A Model of Magnetoreception via Lorentz Force on the Transmission of Action Potential along Peripheral Nerves

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Abstract

动物如何感知微弱磁信号仍是一个未解之谜。在此，我提出假说：感觉输入的传导速度可在被施万细胞包裹的周围神经中得到调控；这些施万细胞含有大量储存在铁蛋白中的超顺磁性铁纳米颗粒，形成六方准晶的有序阵列。通过阵列内的颗粒间相互作用，超顺磁性纳米颗粒被微弱磁化并随地磁场有序排列。当磁感线不平行于离子运动方向时，由准晶体阵列产生的小磁场所产生的洛伦兹力将使动作电位阳离子的运动轨迹在有髓轴突内从直线路径偏转为曲线路径。由于周围神经的弯曲走向呈镜像对称，洛伦兹力可在离子轨迹与轴突弯曲不匹配的一侧延迟信号传导，而在离子能沿轴突曲率半径运动的另一侧则几乎无此效应。该机制可在两侧之间造成到达中枢神经系统核团的时间差，从而激活偏离的巧合检测神经元，实现对外部磁「源」方向的编码与处理。

Full Text

A Model of Magnetoreception via Lorentz Force on the Transmission of Action Potentials along Peripheral Nerves

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Abstract

How animals perceive weak magnetic signals remains a mystery. Here I propose that sensory inputs can be modulated in their transmission velocity along peripheral nerves surrounded by Schwann cells containing huge amounts of superparamagnetic iron nanoparticles stored in ferritins, forming ordered arrays of hexagonal paracrystalline structures. Through interparticle interactions within these arrays, the superparamagnetic nanoparticles become subtly magnetized and align orderly with Earth's magnetic field. The Lorentz force from the small

magnetic field created by the paracrystalline arrays will shift the motion trajectory of action potential cations whenever magnetic field lines are not parallel to ion movement direction, changing their path from straight to curved tracks within myelinated axons. Since bending orientations of peripheral nerves are always mirror-symmetric, the Lorentz force can delay transmission on one side where ion trajectories do not match axon curvature, while having almost no effect on the other side where ions travel along the radian of axon curvature. This mechanism creates a time difference in arrival at CNS nuclei between the two sides, activating deviated coincidence detector neurons so that directions of the external magnetic "source" are encoded and processed.

Keywords: Schwann cell, iron-loaded ferritin, superparamagnetic collective behaviour, Lorentz force, coincidence detector neuron

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Introduction

The Earth's magnetic field is thought to be caused by motion of the Earth's conductive, iron-rich core. It is a vector quantity with three components: 1) inclination, 2) declination, and 3) intensity. The compass was invented by the Chinese between 200 BC and 100 AD, first used in navigation by sailors around 1000 AD [**?**]. Nevertheless, the geomagnetic field has been used by bacteria and animals as an orientation and navigation aid for far longer than human techniques, becoming an important topic in biological and physical fields. This phenomenon represents both a century-long conundrum and one of the 125 questions posed in the 2005 *Science* magazine (vol. 309): "how do migrating organisms find their way" [**?**, **?**, **?**].

While experimental evidence for magnetic sensing in migratory animals, from insects to mammals, is undisputed [**?**, **?**, **?**], it is becoming apparent that a growing number of non-migratory species can respond sensitively to magnetic stimulation, including nematodes, crustaceans, fruit flies, teleost species, amphibians, subterranean rodents, dogs, humans, as well as some resident birds and ungulates [**?**, **?**, **?**, **?**, **?**, **?**, **?**]. In some situations, the adaptive significance has been ecologically elucidated, while in others it remains obscure [**?**, **?**]. Meanwhile, magnetoreception is poorly understood from the primary biophysical detection events, signal transduction pathways and neurophysiology, to information processing in the brain [**?**], although it varies in magnetic field inclination, polarity or intensity, which could be informative for animals.

Several sophisticated models for magnetic sensing have been proposed, but none have been commonly accepted. Two of them—magnetite and radical pairs—have been studied more extensively in laboratories worldwide than others. The

model of chemical reactions that has recently attracted the most attention is based on radical pairs, presumably modulated by magnetic fields as strong as Earth's. The radical pair is a short-lived reaction intermediate composed of two radicals formed in tandem. The hypothesized process begins with electron transfer from a donor molecule to an acceptor, leaving each molecule with an unpaired electron whose spins may be either antiparallel (↑↓ singlet state) or parallel (↑↑ triplet state). As each electron spin has an associated magnetic moment, interconversion between singlet and triplet states, as well as their chemical fates, can be influenced by internal and external magnetic fields [**?**]. The eye and pineal gland are proposed as putative organs for magnetic senses based on their dependence on light with specific wavelengths during orientation and navigation [**?**, **?**, **?**].

Cryptochrome (Cry), the photopigment circadian rhythm molecule located in photoreceptors, is proposed as the substance involved in such a process. However, it has been claimed that, with the exception of Cry4, no cryptochrome from a migratory animal that unequivocally uses a light-dependent magnetic compass has been shown to exhibit magnetic sensitivity [**?**]. Cry4 derived from the night migratory European robin is more magnetically sensitive than those from non-migratory pigeon and chicken under identical measurement conditions *in vitro* [**?**]. The response of Cry to magnetic fields via radical pairs appears theoretically incapable of forming the basis of a polarity compass, being more likely to perceive inclination information from a geomagnetic field. There must be a mechanism that can amplify the weak interaction of the geomagnetic field with the spin of a single electron to the level of photon detection, resulting in modulation of the photoreceptor's response to light [**?**]. This magnetic field-dependent chemical reaction then triggers a signaling pathway that ultimately generates neuronal signals and affects neuronal firing rates [**?**].

The magnetite model is based on small magnetic particles found in the inner ears and/or beaks of birds [**?**, **?**, **?**] and in the olfactory epithelium of fishes [**?**, **?**]. These species appear to use magnetic particle-based magnetoreception (or a magnetic polarity compass) in complete darkness for orientation and navigation. It is proposed that rotation or translation of a magnetic particle can somehow influence the electric field across a sensory nerve membrane to generate membrane potential, eventually eliciting an action potential once threshold is exceeded. Alternatively, magnetite crystals in chain or cluster form are attached to the cytoplasmic membrane via a cytoskeletal linker, through which ion channels can be opened directly by magnetite crystal rotation [**?**]. This linear chain of single-domain crystals attempts to align itself with Earth's magnetic field, behaving like its counterpart in bacteria, thereby exerting torque force or pressure on a mechanosensitive channel. This transiently activates the channel, resulting in cation influx and membrane depolarization [**?**, **?**], finally triggering the action potential [**?**, **?**, **?**].

The electromagnetic induction model regards an accessory structure that converts magnetic stimuli into electrical information. One possible target is the

vertebrate semicircular canals, which may fill with cation-rich endolymph and have sensory cells on both sides of the cupula. When animals rotate around an axis in the plane of the semicircular canal, electromagnetic induction occurs without displacement of the endolymph [**?**, **?**]. Depending on the strength and orientation of the external magnetic field, this induces an electromotive force in the conductive endolymph, leading to charge separation in the circuit and inducing cation influx through highly sensitive voltage-gated ion channels [**?**, **?**]. This model is somewhat supported by the finding that avian hair cells contain an iron-rich organelle, the cuticulosome, consisting primarily of ferritin nanoparticles with only one particle per cell [**?**].

Recently, a putative magnetic receptor protein (MagR), an iron-sulfur cluster protein, was identified in *Drosophila* species. This protein forms a rod-shaped multimeric complex with 40 iron atoms distributed over approximately 24 nm. Individual complexes were visualized by electron microscopy on a sample grid, leading to the conclusion that each rod possesses an intrinsic magnetic moment large enough to align with Earth's magnetic field [**?**]. Afterwards, three types of MagR were identified, each with distinct binding capacity of iron and/or iron-sulfur clusters, indicating evolutionary expansion of MagR functions and protein stability. Furthermore, a gradual increase in iron content of MagRs was observed during evolution [**?**]. Sequence conservation and structural features of MagR and Cry revealed an intermolecular electron transport pathway bridging different models of animal magnetoreception—chemical reaction and magnetite mechanisms [**?**, **?**]. By binding to certain metals, melanin secreted by the pineal gland can acquire magnetic properties that could influence magnetic effects and possibly organisms' response to external magnetic fields and magnetic perception [**?**]. The pineal gland is a rhythmic, light-sensitive circadian organ proposed to be part of a combined compass and sundial system [**?**]. The electrical activity of pineal cells was suppressed by an induced magnetic field and restored when the field was inverted. However, it is unknown whether the pineal organ itself detects changes in magnetic field, as it is strongly innervated by the sympathetic nervous system, which can be affected by magnetic stimuli [**?**]. Studies involving surgical and chemical interventions on neuronal connections of the pineal gland led to identification of intrinsic magnetic sensitivity, consistent with the assumption that detection of magnetic fields is related to activity of photoreceptors [**?**].

Unfortunately, only one convincing model of magnetotactic bacteria has been proposed, with chains of magnetically interacting crystals (magnetosome crystals) used for navigation in coordination with Earth's magnetic field [**?**]. To improve efficiency of magnetotaxis, magnetosome crystals (usually composed of magnetite or greigite) should be magnetically stable single-domain particles. The formation of magnetite chains and magnetotaxis behaviour of bacteria have been demonstrated by consistently verifiable experiments [**?**, **?**, **?**]. In contrast, all proposed models for animal magnetoreception are primarily theoretical, too exquisite to be tested. Even in cases of experimental sensory investigations, the majority are performed *in vitro* and/or with magnetic stimuli much stronger

than Earth's magnetic field [**?**, **?**], providing referential evidence rather than direct proof.

Bottlenecks of Existing Models

Several important issues must be addressed before achieving full understanding of magnetoreception [**?**].

The first is the large gap between energy demanded to generate neural signals (action potential spikes) and that produced by interaction of cellular components with Earth's magnetic field. In the Cry/radical pairs mechanism, the energy of interaction of a molecule with a 50 µT magnetic field is >6 orders of magnitude smaller than average thermal energy kBT (where kB is Boltzmann constant and T is temperature in Kelvin) [**?**, **?**], not to mention generation of action potentials. Giachello et al. (2016) stated that neuronal firing rates of Cry-dependent processes can be significantly potentiated in the presence of an applied magnetic field of 100 mT, which is, however, 2,000-fold stronger than mean strength of Earth's magnetic field [**?**]. No experimental data on the chemical mechanism collected under Earth's magnetic field conditions is available to date [**?**].

The smallest iron particles known to have a permanent magnetic moment at room temperature are single-domain crystals of magnetite (Fe_3O_4), about 30 nm in size [**?**]. For the magnetite model, it is proposed that permanent magnetite particles are anatomically coupled to ion channels so they can be gated by magnetic torque from magnetite rotation, but this envisioned pattern has not yet been found in excitable cells. The force derived from an externally applied magnetic field gradient on iron-loaded protein (ferritin), even superparamagnetic forms, is too weak for mechanically gated ion channels [**?**, **?**]. It is frequently assumed that iron compounds within ferritins are ideally all magnetite (Fe_3O_4) or maghemite (γ-Fe_2O_3), but they are actually hydrated iron oxide minerals or ferrihydrites with much lower magnetic susceptibility compared to magnetite [**?**, **?**]. Regarding non-ferritin iron particles, the densities of sensory cells and numbers of responsive molecules involved in magnetic navigation are noticeably low and seem impotent in inducing behavioral reactions [**?**, **?**, **?**, **?**], or worse, no intracellular magnetite can be identified in putative vertebrate magnetoreceptors by magnetic screening [**?**].

Extracting magnetic direction information embedded in the static geomagnetic field is another major challenge for any animal wishing to use it for long-distance navigation, since geomagnetic characteristics remain almost invariant locally, with magnetic intensity varying only about 0.01% km^{-1} and inclination only about 0.01° km^{-1} on Earth's surface [**?**, **?**]. Therefore, displacement relative to the size of our planet is extremely miniature when moving at physiologically limited speeds on land, underwater, or even in air. So how, if at all, can slow-moving animals distinguish spatial magnetic signals from the geomagnetic field to enable magnetic mapping with resolution below 10-30 km [**?**]? The high

penetration characteristic of magnetic fields through biological tissues ensures that all magnetic sensors are activated simultaneously and homogeneously, eliminating signal differences between two sides of the body. In contrast, other sensory systems—including visual, auditory, thermal, piezo, and olfactory sensors—receive and process localized, varied, or heterogeneous stimuli to locate signal sources. For instance, sound localization is accomplished by comparing acoustic differences in phase, magnitude, and frequency between two ears [**?**, **?**]. For this purpose, biological evolution favors wide separation of paired sensors, like two eyes and ears on opposite sides of vertebrate heads, and paired tips of signal collectors such as reptile tongue forks. If a similar mechanism were applied to magnetic sense, for small animals like insects, anatomically and functionally insulating two paired homogeneous sensors would be disastrous.

To date, four organs and their corresponding cranial nerves have been proposed as typically involved in magnetoreception: photoreceptors in the eyes (nII) and/or pineal glands (nV) of robins, vestibular organs (nVIII) of pigeons, and olfactory epithelium (nI) in trout nostrils and beaks (nV) of pigeons. In the central nervous system (CNS), isolating magnetic signals from those of their "master" organs represents a third major challenge [**?**]. Are there neuronal areas or nuclei in the CNS that have been specified during evolution for exclusive processing of magnetic signals, or have they been intermixed during development with other perceptual systems [**?**, **?**, **?**]? If the neuronal pathway is shared by magnetic sensation and its "master" perception from sensory organ to higher brain region, where is the anatomical bifurcation site for signal division located, and how can the two categories of signals be functionally divided? In all respects, a generally acceptable model of animal magnetoreception must be most compatible with addressing these three problems: extreme weakness of magnetic strength, lack of locally directional information, and existence of a dedicated magnetic neural pathway [**?**].

Schwann Cells as Potential Magnetoreceptors

Peripheral nerves are generally wrapped very tightly with thin multi-layered membranes of Schwann cells, forming a myelin sheath structure that isolates the axon from surrounding tissues, causing insulated axons to behave like wires exposed to air magnetic fields [**?**]. Unlike in the CNS, where an oligodendrocyte makes several myelin sheaths across nodes of Ranvier and even across neurons, a Schwann cell in the peripheral nervous system (PNS) forms only one myelin sheath restricted to a single segment between two nodes, so a full single axon must be folded with several Schwann cells. The majority of Schwann soma does not surround an axon but is mostly located alongside it (Fig. 1 [Figure 1: see original paper]) [**?**, **?**].

Importantly for magnetoreception, Schwann cells contain enormous numbers of tiny iron atoms stored within an 8 nm diameter hollow spherical nanocage of ferritin—a cytosolic protein with external diameter of approximately 12 nm, composed of 24 chain-like subunits categorized into light and heavy chains [**?**, **?**].

Although the ferritin cavity provides space for up to 4500 Fe^{3+} atoms, this space is rarely fully utilized; about 2000-4500 iron atoms form particles of 5-8 nm diameter controlled by multiple metal-protein interactions [**?**, **?**, **?**, **?**]. Ferritin cannot enter the medullary sheath where space is less than 12 nm between adjacent internal membranes of myelin lamellae, so iron nanoparticles are distributed mainly in the Schwann soma with cytoplasm containing up to 3/4 of total iron [**?**]. In the sural nerve, for example, ferritin-reactive staining is densely localized in Schwann cell cytoplasm adjacent to myelinated nerve fibers. Microphotographs support a predominant 1:1 ratio between ferritin-containing Schwann cells and myelinated axonal segments divided by nodes of Ranvier [**?**].

[Figure 1: see original paper]

As one of the most iron-rich cell types in the nervous system, ferritins in Schwann cells would have high concentration with high gene expression because sufficient iron is necessary for development and maintenance of myelin sheath structure in both CNS and PNS [**?**, **?**, **?**, **?**, **?**]. Furthermore, Schwann cells demonstrated iron pools for import and export to axonal segments located far from neuronal soma [**?**, **?**, **?**]. Additional evidence shows Schwann cells can efficiently internalize dextran-coated superparamagnetic iron oxide from culture medium via fluid-phase pinocytosis [**?**]. It is rational that the number of iron atoms per ferritin in Schwann cells is higher than in other cell types; let us assume that fully iron-loaded cores with 8 nm diameter can account for up to 50% of all ferritins, which are more likely to cluster locally [**?**].

Superparamagnetism

Superparamagnetism is the magnetic behavior associated with magnetic nanoparticles, generally made of ferromagnetic or ferrimagnetic materials, corresponding to a single magnetic domain with high magnetic moment. Unlike ferromagnetic materials or permanent magnets, superparamagnetic substances do not retain net magnetization and switch magnetic orientation randomly due to thermal fluctuations once the external field is removed (Fig. 2 [Figure 2: see original paper]) [**?**, **?**]. Consequently, various physiological arrangements of single-domain biogenic magnetite have been suggested as the basis for geomagnetic field sensitivity in animals [**?**, **?**, **?**].

Here, straightforward magnetization and demagnetization of superparamagnetic materials are invaluable for rapid, sensitive, and sustainable detection of external magnetic fields. In this case, magnetization likely corresponds to the magnetic sense process, while demagnetization returns the “sensor” to its initial baseline to restore excitability.

When nanoparticles are subjected to an external magnetic field, their internal magnetic moment quickly and substantially reorganizes, resulting in strong internal magnetization from exchange coupling of electrons within the domain, thus becoming superparamagnetic [**?**]. The essence of this phenomenon is caused by the nano effect of the material: at the nanoscale, electron spin and orbital

motion are affected by quantum effects (Fig. 2). Nanoparticles can align with the external field and their poles orient accordingly, randomly reorienting when the external field is absent. For a single domain in a separate particle, there can be no interactions or domain ordering within a multiple-domain sample [**?**]. Magnetite (Fe_3O_4) is the most magnetic of all natural minerals on Earth [**?**] and comprises a close-packed array of oxide (O^{2-}) ions, forming superparamagnetic particles with diameters reaching up to 25 nm [**?**, **?**, **?**, **?**].

[Figure 2: see original paper]

Within weak fields such as Earth's magnetic field, experimental magnetization curves showed that magnetite particles with 10-12 nm diameters had steeper magnetic saturation curves or higher magnetic susceptibility, while smaller particles had decreased magnetizability. Among them, particles with average diameter of 6.7 nm displayed relatively gentle curves, implying perceptible effects of thermal Brownian motion on small particles even when subtly magnetized [**?**]. In contrast, some studies report that magnetization of superparamagnetic nanoparticles increases significantly in the size range below 10 nm, with saturation magnetization close to 10^6 A/m [**?**, **?**, **?**]. Therefore, in Earth-strength magnetic fields, superparamagnetic crystals can generate fields strong enough to attract or repel other nearby crystals [**?**]. It is imperative that superparamagnetic iron particles respond to external magnetic stimulation with very steep patterns (Fig. 2), acting as magnetic switches that determine high sensitivity and short response time of the "sensors." However, Earth's magnetic field is static and unable to change direction and inclination quickly. Relative changes for signaling only occur when animals move—eastward or westward crossing magnetic lines of force, and northward or southward changing inclination. Through superparamagnetic phenomena, magnetic fields at nanometer scale can be created around individual nanoparticles, but they are too weak and small to be used as magnetic needles [**?**].

Iron-Loaded Ferritin

Biological materials with magnetic properties are primarily iron-containing systems, mostly in oxide form stored in ferritin cores as reservoirs of readily available iron. Due to cellular toxicity, Fe^{2+} must be stored as ferrihydrite within ferritins, where it is oxidized to less toxic Fe^{3+} by heavy chains of ferritins, distinguishing ferrihydrite in ferritin from non-biogenic forms whose main component is Fe^{2+}. Ferrihydrite nanoparticle size typically ranges from 5 to 8 nm in diameter, fitting the hollow cage size [**?**, **?**]. Synthesized ferrihydrite nanoparticles exhibit superparamagnetic properties at room temperature within ferritin spherical nanocages, with characteristic blocking temperature of 23-25 K. Uncompensated moments of ferrihydrite particles are approximately 200 Bohr magnetons, which is 66-fold lower than human-made magnetoferritin (Fig. 1) [**?**, **?**]. Nevertheless, natural ferritins do contain superparamagnetic cores, even though magnetic moment of a single ferrihydrite core is far smaller than magnetite nanoparticles at room temperature [**?**].

In theory, saturation magnetization of an individual Fe_3O_4-loaded ferritin could reach a maximum of 7.8×10^5 A/m when assuming an assigned iron core diameter of 8 nm with moment of 5 μB per iron atom [?, ?, ?], but this calculation may not work for ferrihydrite cores. The magnetic field near the surface of saturated magnetite particles is estimated to be about 0.65 T; correspondingly, for ferritin ferrihydrites this value may be re-estimated by dividing by 66, yielding 9.85 mT [?, ?, ?]. Superparamagnetic properties of ferrihydrite nanoparticles may arise from surface effects (important for such nanometric compounds) and from presence of cation vacancies in the crystal, resulting in small magnetic moment for each ferrihydrite particle within ferritin. Néel relaxation is also observed in particles within ferritins prepared from horse spleen, further supporting its classification as a superparamagnetic compound [?]. Therefore, ferrihydrite presented in ferritin cores can be magnetically ordered and exhibits superparamagnetism, as measured by magnetic resonance imaging (MRI) and Mössbauer spectroscopy [?, ?, ?].

Because of high iron concentration in Schwann cells and thus ferritins, iron particles aggregate densely in local cytoplasmic regions where individual magnetic moments interact and align, leading to collective magnetic states rather than random individual flipping moments. Iron-rich ferritins are typically large particles located exclusively within cytosol clusters, mainly in lysosomes, with the iron-rich variety exhibiting higher electron density than dispersed cytosolic ferritin [?]. Their cores can form hexagonal paracrystalline arrays within a siderosome (Fig. 1) or *in vitro* in solution, showing relatively compact and ordered structure—a type of sublattice [?, ?]—probably due to two causes: 1) mutual attractive force, which is highly significant between two iron-loaded ferritins if iron particles are in superparamagnetic spin configuration [?, ?], and 2) apoferritin-driven process [?, ?]. Many studies show that although these superparamagnetic crystals cannot retain stable magnetic moments, they have much higher magnetic susceptibility than paramagnetic systems when forming collective lattice behavior [?, ?, ?, ?, ?]. Accordingly, paracrystalline arrays of fully iron-loaded ferritins are characterized by collective behaviors and therefore may possess features of both multidomain magnetite and magnetic nanoparticles, such as high magnetic moment and superparamagnetism (Fig. 3 [Figure 3: see original paper]).

[Figure 3: see original paper]

Maximum iron particle size is limited by the protein's internal diameter of 8 nm, while these shells ensure a 4 nm gap between neighboring particle surfaces, enabling interaction between dipolar moments of different particles that favor magnetic ordering and increase magnetic response when nanoparticles are close together [?, ?, ?]. In collective magnetic states, particles can align their magnetic moments in coordinated fashion. Considering that distances between neighboring iron particles are approximately 8 nm, dipole-dipole interparticle interaction may be the dominant effect of their collective behaviors [?, ?, ?, ?, ?].

Local Magnetic Field Generation

It has been established that magnetic properties of iron are notoriously sensitive to structure, and spin coupling configuration (paramagnetic, ferrimagnetic, antiferromagnetic, etc.) is highly variable and depends on chemistry [**?**, **?**]. Ferrihydrite cores appear as paracrystalline hexagonal formations in electron microscopy, suggesting each is most likely an icosahedron when considering the hollow spherical cage and multiple metal-protein interactions (Fig. 3) [**?**, **?**]. This icosahedron shape, with nearly symmetrical characteristics close to a sphere, means there is no obvious easy axis during magnetization, and magnetized direction can be completely determined by external magnetic field. Furthermore, compared to cube-like nanoparticles, sphere-like ones exhibit lower magnetic coercivity and remanence values, enabling faster sensor response due to different orientations of their polycrystalline structure [**?**, **?**].

Therefore, local magnetic fields at micrometer scale based on collective effects of paracrystalline arrays can be subsequently created in Schwann cells (Fig. 3) [**?**, **?**, **?**]. Since magnetic force is dramatically enhanced and its poles align with Earth's polarized magnetic field, the local magnetic field can serve as an internal dynamic compass in animal orientation and navigation [**?**, **?**]. By this mechanism, weak geomagnetic signals are amplified regionally within cells in a manner similar to dense local magnetic field lines around permanent magnets (Fig. 3).

When animals perform a horizontal turn, relative magnetized orientation of superparamagnetic particles may shift by corresponding angle due to Earth's magnetic gradient or force. During this phase, those 50% fully iron-loaded ferritins located in paracrystalline arrays will be magnetized first and then adjust to new polar direction with Earth's magnetic field [**?**, **?**]. Once this process occurs, combined forces of Earth's magnetic field and magnetized neighboring particles (Bt = Be + Be, where Bt is total magnetic strength, is susceptibility of particles, and Be is external magnetic strength) will be generated. Eventually, all particles, including small ones, in paracrystalline arrays can be magnetized and magnetic moments align correspondingly (Fig. 3) [**?**, **?**].

When animals make a new turn, small nanoparticles will first be demagnetized by thermal fluctuation at physiological temperatures, then influence neighboring large particles that have lost alignment force (Be) of Earth's magnetic field. Subsequently, the local magnetic field generated in the last movement turn dissipates and the process of building a new local magnetic field restarts from this chaotic state. By repeating this process, polar orientation of Earth's magnetic field is dynamically represented and signaled within animals.

[Figure 4: see original paper]

Alternatively, if magnetoreception cells possess iron particles with diameters $ $20 nm, as found in pigeon beaks and trout nostrils [**?**, **?**, **?**, **?**], magnetic detection may be more accurate and faster. Although it is claimed these iron

particles were simply macrophages in pigeons [**?**], this does not prevent them from being used in magnetic navigation as well. These types of iron particles can be magnetized with greater susceptibility and affect related neuronal processing over relatively long distances. Based on the present model, it can be predicted that animal species with high magnetoreception sensitivity may possess relatively large non-ferritin magnetite nanoparticles in Schwann cells or glia near PNS axons.

Lorentz Force on Ion Motion

The force required for induction of an action potential is much greater than that provided by cellular magnetic crystals crossing Earth's magnetic field, and therefore magnetoreception in animals may not depend on this process [**?**]. The present study proposes that Lorentz force derived from local magnetic fields in Schwann cells can modulate velocity of ions (especially Na^+, K^+, and even Ca^{2+} involved in generation and transmission of action potentials) moving along peripheral axons with myelin sheaths (Fig. 4). For efficient conduction of action potentials, cations move rapidly from soma to nerve terminal at velocities ranging from 70 to 150 meters per second in fully myelinated axons with diameters of 12-20 µm [**?**].

The local magnetic field is created by superparamagnetic particle arrays in the soma of Schwann cells that stick close to the axon. The effect of Lorentz force can apparently reduce transmission velocity within each sheath segment along PNS axons in specific situations—for example, when Lorentz force drives straight motion pathways of ions to curved tracks while magnetic field lines are perpendicular to motion trajectory (Fig. 4). Peripheral nerves or axons of optic, auditory, and trigeminal nerves are not exactly straight but naturally curled in their innervations from lateral to medial, showing chiral or mirror-symmetrical patterns (Fig. 5 [Figure 5: see original paper]).

[Figure 5: see original paper]

For cation motion of action potentials driven by Lorentz force moving along peripheral axonal curvature (Fig. 4), transmission velocity is rarely disturbed. In another situation where cation motion is propelled in a direction that does not follow axonal curvatures or even opposes them (Fig. 4), transmission velocity is reduced accordingly. Therefore, arrival times from peripheral sensors to the central nervous system will differ between the two sides. Force strength and operating distance from superparamagnetic ferrihydrite arrays can be relatively small, causing large radian of ion trajectory in local areas where ions change direction correspondingly (Fig. 4 & 5). Those ions can advance further in new trajectories when moving out of action range of local magnetic fields. The radius of curvature of ion trajectory path (r) can be determined by:

$$r = \frac{mv \sin \theta}{qB}$$

For K^+, m is $6.4924249 \times 10^{-23}$ g; for Na^+, m is $3.8175458 \times 10^{-23}$ g; v is 70-150 m/s; q is +1 for both ions; while B is magnetic flux density of local magnetic field, which may have uneven spatial distribution in the present model. Here, is the angle of intersection between magnetic force direction (B) and ion motion direction (v), importantly changing correspondingly as animals move in Earth's magnetic field, which then quantitatively encodes orientation information. Accordingly, geomagnetic direction information generated by changes in direction and/or inclination at tiny scales can be sensitively reflected by nervous systems, no matter how close paired nerves are anatomically.

Coincident Detection

There is a type of CNS neuron possessing bipolar dendrites extending on opposite sides that has maximum response probability only when signals from two PNS sensors arrive simultaneously (Fig. 6 [Figure 6: see original paper]). Therefore, it is named a coincident detector neuron. Bipolar neurons are frequently found in visual systems calculating depth of 3D images and auditory systems encoding sound location [**?**, **?**, **?**]. These neurons often arrange in orderly lines in avian auditory brainstems (nucleus laminaris in Fig. 6) and consequently, interaural time differences upon arrival can be encoded by delay-line neurons, following Jeffress's model [**?**]. The Lorentz force-based model can generate such time differences in arrival between two sides of the head and activate "coincidence detector" neurons in delay-lines, so that information about geomagnetic direction and/or inclination is decoded by this magnetoneural system. This panorama is experimentally supported by stereospecific neural responses of vestibular nuclei to magnetic field stimulations with strength comparable to Earth's [**?**].

[Figure 6: see original paper]

The processes described above are mainly based on position of iron-loaded ferritins within Schwann cells relative to axons they wrap around—for example, most if not all molecules must be localized exclusively on the same side, such as the "top" side (Fig. 1). This specific ferritin distribution might be architecturally supported by outer cytoplasmic channels in Schwann cells along wrapped axons in virtually parallel patterns [**?**]. If not, effects of Lorentz force would be cancelled by clustered iron particles distributing randomly around axons. Natural selection pressure would favor this arrangement for systems used in biomagnetic perception. Evolutionary development in one system would usually release selection pressures on systems with the same function; hence for peripherally nonmagnetic nerves, relaxed selection would favor arrangement of iron particle clusters in random spatial patterns (possible minimum energy consumption). Here, a positional switch that "turns on" arrangements of Schwann cells works as evolutionary magnetoreception when they line up and "turns off" when distributed randomly. It is difficult to rule out that two or three sensitive organs or systems (visual + auditory) in one animal may be involved in geomagnetic detection. In such situations, one system should dominate over others.

Signal Processing

The core idea of my hypothesis is that geomagnetic signals are detected and perceived by manipulating electrical signal transmission rather than by inducing action potentials. Logically, this mechanism requires simultaneous, "very uniform" or highly homogeneous electrical signal inputs from both sides of the head. In visual systems, signaling in both eyes stimulated by shortwave light generally satisfies this logical requirement, since both sky and sea provide uniformly blue stimuli reaching both eyes with equal intensity. This essentially explains the phenomenon exhibiting blue-light-dependent patterns in geomagnetic perception [**?**, **?**]. The semicircular canals record body positions highly synchronized between both sides of the head. The horizontal semicircular canal may respond to directional information while the vertical one responds to inclination information of geomagnetic field [**?**, **?**]. All three semicircular canals may work together to encode local magnetic maps with stereotypical combinations. In fish olfactory systems, two nostrils open very closely so that one pulse of chemical stimulation can arrive at both nasal tunnels almost simultaneously to generate synchronized electrical inputs. Interestingly, these signals appear to be captured by the ophthalmic branch of trigeminal nerves [**?**, **?**], probably because the large distance between paired nerves on two sides of the head and/or curvature radian of trigeminal nerves is more pronounced than that of nasal nerves (Fig. 5).

Neural circuits specifically evolved to process magnetic information cannot yet be identified anatomically to date, meaning they may not exist. Alternatively, magnetic signals are processed by existing pathways used in visual, vestibular, olfactory, or multisensory systems of the face/head [**?**, **?**, **?**]. Based on my model, magnetic signals will be isolated and encoded independently at first- or second-order nuclei of CNS vestibular pathways, which is quite applicable for reinterpretation of neural firing patterns recorded by Wu and Dickman (2012) [**?**].

Multiple systems can operate in synergy to detect direction, inclination, and maps of Earth's magnetic field, similar to how vestibular inputs are reinforced by visual information from corresponding rotating images. In absence of visual orientation cues during seasonal bird migration, particularly at night, the "parasitic" magnetic pathway will dominate over its "host" in orientation decision processes, or under repeated stimulation with different variables of strong magnetic fields in the laboratory [**?**], the learning process reinforces magnetic detection.

Detection accuracy and reaction time of magnetic perception in animals are suboptimal compared to other sensory systems but can be adequately characterized using the present model. In addition to comparison with other behavioral patterns, orientation data typically exhibit large inconsistency in probability distribution with relatively high variations [**?**, **?**], although they may pass statistically significant tests. This situation not only reduces accuracy of conclusions

but also leads to contradictory statements, likely due to limitations of initial naked-eye observations in fields with limited visible distance. In some cases, orientation cannot accurately reflect final direction. One solution is to use cyber-animals carrying small devices on their backs, equipped with tracking systems developed in our laboratory, which indicate movement directions in geographic ranges. Vector orientations in polar coordinates can be calculated to manifest subjects' final navigation directions. Finally, it should be noted that while my theory can explain most physiological and behavioral phenomena reported to date, magnetoreception in lower animals such as nematodes with much simpler neural systems is beyond the scope of my model [**?**].

Further Studies

Although the model proposed in the present study is logically rational based on physical and biological advances achieved, a series of studies providing more direct evidence is required to verify its validity:

1. The paracrystalline arrays made of ferritin ferrihydrites must be tested fully *in situ* in terms of chemical components, nano- and microstructures, and cellular locations. The challenge is that related anatomical structures are frequently deformed and dissolved during sample treatments and are also contaminated by iron-made tools [**?**, **?**].
2. The collective susceptibility of the arrays should be measured under 50 $±$25 μT magnetic stimulation to identify existence of a local magnetic field.
3. Formulas must be established to describe mathematical relationships between magnetic force derived from local magnetic fields and curved paths of cations during action potential transmission along axons, based primarily on a single-axon model [**?**].
4. Delay lines derived from neural effects of Lorentz force—for example, different arrival timings of neuronal signals from both sides of the head—should be verified with neurophysiological paradigms under different magnetic field strengths. Therefore, a quantitative correlation can be constituted between temporal differences in signal arrival to the CNS and intensity of magnetic stimulation.
5. Orientation and navigation behavioral responses must be investigated quantitatively with experimental perturbations of delay lines.

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