In Vivo Evaluation of a Fully-Passive Wireless Neurosensing System

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***Abstract*—Neural implants are used to continuously record essential signals in studies of neurological disorders. Existing systems involve the use of invasive procedures and revision surgeries to maintain adequate system performance. Our previous work demonstrated a fully-passive wireless system, tested *in vitro,* and was demonstrated capable of sensing even minute neural signals. This recorder has a minimum detectable signal (MDS) below 15 µV in amplitude and a RF sensitivity down to about - 135 dBm. While results have been promising, this system is yet to be used to study neurological disorders, the final intended application of the system. In this paper, for the first time, we evaluate the wireless neurosensing system's ability to capture the characteristic components of epilepsy, namely interictal epileptiform discharges. The present validation of this technology has great future clinical implications in neuroscience, especially epilepsy studies.**

***Keywords*—Biomedical Telemetry, Brain implant, Electroencephalography, Neuroscience**

I. Introduction

Wireless monitoring of neural activation is a growing field, with endless applications in research, treatment, and even brain-computer interfacing/prosthesis control. When implanted these systems usually apply a technique named electrocorticography (ECoG). This differs from its noninvasive counterpart (electroencephalography, EEG) in that electrodes are placed on the cortical surface [1]. While invasive, ECoG omits the attenuating properties of the skull and can be used to obtain high spatial and temporal resolution recording of neural activity [1]. Current technology requires protruding wires, a heat-generating power source and often times revision procedures, greatly affecting patient quality of life [2].

Previous work has led to the development of a fully-passive wireless neurosensing implant equipped with the necessary neural probes, capable of recording these signals [2], [3]. In this paper, we build on this work, by testing the system using two distinct but clinically-relevant experimental scenarios. To begin with, we use the device to record minute event-related potentials resulting from somatosensory stimulation of an animal hind limb. This allows us to test the system's ability to sense and transmit small time-locked changes in neural activation resulting from a pulse stimulation paradigm.

In addition, we gauge a possible future application for the system by recording neural activity in an animal model for epilepsy. Epilepsy is one of the most common neurological disorders. According to a 2018 report from the World Health Organization (WHO), approximately 50 million people worldwide suffer from epileptic seizures. This is a disorder that about 70% of the time responds to medical treatment. For the remaining 30%, treatment may include excision of the seizure onset area, depending on the source location. A device such as our neurosensing system would allow doctors to continuously monitor patients in an unobtrusive manner, increasing their chances of precisely locating this onset zone for future surgeries and to further study this disorder.

II. Neurosensing System

Fig. 1 presents our fully-passive and wireless system for monitoring neural activation along with its intended method of use [2]. Fig. 1 also depicts the key components of the system, namely a) the implant, b) the interrogator antenna, c) neural probes, and d) demodulation circuit. The implant is meant to be placed beneath the skin using a small incision and is connected to the brain through the neural probes. Fig. 1 also highlights how the implant transmits the neural signal to the exterior interrogator. This signal is then filtered, amplified and extracted at the demodulation circuit.

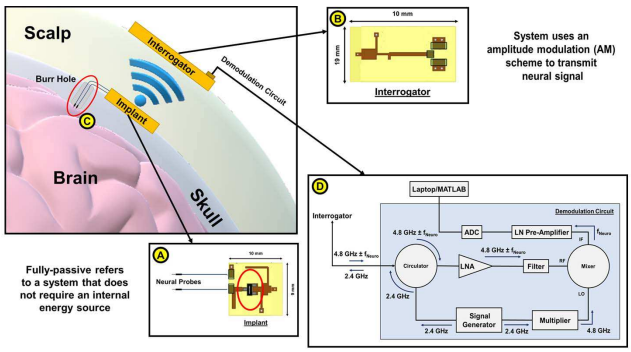


Fig. 1. Neurosensing system set up and major components: a) the implant, b) interrogator antenna, c) neural probes and d) demodulation circuit. Schematic of implant and interrogator obtained from [2].

This work was supported by the U.S. National Science Foundation (NSF) under Award Number 1763350.

The implant and interrogator have dual-band E-shaped patch antennas designed to radiate at 2.4 GHz and 4.8 GHz± f_{neuro} [2], [4], [5]. The implant is triggered by the 2.4 GHz carrier signal generated by an RF source, like a vector signal generator and transmitted using the interrogator. This carrier signal is harmonically mixed in the anti-parallel diode pair (APDP), with minimal conversion loss, with the neural signal sensed at the neural probes[2]. The modulated signal is then backscattered to the interrogator [2]. As previously mentioned, the neural signal can then be extracted using the demodulation circuit reported to have a very low noise figure of 3.8 dB [2]. Since the implant needs the carrier to be modulated by the neural signal the recording continues for the duration the 2.4 GHz signal is supplied.

A characterization of the implant revealed an input impedance several orders of magnitude lower than that of most biopotential recording devices. To be exact, the implant has an input impedance of about 50 Ω compared to ~10 MΩ of most systems [3]. Different developed probes were characterized and tested with the system to closely match the electrode and implant. The objective of this was to make it possible to record diminutive signals in the 10s of microvolts. Parameters essential in lowering the impedance of probes include geometry, material, and surface area as tested and presented in [3]. The recordings presented here were performed using carbon probes and surgical steel probes.

III. Methods and Procedures

All procedures performed as part of this experiment were approved by and carried out in compliance with the Institutional Animal Care and Use Committee (IACUC) at Florida International University (Approval No. 17-042). Wistar rats (Charles River Laboratories, Wilmington, MA) were housed in standard cages at a 12h-12h light-dark cycle with free access to food and water and were allowed to acclimate for at least a week before performing any of the experiments detailed here.

A. Animal Preparation

Prior to the recording, the rats were anesthetized with an isoflurane/ O_2 mixture (1 L/min, 14.7 PSI). During the initial induction a 5% mixture was used and this was reduced to 1.5-2.5% while setting up for the experiment and fixing in a stereotaxy (Narishige, Japan). Before starting the recording, the rat was switched to a sedative (Dexdomitor, 0.25 mg/kg). Body temperature was regulated using a heating pad (TPZ-0510EA, Texas Scientific Instruments, LLC) and a water pump (TP700, Texas Scientific Instruments, LLC). A breathing monitor was used to ensure respiration rate remained between 45-55 breaths per minute. Vitals observed throughout the procedure using AD Instruments PowerLab 8/35 data acquisition device and LabChart software to ensure animal stability.

B. Somatosensory Evoked Potential (SSEP) Recording

Typically, normal neural activation does not exhibit a distinct waveform that is easily recognizable. For the initial

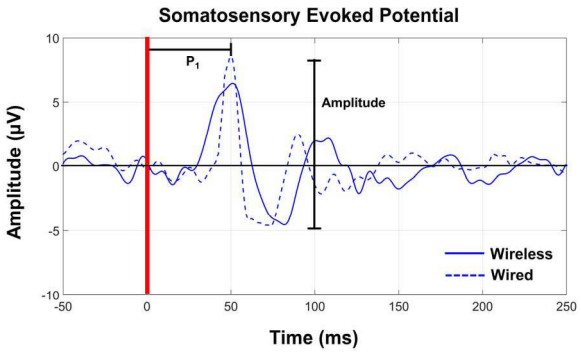


Fig. 2. Overlay of somatosensory evoked potential extracted from the wireless and wired recording.

in vivo recording of neural activity with the neurosensing system, we implemented a somatosensory hind limb stimulation paradigm. During, processing we extracted an evoked potential from the recording. To stimulate the rat hind limb, we generated electrical pulses (3 Hz, 2.5 mA, and 0.5 ms duration) using an isolated pulse stimulator (AM Systems Model 2100) and supplied it using two small needle electrodes inserted subcutaneously. This stimulation induced specific neural activation in the corresponding somatosensory cortex area of the rat and our goal was to record this signal. The AD Instruments PowerLab 8/35 data acquisition device was used to save the demodulated wireless neural signal and a trigger signal from the pulse stimulator denoting the stimulus onset at a 2 kHz sampling rate. This signal played a key role during evoked potential extraction. Our region of interest was limited, this made it difficult to record with the wireless and wired system simultaneously, therefore the two recording were performed sequentially under identical conditions.

At the signal processing stage, a 60 Hz notch filter and a 1 – 125 Hz bandpass filter was used. The wireless and wired somatosensory evoked potential was extracted from approximately 1000 trials, where each trial corresponds to a pulse stimulation of the hind limb. The recordings were divided into 300 ms segments in reference to the stimulus onset trigger. EEGLab, a Matlab-based software was used to average the neuropotentials. We note that during the recording a phantom layer was used between the implant and interrogator to emulate skin dielectric properties at 2.4 and 4.8 GHz, thereby mimicking a fully-implanted scenario.

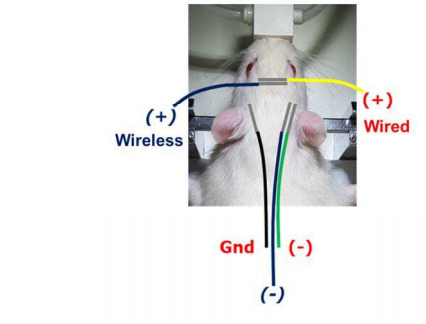
C. Temporal Lobe Epilepsy (IED) Induction

The pilocarpine model for temporal lobe epilepsy (TLE) was used on rats weighing between 120-150 grams at approximately 4 weeks of age. The rats were given an initial dose of N-methyl scopolamine (0.5 mg/kg) intraperitoneally (i.p.) and thirty minutes later an i.p. pilocarpine injection (350 mg/kg). These rats were observed for 90 minutes to confirm status epilepticus onset based on the Racine scale, an established method for quantifying activity associated with seizures. During this observation period, rats displaying Racine scale activity were administered an i.p. phenobarbital injection (20 mg/kg) to reduce the mortality rate. These rats were observed to confirm the development of chronic

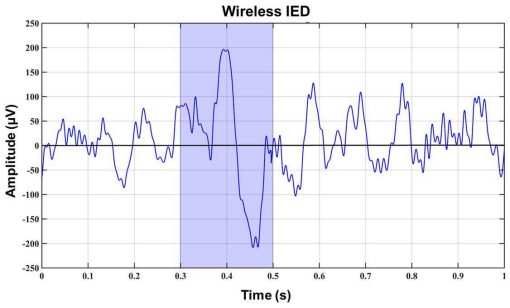
seizures before performing neural recordings. This is an established procedure known as the pilocarpine model, presented in [6] and similar to that presented in [7].

D. Interictal Epileptiform Discharge (IED) Recording

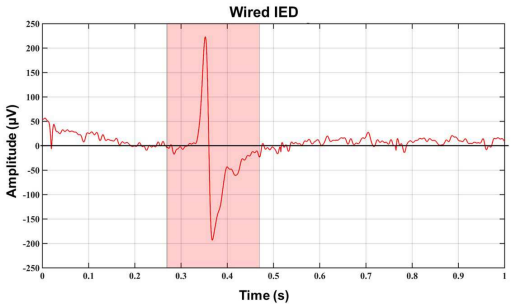
Surgical steel probes were used to record neural activity. Fig. 3 shows our probe set up, which allowed us to record simultaneously with our wireless system and a wired system (AD Instruments Animal Bio Amp). Multiple recordings of spontaneous activity were performed, each with an approximate duration of 20 minutes at a 2 kHz sampling rate. During processing a 60 Hz notch filter was used to remove power line interference. Afterward, the signal was bandpass filtered from 1 – 100 Hz, as is typical when analyzing this epileptiform activity [7]. Matlab was used to identify IEDs in the wireless and wired recording. During the recording, again a phantom layer was inserted between the implant and the interrogator.



(a)



(b)



(c)

Fig. 3. a) Electrode configuration that allowed us to perform simultaneous recording with the wireless and wire system. b) and c) show an interictal epileptifrom discharge (IED) recorded with the wireless and wired system, respectively.

TABLE I

DETECTED IED FREQUENCY

Record #	Wireless	Wired
1	14.4	16.0
2	12.0	16.0
3	10.6	18.4
4	10.0	8.0
5	10.2	11.2
Average	***11.4***	***13.9***

IV. MEASUREMENTS

Fig. 2 shows an overlay of the somatosensory evoked potential extracted from the wireless and wired system. The key components of this type of signal are evident, namely the occurrence of a positive peak (P_1) followed by a negativity. The wireless evoked potential has an approximate amplitude of 11 µV compared to the wired amplitude of 12 µV. The delay between the wireless and wired P_1 is of approximately 1.5 ms.

Fig. 3(b-c) shows a 1-second segment of one of the recordings performed on an epileptic rat. This segment was selected to show a recorded IED, specifically an epileptic spike, with the wireless neurosensing system and wired system, respectively. Epileptic spikes are greater in amplitude than normal background neural activity as is evident in Fig. 3(b-c). They also have a duration of about 70 ms [7]. Fig. 3(b) shows a spike with an amplitude of about 406 µV compared to the 416 µV amplitude in Fig. 3(c). Table I summarizes the results of 5 recordings, along with the average detected IED frequency with each system. A two-sample T-test using this data revealed that there is no significant difference between the average detected frequency with each system.

V. CONCLUSIONS

Here, we presented an in vivo evaluation of the neurosensing system. This included recording a range of clinically-relevant neural signals spanning a range of amplitudes and portraying both normal and abnormal activity. A stimulation paradigm was used to induce specific neural activity and the recorded resulting evoke potential showed a significant correlation with the wired counterpart. In addition, for the first time, we used the system to record neural activity originating from a neurological disorder, specifically epilepsy. Particularly, we presented a segment of a trace containing an epileptic spike and demonstrated the system's ability to sense and transmit this signal with minimal signal distortion. While evidently different, both traces contain the components essential in IED analysis. In addition, we presented a summary of data from different recordings performed with the system, as evidence that the systems have comparable performance. This reinforces the idea that the neurosensing system can record the spectrum of signals generated by the brain, including those resulting from epilepsy and can be used to improve the study of such a disorder.

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