Recording Critical Epilepsy Indicators using a Fully-Passive Wireless System

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***Abstract* – Implantable sensors for recording neural activity are often used for a variety of applications, including epilepsy studies. Current versions of these recorders are highly-invasive impractical implants and undesirable in daily life. To address this, for the first time we present a novel fully- implantable and passive system for recording characteristic epileptic activity. In this paper, we focus on recording interictal epileptiform discharges (IEDs), known indicators of clinical significance. IEDs can serve to identify the location of seizure onset zones. Notably, in the case of temporal lobe epilepsy (TLE). Here, we present IED signals recorded using neural probes previously tested with our system and demonstrated to be capable of sensing signals as low as 15 µVpp in amplitude. These recordings refer to actual animal experiments and are indicative of the broad spectrum of neural signals that can be recorded.**

Keywords – Neurosensing Implants, Impedance Matching, subdural EEG, Electrocorticography

I. Introduction

Implantable neural recording systems offer a method for recording neural functionality to monitor activity continuously. From a treatment point of view, these systems can be used to form a brain-computer interfacing system, enable neural stimulation. and sense critical indicators of neurological disorders.

Past efforts in developing neural recorders relied on battery-powered sensors. However, these recorders are undesirable as they generate heat, are bulky and highly-invasive. To address the need for unobtrusive recording of high-resolution neural activation, we developed and tested a novel fully-passive and implantable wireless neurosensing system with an RF sensitivity of ~-135 dBm and the ability to sense signals down to 15 µVpp [1].

Perhaps, one of the most significant applications of a system like the neurosensing system is as a diagnostic or treatment tool for epilepsy. According to a report by the World Health Organization (WHO) published in 2018 about 50 million individuals worldwide are affected by epilepsy disorders. This makes epilepsy one of the most common neurological disorders. Within the category of partial epilepsy, the most common is temporal lobe epilepsy (TLE); a form that when medical treatment is ineffective, surgical excision of the onset zone is usually the remaining option. Evidently, locating this area of excision is of great importance. This can be done by recording interictal epileptiform discharges (IEDs) that occur between seizures. IEDs have a characteristic duration and shape, for example, spikes and sharp waves with durations of 20-70 ms and 70-200 ms, respectively [2].

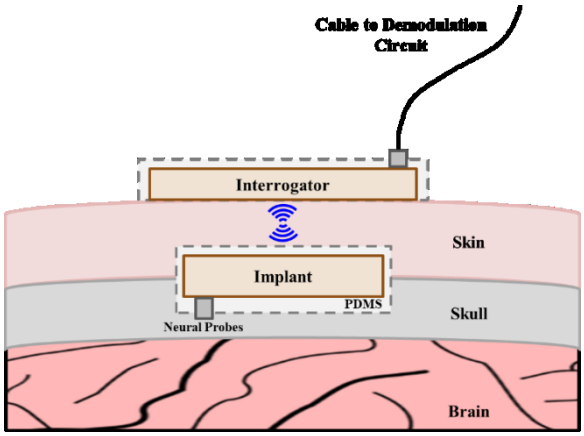


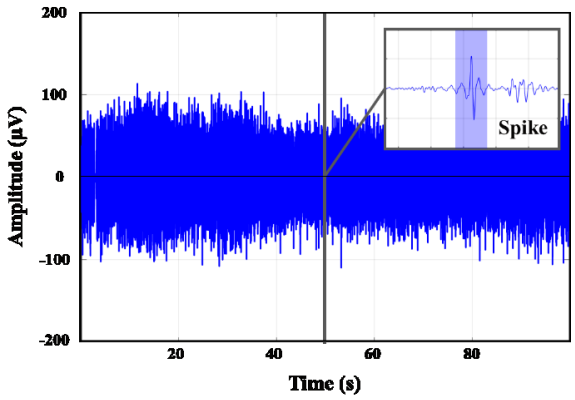
Fig. 1: Wireless neural recorder with its essential components including a depiction of the implant and interrogator location.

In this paper, we present the first fully-passive and wireless recording of TLE and IEDs in an animal model [3]. This is followed by the analysis of neural activity and its related critical markers used in clinical settings for the diagnosis and treatment of epilepsy. Notably, the research presented in this paper builds on previous work where we developed in-house probes to closely match the impedance of the implant and tested it in a series of experiments [1]. Our results in this paper reinforce the pursuit that our wireless neurosensing system can be applied to a variety of neurological studies with performance comparable to an existing wired system.

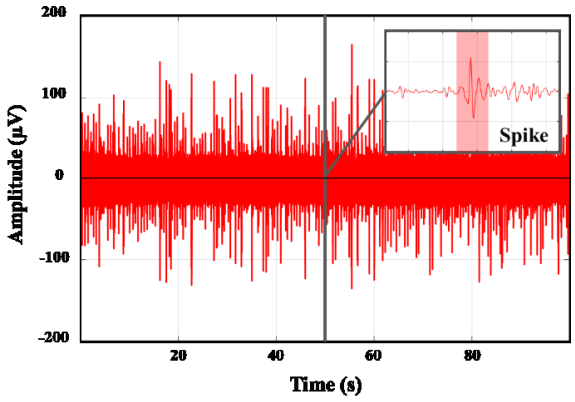
II. Wireless Neural Recorder

The developed wireless neural recorder is comprised of four major components: 1) the implant, 2) interrogator, 3) neural probes and 4) demodulation circuit. Fig. 1 briefly depicts these components except for the details of the demodulation circuit, which can be found in [1]. Fig. 1 also depicts the intended application, where the PDMS-coated implant (10 mm x 9 mm) is placed beneath the skin and completely sealed. This implant communicates wirelessly with the external interrogator (10 mm x 19 mm) from which it receives a carrier signal centered at 2.4 GHz. This carrier is subsequently, mixed with the detected neural signal prior to being backscattered to the interrogator. The mixing is performed by the anti-parallel diode pair (APDP) within the implant to generate the 4.8 GHz ± f_{neuro} signal. Notably, dual-band antenna in both the implant and the interrogator are used for transmitting/detecting the 2.4 GHz and 4.8 GHz mixed signal.

A major challenge when testing the neurosensing system *in vivo* was the low input impedance of the implant. Our implant was designed to have an impedance of ~50Ω, whereas available



(a)



(b)

Fig. 2: Sample traces of the recorded neural activity using the (a) wireless and (b) wired system. Each trace shows a spike recorded, verifying the accuracy of the wireless system.

probes have an impedance in the ~ MΩ scale, making it difficult to match [1, 2]. As is well-known, probe surface area and material, especially at low frequencies (Hz to kHz) are critical to lowering the impedance. Taking these factors into consideration different probes were characterized and evaluated in [1], leading to distinct acceptable probes, including those used in the experiments performed in this paper.

III. Experimental Set-up and Measurements

All of our neural recordings and procedures were first approved by and carried out in compliance with the Institutional Animal Care and Use Committee (IACUC) at Florida International University (Approval No. 17-042). The test animals (Wistar rats, Charles River Laboratories, Wilmington, MA) were housed in standard cages at a 12h-12h light-dark cycle with continuous access to food and water. The rats were acclimated for a week before inducing TLE and performing the recordings. Notably, the pilocarpine model for TLE was used on rats weighing between 120-150 grams. As part of the induction procedure, they were given an initial intraperitoneal (i.p.) dose of N-methyl scopolamine (0.5 mg/kg), followed by a pilocarpine injection (350 mg/kg) and later a phenobarbital injection (20 mg/kg) to reduce mortality rate as detailed in [2, 3] . During this induction procedure, the rats were observed for 90 minutes to confirm "status epilepticus onset" in accordance with the Racine scale. In the weeks following the induction, these rats were observed to confirm the development of spontaneous recurring seizures (SRSs) before performing the neural recordings.

Prior to initiating the recording, the rats were anesthetized with an isoflurane/O_2 gaseous mixture (1 L/min, 14.7 PSI). A 5% solution was used to initially induce the rat and was later reduced to 1.5-2.5% throughout the experiment and set up. In addition, at the time of the recording, the rats were switched to an injectable sedative (Dexdomitor 0.25 mg/kg). Surgical steel probes were used to record the neural activity using our wireless and a wired recorder (AD Instruments Animal Bio Amp) simultaneously. Multiple recordings were performed at a 2 kHz sampling rate. Each recording was processed with a notch (60 Hz) and bandpass (1-100 Hz) filter. Post-processing was then used to identify IEDs in the wireless and wired recordings. A skin phantom (~ 3 mm thickness), mimicking the dielectric properties of human skin, was used between the implant and interrogator to simulate a fully-implanted setting.

Fig. 2 shows a segment of a neural recording performed with the (a) wireless and (b) wired system, along with an IED. An epileptic spike is also highlighted. Notably, the duration of each spike is approximately 70 ms, complying with the description in [2]. As expected, IEDs are greater in amplitude than the typical neural activity observed. A complete analysis of five recordings resulted in an average sensed IED (including both spikes and sharp waves) of ~11 and ~13 per min with the wireless and wired system, respectively, that is, the systems did not have a significant difference in average detected IED (α = 0.05).

IV. Conclusion

Here, we present the use of our novel fully-passive wireless to record IEDs. These waveforms are critical indicators of epilepsy as they are typically analyzed in clinical settings for localization of pathological zones. Particularly, we present the spontaneous nature and detection of this activity. These results build on previous measurements, where we showed an ability to sense signals as low in amplitude as 15 μVpp and speak to the recorders applicability, as it can be used to accurately study epilepsy in a manner comparable with a wired system. Future studies with this device will include completely implanted wireless recordings in a free moving animal.

References

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