Wireless Multichannel Integrated Potentiostat for Distributed Neurotransmitter Sensing

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***Abstract*— Sensing neurotransmitters is critical in studying neural pathways and neurological disorders. An integrated device is presented which incorporates a potentiostat and a power harvesting and telemetry module. The potentiostat features 16 channels with multiple scales from microamperes to picoamperes. The wireless module is able to harvest power through inductively coupled coils and uses the same link to transmit data to and from the potentiostat. An integrated prototype is fabricated in CMOS technology, and experimentally characterized. Test results show RF powering introduces noise levels of 0.42% and 0.18% on potentiostat current scales of 500pA and 4nA respectively. Real-time multi-channel acquisition of dopamine concentration *in vitro* is performed with carbon fiber sensors.**

I. Introduction

The behavior of chemical messengers is crucial to the overall understanding of the entire nervous system. These chemicals play a major role in the mechanisms of several neurological disorders such as Parkinsons disease and epilepsy. Electrochemical sensing of certain electroactive neurotransmitters (e.g. nitric oxide, dopamine) is very attractive due to the high sensitivity, rapidity and the ability to perform distributed measurements with this method [1], [2], [3].

Electrochemical measurements are based on oxidizing or reducing the neurotransmitters at electrodes held at a potential characteristic for that specific neurotransmitter (the redox potential) with respect to a reference electrode. As neurotransmitter molecules get adsorbed at the electrode surface there is an exchange of electrons, leading to a net current into or out of the electrode. These redox currents are directly proportional to the neurotransmitter concentration and range from picoamperes to microamperes for physiological concentrations of neurotransmitters. Traditionally these electrochemical measurements are performed with a bench-top potentiostat, an instrument that is capable of measuring current while maintaining a constant potential (the redox potential). These single channel instruments are large and expensive, making multi-channel recordings beyond the reach of standard laboratories.

A multi-channel VLSI potentiostat has been created to address these concerns. This microchip is compact and has many advantages over traditional devices. However, this device is still unsuitable for implantation in the human body. In order to operate, implantable devices require power and duplex data communication, usually supplied by wires connected through the skin. This wiring or tethering limits the recording range in awake, behaving animals in chronic studies [4], [5]. Techniques to harvest power allow these wires to be removed.

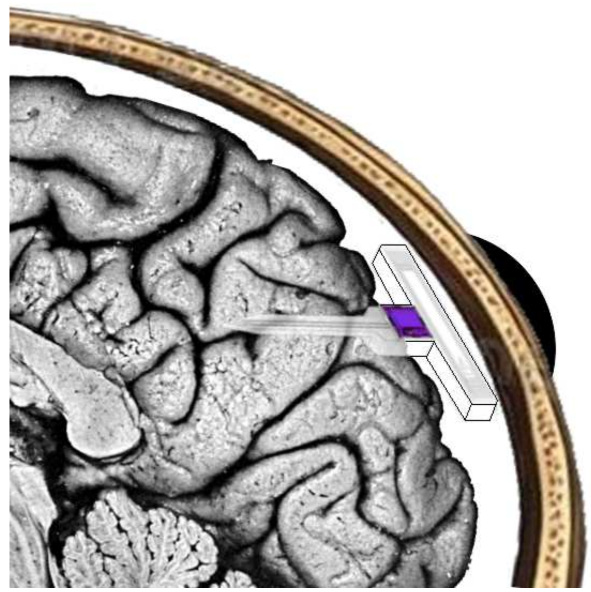

Fig. 1. Envisioned application of the probe with integrated VLSI potentiostat (on the base of the probe), electrochemical sensors (on the shank of the probe), and transponder coil (on the wide end of the probe).

Energy harvesting uses the external environment as a source of energy (e.g. temperature gradients, wind). For example, devices such as the Smart Dust distributed networks make use of many different types of transducers, from solar power to vibration transducers [6]. Unfortunately, most of these types of energy gathering methods are unsuitable for a device implanted in the human body. A very promising alternative for implanted devices is RF power harvesting through inductive coupling [7]. In addition to gathering power, this technology can also be used to send data back to the base station, creating a two-way link. The principles of the technique are the same as those behind the increasingly common RFID (radio frequency identification) tags.

This paper presents a solution to these problems and details the basis of a fully implantable VLSI potentiostat. The VLSI potentiostat circuitry [8] has been paired with inductive coupling and telemetry circuitry [9]. The resulting single

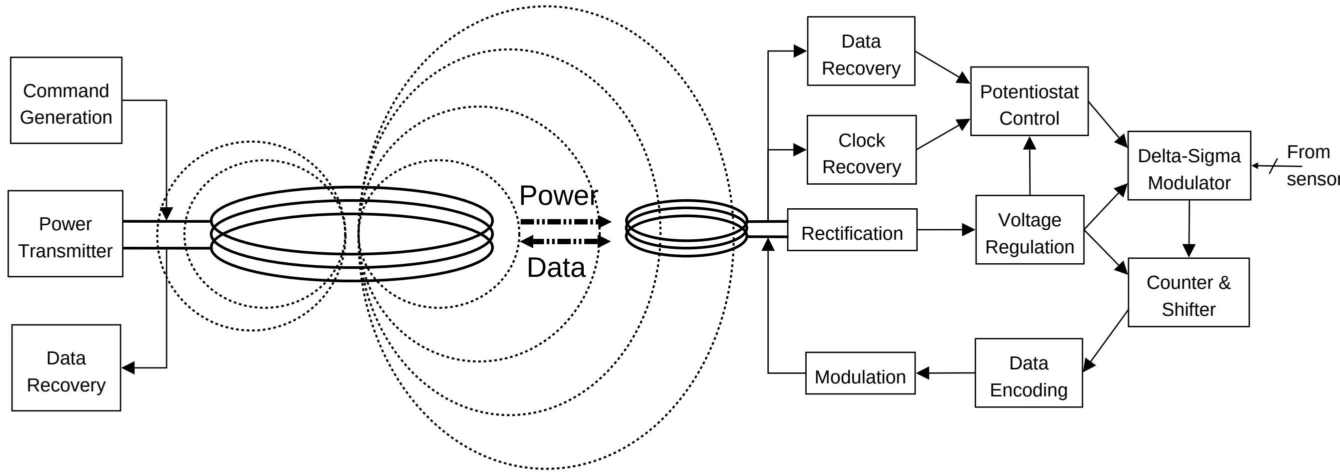

Fig. 2. Block diagram of overall RF Potentiostat system, including external base station.

microchip is able to operate with no hard wired connections apart from those connecting the sensors to the electronics, and thus could be implanted without the need of wires going to the base station outside the body. The design can be integrated along with the sensor arrays developed by our group [10], [11], [12] to create a fully autonomous neural probe, as envisioned in Figure 1.

II. Chip architecture

A block diagram of the entire RF Potentiostat is shown in Figure 2. The system is designed to use a single channel for both communications and power. A base station located outside the body drives the transmitter coil with a current to produce a magnetic field. This field induces a current in the implanted coil that can be converted into a DC voltage through the use of a rectifier and regulator. This voltage is then used as the supply for the potentiostat circuitry. In addition to power, this carrier wave also provides a system clock and can carry commands or data from the external base station. The carrier waveform for this system is a sinusoid of 4 MHz, leading to a basic system clock at this frequency. This clock is then used to generate a 1 MHz system clock for use in the potentiostat control logic.

Commands entered on the carrier wave are decoded via a central potentiostat control unit. This module allows the gain and resolution of the delta-sigma A/D to be set remotely. The control unit is also responsible for the generation of a readout clock that sends data stored in the shift register to the output channel. A command begins the sequence of actions. It can either be for configuring a conversion property (gain, resolution, or reference current are all stored in memory until overwritten by the next command to change these settings) or for starting a conversion cycle. After the conversion cycle, the 16 bits representing the digital value of input current of each channel are shifted out bit-serially using clock independent of system clock and 256 cycles are necessary to read out all 16 channels. As the data is read from the shift register it is encoded for transmission on the back pathway. This is accomplished through the same coils used to transfer power and data (note that while power is continuously transferred, data can only be transferred in one direction at any one time).

III. Chip characterization

For characterization, transmitter coils described in [9] were used to transfer power. A custom PCB was developed with jumpers allowing power, clocks and control signals to be independently routed to the potentiostat from either the power harvesting and telemetry module on chip or external sources. A class-E transmitter board was developed to allow data and power to be transferred to the main system board. This board interfaced with a data acquisition card, allowing data to be recovered by a computer. This pathway was tested to insure proper transfer of data at different frequencies. Data was encoded using a modified Miller encoding scheme, in which a one is represented by a short pulse while no change in state is

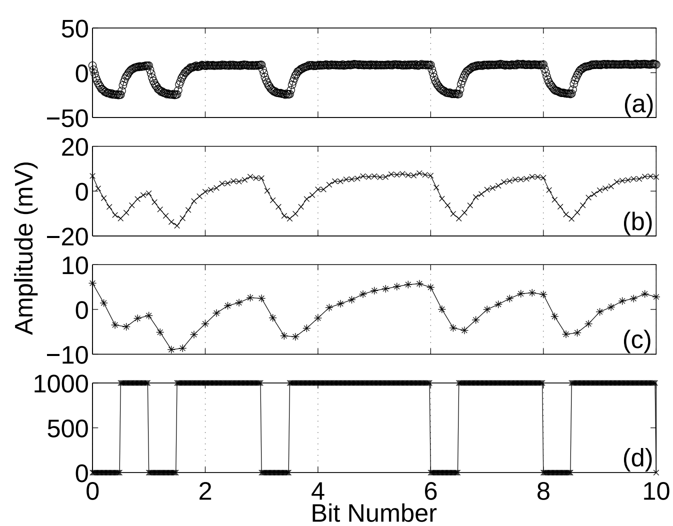

Fig. 3. Comparison of recovered data signal at different frequencies (a: 1kHz, b: 5 kHz, c: 10 kHz, d: original data stream). The Miller encoded data stream is ’1101001010’.

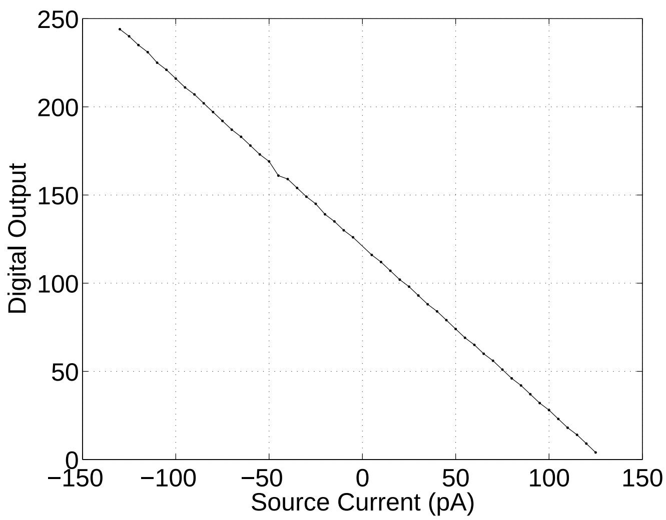

Fig. 4. Digital output (read directly from the RF Potentiostat) as a function of the input current for gain of 8192 and oversampling ratio of 256. Current was supplied by a Keithley source meter.

sent for a zero. Figure 3 illustrates the data signal as ecovered by the computer. Subplot (d) represents the original digital signal. Subplots (a) through (c) represent the recovered signal at frequencies of 1, 5 and 10 kHz respectively.

To test the potentiostat, a Keithley model 236 Source Measure unit (Keithley Instruments Inc., Cleveland, OH) was used to sweep current in the range of -125pA to +125pA with a step size of 5pA. Jumpers were set to autonomous mode of operation without any external source. The potentiostat [8] gain and OSR were set to 8192 and 256 respectively. The reference current was set to 1.2μA and the redox potential to 1V. Figure 4 shows the digital output of the potentiostat as a function of the sourced current.

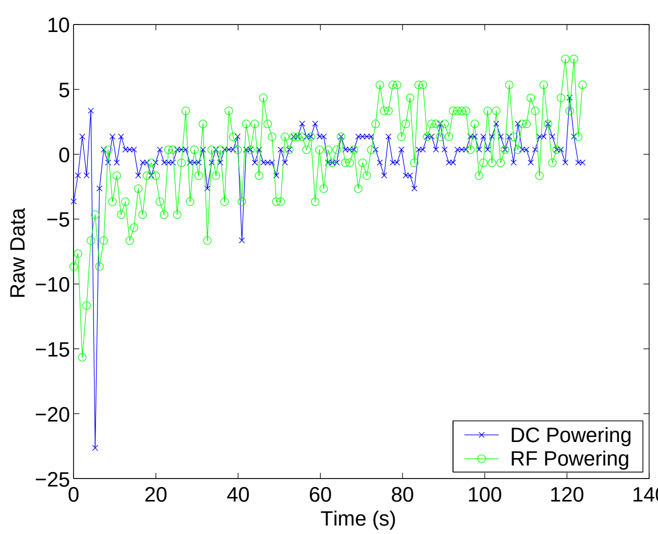

Fig. 5. Comparison of the noise in the two types of powering. The offset of the signals has been removed. The resolution and gain were 128 and 8192, respectively.

Settings		
Input current	Gain	OSR
500pA	2^{10}	2^{10}
4nA	2^7	2^{13}

(a)

RF Powering			
Input current	σ	Equiv. current	% error
500pA	1.093	2.1pA	0.42%
4nA	3.821	7.5pA	0.18%

(b)

DC Powering			
Input current	σ	Equiv. current	% error
500pA	0.705	1.4pA	0.28%
4nA	2.513	4.9pA	0.12%

(c)

TABLE I

Noise levels inherent in the system. (a) shows the potentiostat settings, (b) and (c) show RF and DC powering respectively.

For estimating the noise introduced by the RF power harvesting, a constant current was input to the potentiostat under both DC (external source) and RF (autonomous operation) powering. Figure 5 shows the potentiostat outputs for both cases. The standard deviation of the resulting digital values approximates the noise inherent in that system. The results are summarized in Table I. As can be seen, using an RF supply does introduce more noise than using a DC supply. However, the amount of noise for both current levels is small, always less than 1% of the base current.

IV. Neurotransmitter Measurements

The chip was used for potentiostatic measurements of the neurotransmitter dopamine in a phosphate buffered solution (PBS). A standardized solution of dopamine was prepared thus. 95mg of dopamine hydrochloride (Alfa Aesar, Ward Hill, MA) was dissolved in 99mL of deionized water. 1mL of perchloric acid (Alfa Aesar, Ward Hill, MA) was added to prevent spontaneous oxidation of dopamine. The solution thus obtained is 5mM. A carbon fiber electrode CF30-250 (WPI, Sarasota, FL) and an Ag/AgCl reference electrodes (Bioanalytical Systems, West Lafayette, IN) were introduced into a stock solution of 20mL PBS (Biofluids, Rockville, MD) at pH 7.4. The chip was supplied entirely by power harvested by it over an inductively coupled link with an external power transmitter. The gain and the resolution of the chip were set to 8192 and 8 bits respectively. Reference current was set to 1.2μA. The carbon electrodes was set to a redox potential of 0.9V with respect to the reference electrode. Five boluses of 100μL of the 5mM solution of dopamine, leading to final concentration of 150μM in steps of 25μM, were added to the PBS. The solution was magnetically stirred to avoid diffusion transients. Figure 6 shows the current measured by the potentiostat in response to the various concentrations of dopamine.

Figure 7 shows a static calibration curve with the current measured by the potentiostat plotted against the dopamine

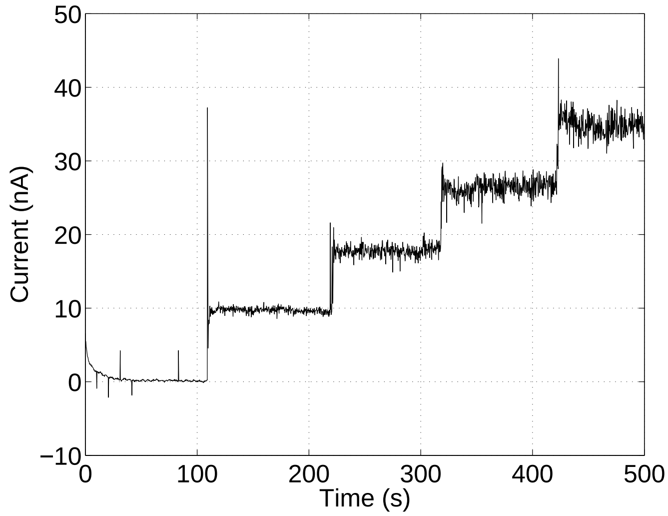

Fig. 6. Real time neurotransmitter monitoring by the chip using the commercial CF 30-250 as the working electrode. Levels correspond to dopamine concentration changes of 25 μM.

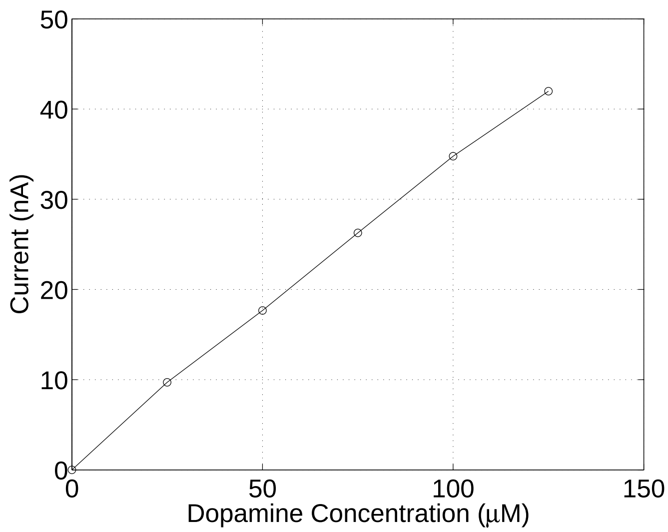

Fig. 7. Calibration curve extracted from real-time measurement of dopamine concentrations in solution.

concentration. The currents are averages of the equilibrium currents for each dopamine concentration shown in Fig. 6.

V. Conclusion

In this paper, we present the design and development of a self-contained wireless multichannel potentiostat for neurotransmitter measurements. A microchip was designed incorporating the 16 channel potentiostat [8] and an inductive power transfer & telemetry module [9] with additional control and interface circuitry. This chip was fabricated and tested. Characterization results show picoampere sensitivity under wireless operation with no external power supply. In this mode, the chip was used to monitor concentration of dopamine in the micromolar range. Good temporal response and linearity were seen.

A long term goal of this work is to develop an implantable, autonomous, monolithic, real-time neurotransmitter monitoring probe. Such a probe would be useful in neuroscience research involving the role of neurotransmitters such as dopamine, glutamate and nitric oxide in the nervous system. Neurochemical measurements would complement electrophysiological measurements for a holistic picture of neural signal analysis. Research on animal models of disorders like epilepsy and stroke would benefit from neurochemical detection using integrated systems. Ultimately, using microfabricated sensors and VLSI circuits in an integrated package could also be useful in developing implantable neural prosthetic devices.

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