33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

A high bandwidth fully implantable mouse telemetry system for chronic ECG measurement

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***Abstract*—We report on the development of a novel system that enables the wireless transmission of high-bandwidth physiological data from a freely moving mouse. The system employs inductive power transfer (IPT) to continuously power a battery-less transmitter using an array of overlapping planar coils placed under the animal. This arrangement provides a minimum of 20mW at all locations and orientations across the mouse cage by selecting a coil which will sufficiently power the transmitter. Coil selection is performed by feedback control across the 2.4 GHz wireless link. A device was constructed utilizing this novel IPT system and was used to capture high-fidelity electrocardiogram (ECG) signal sampled at 2 kHz in mice. Various attributes of the ECG signal such as QT, QRS, and PR intervals could be obtained with a high degree of accuracy. This system potentially provides lifetime continuous high bandwidth measurement of physiological signals from a fully implanted telemeter in a freely moving mouse.**

I. Introduction

The development of fully implantable telemetry has provided researchers the ability to obtain valuable measurements of physiological signals over extended periods of time in freely moving laboratory animals. Their use in mice has been driven by the need to remove stress-inducing tethers, telemetry 'backpacks' and tail cuffs, to avoid potential sources of infection from transcutaneous leads, and to allow conscious freely-moving continuous measurements over the animal's lifetime.

In general, mice are the most commonly used laboratory animal due to their low ongoing maintenance costs and the availability of genetic knockouts. Fully implantable telemetry is extensively used in larger animals such as rats and rabbits. The availability of fully implantable telemetry suitable for continuous lifetime measurement in mice is limited due to technical challenges involved in miniaturization.

There is an inherent tradeoff in the development of mouse telemetry between bandwidth, size and longevity. Longevity and continuous recording are important parameters in chronic research studies for detecting rare events such as cardiac arrhythmia[1] or studying long term trends for example ST interval[2]. High bandwidth is required to capture high frequency components for accurate temporal measurements such as QT, QRS and PR intervals of electrocardiogram (ECG)[3]. A band limited signal of 100 Hz such as in [4] has a very low temporal accuracy, they observed a mean Q-T interval of 54 ms compared to ~25 ms of other investigators. For a 200Hz sampling rate the error based on the temporal accuracy is ±10 ms, while for a 2 kHz sampling rate the error is ±1 ms. Therefore to accurately measure intervals of the ECG waveform a high sampling rate is required.

The problem with providing continuous high bandwidth data relates to the power consumption and size and weight if an implanted battery is used.

Several groups have developed mice telemetry with different approaches. [5] has developed a fully implantable system for mouse biopotentials. This uses an ASIC for circuit miniaturization and a non-rechargeable battery. This approach achieves a good tradeoff with a battery lifetime of 2 months and a bandwidth of 1-200Hz (ETA-F10, Data Sciences International, MN, USA). This system has been expanded to measure other physiological parameters such as pressure and is now commercially available. Other commercial units include those from Mini Mitter (OR, USA), which have a selection of battery-less telemetry for very-low-bandwidth signals such as temperature and activity. Other groups have concentrated on obtaining higher bandwidth measurements. [6] have developed a mouse telemeter which has a bandwidth of 300 Hz but relies on the circuit to be external to the mouse. Inductive power transfer (IPT) has been employed by [7] to develop a 400 mg battery-less telemeter to provide 100 Hz bandwidth with 8-bit accuracy. Continuous measurement is also sacrificed as it relies on sufficiently good field alignment.

For larger animals, such as rats and rabbits, IPT has been used to provide a method of recharging the battery wirelessly to enable high bandwidth measurements without sacrificing longevity. Budgett et al [3] has developed rat telemetry for

Manuscript received March 25, 2011.

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monitoring biopotentials which provides high-fidelity data from a sampling rate of up to 8 kHz. This is achieved via a pad placed under the animal's cage, to continuously recharge the telemeter's internal battery.

The battery in the telemetry unit is the principle obstacle to implant miniaturization. By replacing the battery with an IPT system, the telemeter can be miniaturized, while retaining the ability to make high-bandwidth measurements. However, without a battery to act as a buffer the device must be designed to ensure that the field provides power regardless of the orientation and location on the pad.

There are two approaches which have been explored to maintain IPT over arbitrary orientations and locations: The use of multiple primary coils or multiple secondary coils. The former involves arranging multiple primary coils around the exterior of the powered volume, so that the magnetic field at any given point can be controlled to match the orientation of the pickup. However this is impractical due to the requirement of such a large powered volume [8, 9]. The latter approach uses multiple orthogonal secondary coils, allowing for the use of a single solenoidal primary coil, which can easily fill the cage volume with a sufficiently strong magnetic field for power delivery. Employing multiple secondary coils reduces the complexity of power control at the expense of additional telemeter volume [8, 10].

We have previously reported in [11] on the validation an IPT system for the continuous powering of a mouse telemeter, and have demonstrated 20 mW power transfer regardless of orientation and location on the pad. This approach employed the use of multiple planar primary coils to generate a magnetic field which is aligned with the telemeter IPT pickup.

In this paper we report on the progress on this novel wireless power system to demonstrate uninterrupted high-bandwidth ECG measurement (2 kHz sampling) regardless of orientation and location over the pad from a transmitter suitable for implantation in mice.

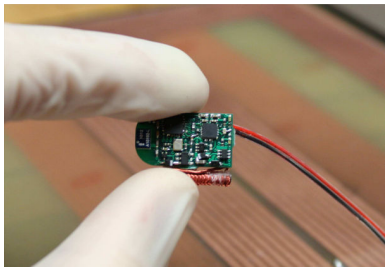

Fig. 2: A photo of the prototype transmitter.

II. System Overview

A. Wireless Power

The wireless power system has previously been described [11]. The coils have a planar arrangement and are distributed over four layers with a repeating pattern which is displaced by half a diameter per layer. This setup creates magnetic fields which are approximately aligned with each of the three axes at all locations. Therefore by selecting the appropriate coil, sufficient power is available in any orientation regardless of the location on the pad.

The coils are driven by a full bridge series resonant inverter. As shown in Fig. 1, the coils (L1…LN) can be electronically switched in parallel to the resonant capacitor (C) via solid state relays (S1…SN). The resonant frequency is tuned using a phase-locked loop, in order to lock the resonant current and gate drive signals in phase.

The telemeter has a parallel resonant pickup coil tuned to the resonant frequency. A 690 uF surface mount capacitor is used as an energy buffer to provide continuous operation during interruptions in the field while changing between coils. This minimizes the transmitter volume as a battery and charging circuitry is not required.

A prototype system has been built which can deliver 20 mW of power to an arbitrarily oriented pickup coil over

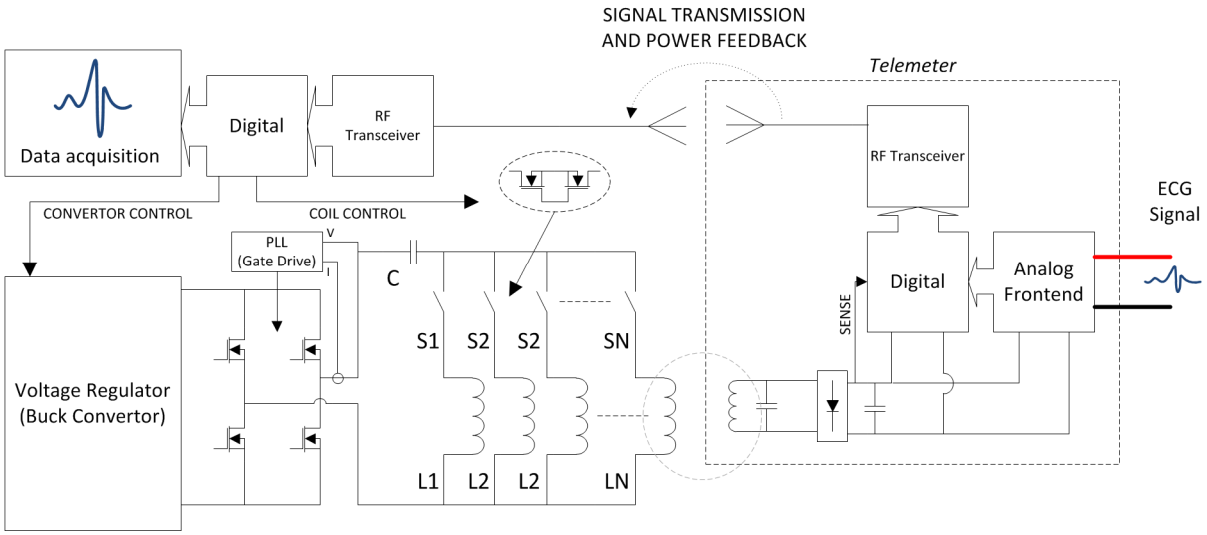

Fig. 1: The fully implantable telemetry system for ECG measurement in a mouse including ECG data acquisition, wireless power generation and power feedback coil control.

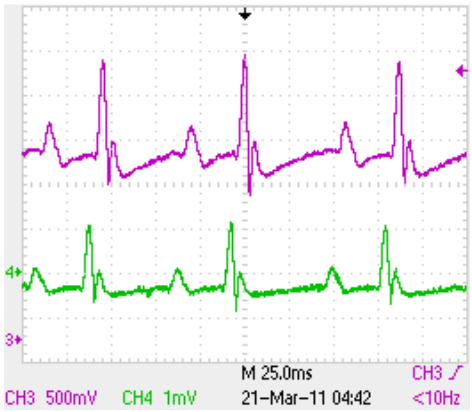

Fig. 3: Validation of ECG from arbitrary waveform generation. Top: ECG waveform acquired from telemeter (amplified and offset for 0-4V acquisition). Bottom: Amplified ECG waveform from output of signal generator.

an area of 150 mm x 375 mm. This design can be scaled up to the size of a mouse cage by adding more coils in the repeating pattern.

B. *Transmitter*

The transmitter has a weight of ~2.4 g, which can be reduced with the use of thinner and flexible PCBs. It contains an nRF24LE1 (Nordic Semiconductor Inc.) microcontroller with embedded 2.4 GHz RF transceiver. The analog front-end has an INA333 (Texas Instruments) instrumentation amplifier which directly drives the input to the 12bit ADC of the microcontroller. The ECG leads are AC-coupled with the instrumentation amplifier to remove the DC component and to allow for a greater gain on the amplifier. The ECG signal is sampled at 2 kHz. The ability to capture ECG was validated by simulating a mouse ECG waveform from an AFG3022 (Tektronix) function generator, attenuated at a ratio of 100:1 to produce an mouse ECG signal with an amplitude of ±1 mV, and a heart-rate of 12 Hz (720 bpm). The signal is fed into the ECG leads on the telemeter, transmitted wirelessly to the receiver where it is acquired digitally and compared against the known arbitrary signal (Fig 3.).

The received power is sampled after the rectifier and averaged over 4 samples for the feedback control of the coils. The RF transceiver packets are divided into three types: a signal packet sent every 12 samples; a power packet sent every 4 samples and a packet warning of imminent power loss.

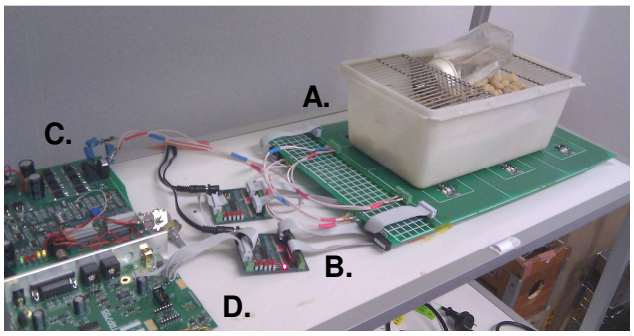

Fig. 4: A. Charging pad with array of planar coils. B. Port expanders to switch coils. C. IPT convertor D. Digital receiver and coil control unit.

C. *Receiver and Power Control*

The receiver used is an nRF24LE1 motherboard and development kit (Nordic Semiconductor Inc.). Data transmitted by the receiver over RS232 included the 2kHz ECG signal, the wireless power monitor line on the transmitter and the coil which is currently selected. These were captured in Matlab 2010a (Mathworks) and later exported to Labchart 7 (AdInstruments Inc.) for ECG analysis. A MCP23S17 (Microchip Technology Inc.) port expander is used to multiplex the coil switches. A SPI output is produced by the receiver unit to select which coil is to be energised.

The control algorithm changes the coil based on reaching a minimum threshold (3.5 V) on the wireless power monitoring on the transmitter. The sequence of coil selection is based on the evidential probability of changing to each coil calculated from previous data sets. The system holds on each coil, taking into account the time it takes for the coil to change and receiver to be updated with a value corresponding to power received for this coil (~3 ms). This provides the capacity to power the telemeter moving linearly between two points up to 0.194 ms^{-1}. In the case where there is no power received, the onboard buffer will power the transmitter for ~180 ms before shutdown. In the worst-case scenario where the transmitter has shut down and no packets are received, it will maintain power to each coil so that it has time to start up the transmitter and to receive a response on the status of the field (~60 ms).

III. Experimental Procedure

All procedures were approved by the Animal Ethics Committee of The University of Auckland (AEC #R810). The mouse was anesthetized with ~2.5% Isoflurane. A tail pinch confirmed a suitable level of anesthesia. A midline incision was made through the skin to expose the muscle layer. A thin layer of muscle was lifted using forceps to place the ECG leads 10mm apart on both side of the chest. With the leads firmly in place the wireless power control was turned on and the transmitter energised. Validation of the analog circuit was effected by capturing the ECG signal of an anesthetized mouse. The wireless power- and control-system's ability to provide continuous operation was validated by moving the transmitter into arbitrary orientations and locations across the pad during ECG data acquisition.

IV. Results and Discussion

The ECG waveform acquired from the transmitter was averaged over 15 minutes to calculate various ECG attributes. These were calculated in the ECG analysis extension in Labchart 7 (AdInstruments Inc.) using the mouse detection and analysis settings. The following averages were calculated: Heartrate: 515.7 bpm (8.6 Hz), QT

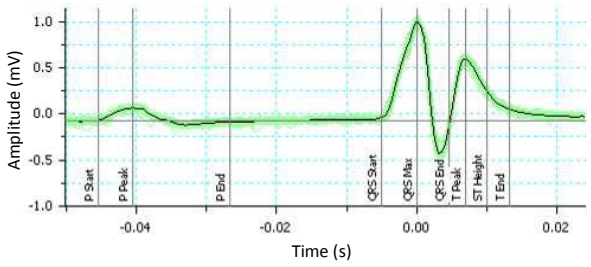

Fig. 5: Black line is ECG waveform averaged over 50 beats, Green lines are individual ECG waveforms used for averaging.

interval: 17.7 ms, QRS interval: 9.1 ms, PR interval: 40.6 ms. The mean amplitude of the R wave: 1.1 mV, and S wave: -0.32 mV, resulting in mean range of 1.42 mV.

The system was able to continuously power the transmitter and continuously acquire ECG data while the transmitter changed orientation and location over the pad. A typical example is shown in Fig. 6. As the transmitter moves across the pad, a misalignment of the pickup coil and the field occurs. This is shown by a drop in the wireless power monitor line. The threshold (3.5V) is reached and the control system compensates by changing the energized coil, to find another one which will sufficiently power the transmitter. The system selects the next coil (#1). Once the time constant is reached a packet is sent to the receiver on the ability of this coil to power the transmitter. The receiver acknowledges this packet and detects that it is also insufficient to power the transmitter. It then selects the next coil (#2) and ultimately detects that this coil can provide sufficient power. This is shown by the power monitor line jumping up to 4.0V. During this process, data acquisition continued uninterrupted and provided continuous measurement of the ECG waveform at 2 kHz regardless of orientation and location on the pad.

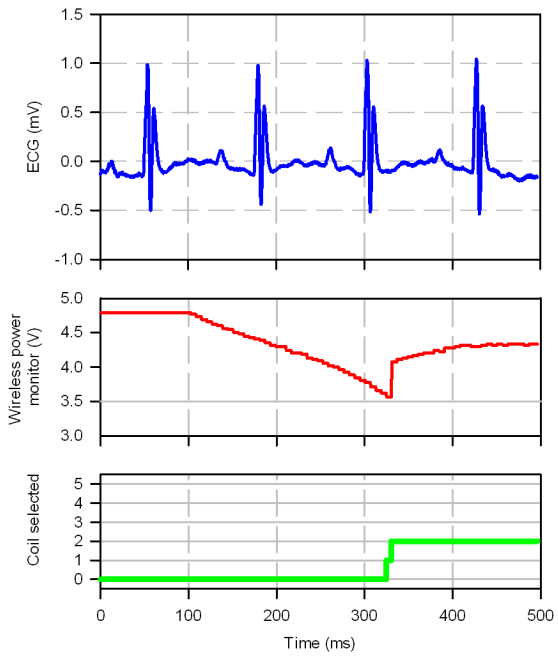

Fig. 6: Continuous ECG measurement while telemeter is moving, illustrating the drop in received power until threshold is reached, and switching to another coil.

V. Conclusion

We present a high bandwidth (2 kHz sampling), fully implantable telemetry system for the continuous (potentially lifetime) measurement of physiological signals in mice. We employ a novel inductive power transfer setup to continuously power the battery-less transmitter regardless of orientation and location of the animal within its home cage. We have validated the ability of this system to continuously obtain high-frequency measurements by capturing electrocardiogram (ECG) data in an anesthetized mouse from the wireless transmitter. We have also shown the ability to continuously power the transmitter and obtain uninterrupted data acquisition regardless of orientation and location of the transmitter over the pad.

Acknowledgment

Matthew Lim, Dr. Sarah Jane Guild, Stephanie Lindsay

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