Resilience of Neural Electronics to High Magnetic Fields

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Abstract
With the advent of neuronal oscillators in bioelectronic medicine, it has become increasingly important to understand the effect of magnetic fields on the biological rhythms they produce. In particular, cardiac pacemakers must be resilient to the magnetic fields applied during magnetic resonance imaging, but it is not known whether the nonlinearity of the neuron response would amplify some the known effects of magnetic fields in semiconductor devices. Here, we have performed a series of experiments probing the oscillations of a silicon neuron in a static magnetic field of 3 T applied in the plane of the substrate and perpendicular to it. The neuron was fabricated from complementary metal-oxide-semiconductor integrated circuits, which integrated currents in the nA range to compute the output of the Hodgkin-Huxley model. The experiment reveals a small magnetic field-induced dephasing of neuron oscillations which is slightly larger when the magnetic field is in the plane rather than perpendicular to the plane. This is interpreted in terms of the differences in diffusion coefficients of cyclotron and magnetoelectric skipping orbits at room temperature.

Keywords Cardiac · pacemaker · neuron · MRI

Introduction
Neuronal pacemakers have the ability to resynchronize cardiac and respiratory rhythms and reverse the effects of heart failure in animal models. Consequently, assessing the robustness of neuronal rhythms to magnetic fields is essential if practical implants are to be made, especially if neuronal circuits on the nanometre scale are to be used to minimize power consumption and extend battery life.

A particular concern of neuronal electronics is the increasing use of transistors operating in the sub-threshold regime, where diffusive transport is sensitive to magnetically induced metal-insulator transitions, with subsequent modifications expected in the threshold voltages of ion channels. Shifts in the thresholds of the activation and inactivation gates can significantly affect neuronal dynamics; hence, it is important to assess and quantify these effects. Magnetic resonance imaging (MRI) scanners use high static magnetic fields (between 1 T and 7 T) to align the protons in water molecules within the body. A dynamic field of around 30 mT is then used to flip the proton magnetic moments and hence provide information on the structure and contents of the scanned area from the resulting spin echoes.

The high static field makes MRI unsuitable for any patient with surgical implants that contain magnetic elements. Additionally, the dynamic fields can induce eddy currents in cardiac leads that behave like antennae, sending erroneous feedback to the pacemaker. These signals can be incorrectly interpreted as the heart going into fibrillation and, as a result, applying unnecessary defibrillation. Large conductive components can also produce considerable torque when moved through the field lines—although this is a secondary effect compared to the potential effect of these fields on sub-threshold currents (typically 10–100 pA) and the resulting changes in neuronal dynamics.

When designing a system that can be used safely within an MRI scanner there are, therefore, two core challenges that must be addressed. Firstly, the system must be safe for insertion into high magnetic fields. This requires the use of non-magnetic components and small metallic surface areas. Secondly, the periodicity of pacing signals must be unaffected by immersion in static and dynamic magnetic fields.
This paper describes initial experiments carried out at the Siemens research laboratory (Siemens Healthineers) at Eynsham (Oxon, UK) to investigate the effect of static magnetic fields on the electrical behaviour of the DC drain current of an NMOS transistor when measured in the field and the firing behaviour of a silicon emulation of a neuron. In both cases the effect of the field on the measured parameters was found to be small.

**Methods**

Two sets of experiments were carried out. Firstly, an integrated circuit (IC) test structure containing a single N-type metal-oxide-semiconductor (NMOS) transistor was characterised at DC in the 3 T static field of the MRI magnet and compared with measured zero-field values. The transistor (\(W = 10 \mu m\) and \(L = 2 \mu m\)) was fabricated in a standard n-well CMOS process (Austriamicrosystems 0.35 \(\mu m\), C35B4) and mounted on a 24-pin DIL package. Although several NMOS and PMOS transistors were available, time pressure and limited access to the magnet only allowed the single experiment reported to be carried out.

Secondly, an electronic analogue emulation of a neuron (with two neurons on each IC) was designed and fabricated based on the Mahowald-Douglas (MD) realisation of the Hodgkin-Huxley (HH) neuron model, fabricated in the same CMOS technology as the single NMOS transistor. Although an approximation to the HH model (itself an approximation to a biological neuron), the MD neuron features separate, independently controllable sub-circuits emulating the sodium and potassium channel conductances and a direct realisation of a sigmoidal conductance-voltage relationship. The form implemented here employs sub-circuits with devices in both the strong and weak inversion (i.e., sub-threshold) regions of operation. The packaged ICs were mounted on a specially designed printed circuit board that was positioned in the magnet by means of a non-magnetic probe (not shown) allowing the ICs to be inserted (and moved) in the magnetic field.

The experiments began with an examination of the single NMOS transistor because it was felt that in addition to the inherent interest in doing this, any deflection in the terminal properties of the transistor due to the magnetic field would affect transistors in the neurons in a similar way, making any observed changes easier to interpret.

**Single NMOS Transistor**

The general test arrangement is shown in Fig. 1a and b. The NMOS test structure was characterised using a source measurement unit (SMU) and a 3-V DC supply connected as shown in Fig. 1a. Programs were developed for the SMU to automate the measurement of the output characteristics of the device, i.e., plots of \(I_{ds}\) as a function of \(V_{gs}\) with \(V_{ds}\) as a parameter. \(V_{ds}\) was varied in the range 0 to 3 V in increments of 0.01 V, with \(V_{gs}\) values of \[0.00; 0.25; 0.50; 0.75; 1.00; 1.25; 1.50\]. This process was repeated 10 times (for averaging) to ensure that the impact of thermal effects and external noise were mitigated (also, the system was switched on for a few minutes prior to taking readings to allow thermal equilibrium to be reached).

Each set of experiments was performed a total of four times, once outside the influence of the magnetic field and once at each of the three orientations within the field. The magnetic field was aligned along orthogonal axes as shown in Fig. 1b. Because of space constraints within the setup, the field oriented along the \(x\)-axis was directed towards negative \(x\).

**Neuron IC**

As already noted, the neuron circuit consisted of an electronic emulation of the Hodgkin-Huxley model, based on circuits first proposed by Mahowald and Douglas. The circuits are not described in detail in this paper but contain

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Fig. 1 (a) The electrical schematic for the NMOS test structure experiments. In these experiments the characteristic \(V_s\) and \(V_{gs}\) curves were recorded while under the influence of different magnetic field orientations. Note that the source of the NMOS transistor is connected to the substrate, i.e., ground, as indicated. (b) The three orientations of the chip in the magnetic field, shown as black arrows with their associated labels.
sub-circuits operating in both the strong and weak inversion (i.e., sub-threshold) regions of operation. Each chip contains four complete neurons, two of which do not have internal feedback and are intended for characterisation analogous to a voltage clamp experiment (not considered in this study). Apart from this difference, the four neurons were identical cells laid out as indicated in Fig. 2 and no special steps were carried out to improve matching between the cells. Two chips were selected at random from a batch of 10 for these experiments. The chip layout and a photograph of the fabricated die are shown in Fig. 2.

Two sets of dynamic measurements were made on the MD neuron: (a) with discrete pulse stimulation and (b) with continuous stimulus (i.e., a current step) resulting in tonic (i.e., free running) spiking. These measurements were carried out at zero field and using the three field orientations, as was done for the single NMOS transistor. For the first MD neuron test, the neuron was stimulated by a current pulse generated using an SMU. This stimulus pulse was used to drive the two neurons incorporated within the MD-Neuron IC. An oscilloscope provided a recording of the neuron’s membrane potential, \( V_{\text{mem}} \), allowing the stimulus response to be assessed. The SMU was programmed to generate 100-µs current pulses ranging from 10 µA to 50 µA, i.e., spanning both the sub- and supra-threshold levels of stimulation.

Results

Single NMOS Transistor

The averaged output characteristics of the NMOS transistor are shown in Fig. 3. The overall effect is small, but a deflection in the drain current \( I_d \) is visible at normal incidence (i.e., Z-plane oriented) and this is clearly seen in the expanded plot of Fig. 3b. The value is about 2.5 µA, or slightly less than 1% of the saturated drain current \( I_d \) for \( V_{gs} = 1.5 \) V. A similar deflection is not seen when the field is applied in the other planes. Similar effects (proportionate deflections of \( I_d \) when the field is applied in the Z-plane) are seen for smaller drain currents, the minimum value measured being approximately 0.5 µA, which is approaching the boundary of the sub-threshold region of operation.

Fitting a 1st order (Shichman-Hodges) model to the data for \( V_{gs} = 1.5 \) V, the shift in \( I_d \) can be interpreted as shift in zero bias threshold voltage (\( V_{T0} \)) as shown in Table I. The transfer characteristics were also calculated but showed no shift in transconductance for any of the orientations.

MD Neuron Chip

The neuron circuits require current pulse stimulation, and this was generated using an SMU as a current pulse generator. The outputs of the two neurons when stimulated by a 100-µs, 49 µA pulse (above threshold by a factor of approximately 2) are shown in Fig. 4a and b. Both neurons were stimulated with the same current pulse (see Fig. 4c) and the slight difference in response appears to be due to process variation and/or small differences in the preset tuneable parameters. At this level of stimulation there was no observable change in the neurons’ response when the magnetic field was applied in any orientation.

Figure 5 shows the effect of reducing the stimulus to a level close to the neuron threshold. With a pulse width of 100 µs, the threshold stimulus current is approximately 24 µA. Note that at this critical level the two circuits, although fabricated on the same die and in close proximity, have small differences in responses. The first neuron, shown in Fig. 5a is clearly sub-threshold, whereas the second (Fig. 5b) is above threshold, although the shape is a little
different from that shown in Fig. 4 (note that increasing the stimulus to 25 µA, which is just above threshold, results in responses similar to those shown in Fig. 4, for both neurons). Application of the 3 T magnetic field to the first neuron (sub-threshold) produced no effect in any orientation (Fig. 5a). However, for the second neuron, applying the field in the Z-plane suppresses AP generation completely. Note that applied to the neuron in (a), the magnetic field had no effect in any orientation.

**Table I** Changes in NMOS Transistor Threshold Voltage With Applied Field

| Field orientation | $V_{TO}$       |
|-------------------|----------------|
| No field          | 0.570 ± 0.005  |
| + Z               | 0.572 ± 0.006  |
| $-$ X             | 0.571 ± 0.003  |
| + Y               | 0.570 ± 0.005  |

**Fig. 3** Measured, averaged output characteristics of the 10 µm × 2 µm NMOS transistor at zero magnetic field and when placed at the different orientations in the field. (a) shows the full set of measurements, while (b) shows detail of the measurement with the largest drain current. While the effect is generally small (about 2.5 µA, or 1% of $I_d$), a deflection of $I_d$ is visible at normal (Z-oriented) incidence.

**Fig. 4** Stimulation of two neurons on one chip with a current pulse of amplitude 49 µA and duration 100 µs (a and b). The pulse was generated using a pulsed current source (c). Note that the magnetic field had no observable effect in any orientation.

**Fig. 5.** Stimulation of two neurons on one chip with a current pulse of amplitude 24 µA and duration 100 µs. At this level of stimulation, the neuron in (a) is below its threshold and does not generate an AP, whereas the neuron in (b) exhibits normal firing behaviour. However, the application of the magnetic field to the neuron in (b) in the Z-plane suppresses AP generation completely. Note that applied to the neuron in (a), the magnetic field had no effect in any orientation.

different from that shown in Fig. 4 (note that increasing the stimulus to 25 µA, which is just above threshold, results in responses similar to those shown in Fig. 4, for both neurons).

Application of the 3 T magnetic field to the first neuron (sub-threshold) produced no effect in any orientation (Fig. 5a). However, for the second neuron, applying the field in the Z-plane suppressed AP generation, an effect that could be reversed by an increase in the amplitude of...
the stimulation current (Fig. 5b). Note that in this case there is a suggestion that applying the field in the $Y$-direction appears to slightly reduce the threshold, which has the effect of reducing the rise time of $V_{\text{mem}}$.

Finally, a step stimulus was applied, allowing the generation of tonic spiking. Any differences in AP timing will present as different spiking frequencies making it easy to identify small changes. Figure 6 is the Lissajous plot of the outputs (i.e., membrane potentials) of both neurons in response to the application of a 49 µA pulse of 10-ms duration, resulting in the production of a train of spikes (colour-coded time records are also included and the accumulation of phase error with time is clear in all the Lissajous plots). Although some dephasing is indicated when the field is applied in all planes, it is more marked in the $X$- and $Y$-directions, in apparent contradiction to the results of the DC and single pulse measurements, all of which showed the strongest effect in the $Z$-direction.

![Image of Lissajous plots](image)

**Fig. 6** Lissajous plots of the response of two neurons to a 10 ms 49 µA pulse, resulting in continuous spiking behaviour. The effects of the application of the field are indicated by the bowing of the plots. The time elapsed along each trajectory is colour-coded in the Lissajous plot.

The most likely explanation for this effect is that for these device dimensions operating at room temperature, no quantization (i.e., Landau quantization and anisotropy in the Landé factor/Zeeman splitting) of the orbital motion is expected to occur (see the Appendix for a more detailed explanation). The residual effect of the magnetic field is, therefore, to squeeze the electron wave functions in the perpendicular direction giving rise to a diamagnetic shift.\(^7,8\) When the field is in the $Z$-direction, the wave function will only be confined by the magnetic field in the $X$–$Y$ plane, whereas when the field is in the $X$–$Y$ plane the electron wave function will be confined by both the magnetic field and the electrostatic potential of the accumulation layer. The diamagnetic shift will differ for each orientation and the resulting change in energy will change the group velocity and hence the diffusion coefficient of electrons. The equivalent classical picture is that of closed stationary electron orbits (low diffusivity) when the magnetic field is perpendicular versus open magneto-electric orbits skipping on the Si/SiO$_2$ interface (higher
diffusivity). This effect will modulate carrier transport properties depending on the orientation of the field and explain the stronger dephasing in the Lissajous curve when the field is in the plane as opposed to when it is perpendicular to it.

In order to investigate the sensitivity of the neuron threshold current to the fundamental threshold potentials of the sodium (Na) and potassium (K) channels, simulations were carried out using the classical Hodgkin-Huxley model equations. The system was stimulated with a supra-threshold current pulse (100 pA) between 50 ms and 150 ms, eliciting a train of spikes. The resting membrane voltage was $-60$ mV. The Na threshold was perturbed in the range $-39$ mV to $-41$ mV and the K threshold in the range $-58$ mV to $-62$ mV. The output pulse trains for the perturbed thresholds were plotted against the nominal oscillations in the form of Lissajous figures (Fig. 7). The change in Na threshold has a large effect on the oscillation period whereas the change in K threshold has virtually no effect other than slight modulation of the AP amplitude. It is likely, therefore, that the effects observed and noted above are the result of modulation of the Na threshold by application of the field.

**Discussion of the Results**

Tests on both the single NMOS transistor and the MD neurons suggest that the effect of a static magnetic field, applied in any of the three orientations, remains small but observable. However, it was also noted that any field-induced deviations are likely to be much smaller than the effects of device mismatch.

A reduction in the saturated value of $I_d$ was noted in the NMOS output characteristics for a magnetic field oriented along the Z-axis of the IC. For the range of currents considered this reduction was consistently about 1% of the saturated drain current. This smallness of the shift appears to conflict with the results of earlier work carried out at the National High Magnetic Field Laboratory (NHMFL) in Tallahassee, FL, USA, in 1998. In these experiments a single transistor was exposed to DC fields of between 1 T and 10 T. No details of the experiment or the device used are provided, so direct comparison with the current work is impossible. However, the zero-field value of $I_d$, 10 mA, suggests a different type of device from that used in our experiment. Also, the reported reduction in $I_d$, 20%, is much larger than that observed in our experiment.

The deviation noted in the NMOS transistor characteristics due to the applied field in the z-direction was quite small and was broadly repeated in the observed neuron responses as shown in Figs. 5 and 6. Simulations using the classical HH model equations suggest that the observed change in neuron threshold voltage were probably attributable to modulation of the sodium (Na) channel threshold by the applied field. In addition, when the neuron was stimulated with an extended pulse resulting in a train of spikes (tonic spiking), some frequency deviation was noted when the field was applied (Fig. 6). However, unlike the case where a single spike was elicited, the frequency shift was maximum when the field was applied in the plane of the device, i.e., the X−Y direction. As suggested above, the most likely reason for this

![Fig. 7 Lissajous plots showing simulations of the classical Hodgkin-Huxley (HH) model of a neuron in response to a supra-threshold current pulse. The output (membrane voltage) is a train of spikes, and the figures plot the nominal output (X-axis) against the outputs when the Na and K threshold potentials are perturbed relative to the mean parameter value as indicated in the figures (Y-axis). The motion is from clockwise to anticlockwise when the threshold is above or below the reference threshold.](image)
variation are corrections in electron diffusion coefficients due to the diamagnetic shift.

**Conclusion**

The magnitude of the action potential dephasings observed in large magnetic fields remain very small compared to the shift in peak-to-peak intervals which are biological meaningful. They are also small in comparison with the likely changes due to on-chip component mismatches. These dephasings remain well under the 1–3% shift observed in respiratory sinus arrhythmia. It may therefore be concluded that neural pacemakers would be largely unperturbed by static MRI magnetic fields.

**Appendix**

The physics of two-dimensional electron systems in high magnetic fields has been extensively studied at low temperatures where the mean free path is greater than the cyclotron radius and magneto-oscillations are observed. The 2D electrons in our MOSFETs have a maximum mean free path \( l = 59 \text{ nm} \) at a density of \( n_s = 2 \times 10^{11} \text{ cm}^{-2} \) which is comparable to copper. However, the mean free path near the conduction threshold where the devices operate here will be much shorter. The cyclotron radius in the 3-T magnetic field is 25 nm. Therefore, no quantization of the orbital motion is expected to occur. The residual effect of the magnetic field is to squeeze the wave functions of electrons in the perpendicular direction giving rise to a diamagnetic shift:

\[
f_B = \frac{\hbar^2}{2m} \left( \langle x^2 \rangle - \langle x^2 \rangle \right)
\]

This is proportional to the variance of the wave function spread where the averages of \( x \) and \( x^2 \) are over the electron wave function. Here \( m \) is the effective mass and \( e \) is the electron charge. The diamagnetic shift adds a correction to the total energy:

\[
E = E_0 + \frac{\hbar^2}{2m} (k_y - k_0(B))^2 + f_B
\]

where \( E_0 \) is the ground state energy, and the second term represents the orbital kinetic energy centred on the oscillator centre \( k_0(B) \). The latter averages to zero in the diffusive regime at 300 K.

When \( B \) is in the \( Z \)-direction, the wavefunction will only be confined by the magnetic field in the \( X-Y \) plane, whereas when \( B \) is in the \( X-Y \) plane the electron wave function will be confined by both the magnetic field and the electrostatic potential of the accumulation layer. Therefore, the diamagnetic shift will differ for each case because the averages \( \langle x \rangle \) and \( \langle x^2 \rangle \) will be different. The change in energy will subsequently change the group velocity of electrons and hence modulate transport properties depending on the orientation of \( B \).

The observation of a stronger dephasing in the Lissajous curve when \( B \) is in the plane as opposed to when \( B \) is perpendicular is consistent with the different confining potentials experienced by the wave functions in each case. Another potential source of anisotropy with respect to magnetic field orientation is the Landé g-factor. However, given the weak spin-orbit interactions in silicon, a spin induced anisotropy of transport properties may be neglected compared to the correction brought by the diamagnetic shift.

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