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Brief Communication

On the Cyclotron Resonance Mechanism for Magnetic Field Effects on Transmembrane Ion Conductivity

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The cyclotron resonance model, recently proposed to account for physiological response to weak environmental magnetic fields, is shown to violate the laws of classical mechanics. Further, it is argued that the ubiquitous presence of dynamic friction in fluid media precludes significant magnetic effects on membrane ion transport.

Key words: membrane channels, ion transport, dynamic friction

The possibility that weak electromagnetic fields in the environment can interfere with biological cell function deserves serious consideration. While a variety of such effects have been reported, their mechanistic basis remains to be established [Adey, 1981]. Motivated by the experimental finding [Blackman et al., 1985] of an enhanced calcium ion efflux from brain tissue subjected to a combination of weak static and low-frequency oscillating magnetic fields, Liboff and McLeod have proposed a molecular mechanism [Liboff, 1985a,b; McLeod and Liboff, 1986; Liboff and McLeod, 1988]. The alleged basis of this so-called cyclotron resonance model (CRM) is that ions moving through helical membrane channels in the presence of a static magnetic field B exhibit a resonance frequency, $\omega_c = (Q/M)B$, at which energy can be transferred from an oscillating electromagnetic field to the molecular system. A variety of experimental results, interpreted as supporting the CRM, have recently been described [Thomas et al., 1986; Smith et al., 1987; Liboff et al., 1987]. The purpose of this report is to point out that the CRM violates the laws of classical mechanics and, hence, cannot explain the observed effects. Furthermore, it is argued that the role of dynamic friction has been severely underestimated.

All classical resonance phenomena share two essential ingredients: i) a periodic motion in the system with a natural frequency, and ii) an external time-dependent

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driving force which, when tuned so that the driving frequency matches the natural frequency, can excite the natural mode of motion and, hence, transfer energy to the system. The natural motion may be the swinging of a pendulum, the Larmor precession of a nuclear magnetic moment in a magnetic field or, as in the CRM, the motion of an ion through a helical membrane channel in a static magnetic field. In the CRM, the natural (cyclotron) frequency exists only in the presence of a magnetic field. For the CRM to be valid, it is thus necessary that the ionic motion be affected by the static magnetic field. If this is not the case, then, of course, the time-dependent electromagnetic field cannot produce a resonance phenomenon. To disprove the CRM, it is therefore sufficient to consider the first ingredient of the proposed resonance mechanism, viz. the natural (cyclotron) motion induced by the static magnetic field.

We thus consider the motion of an ion of mass M and charge Q in the presence of static electric (**E**) and magnetic (**B**) fields. We shall assume that the fields are uniform; this simplifies the algebra, but is not essential for our arguments. The ion obeys Lagrange's equations of motion [Goldstein, 1950]

$$\frac{d}{dt}\left(\frac{\partial L}{\partial \dot{q}_\alpha}\right) - \frac{\partial L}{\partial q_\alpha} = 0, \tag{1}$$

where the q_α are independent generalized coordinates ($1 \leqslant \alpha \leqslant f$ = number of degrees of freedom) and $\dot{q}_\alpha = dq_\alpha/dt$. The Lagrangian is given by

$$L = \tfrac{1}{2} M v^2 + Q \mathbf{r} \cdot \mathbf{E} + \tfrac{1}{2} Q \mathbf{r} \times \mathbf{v} \cdot \mathbf{B}, \tag{2}$$

where $\mathbf{v} = d\mathbf{r}/dt$ is the velocity of the ion.

For the case of unconstrained motion (f = 3), it is easily shown that equations (1) and (2) reduce to Newton's equations of motion

$$\frac{d\mathbf{v}}{dt} = \frac{Q}{M}\mathbf{E} + \mathbf{v} \times \omega_c, \tag{3}$$

with the cyclotron frequency

$$\omega_c = \frac{Q}{M}\,\mathbf{B}. \tag{4}$$

The solution to Equation (3) in the absence of electric field is well-known [Jackson, 1975]. The ion, with initial velocity components $v_\parallel$ and $v_\perp$ (with respect to **B**), executes a uniform rotation around **B** with angular frequency ω_c superimposed on a uniform translation along **B** with velocity $v_\parallel$, thus tracing out a helical path of radius $R = v_\perp/\omega_c$ and pitch $h = 2\pi\, v_\parallel/\omega_c$. This simple example illustrates the crucial fact that a magnetic field can alter the direction of the ionic velocity, but not its magnitude (the energy of the system is conserved).

In the CRM, the ion is constrained to follow a helical path with radius R_0 and pitch h_0. The position of the ion is then given by $\mathbf{r} = (R_0 \cos\theta, R_0 \sin\theta, \hbar_0\theta)$, where

θ is the angle of rotation around the helix axis and $h_0 = \hbar_0/(2\pi)$. To include this constraint in the dynamical description, we simply substitute **r** into Equation (2) to obtain the Lagrangian

$$L\,(R_0^2 + \hbar_0^2)^{-1} = \tfrac{1}{2}\,M\,\dot{\theta}^2 + Q[\kappa(E_x \cos\theta + E_y \sin\theta) + \tau\,E_z\,\theta]$$
$$+ \tfrac{1}{2}\,Q\,R_0\,\{\tau\,[B_x(\sin\theta - \theta\cos\theta)\,\dot{\theta} - B_y(\cos\theta + \theta\sin\theta)\,\dot{\theta}] + \kappa\,B_z\,\dot{\theta}\}, \quad (5)$$

where we have introduced the helix curvature $\kappa = R_0/(R_0^2 + \hbar_0^2)$ and torsion $\tau = \hbar_0/({R_0}^2 + {\hbar_0}^2)$. Inserting this Lagrangian into Equation (1) (with $f = 1$ and $q = \theta$), we obtain the equation of motion for an ion in a helical channel

$$\frac{d^2\theta}{dt^2} + \frac{Q}{M}\,[\kappa\,(E_x \sin\theta - E_y \cos\theta) - \tau\,E_z] = 0. \quad (6)$$

Equation (6) shows that the motion of the ion is entirely unaffected by the magnetic field. This conclusion remains true for motion along an arbitrary (not necessarily helical) prescribed space curve in the presence of an arbitrary (not necessarily uniform and not necessarily static) magnetic field. In fact, this follows directly from the observation that the magnetic force, $Q\,\mathbf{v} \times \mathbf{B}$, is orthogonal to **v** and that the motional state of a particle with a single translational degree of freedom can be altered only by a force with a nonzero component along **v**. In the absence of an electric field, the ion thus maintains its initial state of motion through the helix. In contrast, Liboff insists that the ion experiences a magnetic force of magnitude Q v B, which causes it to move through the helix with the natural (cyclotron) frequency ω_c given by Equation (4). This erroneous conclusion was deduced from a balance equation for the radial (perpendicular to the helix axis) component of the forces acting upon the ion in the channel [Liboff, 1985b]. However, since the ion encounters an infinite (in the model) constraining force at the channel walls, a purely radial force cannot affect its motion. In another paper, Liboff seeks to consolidate his claim by deriving the equation of motion for an ion in a helical channel under the influence of a static magnetic field [Liboff, 1985a]. Again, he finds that the static magnetic field drives the ion through the channel with a natural frequency ω_c. However, as is evident from Equation (6) with $\mathbf{E} = 0$, $\dot{\theta}(t) = \dot{\theta}(0)$ independently of the magnetic field. Liboff's derivation is based on Newton's equations of motion. This is a force balance equation and, hence, must include all the forces experienced by the ion, including the constraining force that keeps the ion on its prescribed helical path. Liboff's erroneous conclusion is a direct result of his omission of this constraining force. In the present treatment, by adopting the Lagrangian formulation of classical mechanics, we implicitly include the constraining force via its (prescribed) effect on the motion of the ion.

If the translocating ion were not constrained to a one-dimensional path through the membrane, a magnetic field could conceivably affect its motion. To explore this possibility, we consider the case of completely unconstrained motion. To account for the dynamical coupling of the ion with its fluctuating molecular environment, we replace Equation (3), which applies to ionic motion in a vacuum, by the Langevin equation [van Kampen, 1981]

$$\frac{d\mathbf{v}}{dt} = \frac{Q}{M}\mathbf{E} + \mathbf{v} \times \omega_c - \omega_f\,\mathbf{v} + \mathbf{R}(t). \quad (7)$$

In this equation, the fluctuating environment appears through the random force M $\mathbf{R}(t)$ (with zero mean and no temporal correlation), which drives the thermal motion, and the associated dissipation force $\zeta\,\mathbf{v}$, which returns the acquired energy to the medium. The ionic friction coefficient ζ (= M ω_f) is assumed to be unaffected by the applied fields.

The transmembrane current is proportional to the ensemble-averaged steady-state velocity $\mathbf{v}^s$, which satisfies

$$\frac{Q}{M}\mathbf{E} + \mathbf{v}^s \times \omega_c - \omega_f\,\mathbf{v}^s = 0. \tag{8}$$

Hence, the steady-state velocity components (with respect to **B**) are

$$v_{\parallel}^s = Q\,E_{\parallel}/\zeta\,, \tag{9a}$$

$$v_{\perp}^s = (1 + \alpha^2)^{-1/2}\,Q\,E_{\perp}/\zeta\,, \tag{9b}$$

where $\alpha = \omega_c/\omega_f = Q\,B/\zeta$ is a measure of the relative importance of the magnetic and frictional forces.

On the basis of the current knowledge about the structure and dynamics of biological membranes and channel-forming molecules [Hille, 1984; Mackay et al., 1984; Jordan, 1987; Skerra and Brickmann, 1987], it is clear that the translocating ion experiences an essentially fluid environment of mobile water molecules and polypeptide structures strongly coupled to the fluctuating lipid membrane interior. The ionic friction coefficient ζ should therefore approach that of a dense fluid. Accordingly, we take $\omega_f = 10^{14}\ s^{-1}$ [Wilson et al., 1985], which, for an ion in the geomagnetic field ($B \approx 50\ \mu T$), corresponds to $\alpha = \omega_c/\omega_f \approx 10^2/10^{14} = 10^{-12}$. From Equation (9), it is evident that the magnetic effect is completely negligible (since $\alpha^2 \approx 10^{-24} \ll 1$). This conclusion remains valid even if the estimated friction is too high by several orders of magnitude (which is unlikely).

In conclusion: we have demonstrated that the cyclotron resonance model is untenable. If the ionic trajectory is prescribed, the magnetic effect vanishes identically. And even if the motional constraint is relaxed, dynamic friction ensures that the magnetic effect is utterly insignificant. It seems clear, therefore, that the origin of a physiological response to a weak magnetic field should be sought within the realm of collective phenomena, rather than at the level of local single-ion dynamics.

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