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A fully implantable stimulator for use in small laboratory animals

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Abstract

This paper describes a low cost, fully implantable, single channel stimulator that can be manufactured in a research laboratory. The stimulator generates charge-balanced biphasic current pulses which are delivered to a bipolar electrode array for chronic stimulation of neural tissue in free-running laboratory animals such as rats and mice. The system is magnetically coupled and contains no batteries or external leadwires. The subject is placed in a chamber surrounded by three orthogonal coils of wire which are driven to generate a magnetic field. Currents are induced in wire coils in the implanted stimulator then regulated to produce biphasic current pulses with fixed amplitude of up to 500 μ A. Phase duration is adjustable from 25 – 250 μ s per phase. Charge balance is maintained by capacitive coupling and shorting of the electrodes between pulses. Stimulus rate can be continuously varied, and the temporal precision of the stimulus means that the stimulator can be used in behavioural experiments or for generating electrically-evoked potentials. We describe the application of this stimulator for chronic electrical stimulation of the auditory nerve (i.e. a cochlear implant); however it will have application in other areas of neuroscience requiring controlled safe electrical stimulation of neural tissue over extended periods. Circuit diagrams and manufacturing details are provided as supplementary data.

Keywords

electrical stimulation; cochlear implant; neural prostheses; stimulator; mouse

1. Introduction

Chronic electrical stimulation of excitable tissue in experimental animals has important application in evaluating the safety and efficacy of neural prostheses (e.g. motor neural prostheses, cochlear implants, deep brain stimulators, respiratory muscle stimulators, visual prostheses), as well as more broad application in neuroscience wherever controlled stimulation of neural tissue is required.

We describe a low cost, fully implantable stimulator suitable for chronic stimulation in small laboratory animals. We have successfully used this stimulator to chronically stimulate the auditory nerve in deaf rodents (Widijaja et al., 2006), however given appropriate stimulation electrodes, this device could be used to safely stimulate any target neural population in the peripheral or central nervous system.

Our design criteria (Table 1) called for the development of a fully implantable stimulator for use in unrestrained small laboratory rodents including rats and mice. The stimulator must be

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capable of delivering precisely timed biphasic current pulses at variable rates suitable for chronic electrical stimulation, behavioral experiments and to generate electrically-evoked potentials. The output of the stimulator must deliver charge balanced biphasic current pulses to a bipolar electrode array; stimulus intensity is varied externally by varying the phase duration (i.e. varying charge/phase as neurons are charge sensitive; Grill, 2004), a voltage compliance of at least 5V, and a charge recovery technique similar to that used in clinical devices to minimize the generation of DC (i.e. electrode shorting between pulses and capacitive coupling; Huang et al., 1999). Finally, the implantable stimulator must be encapsulated to ensure it is protected from body fluids over its required implant life (at least 10 weeks) and be biocompatible. While there are systems described in the literature which address some of these issues (Cools et al., 1978; Winter et al., 1998) the size of these implants precludes their use in small rodents such as mice. Moreover, the present stimulator is designed to drive implanted electrodes in the same way as a commercial cochlear implant by generating charge-balanced biphasic current pulses and shorting the electrodes between pulses. Other experimental stimulators lack one or more of these features. A comparison of the output characteristics of the present stimulator with those of typical commercial devices is summarised in Table 2.

We have attempted to design an implant that is small, reliable and may be manufactured in a laboratory at modest cost. It is powered and driven by a pulsed magnetic field generated by coils of wire wound around the outside of the animal enclosure. The ability to manufacture the device in-house is important as it allows researchers to readily alter the device to suit different experimental requirements (e.g. the incorporation of a neurotrophin delivery system into the electrode array; Shepherd and Xu, 2002).

We have developed two implantable stimulators; one for implantation in the mouse and a larger stimulator with additional options suitable for implantation in larger rodents such as the rat. The larger stimulator differs from the one designed for mice by including light-emitting diodes (LEDs) which are visible through the skin of the animal in order to provide confirmation that the stimulator is functioning. It also uses coils that enable a longer pulse period than the mouse design, and has an active electrode shorting circuit which may enable higher rates of stimulation (Huang et al., 1999).

2. System Description

2.1 Overview

A pulsed magnetic field is generated by applying a voltage to an external coil of wire wound around a chamber containing the implant stimulator (the “excitation” coil; Fig. 1a). In our application a 230 V biphasic voltage pulse is applied to the excitation coil (Fig. 1b). The current through this coil increases with time at a rate proportional to the applied voltage (Fig. 1c). Because the voltage is constant during the phase period of the pulse, the rate of change of current is also constant, producing a triangular current waveform. The intensity of the magnetic field is directly proportional to the current and is therefore also triangular.

A biphasic voltage pulse, which is proportional to the rate of change in the intensity of the magnetic field, is induced in the implant coil (Fig. 1d). The coil system therefore acts like a very leaky electrical transformer. The induced bipolar voltage pulse is applied to a current regulator producing a biphasic constant current pulse which is delivered to the electrodes (Fig. 1e). The voltage pulse in the implant coil will vary in amplitude as the coil is positioned at different angles within the field. Because this application called for freedom of movement of the implanted animal, excitation coils are wound in orthogonal planes so that the implant coil can never be at an angle of more than 45° to the excitation field from one of the coils (see Fig. 5). The three orthogonal coils are independently driven in a sequential order. When the implant coil is at 45° to an excitation coil the induced voltage will be reduced to 0.7 of maximum. The

field is also reduced by a factor of 0.7 near the ends of the coils, resulting in an overall reduction in induced voltage in the implant coil to half the maximum induced voltage. With these reductions the voltage compliance of the stimulator is 5 V. Finally, the electrode voltage waveform shows the typical resistive and reactive components normally associated with a current pulse (Fig. 1f; Newbold et al., 2004).

With this configuration, the animal is guaranteed to always receive at least one current pulse per cycle from one of the three orthogonal coils, for any orientation of the stimulator. If it is aligned at 45° to two coils the stimulator will generate two current pulses per cycle; if it is aligned at 45° to all three excitation coils it will generate three current pulses per cycle. For orientations greater than 45°, in addition to the one or two current pulses generated, there will be two or one smaller pulses generated with the current source operating out of voltage compliance (Fig. 2). These smaller pulses may not reach threshold excitation and may not be symmetrical, however, charge balance is maintained by the coupling capacitor and electrode shorting between the pulses (Huang et al., 1999; Shepherd et al., 1991).

The stimulus rate in the free-running cube can be specified to be between a minimum (oriented for only one pulse) and a maximum which is three times the minimum. For behavioural or evoked response measurements the animal is constrained within a single coil so that it is always aligned to the field and the rate and timing of the stimulation is precisely known.

2.2 Implant design

2.2.1 Mouse implant—This stimulator consists of a coil of wire, a bi-directional current regulator, a capacitor and bipolar electrodes (Fig. 3a). It is driven by a magnetic field that produces a biphasic constant-voltage waveform across the inductor which forces a current through the current regulator and capacitor to the electrodes. The coil (Sonion; Passive Telecoil T20 AG 12, 9012-1050184, www.Sonion.com) used has a core of magnetisable material which saturates at high field strengths limiting the maximum pulse period to 150 μ s. The bidirectional current regulator uses depletion-mode field-effect transistors (BSS139), which conduct between the source and the drain when there is no potential between the gate and the source. When there is a potential applied across the circuit, current flows through both devices and the voltage drop across the source resistor (R, Fig. 3a) creates a gate-to-source voltage for both devices. For one device this voltage will be positive, which enhances its conduction. For the second, the voltage will be negative which will reduce conduction and establish it as the regulating device. There is an equilibrium point established where the current is determined primarily by the input characteristics of the transistor and the value of the resistor. The resistor value is selected to set the required current and is typically 3 k Ω with a BSS139 transistor for 350 μ A. The transistors could also be selected into pairs but devices from the same batch appear well matched. They have a parasitic diode between the source and the drain, which will conduct when the voltage across the non-regulating transistor exceeds the forward voltage threshold. The output impedance of the stimulator was measured at the 10 M Ω (Table 2). The shorting resistance of this stimulator is the resistance of the coil plus the current regulator resistor (~5 k Ω in total). After encapsulation (see 2.3), this stimulator is ~10 mm in length, 3 mm in diameter and weighs ~1 g.

2.2.2 Larger rodent implant—Using the same principles utilized in the mouse stimulator, this implant incorporates an additional coil, light-emitting diodes (LEDs) to provide a visual indication that the stimulator is generating a current pulse, and a shorting switch allowing the stimulator to safely operate at higher stimulus rates (Fig. 3b). Like the mouse stimulator, this design delivers charge balanced biphasic current pulses to a single bipolar electrode pair.

LEDs were added to this design to provide visual indication that current pulses are being delivered to the electrodes; red LEDs are visible through the skin and fur of a rat. The LEDs

are effectively open-circuit once the voltage across them drops below about 1.5 V, and what discharge could otherwise occur through the resistance of the coil is effectively blocked, so a complementary pair of junction field-effect transistors plus over-voltage protection for their gate to source junctions were added to effect the shorting. Because there is a voltage drop across the LEDs, another coil is included in series in this design in order to maintain voltage compliance. After encapsulation (see 2.3), this stimulator is 14 mm in length, 12 mm wide, 6 mm thick and weighs 2.5 g.

2.3 Encapsulation procedure

It is important to remove any contaminants produced during manufacture prior to encapsulation of the stimulator. The PCB is cleaned with detergent followed by isopropyl alcohol and components are then soldered using 2% silver solder. Flux is removed with isopropyl alcohol and the stimulator is dried overnight at 80 °C. Once cleaned, the stimulator is only handled using clean plastic tweezers. After cooling, the PCB board is coated with conformal coating (Electrolube DCA SCC3) which is cured overnight at 80 °C. The following day the assembled board is coated with a silicone elastomer (Permatex 65AR; www.permatex.com/), taking care not to cover the electrode connection pads. The silicone is allowed to cure overnight at room temperature.

Platinum/iridium (90/10) electrode leadwires are soldered to the PCB using 2% silver solder. These connections are cleaned with isopropyl alcohol to remove residual flux, dried for 30 minutes and then coated with silicone elastomer. The proximal leadwire is fixed to the encapsulated stimulator with silicone in order to provide stress relief to these connections. Figure 4 illustrates an encapsulated rodent stimulator containing a leadwire and electrode assembly suitable for cochlear implantation. The design of bipolar electrode arrays and Pt/Ir leadwires used in the rat (Shepherd and Xu, 2002) and the mouse (Pettingill et al., 2006) have been described previously.

2.4 Testing the implant assembly

During the assembly process the board is tested by placing it in the field of an excitation coil (see 2.5) and the voltage waveform is recorded on an oscilloscope connected across the electrode connection pads (Fig. 1d). A rectangular biphasic waveform of at least 10 volts peak indicates normal function. The voltage recorded across a resistor placed across this output is used to check the amplitude of the biphasic current waveform (Figs. 1e & 2). Finally, the encapsulated assembly is tested prior to sterilization (see 2.7) by measuring the current waveform using a resistor connected across the bipolar electrodes (Figs. 1e & 2) with the stimulator placed within the test coil.

2.5 The excitation coil assembly

Figure 5 illustrates the excitation coil assembly used for chronic electrical stimulation in the awake unrestrained animal. This assembly is suitable for both the mouse and large rodent stimulators. The use of three orthogonal coils is designed to allow the subject(s) complete freedom of movement within the clear acrylic cube. The inductance of the excitation coils is related to the number of turns and the volume enclosed. The inner clear acrylic box (arrowhead, Fig. 5a) has outside dimensions of $0.16 \times 0.16 \times 0.17\text{m}$ and a volume of 0.0044m^3 . There are 150 turns on each box in 5 groups of 30 turns to allow the animals to see out of the box. The inner box is completely removable for cleaning, and has no openings in the bottom or sides, although the top is open. Because of dielectric heating and the current in the coils warming the clear acrylic (a 400 ml beaker of water will increase in temperature by $\sim 1^\circ\text{C}$ in an hour at maximum field strength), the two additional clear acrylic cubes have holes to enable air to be replaced and the assembly contains a small fan (rated at 0.6m^3 per minute; Fig. 5b). Finally,

food and water are supplied to the animals during stimulation using standard rodent feed and water containers.

The excitation coils receive voltage pulses from the excitation coil control unit (Fig. 6). This unit is designed to send precisely timed voltage pulses to the coils and has variable pulse width of 25 to 250 μ s and stimulation rate of 50 to 5000 Hz. It may also be controlled via an RS232 interface by a computer, and accepts an external trigger pulse for electrophysiological experiments. Moreover, in our application (cochlear implants) a computer can process environmental sounds and command the exciter to produce pulses which represent some properties of that sound, so the subject will have some connection to its acoustic environment.

The voltage induced in the implant coils is proportional to the number of turns in the coil and the rate-of-change of magnetic flux through the coil. Since commercial coils are used, the intensity of the field used has been chosen to suit these coils. To generate a rectangular voltage pulse in the implant, i.e. a constant voltage over the period of the pulse, a constant rate-of-change of the magnetic field must be generated. The flux density (B) in air is related to the magnetising force (H):

$$B = \mu H$$

where the permeability $\mu = 4\pi \times 10^{-7}$

The excitation coils approximate a solenoid and the magnetising force H in a solenoid is given by:

$$H = I * (N/L)$$

Where I = the current and N/L = the number of turns per unit length of the coil.

Therefore the current in the excitation coils also needs to have a constant rate-of-change. Such a current waveform can be generated by applying a constant voltage to the excitation coil. Because the voltage across an inductance is proportional to the rate-of-change of current:

$$V = L * di/dt$$

applying a constant voltage will produce a linearly changing current.

There are a number of competing factors that must be considered in the selection of the size of the excitation coils. For the same field strength, more turns results in less current but a higher resistance, producing a more exponential waveform. A compromise is reached using 230 volts and a peak current of 12A. The excitation and implant coils may be considered to act like a very leaky transformer. A rectangular pulse voltage waveform is input to the primary (excitation) winding, and a similar voltage waveform is obtained from the secondary (implant) winding.

Moderate levels of energy are generated during the pulses. The excitation electronics uses a flyback principle to recover the energy from the magnetic field and so reduce power consumption. The coils are driven by a bridge configuration (Fig. 7). The first phase of the stimulation is generated by closing both the switches. Current then flows from the 270V power supply following the path labelled "Phase 1 Current" (Fig. 7a). The current linearly ramps up ($di/dt = V/L$ where the inductance L is approximately 10mH). To end phase 1, the switches are both opened. Once the coil no longer has a source of current, the field begins to collapse, and the polarity of the voltage across the coil reverses and rises, forward-biasing the diodes to

pass current which now follows the path labelled “Phase 2 Current” (Fig. 7b), returning energy back to the supply.

Because of the forward voltage drop across the diodes, other losses and lack of regulation of the power supply, the second phase would be of higher voltage and of shorter duration. To correct for this, the anode of the lower diode is returned to a power supply of 40 volts.

2.6 Operator safety

The maximum magnetic field intensity (up to 30 mT) that may be generated within the exciter exceeds the recommendations of the International Commission on Non-Ionizing Radiation Protection (ICNIRP) for workplace exposure (International Commission on Non-Ionizing Radiation Protection, 1998). To set a safe distance for operators of this equipment the fields were measured with two different survey meters (GaussMaus B7461; www.dindima.com and an HMI-1; www.hmisystems.com.au/). The fields were also measured with a small search coil connected to an oscilloscope, and the magnitude of the field calculated:

$$B=(V * t)/(A * n)$$

Where: V = Field intensity (Tesla), t = time (seconds), A = Area of coil (m²), and n = number of turns

These measurements indicated that the safety limits as recommended by the ICNIRP guidelines are reached at 30cm from the equipment. As a result, we recommend that personnel do not remain within 1 meter of the equipment when it is operating.

2.7 Surgical implantation

Prior to implantation the stimulator is cleaned by rinsing in double-distilled H₂O for 20 minutes followed by 20 minutes in an ultrasonic cleaner in 100% ethyl alcohol followed by double-distilled H₂O. After drying at 37°C the implant assembly is sterilized using H₂O₂ gas sterilization (Sterrad® 100S).

Surgery is performed under sterile conditions using anaesthetic protocols described previously (Lu et al., 2005). In our application, after the bipolar electrode array is implanted into the cochlea, the leadwire is fixed in the middle ear cavity using bone cement (Durelon®, ESPE Dental AG, Germany) and onto the skull with polyethylene mesh (Lars Mesh, Meadox Medicals, New Jersey, USA). A subcutaneous pocket is then created between the scapulae into which the stimulator is placed (Fig. 8). The wounds are sutured in two layers and sprayed with Opsite (Smith & Nephew Pty. Ltd., Hull, U.K.).

2.8 In vitro and in vivo trials

Two stimulators encapsulated using these techniques were tested *in vitro*. One stimulator failed after 48 weeks due to the implant coil becoming open circuit; a second stimulator functioned normally for 52 weeks of continuous stimulation while immersed in saline at 20°C. This *in vitro* evaluation gave us confidence that the encapsulation technique would be suitable for the required *in vivo* application.

Initial animal trials were performed in young rats without implantable stimulators. Two rats were placed into the clear acrylic excitation box and pulsed with magnetic fields for 2 hours/day over a period of 1 month. Their weight gain over this period showed no significant difference to that of age matched control animals placed in the box for similar periods but not stimulated, and control animals not placed in the box.

There are reports that magnetic and electric fields of the magnitude that this device generates can induce currents in tissue which will directly stimulate nerves (International Commission on Non-Ionizing Radiation Protection, 1998). When exposed to the maximum fields, the unimplanted animals placed in the magnetic field showed no evidence of detection when the device was turned on. They continued to groom, eat and rest with no sign of distress during stimulation.

We recently completed our first chronic stimulation study using these stimulators connected to a bipolar intracochlear electrode array implanted in deafened rats (Fig. 8; Widijaja et al., 2006). The stimulators were implanted for a period of up to 16 weeks and the animals stimulated four hours/day for up to 14 weeks at a level of 3dB above their electrically-evoked auditory brainstem response threshold (see 2.9). All five implanted stimulators performed normally over the implantation period, moreover the animals maintained good health throughout the stimulation program.

2.9 Recording electrically-evoked potentials

Recording electrically-evoked potentials is important in applications where it is necessary to demonstrate functional activation of the target neural population. We routinely record electrically-evoked auditory brainstem responses from anesthetized animals stimulated via this magnetically coupled stimulator (e.g. Fig. 9). These potentials are recorded from the scalp using differential recording and signal averaging techniques (Shepherd et al., 2005). Because the amplitude of these responses are in the order of micro-volts, the technique requires careful electric and magnetic shielding (Fig. 10).

For this application, the magnetic field is generated from an 8 cm long single solenoid coil wound onto an 8cm diameter tube whose inside is coated with a conductive layer running the length of the tube (but containing a small gap to prevent the formation of a shorted turn), to shield the electric field from the coil (Fig. 10). The field is adjusted to be similar to the weakest of the 3 axial fields generated in the 3-axis clear acrylic stimulation box by inserting an air-cored inductor in series to set the current. The tube is then surrounded by a metal box made from 0.2mm thick tin plated steel. Space within this box is filled with expanding foam to reduce acoustic noise generated from the movement of the coils and the box by the pulsed magnetic field. The anaesthetized subject is placed in the tube so that the implanted stimulator – located between the animal's scapulae – is within the field of the excitation coil (Shielding box B; Fig. 10). Recording electrodes (30G stainless steel needles) are placed at the vertex and nape of the neck; a common reference electrode is also located outside the excitation coil; wires connecting the recording electrode to the amplifier are twisted together to minimise induced electrical artefact. The animal's head - positioned outside the excitation coil - is separately shielded by a second metal box designed to enclose the recording electrodes (Shielding box A; Fig. 10). The two shielding boxes are electrically isolated and separately connected to a common ground. Standard differential recording procedures are used to generate the evoked response (Shepherd et al., 2005).

In order to ensure that the pulsed magnetic field used in this application does not directly stimulate the peripheral or central nervous system, we used identical recording techniques in a deafened control animal (i.e. without a functioning stimulator/electrode assembly) and could not evoke a physiological response at maximum field strength.

3. Discussion

We describe a low cost, fully implantable single channel stimulator that can be used to chronically stimulate target neurons using charge balanced biphasic current pulses – a stimulus widely considered safe for use in chronic applications and used extensively in neural prostheses

(Seligman and Shepherd, 2004). The design also incorporates charge recovery techniques used by neural prostheses, including capacitive coupling (Huang et al., 1999), to ensure long-term safety of the stimulus.

One version of this stimulator is the first – to our knowledge – suitable for implantation in an animal as small as a laboratory mouse. A second, larger stimulator has been successfully used in laboratory rats to provide chronic electrical stimulation of the auditory nerve (i.e. a cochlear implant) in pathophysiological studies (Widijaja et al., 2006).

The stimulator is designed for use in unrestrained animals, and contains no batteries or external leadwires, therefore minimizing the risks of infection associated with a percutaneous connector. The amplitude of the output current of the stimulator is fixed (typically 350 μ A but this can be varied for a given application), and stimulus intensity is varied by varying the phase duration of the current pulse. The bipolar electrodes must be designed for each application, however, given that the voltage compliance of the stimulator is 5 V, the impedance of the electrodes need to be no greater than ~14 k Ω (the electrode impedance in our application is ~2 k Ω).

Adjusting stimulus intensity by varying phase duration rather than current amplitude may have a number of physiological consequences that should be taken into consideration when using this stimulator. For example, narrow phase duration current pulses have greater spatial selectivity compared with the same charge delivered using wider phase durations (Grill and Mortimer, 1996). In addition, the careful selection of phase duration can be used to selectively stimulate one group of neurons within a non-homogeneous neural environment (Voorhees et al., 1992).

An important feature of the present design is the ability to produce precisely timed current pulses via computer or external trigger control of the excitation coil control unit, allowing the stimulator to be used in electrophysiological and behavioral experiments. The generation of electrically-evoked potentials are particularly important in this application as they provide confirmation that the stimulus is depolarizing the target neurons, and therefore provides a physiological measure of threshold that is required in setting stimulus intensities for chronic stimulation in awake animals.

As noted by Winter et al., (1998), the long-term effects of exposure to pulsed magnetic fields on animals are unknown. The maximum magnetic field generated in this design (30 mT) is nearly two orders of magnitude less than the 1.4 – 2.0 T fields typically required to evoke activity in neural tissue (Benecke et al., 1988a; Benecke et al., 1988b; Schmid et al., 1992). However, as the field in close proximity to the excitation coils was above ICNIRP guidelines, safe operation of this equipment requires that staff do not remain within 1 m while it is in use.

Because the stimulators could unintentionally be driven by stray electromagnetic fields, it is necessary to monitor the laboratory for stray fields before use. However, an advantage of the relatively high field strengths used in this design means that such stimulation is most unlikely. A more common problem may be associated with the electrical noise generated by this equipment interfering with other laboratory equipment.

Because the stimulator is fully implantable, one clear disadvantage is the lack of direct access to the electrode waveforms (current and electrode voltage). LEDs were added to the circuit to provide confirmation of delivery of a current pulse to the bipolar electrodes. While this addition has provided a level of reassurance regarding device function, the recording of electrically-evoked potentials is the definitive test of function.

Future development of these fully implantable, magnetically coupled stimulators includes the development of devices with variable current amplitude output and multichannel stimulation capabilities. At least initially, it would not be envisaged that these advanced stimulators would be of a size suitable for use in mice.

In conclusion, we describe the manufacture of a fully implantable small animal stimulator for use in chronic pathophysiological and behavioural experiments, and its use in the study of electrical stimulation of the auditory nerve (i.e. a cochlear implant). With simple modification of the bipolar electrode array, this stimulator would have application in many other areas of neuroscience. Circuit diagrams and manufacturing details are available as supplementary files.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

(a) Schematic diagram illustrating a single excitation and implant coil. These coils induce a biphasic current pulse in the implant stimulator in response to a pulsed magnetic field. Representative voltage and current waveforms illustrating the sequence in the generation of a biphasic current pulse: (b) voltage pulse delivered to the excitation coil; (c) the induced current in the excitation coil; (d) the induced voltage in the implant coil; (e) the biphasic current pulse generated by the current regulator; and (f) the electrode voltage waveform developed across the bipolar electrode.

Figure 2.

Plots of the current waveform recorded from a stimulator with the stimulator coil placed at different angles (0, 15, 30, 45, 60, 75 & 90 degrees) relative to a single excitation coil. The output of the stimulator was connected to either an 18 k Ω resistor in series with a bipolar electrode array (a); or the bipolar electrode array alone (b). In both cases the electrodes were immersed in normal saline. For orientations of at least up to 45 degrees there was little change in the current pulse waveform (i.e they are superimposed). At greater angles the current pulse decreased in amplitude as the stimulator begins to operate outside its voltage compliance. It is important to note that while operating outside voltage compliance the electrode shorting and capacitive coupling ensured charge balance.

Figure 3.
Schematic (a) mouse and (b) rat stimulator circuits.

Figure 4. Photograph of the large rodent stimulator and electrode assembly. The stimulator and leadwire have been encapsulated in silicone in preparation for implantation. A 0.3 mm diameter bipolar platinum electrode array (arrowhead) is designed for insertion into the rat cochlea. Scale bar = 10 mm.

Figure 5.

Excitation coil assembly for chronic electrical stimulation of small laboratory animals using a pulsed magnetic field. Animals are placed within the inner acrylic box (dimensions $0.16 \times 0.16 \times 0.17\text{m}$; arrowhead; a), which is then closed (b) to place the animal within the field generated by three orthogonal excitation coils. The coil assembly receives voltage pulses from the excitation coil control unit (Fig. 5). Holes in the top of the acrylic cubes (arrows; a) and a small electric fan (double arrowhead, b) are used to provide air circulation during stimulation.

Figure 6.
Photograph of the excitation coil control unit. This unit is assembled in a standard 19" 1 U rack mounted case.

Figure 7.
Schematics illustrating the principles of operation of the exciter electronics.

Figure 8. Micro-focus x-ray image of a live rat implanted with the electrode array/stimulator assembly. Bipolar platinum electrodes are located in the cochlea (arrowhead), while the leadwire system – consisting of helically coiled Pt/Ir wires encapsulated in silicone (double-arrowhead) – courses back to the stimulator located in a subcutaneous pocket overlying the scapulae. Charge balanced biphasic current pulses, induced in the implanted stimulator via an external magnetic field, are delivered to the bipolar electrodes. Scale bar = 10 mm.

Figure 9.

Representative mEABRs evoked from a chronically implanted animal two months following implant surgery. The implantable stimulator induces a charge balanced biphasic current pulse of fixed current ($500\ \mu\text{A}$ in this example) in response to a pulsed magnetic field. Charge delivery is controlled by varying the duration of the phase (in this example $15\text{--}100\ \mu\text{s}/\text{phase}$; threshold at $20\ \mu\text{s}/\text{phase}$). High quality mEABRs have been recorded during the chronic implantation period. The waveform morphology is similar to conventional EABRs recorded in the same species (Lu et al., 2005).

Figure 10.

Schematic diagram illustrating the recording and shielding configuration required to record electrically-evoked potentials via the implantable stimulator (S). The anesthetised animal is placed so that the implanted stimulator lies within, and is aligned with, a single excitation coil. This coil is wound around an 8 cm diameter tube (B); a conductive layer inside the tube shields the electric field from the coil. The coil is also surrounded by a metal shielding box which is connected to ground (B). Scalp potentials, recorded from the subcutaneous recording electrodes placed at the vertex and the nape of the neck, are fed to a differential pre-amplifier (P) via leadwires twisted together (t) to minimize induced electrical artefact. A reference electrode connects the animal to a common ground. These recording electrodes are positioned outside the excitation coil and are separately shielded by a second metal box (A). The two shielding boxes are electrically isolated and, together with the shielded pre-amplifier, are separately connected to a common ground.

Table 1

Design criteria

General:	Fully implantable
	Implantable in an adult mouse
	Minimum implant period of 10 weeks
Output:	Charge balanced biphasic constant-current pulses
	Bipolar (i.e. single channel) electrode array
	Minimum of 5 V voltage compliance
	Fixed current amplitude in the range 100 – 500 μ A
	Variable phase period of 25 – 250 μ s per phase
	Ability to vary stimulus intensity
	Electrodes capacitively coupled
	May be used in behavioural experiments
	May be used to generate electrically-evoked potentials

Table 2

Comparison of output characteristics of a commercial cochlear implant with the experimental stimulator described in this paper.

Parameter	Commercial stimulator	Experimental stimulator
Current amplitude	10–1750 μ A	100–500 μ A
Current rise time	2 μ s	10 μ s
Current phase period	10–400 μ s	15–250 μ s
Output impedance	100 k Ω –1 M Ω	10 M Ω
Shorting impedance	300 Ω	5 k Ω