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Review

Hypomagnetic Fields and Their Multilevel Effects on Living Organisms

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Abstract: The Earth's magnetic field is one of the basic abiotic factors in all environments, and organisms had to adapt to it during evolution. On some occasions, organisms can be confronted with a significant reduction in a magnetic field, termed a "hypomagnetic field—HMF", for example, in buildings with steel reinforcement or during interplanetary flight. However, the effects of HMFs on living organisms are still largely unclear. Experimental studies have mostly focused on the human and rodent models. Due to the small number of publications, the effects of HMFs are mostly random, although we detected some similarities. Likely, HMFs can modify cell signalling by affecting the contents of ions (e.g., calcium) or the ROS level, which participate in cell signal transduction. Additionally, HMFs have different effects on the growth or functions of organ systems in different organisms, but negative effects on embryonal development have been shown. Embryonal development is strictly regulated to avoid developmental abnormalities, which have often been observed when exposed to a HMF. Only a few studies have addressed the effects of HMFs on the survival of microorganisms. Studying the magnetoreception of microorganisms could be useful to understand the physical aspects of the magnetoreception of the HMF.

Keywords: hypomagnetic field; magnetic zero; magnetoreception

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1. Introduction

Every living organism on Earth has adapted to the geomagnetic field during an evolutionary process lasting billions of years. The presence of a geomagnetic field (approximately 50 uT) is natural to each cell [1]. However, in a few circumstances, organisms can face the absence of magnetic fields. Understanding its effect can enhance our knowledge of magnetoreception mechanisms, with applications in space research, biotechnology or medicine. The terms "hypomagnetic", "conditionally zero magnetic field" or "magnetic vacuum" generally refer to fields with a magnetic flux density (B) below 100 nT [2], but according to some authors, we can speak of a magnetic field weaker than 5 μT as being hypomagnetic [3].

Hypomagnetic fields (HMFs) commonly occur in the interplanetary space of the solar system and fluctuate in the range of several nanoteslas (nT). For example, the lunar magnetic field is less than 300 nT, and the magnetic field on Mars is approximately 1 μT [3]. The planetary magnetic field of Mars is extremely small, and the planetary magnetic field of Venus is practically non-existing [4] (Figure 1).

New technologies are currently being developed to enable space exploration and interplanetary flights. In the future, organisms will be exposed to a HMF during space travels, which is significantly weaker than the geomagnetic field (GMF) and expected to have diverse biological effects. During these travels, organisms will be exposed to tedious periods of a HMF that is approximately 10,000 times weaker than the Earth's magnetic field, ranging from 0.1 to 1 nT [5]. However, attenuation of the Earth's magnetic field is not limited to staying in space but occurs in daily life, for example, in buildings with steel

walls or steel reinforcement [2]. Building walls are a natural shield against low- and high-frequency electromagnetic fields. However, a magnetic field (such as a geomagnetic field) is more difficult to shield. In contrast to radiofrequency and low-frequency electric fields, thin sheets of metal have no effect on magnetic fields [6]. However, there is evidence that buildings with steel in their construction magnetise and deform the natural geomagnetic field [5], causing an even 50-fold magnetic field attenuation according to the building size and the complexity of the steel [7].

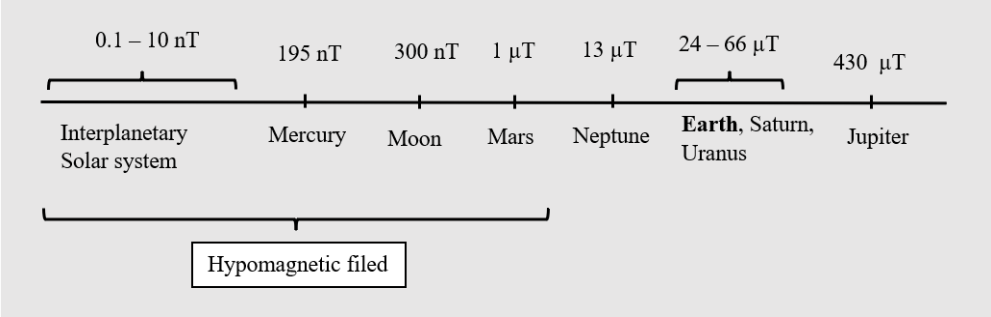

Figure 1. Presence of hypomagnetic field in the solar system [3].

Hypomagnetic fields can have various effects on organisms, although the underlying mechanisms remain unknown. Erdman et al. [8] suggest that the magnetoreception of the HMF differs among different organisms. The authors assume that the magnetoreception of the HMF is a nonspecific mechanism and manifests in highly different biological systems as mostly random reactions as a result of magnetic interaction with magnetic moments at a physical level. This moment, which is present in each molecule, could transfer the magnetic signal at the level of downstream biochemical events [2].

In this study, we summarise information about the observed biological effects of the HMF on eukaryotic and prokaryotic organisms and show the possible underlying mechanisms.

2. Materials and Methods

We used the scientific databases PubMed and ScienceDirect to select papers that contained the terms "hypomagnetic", "magnetic zero", "magnetic vacuum" or "magnetic shielding" in their titles, abstracts and keywords. This gave, after a subsequent semantic control, 65 experimental and theoretical articles that included original results suitable for further investigation. This type of search was repeated with each new relevant article iteratively until no new articles could be detected.

3. Mechanisms of Magnetoreception of HMFs

Magnetoreception is the universal ability of a biological system to detect magnetic and electromagnetic fields, although it may manifest itself differently in different organisms. Any changes in magnetic field intensity may affect the organisms in many ways, including the basic metabolism of prokaryotic and eukaryotic cells [8]. Magnetoreception relates not only to geomagnetic fields and higher magnetic and electromagnetic fields, but it also explains the perception of HMFs. The hypothesis of nonspecific nonthermal magnetoreception on the physical level has not been studied since none of those has yet been identified experimentally. Typical for hypomagnetic magnetoreception experiments is a high sensitivity to the physical, chemical and physiological conditions, as well as a low reproducibility [2] and a great variety of effects in different organisms. It has not yet been possible to establish any common conditions controlling the magnetic effects in different organisms or populations rather than in their individual forms [9]. Several mechanisms have been described that could explain the mechanism of magnetoreception, such as the cyclotron resonance model, macroscopic charged vortices in the cytoplasm and the parametric resonance model, among others [10]. The most likely physical mechanisms

with expected biological responses are: (i) the radical pair mechanism, (ii) the universal physical mechanism and (iii) the molecular gyroscope mechanism. However, according to Binhi and Prato [2], the radical pair mechanism is unlikely to explain all HMF effects on living organisms. The authors assume that the universal physical mechanism and the molecular gyroscope mechanism are more accurate.

These primary physical mechanisms can lead to secondary biophysical responses, which can include changes in ROS concentrations, Ca2+ ion homeostasis or influence enzymes that are involved in the electron transport chain in mitochondria or in cell cycle promotion.

1. Radical pair mechanism

Traditionally, radicals (for example, reactive oxygen species (ROS)) are considered harmful because they can cause cell death via oxidative intracellular damage in the metabolism of sugars, fats and nucleic acids. Several studies have also shown the importance of ROS in intracellular signalling cascades such as apoptosis initiation [11–13]. Radicals are magnetic because an electron (along with a proton and a neutron) has a property known as spin or, more precisely, a spin momentum [14].

The radical pair consists of two radicals that have been formed simultaneously, usually by a chemical reaction. The spins of two unpaired electrons can be either parallel to each other (↑↑ which gives S = 1) or anti-parallel (↑↓, which gives S = 0, where S is the spin quantum number). The two forms of the electron pair are therefore known as triplet (S = 1) and singlet (S = 0) [15]. Influencing either singlet or triplet formations of electron pairs could be associated with the presence of an external magnetic field and leads to a longer life of the radical pairs (triplet states) [16].

This mechanism can cause a difference in the stability of radical pairs and affects the shift of the chemical reaction equilibrium. Thus, during the formation of radical pairs, external magnetic fields change the recombination rate of these radical pairs, which in turn changes the concentration of radicals such as O2 • and molecules such as H_2O_2 [17]. In general, the coupling between unpaired electrons and nuclei in each fragment of a radical pair can be achieved by magnetic fields in the range of 10 µT–3 mT [18]. Magnetic fields could interact with the magnetic moments of radical pairs at physical levels, which are ubiquitous in macromolecules with unpaired electrons, protons, paramagnetic ions or other magnetic nuclei in biological cells, and then transmit the magnetic signal to subsequent biochemical events such as cell oxidative stress reactions. This procedure would therefore lead to highly different biological observables and mostly random reactions [19].

This mechanism does not have frequency selectivity because the development of a magnetosensitive spin state occurs over an extremely short life of the radical pair, usually in the order of 10^{-9}–10^{-7} s [20]. Many authors explain the observed results by this mechanism [21–23].

2. Universal physical mechanism

The rotation of magnetic moments in a magnetic field precedes any biophysical or biochemical mechanism of magnetoreception and largely determines the spectral and nonlinear characteristics of the biological effect of the field. The mechanism is based on the external magnetic field, which influences the magnetic moment of the molecules and leads to the terminal relaxation of the magnetic moment [19]. Magnetic relaxation is known as the approach to equilibrium after a magnetic system was exposed to magnetic field change. Relaxation processes allow nuclear spins to return to equilibrium following a magnetic disturbance [24].

The biological effect is observed only when changes in the magnetic momentum dynamics go through the stages of transformation at the biochemical, physiological and biological levels of the system. A special characteristic of this mechanism is that it predicts the effects of weak magnetic fields but also those of electromagnetic fields induced by alternating electric currents (ACs) in the same biological system [2].

3. Molecular gyroscope mechanism

The molecular gyroscope mechanism can be explained as the rotation of large fragments of macromolecules or amino acid residues with a distributed electric charge. This movement can be influenced by a magnetic field.

In some stages of protein assembly, in the final stage of their synthesis, virtual cavities without water molecules, of the order of 1 nm or less, may occur in the protein [25]. In these cavities, amino acid residues (molecular gyroscopes) rotate over milliseconds, searching for the best position. As a result of such rotation, a magnetic moment interacts with an external magnetic field [2]. The magnetic field affects these rotations, which results in possible changes in protein folding. The folding of protein chains is an evolutionarily conserved process, and improper folding can prevent a protein from performing its specific function [26]. Mostly, random changes in the proteome of the cell can explain various biological responses after HMF exposure.

4. Influences of HMFs on Organisms

In many areas, the biological effects of HMFs are contradictory, which might be explained by the length of exposure to the HMF. The authors of [27] reported that exposure to a HMF for a shorter time (1 h) could promote cell respiration, but a longer exposure time (6 h) has an inhibitory effect.

Another parameter causing conflicting results may be the method of generating the HMF. The authors used either the shielding of the present HMF or its compensation by another magnetic field, which may have caused a different result. For example, the production of free radicals caused by direct-current (DC) HMFs differs from the effect of AC HMFs. A similar difference was observed when the HMF was induced by a static field or a variable frequency-alternating magnetic field [28].

The type of organism is an important factor of the HMF effect [29]. Not only does the biological effect of HMFs vary between plant and animal cells, but according to Binhi and Prato [2], there are different targets of HMFs for different organisms or even for individuals of the same species. The observed effect of the HMF differs between eukaryotic and prokaryotic organisms, even in plant and animal cells. Few effects of HMF exposure could be similar for various organisms and are on the level of individual ions and proteins; they are generally related to cell signalling.

Regarding the spectrum of the hypomagnetic effect in various types of organisms according to their basic differences in structure and life cycle, we will separately discuss plant, animal and prokaryotic organisms.

4.1. Animals and Animal Cell Cultures

The observed effects can differ at various levels of the organization of the living organism. According to the observations described in various studies, we will discuss cell transport and respiration in a separate subsection (Section 4.1.1), and subsequently, we will discuss animals at the level of the organism or organ systems (Section 4.1.2).

4.1.1. Cell Transport and Respiration

The effects of the HMF on a single-cell level may include the effect on ion transport and concentration as well as cellular respiration (Table 1).

Table 1. Impact of hypomagnetic field on cell transport and metabolism (B—magnetic flux density in Tesla (T)).

Impact on	Effect	Hypomagnetic Field Properties				
		Organism	Mechanism	B (nT)	Duration	References
Mineral density of bones	Reduction	Sprague-Dawley rats	Shielding	<300	3 days	[30]
The concentration of Fe, Mn, Cu, Cr	Reduction	Fur of laboratory rats Wistar	Shielding	<20	7 months	[31]

Table 1. *Cont.*

Impact on	Effect	Hypomagnetic Field Properties				
		Organism	Mechanism	B (nT)	Duration	References
Ca^{2+} dependent proteases	Inactivation	Enzymes from fish and invertebrates	Compensation		1 h	[32]
The concentration of Co, Ni	No effect	Fur of laboratory rats Wistar	Shielding	<20	8 months	[31]
Mitochondrial activity	Reduction	Skeletal muscle cells	Compensation	<200	7 days	[33]
Mitochondrial activity	Reduction	Mouse (C57BL/6)	Compensation	0–500	30 days	[34]
ATP levels	Reduction	Skeletal muscle cells	Compensation	<30,000	3 days	[35]
Cell respiration	Reduction	*Drosophila melanogaster*	Compensation	1	6 h	[27]
Cell respiration	Promotion	*Drosophila melanogaster*	Compensation	1	1 h	[27]

The cellular transport mechanisms of various nutrients can be affected by near-zero magnetic field exposure. Some studies have reported changes in the Ca^{2+} ion concentration in the cytosol after being subjected to hypomagnetic conditions. The effect of the HMF on Ca^{2+} ion concentration in tissues is the basis of the parametrical resonance theory [35], which deals with magnetoreception; it is caused by the effect of HMF on Ca^{2+} ions and proteins with Ca^{2+} binding sites. This theory agrees with the results of Kantserova et al. [32], who showed that the production of Ca^{2+}-dependent proteases was inactivated after HMF exposure. It can be assumed that the inhibition of Ca^{2+}-dependent enzymes under hypomagnetic conditions may negatively affect the basic calcium-mediated transduction in the cell. In eukaryotic cells, the Ca^{2+} ion plays a role as a primary and secondary messenger, and Ca-dependent enzymes, including calcium-dependent kinases or proteases, may participate in cell membrane fusion, cell division and apoptosis [36].

Several studies have found that a stronger magnetic field (≥100 μT) can increase the levels of reactive oxygen species (ROS) [37–39], whereas the HMF can significantly decrease the level of ROS in cells [21,40]. There is experimental evidence of the correlation between HMF-induced changes in cellular ROS concentration and biological effects, such as cell growth in vitro [28]. Therefore, ROS may represent a potential target for the magnetic field, which may cause the modulus of biological functions [2]. The changes in ROS concentrations in the cell are directly related to the presence of free radicals, and the authors investigating ROS lean towards the theoretical radical pair mechanism as the magnetoreception mechanism of the HMF influence.

The main source of cellular ROS are the mitochondrial electron-transport chain complexes I, II and III, which are present in the inner mitochondrial membrane. Complexes I and II are the primary sources of O2• under either physiological or pathological conditions [40]. For an individual cell, the rate of ROS generation varies depending on the availability of cellular O_2, the redox state of the electron carriers, the respiration rate, the state of the electron carrier, the mitochondrial inner membrane potential and the post-translational modifications of the respiratory protein chain [28]. Mitochondria are the organelles most sensitive to HMF exposure due to their electron-transparent matrix and lower mitochondrial membrane potential in both plant and animal cells [41,42].

Ogneva et al. [27] reported a decrease in Drosophila melanogaster sperm cell respiration as a consequence of affecting the I. mitochondrial electrical transport chain complex after 6 h in a HMF. Mitochondria may also undergo morphological rearrangements under HMF conditions. In another study, the size and relative volume of mitochondria in plant cells increased and cristae size decreased after hypomagnetic field exposure, as described in [41].

However, the mechanism by which the level of ROS is modulated by the magnetic field remains unclear. It is assumed that weak magnetic fields can alter the free radical level response and, consequently, affect specific cellular functions and inhibit or reduce cell growth [43]. In addition to metabolic changes, it is possible to consider changes at the morphological level, namely the accumulation of lipid bodies, the development of a lytic compartment (vacuoles and cytosegresomes) and the reduction of phytoferritin in plastids after HMF exposure [41].

4.1.2. Animals

On the level of the whole organism, studies dealing with HMFs mostly focus on animals, humans, tissue cultures and embryos. The most common areas of study are the influences of HMFs on prenatal development as well as cardiovascular and nervous systems (Table 2).

Table 2. Impact of hypomagnetic field on animal neural systems (B—magnetic flux density in Tesla (T)).

Impact on		Effect	Organism	Hypomagnetic Field Properties			
				Mechanism of Generation	B (nT)	Duration	References
Neural system	ROS levels	Reduction	Mouse (C57BL/6 J), males	Shielding	170	Every 3 days/ 150 days	[23]
	ROS levels	Reduction	Peritoneal mice neutrophils	Shielding	20	1.5 h	[21]
	Growth	Promotion	Primary neural progenitor/mouse stem cells	Shielding	0–200	7 days	[42]
	ROS levels	Reduction	Human cells of neuroblast	Shielding	0–200	16 h	[44]
	ROS genes expression	Reduction	Mouse (C57BL/6 J), males	Shielding	170	3 day/150 days	[23]
	Gene expression	Reduction (down-regulation)	Human neuroblast cells	Compensation	<200	2 days	[45]
	Migratory properties	Reduction	Human cells of neuroblast	Shielding	0–200	48 h	[46]
	Proliferation	Promotion	Human cells neuroblast (SH-SY5Y)	Shielding	0–200	3 days	[46]
	Memory	Reduction	*Drosophila melanogaster*	Compensation	100–680	10–19 generations	[47]
	Proliferation	Promotion	Human neuroblastoma cells	Shielding	-	-	[48]
	Cognitive abilities	Reduction	Human (volunteers)	Compensation	400	45 min	[49]
	Proliferation	Promotion	Human neuroblastoma (SHSY5Y) cells	Shielding	<200	3 days	[50]
	Hippocampal neurogenesis	Inhibition	Mouse (C57BL/6 J), males	Shielding	170	every 3 day/ 150 days	[23]
Cardiovascular system	Blood pressure	Promotion	Human (volunteers)	Compensation	±10	60 min	[51]
	Blood circulation	Promotion	Human (volunteers)	Compensation	±10	60 min	[52]
	Haemolysis	Promotion	Human blood	Compensation	100	72 h	[53]
	Haemolysis	Promotion	Blood of rats	Compensation	192	6 h to 4 weeks	[54]
Life cycle and survival	Survival	Reduction	Milnesium inceptum	Shielding	-	21 days	[29]
	Survival	Reduction	Tardigada (Echiniscus testudo and Milnesium inceptum)	Shielding	-	21 days	[29]
	Life expectancy	Reduction	Daphninia magne	Compensation	15	Generational period	[55]
	Larval development	Inhibition	Mythimna separata	Compensation	<500	12 h	[56]
	Development of eggs and nymphs	Delayed	Nilaparvata lugens	Compensation	0–1060	Generational period	[57]

Table 2. *Cont.*

Impact on		Effect	Organism	Hypomagnetic Field Properties			
				Mechanism of Generation	B (nT)	Duration	References
Life cycle and survival	Fertility	Reduction	Nilaparvata lugens	Compensation	0–1060	Generational period	[58]
	Production of abnormal embryoys	Promotion	Xenopus larvae	Shielding	104 ± 12.6	4 days	[59]
	Fertility	Reduction (sterility)	NMRI mouse zygotes	Shielding	200	12 days	[60]
	Abortion	Promotion	Pregnant NMRI mice	Shielding	200	3–12 days	[60]
	Survival of cells exposed to X-rays	Promotion	Immortalised human bronchial epithelial cells	Shielding	<50	24 h	[61]
	Chromatic condensation	Changes	Human fibroblasts and lymphocytes	Compensation	1800	20–70 min	[62]

Hypomagnetic fields can delay the development of insect eggs and nymphs, reduce the fetal size and body length, reduce female fertility in adult insects [41] and reduce the life span of daphnia [56]. Yan et al. [22] also reported negative effects on the mating ratio and developmental stages of insects (Mythimna separata) and on the foraging orientation of Nilaparvata lugens [57], but a stimulating effect on positive phototaxis and flight capacity of Sogatella furcifera [58]. Similar to insects, adverse effects on embryonal development in Xenopus laevis have been observed [59], along with the induced loss of the ability to bear offspring in pregnant mice [60]. Adverse effects of the HMF were observed even in the case of extremophilic invertebrates from the phylum Tardigrada. The obtained results showed that even partial isolation from the geomagnetic field has a negative effect on the anhydrobiotic (resting) stage of both tested species (Echiniscus testudo and Milcium inceptum). Both species exhibited lower survival rates during entering anhydrobiosis, in the anhydrobiotic state, and upon returning to the active state. The authors also observed higher mortality in E. testudo compared to M. inceptum, which suggests that different species respond to hypomagnetic conditions in different ways [29]. Developmental abnormalities caused by HMFs may be related to epigenetic modifications of embryonic stem cells, such as abnormal DNA methylation. The results suggest that a suitable electromagnetic field may be necessary for favorable epigenetic remodelling and, thus, for differentiation during the embryonic stage [63].

An effect of HMFs on the nervous system has also been observed. The results suggest that specific brain structures represent neural substrates for the orientation of the magnetic compass in certain magnetosensory animals. In several experiments, HMFs accelerated the proliferation of neuroblastoma cells and neural progenitor/stem cells [42], and this proliferative effect may be related to decreased levels of cellular reactive oxygen species (ROS). After exposure of neuroblast cells to the HMF, a Warburg effect (commonly observed in cancer metabolism) was observed, when cell metabolism is induced by the repression of oxidative stress and the up-regulation of anaerobic glycolysis. In this case, the increased activity of LDH (lactate dehydrogenase), a key member of glycolysis, could be a direct response to a HMF [49]. The other explanation for the enhanced cell proliferation, according to Mo et al. [50], is the acceleration of proliferation by a forward shift of the cell cycle in the G1 phase. In contrast to the G1 phase, G2 and M phases were not affected during the experiment. The same results could be recorded when Belyaev et al. [62] observed that the effect of the zero magnetic field on chromatin condensation is more pronounced at the beginning of the G1 phase.

A comprehensive study examining the human transcriptome after exposure to a HMF (<200 nT) for 2 days showed a change in the gene expression of 2464 genes associated with the neural system. Mentioned genes were significantly grouped into a few key processes, for example, protein transport, macromolecule localization, RNA processing and brain

function. These results suggest the involvement of the MAPK pathway and cryptochrome in the early biological responses to the presence of a HMF [45].

In addition to the effects on the neural system, effects of the HMF on the cardiovascular system have been observed. Capillary blood velocity increased by 17%, cardio intervals increased by 88.7% [51], and capillary circulation rate increased by 22.4% [52] during HMF exposure. At the end of exposure, diastolic blood pressure dropped considerably relative to mid-exposure values, whereas systolic blood pressure, on the contrary, showed a significant increase [52]. One of the crucial parameters which influence the observed effects of HMFs is exposure time. Both previous studies claim to have simulated hypomagnetic conditions during interplanetary flight, but the time of HMF exposure was only 60 min. We assume that the time of exposure was not sufficient to demonstrate hypomagnetic conditions during a longer stay in space. In comparison, in two studies with a longer exposure time of 72 h [53] and up to 4 weeks [54], the authors recorded an increase in haemolysis and the weakening of the deformation and aggregation properties of human blood, along with a reduction in enzymatic activities. The reduction of these enzyme activities and the promotion of haemolysis can be related to increased protein denaturation and decreased efficiency of the proteolytic system [53].

4.2. Plants

Recent studies have shown that plants respond to near-zero magnetic fields through morphological and developmental changes, including delays in flowering time and germination [64], breath conductivity, chlorophyll content [65], photoreceptor involvement [66] and changes in auxin [67], and gibberellin concentrations [68] (Table 3).

Table 3. Impact of hypomagnetic field on plants (B—magnetic flux density in Tesla (T)).

Impact on	Effect	Organism	Hypomagnetic Field Properties			
			Mechanism of Generation	B (nT)	Duration	References
Growth	Reduction	*Glycine max*	Shielding	111 ± 15	24 h	[69]
Growth	Reduction	*Arabidopsis thaliana*	Compensation	0–1330	35 days	[70]
Growth	Reduction	*Arabidopsis thaliana*	Compensation	40–44	96 h	[71]
Epicotyl elongation	Promotion	*Pisum sativum*	Shielding	-	24 h	[72]
Gene expansion	Reduction	*Arabidopsis thaliana*	Compensation	0–1330	33 days	[68]
Activity of photoreceptors phyA	Reduction	*Arabidopsis thaliana*	Compensation	40	3 h	[64]
Activity of *phyB* photoreceptors	Promotion	*Arabidopsis thaliana*	Compensation	40	3 h	[64]
The content of auxin in flower	Reduction	*Arabidopsis thaliana*	Compensation	0–1330	33 days	[67]
Gene expression (associated with flowering)	Promotion	*Arabidopsis thaliana*	Compensation	50	33 days	[73]
Auxin content in roots	Promotion	*Arabidopsis thaliana*	Compensation	1–1330	33 days	[67]
Iron intake by roots	Reduction	*Arabidopsis thaliana*	Compensation	40–44	96 h	[71]
Concentration of Ca^{2+} ions	Promotion	*Pisum sativum* (root system)	Shielding	0.5–2	3 days	[41]

The HMF can either have inhibitory or stimulating effects on plants, depending on the part of the growth to which the plant is exposed. Hypomagnetic fields can inhibit [41] but also promote vegetative growth, e.g., by increasing the percentage of the germination rate [69]. On the other hand, they may have a reducing effect on reproductive growth by inhibiting seed production [70]. The magnetic field, in this case, is thought to affect the activity of cryptochromes and their gene expressions [64,74]. Plant hormones are also involved in cryptochrome-mediated flowering. Exposure to HMFs reduces the gibberellin content and the expression of their biosynthetic genes in wild-type Arabidopsis thaliana but not in the cryptochrome mutant strain (cry1/cry2). Similar results have been obtained for another plant hormone, auxin [67].

As in the case of animal cells, changes in the ion concentrations of some nutrients (NH_4^+, K^+, Ca^{2+} Mg^{2+}, Cl^-, SO_4^{2-}, NO_3^- and PO_4^{3-}) in plant cells after exposure of the A. thaliana root system to the HMF were recorded. A few minutes of exposure to a zero magnetic field resulted in a significant reduction in the intake of all studied nutrient ions, which can be explained by the existence of a plant magnetoreceptor responding to the HMF by modulating mineral nutrient transport genes. According to Narayan et al. [75], the response to an almost zero magnetic field is rapid, suggesting that some ion channels and all transport activities may not necessarily be related to gene expression. Ion channel changes have been reported in other studies and may influence flowering time [64], photoreceptor signaling [76], and seed germination [77].

In plant cells exposed to HMFs, the functional activity of the genome declined in the early pre-replication period. The HMF can intensify protein synthesis. At the ultrastructural level, changes in condensed chromatin distribution and nuclear compaction, the accumulation of lipid bodies, the development of the lytic compartment (vacuoles, cytosegresomas and paramural bodies), and the reduction of phytoferritin in plastids in meristem cells have been observed in pea roots [39].

In contrast to the animal cell, where the HMF stimulated proliferation and accelerated the passage through the G1 phase, the observed effect on the plant cell was the opposite. The HMF had a negative effect on the speed and progress of the cell cycle. The reproductive cycle of the cells slowed down due to the expansion of the G1 and G2 phases, whereas the other phases of the cell cycle remained relatively stable. The HMF also caused a remarkable decrease in proliferating plant cells (from 68% to 95%) [41].

Tsetlin et al. [78] also recorded remarkable results when they described a synergistic inhibitory effect of HMF and ionizing radiation (α and γ) on plant germination. This experiment simulated another environmental parameter to which the plants will be exposed during interplanetary flights.

4.3. Prokaryotes

Only a few studies have examined the effects of the HMF on microorganisms. Magnetotactic bacteria, i.e., bacteria capable of perceiving the Earth's geomagnetic field by means of magnetosomes, have been investigated most frequently [5] (Table 4).

Table 4. Impact of hypomagnetic field on procaryotic microorganisms (B—magnetic flux density in Tesla (T)).

Impact on	Effect	Organism	Field Properties			
			Mechanism	B (nT)	Duration	References
Growth and number of cells	Reduction	Magnetotactic bacteria (MO-1)	Shielding	2	2 days	[79]
Tolerance to antibiotics	Both reduction and promotion	*Escherichia coli*	Compensation	-	6 days	[80]
Tolerance to antibiotics	Both reduction and promotion	*Pseudomonas* and *Enterobacter* strains	Field compensation	-	6 days	[81]
Magnetosome size	Promotion	*Magnetospirillum magneticum* AMB-1	Compensation	500	16 h	[82]
Gene expression	Modification	*Magnetospirillum magneticum* AMB-1	Compensation	500	16 h	[82]

Studies on the magnetotactic bacterium Magnetospirillum magneticum AMB-1 have shown that after 16 h of magnetic compensation (500 nT), AMB-1 synthesises larger magnetosomes due to the up-regulation (stimulation) of genes encoding larger magnetosomes and the down-regulation (inhibition) of genes encoding smaller magnetosomes. The gene responsible for magA iron transport remained unchanged [82]. Inhibition of the growth and viability of magnetotactic bacteria (MO-1) after exposure to a 2-nT magnetic field for 2 days has also been noted [79].

In addition to magnetotactic bacteria, changes in antibiotic resistance in human pathogenic bacteria have been studied. The susceptibility of 26 strains of Escherichia coli to selected antibiotics was examined after HMF exposure. Susceptibility to antibiotics (ampicillin, ceftazidime, tetracycline, ofloxacin, and kanamycin) either increased or decreased in different strains, depending on the studied drug. The authors detected two types of *E. coli* strains: non-sensitive and sensitive to geomagnetic field compensation, which represents about one-third of the strains. Magneto-sensitive *E. coli* strains showed modified minimum inhibitory concentration (MIC) values to two of five tested antibiotics after HMF exposure [80]. According to Creanga et al. [81], half of the eight tested human pathogen strains (Pseudomonas and Enterobacter strains) were magnetosensitive and showed a change in antibiotic susceptibility (increase or decrease, depending on the tested antibiotics) from 2- to 16-fold.

Ilyin et al. [83] have recently isolated bacteria from the nasopharynx of cosmonauts after their return to Earth from a space mission. The authors observed multiple decreases in antibiotic resistance after exposure to space conditions. Although the effect of the HMF was not especially investigated in this study, its effect on bacterial life is undeniable and can be related to the observed changes in resistance.

The authors further suggest that the HMF can affect cell metabolism by changing the ion transport mechanism in cell plasma membranes in the prokaryotic cell, and this can be applicable in eucaryotic magnetoreception by influencing endoplasmic reticulum (including ribosomal membranes) and mitochondrial membranes [81].

5. Conclusions

So far, the impacts of HMFs on biological systems have been rarely investigated, and the exact mechanism of action remains unclear. The authors explain their results by several theoretical mechanisms, most often by the mechanism of radical pairs which influence the reactive oxygen species concentration. Experimental studies on HMFs yielded conflicting results on the development and functioning of the nervous and cardiovascular systems. However, HMFs are likely to have a negative effect on early developmental stages and fertility in both plants and animals. The conflicting results may have been due to the different exposure times, organism types, and methods of creating a HMF, which seem to be the key factors in the observed biological effects.

However, fewer studies have focused on the effect of the HMF on microorganisms. In our opinion, it is the research of prokaryotic models that can offer useful insight into the magnetoreception of the HMF. Based on this review, the level of magnetoreception can take place at the level of ions, protein complexes, or the cell membrane, and thus, the primary targets of the HMF could be similar for both prokaryotic and eukaryotic organisms.

Hypomagnetic fields seem to affect cell signaling on the level of ion transport and ROS, which has been demonstrated for disruptive embryonal development.

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