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Theoretical evaluation of cell membrane ion channel activation by applied magnetic fields

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Abstract This letter re-examines a recently published calculation of the forces exerted on a membrane ion channel by a cation passing through in the presence of an externally applied magnetic field. We show here, in contradiction to the originally published calculation, that the forces generated due to the Lorentz force of the magnetic field on the cation are negligible compared with the forces required to activate an ion channel protein conformation change associated with the gating of the channel.

Key words Ion channel · Cell membrane · Magnetic field · Lorentz force

Introduction

During the past two decades a scientific controversy has arisen concerning the effects of weak, environmental magnetic fields on humans. Many epidemiological and laboratory studies have been undertaken in an effort to resolve this controversy, yet there are credible results supporting both positions: those arguing that there are adverse health effects resulting from exposure and those arguing against these effects (Moulder and Foster 1995). Most of this work has focused on the effects of exposure to extremely low frequency (ELF: 50–60 Hz) magnetic fields.

In order to determine whether there are effects, however, it is necessary to establish a plausible mechanism by which these effects might arise. Several mechanisms have been proposed and, while many have been rejected, a few remain as credible explanations, although their validity has not yet been established experimentally (Adair 1992; Kirschvink 1992; Dobson and St Pierre 1996).

Recently, a new and straightforward mechanism explaining the effects of weak, ELF magnetic fields on biological systems has been proposed (Balcavage et al. 1996). This theoretical mechanism is based on the Lorentz force acting on ions as they move through transmembrane ion channels in the presence of a magnetic field. The force on the ions within the channel, according to the original calculations, is strong enough to activate nearby voltage gated ion channels. It was proposed that this can explain effects on biological systems exposed to ELF magnetic fields as weak as 100 μ T. We demonstrate here that the calculations presented by Balcavage et al. (1996) were flawed and that the Lorentz force exerted on the ions in the channels has a negligible effect even in extremely large magnetic fields.

The model

Balcavage et al. (1996) discuss the passage of cations such as Na^+ through gated membrane ion channels such as the channel described by Noda et al. (1986). These channels are formed by proteins that span the lipid bilayer membrane of the cell. The structure of the protein results in a channel through the membrane, through which Na^+ ions may diffuse. Gated channels are constructed from proteins which can change their conformation on application of a mechanical force or an electric field such that the new conformation results in an opening or closing of the channel. The magnitude of force required to effect such a change has been estimated to be in the region of 0.2–0.4 pN (Howard and Hudspeth 1989). For some channels, this mechanical force can be actuated by application of an electrical potential difference across the membrane. Charged centres within the protein respond to the electric field within the membrane, thus acting as transducers of the force (Conti and Stühmer 1989). Such channels are usually described as voltage-gated channels and are typically activated by transmembrane potential differences in the order of

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20 mV. Assuming a membrane thickness of approximately 5 nm (Mouritsen 1987) and a charged centre in the ion channel protein of approximately two elementary charges (Conti and Stühmer 1989), this again translates to typical forces in the order of 1 pN on the charged centre in the protein.

Balcavage et al. (1996) proposed that, in large enough magnetic fields, the component of the Lorentz force perpendicular to the motion of a cation through an ion channel would be large enough to activate channel protein conformation changes and hence result in biological effects on the cell. Their calculations indicated that magnetic fields as low as 100 μ T would be enough to induce such changes. However, their calculation was flawed in that they did not take into account the forces of the ion channel on the cation during its transition through the channel. The following is a corrected version of the calculation.

Revised calculation

The calculation is based on the following typical data. Na^+ concentrations in plasma are typically 100 mM. Lipid bilayer membranes are approximately 5 nm thick (Mouritsen 1987). The minimum cross-sectional area of an ion channel is thought to be 0.3×0.5 nm (Hille 1971, 1972; Noda et al. 1986). Typical channel currents are approximately 1 pA (Neher 1987). The 1 pA channel currents imply an ion flux of approximately $6 \times 10^6 \text{ s}^{-1}$ through the channel when open.

Na^+ concentrations of 100 mM imply mean Na^+ – Na^+ distances of approximately 3×10^{-9} m and the cross-sectional areas of the ion channels are such that the Na^+ ions pass through in “single file”. Thus mean drift velocities of particles in the channel are of the order of $3 \times 10^{-2} \text{ m s}^{-1}$.

We now consider the extra force exerted by the Na^+ ion (with charge q) on the channel due to its movement at velocity v in the presence of a magnetic field \mathbf{B} directed in the plane of the membrane. This force is given by the magnetic field component of the Lorentz force:

$$\mathbf{F} = q\mathbf{v} \times \mathbf{B} \quad (1)$$

Thus the field required to produce a force of 1 pN is approximately 3×10^8 T, given the calculated drift velocities. Even if we took instantaneous ion velocities of the order of 10^2 m s^{-1} , magnetic fields of the order of 10^5 T would still be required. This is several orders of magnitude greater than any magnetic field ever generated on Earth. Thus we can conclude that this model does not predict any biological effects of ambient magnetic fields on cells.

Discussion

The main flaw in the original paper published by Balcavage et al. (1996) is neglect of the forces of the mem-

brane channel on the ion. The deflection of the Na^+ ion was calculated as if it were travelling in a vacuum. The Lorentz force on a Na^+ ion due to its thermal movement in a static magnetic field of 100 μ T will be at most 1×10^{-21} N. This value is calculated using instantaneous velocities expected at ambient temperatures (approx. 10^2 m s^{-1}), which are somewhat larger than the drift velocities of the ions through the ion channels. Even in the relatively large fields experienced in nuclear magnetic resonance imaging, these forces still will be only 1×10^{-17} N, a factor of 10^5 smaller than that required to activate a conformational change in an ion channel protein.

It appears then that the Lorentz force acting on ions passing through transmembrane ion channels will be negligible even in extremely large fields and as such cannot be considered a plausible mechanism for the interaction of biological systems with environmental magnetic fields.

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