Published in final edited form as:

Ann Biomed Eng. 2010 March ; 38(3): 707–713. doi:10.1007/s10439-009-9876-x.

Powering an Implantable Minipump with a Multi-layered Printed Circuit Coil for Drug Infusion Applications in Rodents

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Abstract

We report the use of a multi-layer printed coil circuit for powering (36–94 mW) an implantable microbolus infusion pump (MIP) that can be activated remotely for use in drug infusion in nontethered, freely moving small animals. This implantable device provides a unique experimental tool with applications in the fields of animal behavior, pharmacology, physiology, and functional brain imaging. Two different designs are described: a battery-less pump usable when the animal is inside a home-cage surrounded by a primary inductive coil and a pump powered by a rechargeable battery that can be used for studies outside the homecage. The use of printed coils for powering of small devices by inductive power transfer presents significant advantages over similar approaches using hand-wound coils in terms of ease of manufacturing and uniformity of design. The high efficiency of a class-E oscillator allowed powering of the minipumps without the need for close physical contact of the primary and secondary coils, as is currently the case for most devices powered by inductive power transfer.

Keywords

Electromagnetic field; Class-E oscillator; Infusion pump; Printed coil; Radio frequency identification device

BACKGROUND

The microbolus infusion pump (MIP) is an implantable, remotely activated miniature pump developed in our laboratory for bolus administration of pharmaceutical compounds in freely moving animals for applications in the study of animal behavior, pharmacology, physiology, and functional brain imaging.³ The 1st generation of the MIP had three main components:

an electronic module powered by a primary battery that included a miniature solenoid valve, a coiled ejection chamber containing the pharmacologic agent (total volume = 0.5 mL) and an elastomeric reservoir that provided the hydraulic pressure to push the content of the ejection chamber forward (outlet pressure ~124 mm Hg, total volume 1.1 mL)^{4–6} (Fig. 1). The 2nd generation of the MIP replaced the primary battery by a hand-wound inductive coil made of Litz wire that powered the implant through a radio frequency link to an external resonating inductive coil driven by a class E oscillator.¹² Hand winding the Litz wire coil was time consuming and made it difficult to obtain coils that were uniform in shape and electrical characteristics. The inductance had to be measured for each individual hand-wound coil, and then, using the formula $LC\omega^2 = 1$ ($\omega = 2\pi f$), the matching capacitor had to be individually selected for the frequency of the oscillatory electric field.

The electronic module and its inductive coil are substantially modified in the new MIP design. In particular, the hand-wound coil has been replaced by a coil trace embedded in the printed circuit board. Two pump designs are described: (1) A battery-less pump which can be triggered when the animal is moving inside a cylindrical cage surrounded by an inductive wire coil powered by a 2 MHz class-E oscillator. (2) A pump containing a rechargeable battery for use in open-cage paradigms. In the latter design, the battery can be trickle charged in the animal's home-cage when not in use and triggered transcutaneously by infrared illumination while the animal is outside its cage.

METHODS

Primary Coil Transmitter

Power was supplied to the MIP by an external inductive cylindrical primary coil driven by a class-E oscillator.^{9–12} The primary coil ($L \sim 12 \mu\text{H}$, Diameter, $D = 33 \text{ cm}$, Height, $H = 8 \text{ cm}$) was made of five turns of 10-gage wire spiral-wound around a cylindrical plastic rat cage ($D = 33 \text{ cm}$, $H = 26 \text{ cm}$). The coil extended in height between 5 and 13 cm above the floor of the cage, which placed a dorsal implant in an adult rat at the coil's mid-height, where the induced field was the strongest. This primary coil and the cylindrical secondary coil in the implant formed an air-core transformer that transferred electric energy from the transmitter (primary) to the implant (secondary). The combination of a class-E tuned power oscillator and inductive link has been previously described.^{13–16} The class-E amplifier contained a single transistor, which operated as a switch (Fig. 2). The second transistor was used to phase lock the circuit to an external reference frequency oscillator ($f = 2 \text{ MHz}$) in a manner that kept constant the frequency and phase of the electric current waveform in the primary coil despite changes in the local electrical environment. This allowed the secondary receiver circuitry to be as close to resonance as possible within the transmitter coil and maximized the power transfer.^{10,12}

Secondary Receiver Circuit

Battery-less MIP Design—The controller circuit (Fig. 3) of the battery-less MIP was similar to a previous implementation,¹² except for the replacement of the hand-wound coil with a trace in the printed circuit board (PCB). In the design of the implanted receiver with its printed coil, a number of different topologies were considered. Experiments were

performed to optimize the number of turns and the trace width of the printed secondary coil to achieve maximum power transfer from the primary coil to the printed secondary coil of the implant. Experiments with different trace widths showed that a coil trace width of 1.0–1.1 mm produced the largest voltage and current within our primary coil emitter. Using two four-turn spirals on two layers, as opposed to a single eight-turn spiral on one layer, increased the average cross section of the coil by 20% resulting in a stronger induced current. The final configuration had the printed coil laid out on the top and bottom layers of the PCB in the form of two four-turn, square-angled spirals (copper trace, width = 1.02 mm) interconnected to form a single electric coil ($L = 0.93 \mu\text{H}$). The PCB dimensions (2 cm $\times$ 4 cm) kept the implant compatible with the size of the host rat. The space in the middle of the spiral coil was used to mount the other electronic components.

Ex Vivo Characterization—The DC valve current (I_{valve}) was measured with the circuit placed on a grid (2 cm increment) at an altitude (h) equal to 0, 5.5, and 10 cm relative the mid-height of the primary coil. To simulate operation of the implant in animal in a bipedal posture (rearing), I_{valve} was measured for an angle (α) of misalignment between the coil axes equal to 0°, 22.5°, 45°, and 67.5°. These measurements were taken in the primary coil with diameter of 33 cm and at altitudes $h = 0, 5.5$, and 10 cm, and for radial distances $r = 0$ cm (center of the primary coil) and $r = 12$ cm (periphery of the primary coil).

In Vivo Testing in the Animal—All experiments were conducted under a protocol approved by the Institutional Animal Care and Use Committee of the University of Southern California. The circuitry (weight = 14.5 g, length = 40 mm, width = 21 mm, height = 8.4 mm) was embedded in a two-part, medical grade silicon rubber (VST 30, Factor II, Lakeside, AZ) and connected to the hydraulic components of the MIP. Functionality of the implant (weight: 24.5 g) was tested in 30 rats after 10 days of implantation by repeatedly triggering the pump while the animal was freely moving in its cage.

MIP with Rechargeable Battery—The implant circuit (Fig. 4a) was powered by a rechargeable Lithium–Ion coin cell battery (Lir2032, 3.7 V nominal, Power Stream, Orem, Utah), and it included circuitry that (1) conditioned the charging voltage for the battery and (2) controlled the pump's solenoid valve remotely. The battery charging system was powered by the receiver coil PCB trace and tuning capacitors forming a resonating circuit at the 2 MHz frequency of the primary coil transmitter. A Schottky diode (BAS70, 0.4 V nominal, NXP Semiconductors, Taiwan) rectified the voltage waveform produced by the resonating circuit, which was further conditioned to remain 4.0 V (maximum charging voltage for the battery) using a switching diode (1 N 914) and a 4.7-volt Zener diode (BZX84C4V7 W-7, Diodes Inc, China). The battery was trickle charged when the receiving coil was placed inside the cross section of a primary coil.

Two requirements for the controller circuitry were (1) to allow for remote optical triggering of the valve that was not sensitive to illumination changes in the environment; and (2) to raise the battery voltage to a level compatible with the solenoid valve (9–12 V). This voltage (9–12 V) was required only for a fraction of second, after which a minimal voltage of 2.4 V was sufficient to keep the valve open. The circuit was activated when a train of near-infrared light pulses shone on a photodetector (Vishay TSOP 32230, Philippines). The photosensor

output (active low) activated a PNP bipolar junction transistor operating as an inverter, which itself gated a silicon-controlled rectifier (SCR). The SCR current powered a miniature DC–DC converter (NKA0312S, C&D Technology, China) to raise the 3.7 V battery voltage to 12 V and energize the solenoid valve. Because of the operation of the SCR, the valve remained open even after the light pulses that activated the photodetector ended. A normally closed magnetic reed switch (KSK-1C29-1525, Meder Electronics; Mashpee, MA) that was opened by passing a small hand-held magnet over the implant broke the electric current flow through the SCR and turned off the valve. A red LED in series with the valve was visible through the animal's skin, and provided visual feedback on the proper operation of the valve controller.

For the MIP with the rechargeable battery a multilayer board was used because more components were involved than in the battery-less MIP circuit design (Fig. 4b). The printed circuit board (Fig. 4b) included four copper layers. The top layer was populated by electronic components, including the sensor and the dc–dc converter, and interconnections between these components. The bottom layer carried the rechargeable battery and the tuning capacitors ($C = 6500$ pF). The printed coil ($L = 1.04$ μ H, $Q = 15$) was laid out on the two internal layers and was similar to the coil in the battery-less MIP (two four-turn spirals on two layers, 1.0–1.1 mm trace width).

The MIP was triggered by shining five near-infrared LEDs (Lumex opto, USA) placed individually on the walls and ceiling of the room (4.3 m $\times$ 3.4 m $\times$ 3.0 m) in which the testing was conducted. The LED controller was designed to generate the optimal activation pattern for the photodetector in the implant. Three independent square wave oscillators (30 kHz, 420 Hz, 2.8 Hz) had their outputs logical-ANDed and connected through a manual push-button switch to the LED transistor drivers. Trains of at most 70 light pulses at the 30 kHz carrier frequency of the implanted receiver occurred within 360 ms to activate the MIP when the switch was depressed. The receiver was insensitive to the illumination level in the room and to light level changes when the room lights were turned on or off.

Ex Vivo Characterization of Battery Charge Time—The charging circuit of the electronic module connected to a drained battery was placed in the center and mid-height of the primary coil (the weakest point of the induced energy field). The battery voltage was monitored during charge and the time required to reach a full charge ($V = 3.7$ V) was measured. The experiment was repeated while the secondary coil was placed near the edge of the primary coil (the strongest point of the induced field). These measurements were performed for two primary coil dimensions:

1. A 33 cm diameter cylindrical coil with a height of 8 cm and an inter-winding spacing of 1.6 cm ($L = 12.2$ μ H, peak voltage = 320 V, peak current = 2.13 A);
2. A 23.5 cm diameter cylindrical with a height of 4 cm and windings in contact with each other ($L = 11.8$ μ H, peak voltage = 432 V, peak current = 2.4 A).

The larger primary coil was sufficiently large to be placed around a regular size rat cage so the animal could remain in its natural environment while the battery was charged. The smaller coil generated a much stronger electromagnetic field than the larger coil to allow for

a rapid charge of the battery just before the experiment but it required the animal to remain in a less familiar and more restrictive environment. Both coils were energized with the class-E amplifier as described above.

In Vivo Testing in the Animal—The electronic controller (weight = 22.5 g, length = 40 mm, width = 22 mm, height = 8.7 mm) was embedded in a two-part, medical grade silicon rubber (VST 30, Factor II, Lakeside, AZ) and connected to the hydraulic components of the MIP. The implant (weight: 32.5 g) was placed subcutaneously in the dorsal midline of a 400-g adult rat. The rat was returned to its home-cage and the primary coil antenna wound around the cage was powered for 2.5 h to charge the battery. The discharge time (the time that the LED was shining) was measured and compared to observations of the circuit *ex vivo*. Functionality of the MIP was tested at postoperative days 3, 7, and 10 in 19 rats as described in the “Results” section.

RESULTS

Ex Vivo Characterization of Battery-less MIP

When the secondary coil was moved from the center to the periphery of the 33 cm diameter primary coil, the voltage across the terminals of the energized valve increased from 4.5 to 7.2 V (angle $\alpha = 0^\circ$). The corresponding DC current (power) ranged between 8 and 13 mA (36 and 94 mW), respectively. The valve could be activated for angle α between 0° and 60° when the circuit was placed in the center of the primary coil and α up to 80° when the circuit was placed against the edge of the primary coil.

Ex Vivo Characterization of MIP with Rechargeable Battery Design

The time required to charge the battery to 3.7 V (Fig. 5) was approximately 2.5 h in the center of a 33 cm diameter primary coil and 40 min in the center of a smaller 23.5 cm diameter primary coil. These values represented worst-case estimates, with best-case figures being 42 min for the larger primary coil (14 min for the smaller one) with the charging circuit against the wall of the primary coil. The total time a fully charged battery could keep the MIP circuitry energized continuously was about 7 min (Fig. 6), far more than would be needed for applications involving bolus drug administration.

In Vivo Testing in the Animal

In the battery-less MIP, the LED became brightly lit and visible through the animal's skin immediately following powering of the primary emitter circuit around the rat cage.¹² This demonstrated that the implanted circuit was producing sufficient energy to trigger the valve. During ambulation of the animal, the implanted MIP could be triggered at all points in the cage. For rearing positions in which the animal placed its forepaws on the walls of the cage, while maintaining its hind paws on the floor, the implant moved to a position 8 cm above the center plane of the primary coil. Functionality was maintained during rearing for angular misalignment of the primary and secondary of up to 45 degrees. All 30 *in vivo* experiments were performed with the battery-less MIP design without failure and with adequate power transfer from the primary coil to the implanted secondary. There was one malfunction of the pump due to a valve failure (success rate = 97%).

The MIP with rechargeable battery was able to be successfully triggered at 3, 7, and 10 days postoperatively outside the home cage. Optimal alignment of the primary and secondary coils for charging of the battery was less critical, since the battery could be trickle charged overnight with the large 33 cm diameter primary coil wrapped around the outer wall of the home cage. The MIP with rechargeable battery was successfully used in 19 animals in which a radiotracer was injected by remote activation while the animal was freely moving inside a 1.2 m diameter circular maze (Barnes maze, manuscript in preparation).

DISCUSSION

The novelty of our current MIP design was the amount of power we transferred from our patented primary coil and its driver to the implanted receiver. We were able to transfer power of nearly 100 mW through an air gap of 16.5 cm, substantially more than is typical for RFID tags that transfer power in the μ W range. Since the implant's size had to be minimized to not interfere with the animal's normal behavior; very limited space was available for the printed coil trace. To allow sufficient power transfer, we chose a contactless power system based on a Class E oscillator. Class E oscillators are a relatively young technology, introduced in the 1970s that have found new applications since the 1990s, when it was discovered that by phase-locking the oscillator, substantial power transfer could be achieved to a receiver coil.¹⁰ Class E oscillators are presently used in clinical trials to power subminiature, injectable muscle stimulators (BIONs) for uses in physical rehabilitation.^{7,8} Our application of this technology to power our minipump is more challenging than the BION and most RFID applications for several reasons: (1) the power requirements of the MIP (mW) are a thousand times higher than that of the BION or RFID applications (μ W). (2) Unlike the BION, whose primary and secondary coils typically remain stationary and in close physical contact across the subject's skin, the MIP application requires mobility, such that the inter-coil distance changes from moment-to-moment. Given that the coefficient of inductive coupling between a large primary coil and a distant, small secondary coil across an air gap is very low, typically less than 2%, the current application presents a formidable challenge. In addition, changes in the angular alignment of the primary and secondary coils resulting from the animal's movement have to be accounted for, since these too can result in substantial degradation of power transfer. (3) In the BION and in RFID applications, the primary coil is constructed as a high-density, narrow diameter coil, which produces a strong localized electromagnetic field, thereby optimizing inductive power transfer to the secondary coil. By comparison, in the MIP application, the primary coil has to be wrapped around the animal's home-cage in order to allow for movement of the animal. This makes the coil substantially larger and the strength of the induced electromagnetic field weaker.

The use of a multi-layered printed coil virtually eliminated the individual 'tuning' of the electronic module, previously needed with hand-wound coils.¹² The current provided by this new design far exceeded the minimum current and voltage required to keep open the solenoid valve in the MIP. The use of a multilayered printed circuit coil to provide power to electronic devices is novel in that prior applications have relied almost exclusively on wire-wound coils.

The electronic module of battery-less MIP was appropriate for experimental studies carried out in a regular-sized animal cage. Adding a rechargeable power source to the MIP rendered possible applications in which the animal moved in a large experimental area such as a maze, which because of its size typically would make inductive power transfer impossible. Addition of a rechargeable power source also allowed for long-term implantation and the use of more energy-demanding components.

The battery-powered MIP included a near-infrared sensor that could be used to optically activate the implanted circuit from several meters distance, with a minimal amount of light provided by 5-pulsed LEDS, provided that the pulse pattern of these LEDS complied with the sensor requirements. Concurrently, the characteristics of the sensor rendered the circuit insensitive to ambient light levels or changes. The current provided by the new design far exceeded the minimum current required to keep the valve open.

The time required to charge the battery in the battery-powered MIP depended on the primary coil's field intensity (and thus, its diameter), the location of its charging circuit in the primary field and the cosine of the angle formed by the axes of the primary and secondary coils.¹ As the induced field density decreases and the angle increases (cosine decreases), the coupling between the two coils becomes less efficient. A similar mechanism explains our observation that the induced voltage and current decreased as the secondary coil in the implant was tilted relative to the axis of the primary coil.^{2,15,16} This progressive current and voltage loss with increasing angular misalignment was amplified when the secondary coil was placed at the periphery of the cage compared to its center. It was further accentuated with increasing heights of the secondary coil above the center plane of the primary coil. Thus, the implant circuitry was most sensitive to angular misalignment when the secondary coil was placed at the primary coil's periphery above mid plane. Such extreme angles of misalignment are typically seen during rearing behavior, in which the animal stands on its hind paws, placing its forepaws on the cage wall. Rearing could in principle interfere with the triggering of the battery-less pump. However, rearing of the animal is infrequent and short-lived, lasting no more than a few seconds at a time. The animal will typically spend >95% of the time in a 'horizontal' (four paws on the ground) position. Hence, coil misalignments that may exceed 45° during rearing are very brief and do not represent a substantial limitation. The larger primary coil ($D = 33$ cm) was preferred for overnight charging of the implant since it allowed for greater animal mobility in a familiar environment. Here as well, misalignments exceeding 45° due to rearing were infrequent and short-lived, delaying the charging process of the implanted minipump by a few minutes at most.

Acknowledgments

Supported by the NIBIB (1 RO1 NS050171). We would like to thank Drs. Jun Yang, Zhou Wang and Theodore Sadler and Ms. Yumei Guo for their contributions.

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FIGURE 1.
Volume discharge over time for the reservoir of the MIP.

FIGURE 2. Emitter circuit consisting of a class-E oscillator and switched reactance circuit. The resonant frequency of the tank circuit is set by transmission coil L and capacitor C_1 . Tuning is accomplished by proportional application of C_2 .

FIGURE 3.

(a) Circuit diagram for implant receiver circuit for battery-less MIP design. Prototype of the battery-less MIP electronic module prior to casting in silicone (length = 40 mm, width = 21 mm, height = 8.4 mm). (b) Front of the circuit. (c) Back of the circuit.

FIGURE 4.

- (a) Circuit diagram for implant receiver circuit for MIP design with the rechargeable battery.
 (b) Prototype of the MIP electronic module (prior to casting in silicone) with printed coil inside the layers of circuit board (length = 40 mm, width = 22 mm, height = 8.7 mm).

FIGURE 5.

Time to charge the battery to 3.7 V (*ex vivo* testing, in the center of the primary coil). Data was obtained with the implant placed at the mid height of primary coils with diameter = 33 cm (■) and 23.5 cm (▲) and with the axes of the primary and secondary coils in alignment.

FIGURE 6. Time course of the battery current and voltage during powering of the MIP on the bench-top. The threshold voltage to keep the valve open was 2.4 V.