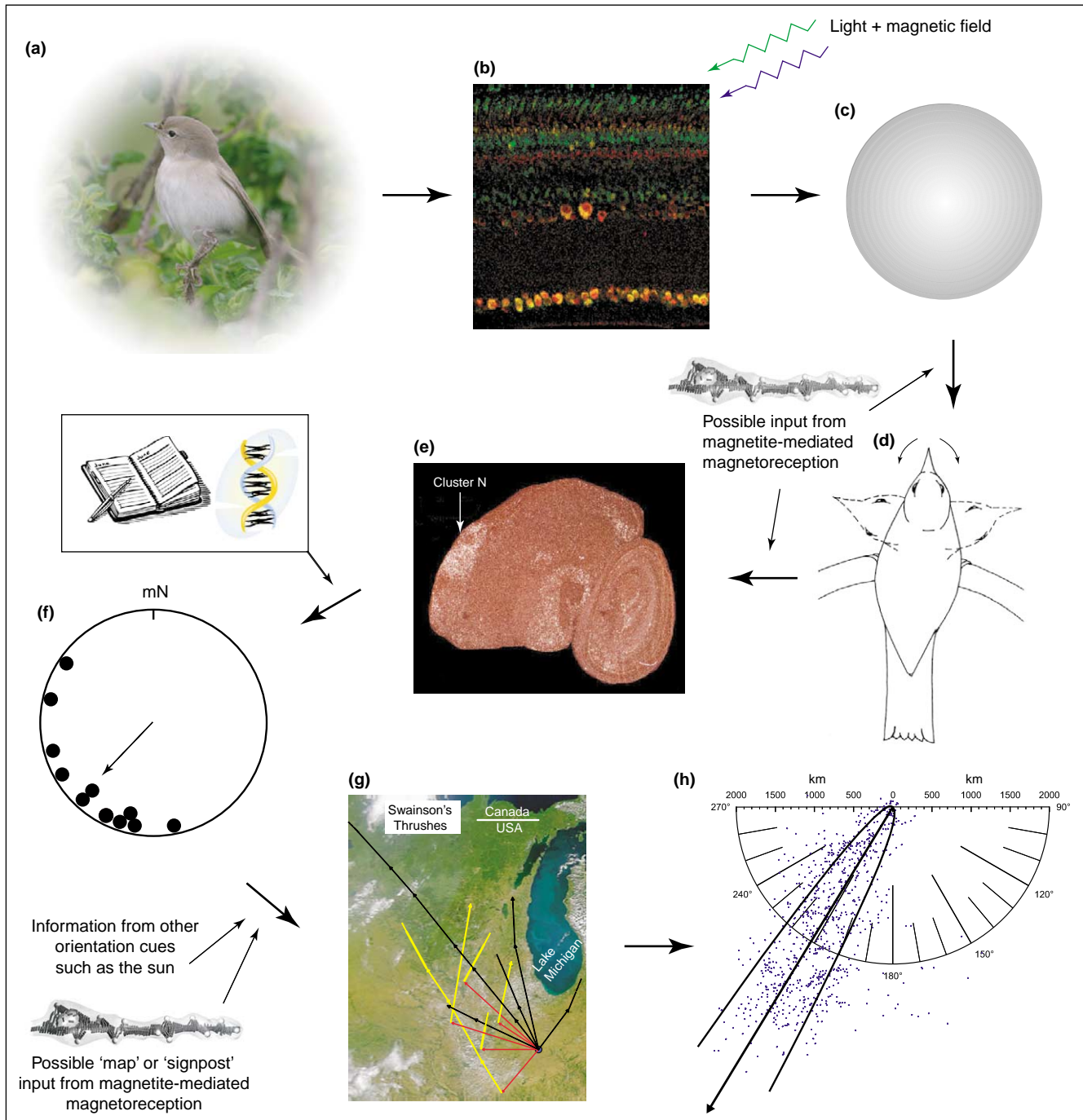
If scanning movements of the head are used in magnetite-mediated magnetoreception, the birds probably scan for the maximum or minimum magnetic field strength direction [54•]. This might, for example, help birds to measure magnetic inclination required for position determination precisely. If scanning head movements are used in light-dependent magnetoreception, they might function to detect the symmetry axis of the magnetically modulated visual patterns that characterize the magnetic field axis [54•]. Furthermore, head scanning behaviour would ease the bird’s recognition of the putative magnetically modulated virtual images, because it is much easier for the visual system to detect moving graded images than it is to detect stationary ones. Free-flying birds might not need to make head scanning movements, because the normal visual input would move across the retina during flight, whereas the magnetically modulated light-patterns would remain stationary. The visual system is also good at extracting stationary images against a moving background. In this respect, the distinct differences in cryptochrome expression in the displaced ganglion cells between migratory garden warblers and non-migratory zebra finches are particularly interesting, because the nBOR, to which the displaced ganglion cells connect, processes large-field visual flow-fields [55].

If birds use head scanning movements to detect the Earth’s magnetic field, it is likely that somewhere in higher centres of the brain, magnetic input is integrated with information identifying head direction in relation to the bird’s body axis. This means that electrophysiological recordings from these higher brain centres in anesthetized animals fixed in a stereotactic setup could be problematic.

Light-dependent effects on behaviour

The limited number of behavioural tests that can be performed with migratory birds within a year precludes straightforward determination of an action spectrum of magnetic orientation under different light wavelengths and intensities. However, progress towards such an action spectrum has been made, resulting in a complicated picture. Under low-intensity monochromatic light, birds orient well in blue and green, but not in yellow or red light. Under mixed colours or higher intensities of monochromatic light, birds show responses that do not coincide with the expected migratory direction and are often bipolar [56•,57]. One can speculate that two magnetoreception mechanisms interact: a dominant, light-depen-

Figure 1



The figure illustrates the current working hypothesis suggesting how a night-migratory songbird might detect and use its magnetic compass to guide its migratory journeys. This figure is not intended to be comprehensive, but is aimed at presenting, to a broad readership, a relatively simple graphical representation of how birds might detect and use magnetic compass orientation during migration. We stress that several details of this figure might not in the end turn out to be exactly true, but the general principles are likely to hold. We refer the reader to the main text for detailed discussion of the evidence supporting each aspect of this hypothesis. The main text also points to the many remaining unresolved questions. **(a)** During the day, the bird forages in order to fuel up for its nightly journey. **(b)** During the twilight period and during the night, dim light, predominantly in the blue-green spectral range, excites photoreceptor molecules, probably cryptochromes, located in the bird's retina (picture shows a transversal cut through a retina — photoreceptors at the top, ganglion cells at the bottom — of a garden warbler, which performed magnetic orientation at night). Green signal: cryptochrome 1a protein. Red signal: neuronal activity marker c-fos. Green + red = yellow signal: co-localization of cryptochrome 1a and neuronal activity during night-time magnetic orientation. Reproduced from [43**]. The light excitation initiates an unknown signalling pathway involving radical-pair formation and electron-transfer, which is modulated by the Earth's

dent mechanism requiring light in the blue–green range of the spectrum, and a secondary mechanism that operates under long-wavelength light or that might not require any light at all [29,57,58].

In principle, a mixture of the fully reduced and semi-quinone forms of flavin photopigments in cryptochrome could result in an absorption spectrum matching the spectral range expected from behavioural experiments. Moreover, some cryptochrome forms use a secondary antenna photopigment as the main light absorber, enabling further variability in the absorption spectrum. In this respect, it is interesting that at least four different cryptochromes have been detected in the retina of migratory birds (M Liedvogel, U Janssen-Bienhold, R Weiler, S Sagasser, H Mouritsen, unpublished [43^{••},44^{*}]). Identification of the absorption spectra of the migratory bird cryptochromes would be a major advance, and one that is needed before we can formulate more precise hypotheses regarding their possible interactions.

Conclusions: two mechanisms

In conclusion, there is quite strong experimental support for both a magnetite-mediated and a light-dependent magnetoreception mechanism in birds. We support the view of Wiltschko and Wiltschko [7] that many birds are likely to have and use both magnetoreception mechanisms. There is strong evidence that the light-dependent mechanism is involved in the magnetic compass of night-migratory songbirds and possibly also in that of homing pigeons (for a summary see Figure 1). The role of the

magnetite-mediated mechanism in birds is less clear. Most evidence suggests that it is used to detect changes in magnetic field intensity and/or inclination and, thus, is used to detect magnetic signposts or is part of a putative magnetic map sense. It cannot be excluded, however, that magnetite-mediated magnetoreception might also provide compass information in some animals including birds [4], and it could transpire that the two systems interact or that they are each of primary importance during different stages [11] of the orientation process. Considering the existing evidence for both a magnetite-mediated and a light-mediated magnetoreception mechanism, one should refrain from using the term ‘the magnetic sense’ in the singular.

Future research directions

There are still many open questions that must be answered before we can explain exactly how birds and other animals can detect the Earth’s magnetic field. This is the case both for the magnetite-mediated mechanism and for the light-mediated, radical-pair mechanism that is probably mediated by cryptochromes. In Box 1, we have listed some of the key questions that researchers should aim to answer during the next 5–10 years.

When evaluating future progress in this field, it should be remembered that the magnetic sense(s) still remains the least researched major sense of the animal kingdom. Because no migratory bird species are bred commercially in captivity, ethical considerations limit the number of wild-caught test birds that can be tested in each group and

magnetic field. **(c)** Because of the putative fixed orientation of the radical-pair forming molecules within the retinal cells and the half ball shape of the retina, the magnetic field modulates the light sensitivity of the radical-pair forming molecules differently in different parts of the retina. Thereby, the magnetic field direction is translated into a virtual visual pattern, which is sent to the brain through the retinal ganglion cells. If the radical-pair forming molecules are oriented normal to the eyeball in all cells and if the light-sensitivity is highest when the magnetic field is parallel to the molecules, the virtual visual pattern would look somewhat like what we show in (c) when the centre of the retina is looking in the direction of the field lines. **(d)** While the bird is stationary it might find it difficult to detect this virtual visual pattern, but during free flight or scanning head movements the virtual pattern and/or the background moves across the retinae, which makes it much easier for the visual system to detect the virtual visual pattern that emerges from magnetic field modulations. The picture shows a schematic drawing of head scanning behaviour. Reproduced from [54^{*}]. **(e)** All night-time visual input from the eyes is relayed to the brain, probably to a specialized brain cluster called Cluster N via the nBOR and/or the thalamus. (Picture shows a parasagittal section through the brain of a migratory garden warbler sitting still but awake during the night [left = frontal].) White signal indicates expression of the immediate early gene ZENK, which indicates that a brain area was active during the last hour of the bird’s life. The whitest area in the top left part of the brain is ‘cluster N’, which is processing seemingly specialized, night-time visual input from the eyes in garden warblers. Reproduced from [50^{••}]. The brain extracts the reference compass direction provided by the geomagnetic field from the visual inputs it receives from the retina. It is a distinct possibility that input from magnetite-clusters in the beak is also integrated into the avian magnetic compass at this stage (insert shows magnetite-cluster from the beak of a homing pigeon). Reproduced with permission from [21^{••}]. **(f)** If the bird’s circannual clock and its hormonal and genetic machinery are in migratory mode, a comparison between the reference direction and the bird’s genetically coded migratory direction [59] fixes its magnetic compass orientation (picture shows typical result of magnetic orientation experiment in an orientation cage). Each black dot indicates the mean orientation of one experimental bird. The arrow represents the group mean vector. mN = magnetic North. Modified after [43^{••}]. **(g)** In the wild, magnetic compass information is integrated with input from other orientation cues such as sun-related twilight information, which reassures that the bird’s orient in the seasonally appropriate migratory direction that night. Input from a magnetite-based magnetic signpost or map sense could also be integrated at this stage (picture shows the orientation of free-flying Swainson’s Thrushes, *Catharus ustulatus*). Black arrows indicate control flights of individuals experiencing the normal geomagnetic field prior to takeoff. Red arrows indicate flights of birds that experienced a magnetic field turned 80 degrees towards the east during the sunset period. Yellow arrows: subsequent flights of birds treated in the changed magnetic field 1–7 days earlier. Connected arrows indicate consecutive flights of same individual. The results suggest the *Catharus* thrushes primarily use a magnetic compass in mid-air, but that its directional meaning is calibrated daily from sun-related cues during twilight. Reproduced with permission from [10^{••}]. **(h)** The bird’s spatiotemporal orientation programme [60] ensures that it arrives at the appropriate wintering or breeding ground (picture shows the distribution of same-autumn ringing recoveries [blue dots] of young European robins relative to the ringing site [0,0 in the coordinate system]). Parabola indicates the predicted distribution of 68% of the recoveries, if young birds use compasses but no map for navigation. Arrow: mean migratory direction. Modified after [61].

Box 1 Examples of key open questions that should be addressed in the coming years.

- (1) Can we use oscillating fields as a diagnostic tool for the magnetodetection mechanism in other animals? The threshold intensity for which oscillating fields produce effects can provide information about the underlying biophysical mechanism in many behavioural setups, not only for that of migratory birds.
- (2) Do cryptochromes from migratory birds produce a radical-pair excited state and does this state survive long enough ($>1\mu\text{s}$) to be differentially affected depending on the direction of Earth-strength magnetic fields?
- (3) Can magnetic field effects be detected on isolated cryptochrome proteins from migratory birds?
- (4) What are the spectral sensitivities of migratory bird cryptochromes and how do they compare with the results from behavioural experiments?
- (5) How can cryptochromes be fixed in cells, so that directional effects can arise?
- (6) Do cryptochrome-containing cells in the retina change their membrane potential in response to changes in Earth-strength magnetic fields?
- (7) What are the signalling pathways by which an initial magnetic effect on cryptochromes or a magnetite structure is linked to a nervous signal?
- (8) Does light-mediated magnetoreception work at all times of day in all bird species? Variation of receptor signalling in the time course of a day infers that neurobiological measurements could yield inconsistent results at different times of day.
- (9) Are the clusters of magnetite crystals that are found in pigeons also found in migratory birds? If yes, what is their function in the orientation mechanisms of migratory birds?
- (10) Do magnetite-mediated and light-mediated magnetoreception interact with each other?

in each study. In addition, no commercial antibodies are made specifically against proteins from migratory birds, and to date nobody has produced a transgenic migratory bird. All of these factors limit the sample sizes, multitude of techniques, and technical sophistication that can be expected in investigations of the magnetic senses of birds. Answers to relatively simple fundamental questions related to light- and/or magnetite-mediated magnetoreception require a lot of effort and should be seen as major advances.

Despite the fact that there are still many open questions, for the first time in this field we now have magnetic sensory hypotheses that are based on strong behavioural evidence, some molecular evidence, a sound theoretical framework and named putative primary receptor molecules and structures. We, therefore, believe that it will finally be possible to obtain a molecular, physiological and cognitive understanding of the magnetic senses in birds and other animals.

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