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ION cyclotron resonance: Geomagnetic strategy for living systems?

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ABSTRACT

Except for relatively few polarity reversals the magnitude of the magnetic dipole moment of the earth has remained constant since life first began, allowing evolutionary processes to integrate the geomagnetic field (GMF) into several biological functions. One of these, bearing the classical signature of an ion cyclotron resonance (ICR)-like interaction, results in biological change associated with enhanced proton transport. The wide range of cation masses over which this effect is found suggest a fundamental biological dependence on the GMF, one that functions equally well for electric as well as magnetic fields. Such generalization of ICR requires two things: transparency of tissues to the GMF and suitably tuned ELF resonant magnetic or electric fields. To complement the widely reported ICR responses to applied AC magnetic fields, we hypothesize the existence of weak endogenous ICR electric field oscillations within the cell. This equivalence implies that even in the absence of applied AC magnetic fields, biological systems will exhibit intrinsic GMF-dependent ion cyclotron resonance intracellular interactions. Many ICR effects that have been reported appear as antagonist pairs suggesting that the characteristics of the GMF have not only been incorporated into the genome but also appear to function in an endocrine-like manner.

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Introduction

To date, the geomagnetic field has not been considered a key factor in biology. The few interactive effects with living things, for example, those involving animal navigation (Wiltschko and Wiltschko, 2002), magnetic bacteria (Frankel et al., 1979), and the influence of GMF perturbations on the incidence of stroke (Feigin et al., 2014) and other cardiovascular problems (Novikova and Ryfkin, 1977) are regarded as merely phenomenological and specific to certain organisms. Even the numerous observations surrounding both ion cyclotron resonance (ICR) effects (Liboff, 1985, 2007a) and retinal cryptochrome magnetosensitivity (Gegear et al., 2008; Mouritsen et al., 2004) are not usually thought of in geomagnetic terms but rather as still unresolved problems in molecular biophysics.

However a recent report (Baek et al., 2019) has convincingly demonstrated that removing the GMF greatly impacts the fate of embryonic stem cells, thereby showing that the earth's magnetic field is essential for favorable epigenetic remodeling and stem cell differentiation. Further, the biological relevance of the GMF may be quite important, given that the magnetic dipole of the earth, save for relatively short-lived polarity reversals has been otherwise constant for billions of

years (Tarduno et al., 2015). Worth noting is that the GMF field in its present form, with a surface intensity ranging from roughly 25 to 65 μT , has been part of the planetary environment for a time close to the first appearance of life on earth (Dodd et al., 2017), and far preceding the worldwide abundance of atmospheric oxygen (Holland, 2006). It goes without saying that there has been more than enough time for evolution to have integrated the GMF into biological processes.

In the following we offer the argument that life on earth is especially dependent on the GMF. In particular the biological usefulness of this field derives from the fact that weak static magnetic fields pass through tissue without absorption, exposing even the innermost cellular components to the identical magnetic intensity everywhere within the cell. This uniformity of field has the effect of providing a sharply specific basis for cell-wide interactions shared both intra- and extra-cellularly. This allows one to invoke the possibility of ion cyclotron resonance not only for cell-wide interactions, but also for multi-cell modes of information transfer (Foletti et al., 2013).

ICR and proton hopping

We argue that all observed ICR biological effects consists of, in principle, two steps: first the interaction

involving a magnetic or electric field that is “tuned” to the classical resonance signature characterized by the charge to mass ratio, and second, a resulting displacement of positive charge. In other words, the biological effects observed in ICR experiments are not directly due to the resonance per se but rather to the subsequent motion of charge. In support of this argument it was recently hypothesized (Liboff et al., 2017) that the effectiveness of ion cyclotron resonance in living systems is connected to the long-standing question of proton-hopping (Agmon, 1995). This is in part suggested by the fact that only cations have been reported as sensitive to ICR stimulation. Not only does ICR exposure of water result in sharply increased electrical conductivity (D’Emilia et al., 2017; Mohri and Fukushima, 2003), but a similar effect is found in the resonance exposure of living tissue (Liboff, 2007b). Increased electrical conductivity is readily associated with the phenomenon of proton hopping.

The details of the hypothetical connection between ICR-related biological effects and proton hopping rest on the associated structural changes in vicinal water structures adjacent to the stimulated cation. Hydronium ions in this nearby water are affected by the associated magnetostatic field, following a helical path conforming to the rotating electric dipole established by hydronium and the hydroxyl ion (Liboff et al., 2017). The net effect is the associated transport of protons usually described as proton-hopping, but with a path slightly different from how this effect is usually described, helical instead of simply directional.

Proton transport, of fundamental importance in biology (Aoi and Marunaka, 2014), plays a key role in a wide variety of expressions, ranging from oxidative phosphorylation and immune response to bioluminescence (Miyake and Rolandi, 2016). One reasonable explanation for the effects observed in ICR stimulation is that the

response of living tissues to ELF weak ICR-tuned magnetic fields frequencies is related to enhanced electric conductivity. In short, the various ICR effects reported are likely the result of enhanced proton transport.

Contrasting B-field and E-field ion resonances

In physics the phenomenon of ion cyclotron resonance is obtained equally well for time-varying magnetic fields as for time-varying electric fields, for the case where both types of field are generated at the same resonance frequency, the sole difference being the relative orientation of the E- and B-fields (Liboff, 1997) with respect to the magnetostatic field (Figure 1). The fact that magnetostatic fields do not interact with living tissue except insofar as they provide a means of selective resonance carries great significance in this regard. Indeed this is the primary reason for ion cyclotron resonance processes in living things, as expressed for both time-varying magnetic fields and time-varying electric fields.

One can estimate the Electric-field intensity for such an ICR equivalent application by first assuming that the energy contents of the resonant electric and magnetic fields are the same. This is achieved by setting the magnetic field B energy density equal to the electric field E energy density, or by writing $B^2/2\mu_0 = \epsilon_0 E^2/2$, where μ_0 and ϵ_0 are respectively the permeability and permittivity of free space, universal constants that are related through the velocity of light, as $c^2 = 1/(\epsilon_0 \mu_0)$. This allows us to express in mks units the relation between an ICR magnetic field B and its equivalent ICR electric field as simply $E = cB$.

The latter expression enables one to find the range of expected electric fields E_{AC} equivalent to that of those time-varying magnetic fields B_{AC} that have been

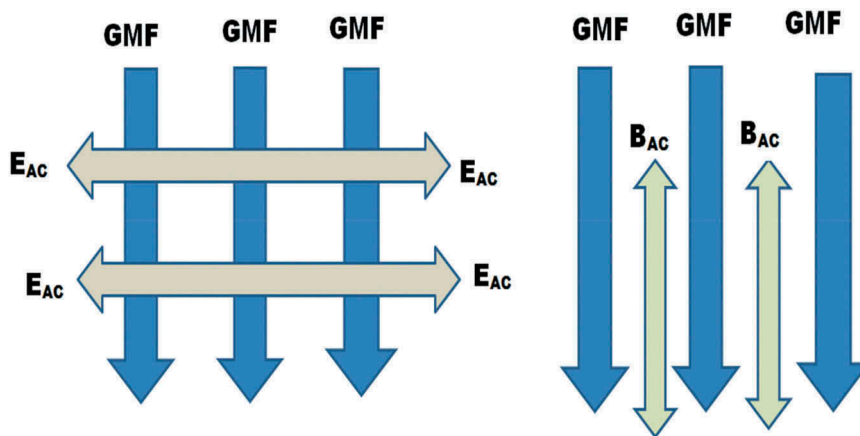


Figure 1. Two equivalent orientations of a weakly intense ELF electric-field (E_{AC}) or ELF magnetic-field (B_{AC}) relative to the static geomagnetic field (GMF) either one of each can result in ion cyclotron resonance.

reported in ICR experiments. The smallest B_{AC} reported is that used in the highly replicated experimental result first obtained by Zhadin et al. (1998) where changes in the aqueous conductivity of glu^+ were found for the vanishingly small magnetic field of 40 nT. Multiplying by the velocity of light this equivalent electric field E is $3 \times 10^8 \times 40 \times 10^{-9} = 12$ V/m. The upper end of AC magnetic intensities utilized in ICR experiments is about 1000 times larger, or 40 μ T, corresponding to 12×10^3 V/m. Thus the range of expected ICR electric fields is roughly 10 V/m to 10^4 V/m, from which it follows that even the largest ICR electric fields are well below the 10^7 V/m cell membrane electric field. Thus the magnitudes of electric field consistent with ICR intracellular interactions are not large enough to impact the insulating nature of the protective cell wall

Cellular electric field oscillations

Electric-field ICR effects fully equivalent to those resulting from magnetic ICR fields are therefore possible with intensities that are orders of magnitude below that of the cell membrane electric field. This begs the question as to the origin of such intracellular electric fields E_{AC} that are required for resonance. These are likely associated with cellular oscillatory states. Other than in the Central Nervous System (Buschman et al., 2012), oscillations are often described in ways that do not explicitly involve the E-field, but rather as chemical changes involving specific molecules. Although it is difficult to conceive of any local change in living systems, oscillatory or one-time, which is isoelectric, that is, not involving some measure of change in electric-field, such changes in field are not necessarily oscillatory. Our proposed E_{AC} concept requires that electric-field oscillations are already in place, perhaps not previously reported because they are too weak.

A number of electric field intracellular oscillations have already been observed or proposed. Most interesting, from the standpoint of our present work, are the electrical oscillations widely associated with microtubules (Pohl, 1983). Although usually thought of as generating very high frequencies, in the tens of GHz (Pokorny et al., 1998; Tuszyński et al., 2005), their structure and size could also readily be the source of ELF electric fields (Sirenko et al., 1996). Worth considering is the possibility that microtubule oscillations occur in a systematized synchronous manner over many single units. Other potential sources of oscillatory electric fields include those occurring in mitochondrial membranes (Aon et al., 2008), calcium oscillations (Berridge, 1993; Berridge et al., 1999; Schuster et al.,

2002), and Belousov/Zhabotinsky reactions (Blank and Soo, 2003; Winfree, 1984; Zhabotinsky, 1984). Clearly, despite the lack of further specificity the living cell exhibits a variety of intracellular ELF oscillatory electric fields that could conceivably serve as sites for E-field ion cyclotron resonances.

This leads to the likelihood that, independent of any applied low-frequency magnetic field, there are endogenous resonance conditions E_{AC} in living things determined by the coupling of the GMF to local oscillatory E-fields. Further, because there is no intrinsic preferred electric direction at the intracellular level, these conditions will not be unique to any one component of the GMF, but are expected to be found throughout the cell.

Extended cation masses

Following the initial ICR studies, which involved simple atomic ions such as Ca^{2+} , K^+ , and Mg^{2+} (Liboff, 1985; Rozek et al., 1987; Smith et al., 1987), it was shown by Zhadin et al. (1998) that more complex molecular ions, in particular the amino acid glu^+ , were similarly sensitive to resonance stimulation. Subsequent studies revealed that other large charged molecules, for example, NAD^+ (Novikov et al., 2010) and H_3O^+ (D'Emilia et al., 2017), were also sensitive to ICR excitation. Thus, ion cyclotron resonance effects are observed over a wide range of ionic masses, extending over three orders of magnitude. This suggests an effect that is not merely phenomenological, but rather a more fundamental, widely applicable biological interaction involving the influence of the GMF in a great many key charge-sensitive reactions.

Adding to this is the widely observed “opposites” nature for many ICR observations (Table 1) showing that many of the ICR effects reported can be reversed by simply tuning to a different ion. This effect was discovered by Smith (McLeod et al., 1987) who observed an enhancement in diatom motility under Ca^{2+} tuning but reduced motility for K^+ tuning. Others subsequently (Lovely et al., 1993; Zhadin et al., 1999) extended these observations to rat behavior, finding that aggressiveness and memory were sharply altered by changing the ICR tuning frequency from Ca^{2+} to Mg^{2+} . Although it is tempting to think of this as a sort of geomagnetic homeostasis, more detailed analysis suggests something else. The notion of homeostasis in biology essentially provides a number of autonomic pathways that serve to maintain the proper “setpoint” of the individual system. ICR stimulation is clearly different from homeostasis, in that in the latter case attempts are made to maintain the state of the system whereas ICR serves to alter the biological state.

Table 1. ICR effects in various model systems, each effect with a clearly evident antagonist response.

Model system	Reference	Freq Hz	B _{DC} μ T	ION	Response
Diatom Motility	McLeod et al., 1987	16	20.9	Ca ²⁺	Motility Up
		16	41.0	K ⁺	Motility Down
Embryonic Bone	Smith et al., 1991	16	20.9	Ca ²⁺	Growth Up
		16	41.0	K ⁺	Growth Down
Plant Growth	Smith et al., 1993	60	78.3	Ca ²⁺	Growth Up
		60	153.3	K ⁺	Growth Down
Rat Learning	Lovely et al., 1993	60	48	Mg ²⁺	Faster Learning
		60	27	Ca ²⁺	Slower Learning
Rat Behavior	Zhadin et al., 1999	63	50	Mg ²⁺	More Active
		38	50	Ca ²⁺	Less Active
Root Gravitropy	Belova and Lednev, 2000	35.8	46.5	Ca ²⁺	Growth Up
		54.7	46.5	K ⁺	Growth Down
GAGS Concentration	Regling et al., 2002	16	20.9	Ca ²⁺	More GAGS
		16	40.7	K ⁺	Less GAGS

Note that this set of results involve different ICR settings for merely three simple cations (Liboff, 2005).

In one sense the action of the ICR field is similar to what the endocrine system does. The endocrine system directs a specific expression of the system to be either enhanced or reduced one way or the other, by means of pairs of antagonistic hormones (insulin/glucagen, estrogen/androgen, diuretic/vasopressin...). The ICR analogy is that instead of selected chemicals we find interactive resonance frequencies.

Discussion

Our work leads us to the conclusion that the various widely reported ICR effects (Liboff, 2007b) are best described in terms of a two-step process: first, a resonance interaction between an electric or magnetic field and cation and second, a resulting charge transfer. In this view ICR biological effects are not directly attributable to the resonance process itself but are instead related to the consequent proton transfer accompanying the resonance interaction.

One of the many puzzling things about the long list of ion cyclotron resonance reports, apart from the overarching problem of exactly how cyclotron resonance paths can be obtained in the fairly dense fluids found in biological systems, is the difficulty in considering an effect that is dependent on the Lorentz force, a force that is nonexistent for charged particles that are not in motion. The Lorentz force explicitly includes the vector term $\mathbf{v} \times \mathbf{B}$, which not only provides a direction for the resulting force, namely perpendicular to both \mathbf{v} and to \mathbf{B} , but it also requires that the charged particle is moving to begin with. There is evidence for inherent motion of the net positive charge associated with simple cations such as Ca²⁺, K⁺, Mg²⁺, under conditions where ICR effects have been reported. In these cases one can simply argue that charge transport occurs because the ion itself is in motion, a statement consistent

with the accepted biological notion of ion transport as a signaling mechanism. However as mentioned above, ICR is also observed in much more massive charged molecules that are not biologically effective because of their transport but rather because they contribute electrically positive charge to specific reactions. We conclude that ICR effects do not arise solely as a secondary consequence of ion transport.

One way of resolving this question is to suggest that ion cyclotron resonance effects are limited to those biological reactions already underway, where it can be assumed that some degree of charged particle motion is happening, even if this is only a loosely bound hydrogen charge. Although this seems to be at variance with the ICR eigenfrequency requirement that is based on the entire mass of the stimulated molecule, this picture fits in with the notion of proton-hopping, where many identical molecules merely transfer protonic charge. Thus, we postulate that the ICR reactions in living systems include some degree of actual motion for positively charged components. This is again consistent with our earlier comments linking ICR interactions with the phenomenon of proton-hopping.

We also note that in order for ion resonance to occur there must be an endogenous interactive process already in place. This idea can be further generalized by associating an appropriately changing electric field with this process, thereby making it possible for the GMF to resonantly couple to the process in a manner described above as E_{AC} ICR. This allows us to view ICR interactions, nominally induced by the application of suitably tuned magnetic fields, as fundamentally electric in nature. The ICR effect, in other words, necessarily requires a corresponding electric field at the local level. This is consistent with our conclusion that E_{AC} ICR

processes making use of the GMF are endogenous. There is the interesting possibility that all electric-field driven biological processes function best under resonance conditions.

The most remarkable thing about the generalized ICR concept we have described is that it reveals the pivotal importance of the GMF in biology. A number of factors combine to suggest that the long-time constancy of this field has enabled it to be inextricably interwoven into life on earth, to the point where it serves a key role in biological function.

This work adds to the notion that certain intrinsic biological properties are functionally dependent on the long-term constancy of physical components of the environment. The best example, of course, is the sun. DNA expression has been uniquely shaped by billions of years of exposure to the sun's light, to its delivery of heat, even to visual processes being primarily sensitive to the maximum wavelength in the solar spectrum (Stair et al., 1954). Most, if not all, living things are sensitive to the rate of spin of the earth, as evidenced by diurnal metabolic cycles. The force of gravity manifests itself in skeletal structures using piezoelectric proteins such as collagen to satisfy Wolff's Law (Frost, 1994; Wolff, 1892), ensuring greater bone growth with increasing loading (Marino and Becker, 1970; McElhaney, 1965). The present work adds the geomagnetic field to those long-term earth-specific constraints that have helped contribute to life on earth. Above all, the fact that the geomagnetic field enjoys a prominent biological role is consistent with our belief that despite widespread reliance on biochemistry and molecular biology to describe living systems, life at its core is a manifestation of the electromagnetic field.

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