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Wireless Hippocampal Neural Recording via a Multiple Input RF Receiver to Construct Place-Specific Firing Fields

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Abstract—**This paper reports scientifically meaningful *in vivo* experiments using a 32-channel wireless neural recording system (WINeR). The WINeR system is divided into transmitter (Tx) and receiver (Rx) parts. On the Tx side, we had WINeR-6, a system-on-a-chip (SoC) that operated based on time division multiplexing (TDM) of pulse width modulated (PWM) samples. The chip was fabricated in a 0.5-µm CMOS process, occupying 4.9 × 3.3 mm^2 and consuming 15 mW from ±1.5V supplies. The Rx used two antennas with separate pathways to down-convert the RF signal from a large area. A time-to-digital converter (TDC) in an FPGA converted the PWM pulses into digitized samples. In order to further increase the wireless coverage area and eliminate blind spots within a large experimental arena, two receivers were synchronized. The WINeR system was used to record epileptic activities from a rat that was injected with tetanus toxin (TT) in the dorsal hippocampus. In a different *in vivo* experiment, place-specific firing fields of place cells, which are parts of the hippocampal-dependent memory, were mapped from a series of behavioral experiments from a rat running in a circular track. Results from the same animal were compared against a commercial hard-wired recording system to evaluate the quality of the wireless recordings.**

I. Introduction

Advanced research in electrophysiology and behavioral neuroscience aims at forming a better understanding of the underlying principles of the human brain and root causes of malfunction in its neuronal circuits. In particular, understanding the mechanisms behind effective therapies, such as deep-brain-stimulation (DBS), which has shown very promising clinical results in Parkinson disease, tremor, and other movement disorders, is important. To extend these medical breakthroughs to other neurological diseases, such as epilepsy, dementia, and Alzheimer's disease, multisite monitoring of brain activities is essential. In recent years, researchers have been trying to engineer multichannel neural recording systems to meet the above needs. The majority of neural recording systems that are in use today are wired both in research labs and epilepsy monitoring clinics. Wireless operation of such systems has a few clear advantages, such as no tethering effects, less irritation or risk of infection, smaller size, comfort, and ease of use. Hence miniature-sized wireless neural recording systems with the ability to simultaneously acquire neural signals from a large number of channels are highly desired. A key application is to monitor the interactions among large populations of neurons as the animals perform certain tasks that involve processing sensory inputs or cognitive abilities, such as learning and memory [1].

Because of the clear advantages of eliminating wires, there have been tremendous efforts on developing wireless neural recording systems to conduct *in vivo* experiments. For instance, previously, we reported a short *in vivo* recording on using earlier version of the WINeR system [2]. However, the hard-wired systems are still far more popular than their wireless counterparts in the majority of neurophysiology labs. This is because wireless systems still have problems such as limited wireless coverage area and poor connectivity, which render wireless systems unreliable for behavioral neuroscience studies.

To address these challenges, we have developed a multi-receiver, multi-antenna solution. Next section describes the WINeR Tx and Rx architectures. Section III describes the synchronization among multiple receivers. Section IV covers *in vivo* testing results on rats, followed by conclusions.

II. WINeR System Architecture

The WINeR system consists of a 32 channel ASIC on the Tx side and a custom-designed Rx. The entire WINeR block diagram is shown in Fig. 1.

A. WINeR Transmitter

Simplified block diagram of the WINeR-6 SoC is shown in Fig. 1a [3]. Its analog front-end (AFE) amplifies and filters neural signals from microelectrode arrays (MEA) with adjustable gain and bandwidth. The 32 AFE outputs are combined with 4 monitoring signals, and fed into the PWM block which consists of a 36-bit circular shift register (CSR), 36 comparators, and a triangular waveform generator (TWG). The CSR converts the analog signals into pulse width modulated (PWM) signal by comparing the AFE outputs with the triangular waveform. The next step is time division multiplexing (TDM) of PWM pulses, following which there is a PWM mask that restrains PWM signal within a predefined range. The trimmed PWM-TDM signal drives a VCO to be up-converted to a 424/442 MHz frequency shift keyed (FSK) signal. The FSK-TDM-PWM signal is then transmitted by a loop antenna after passing through a power amplifier [3].

B. WINeR Receiver and Computer Interface

The WINeR Rx block diagram is shown in Fig. 1a. The RF signal (FSK-TDM-PWM) is picked up by two individual antennas, amplified, and filtered by two identical RF front-end blocks to increase wireless coverage. Depending on the power of the received signal from each RF path, the one that receives

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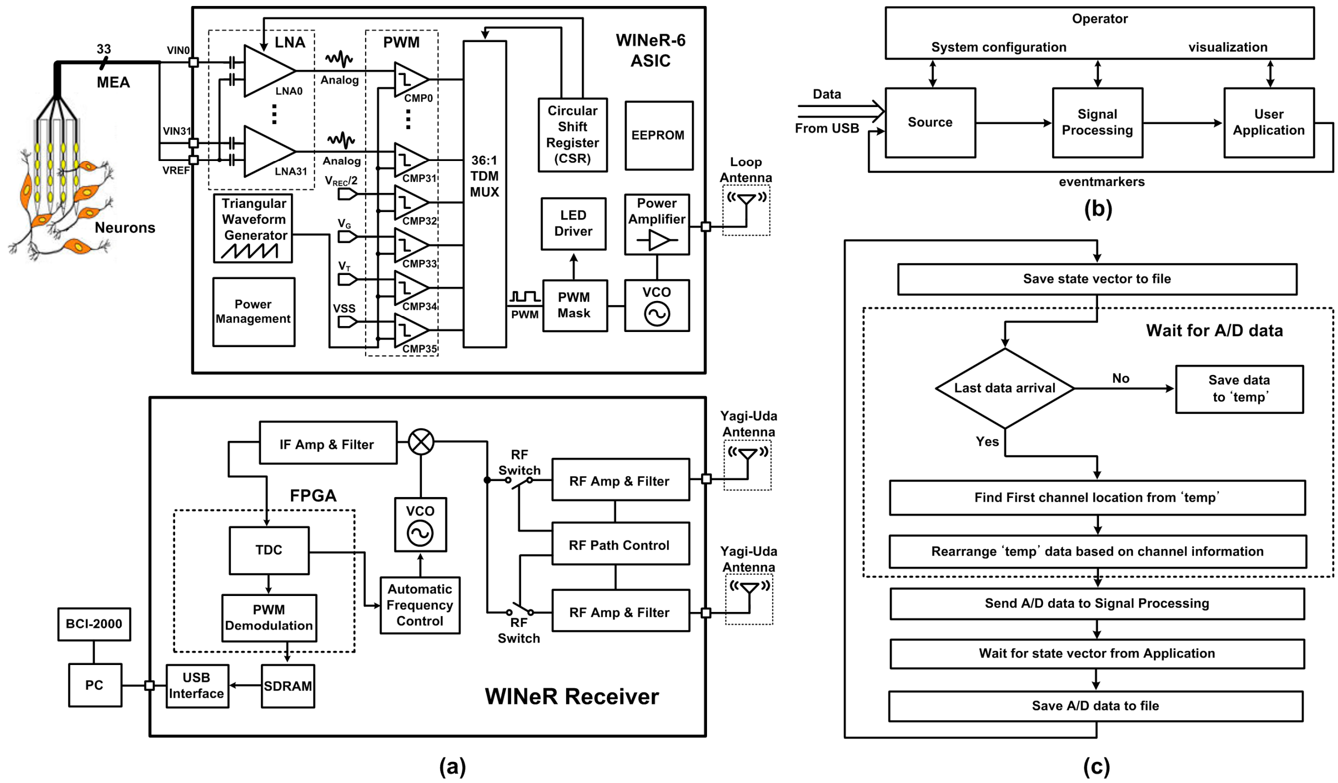


Fig. 1. (a) 32-channel WINeR Tx and Rx block diagrams, (b) The core modules of the BCI2000 [4], (c) Data acquisition flowchart within the Source module.

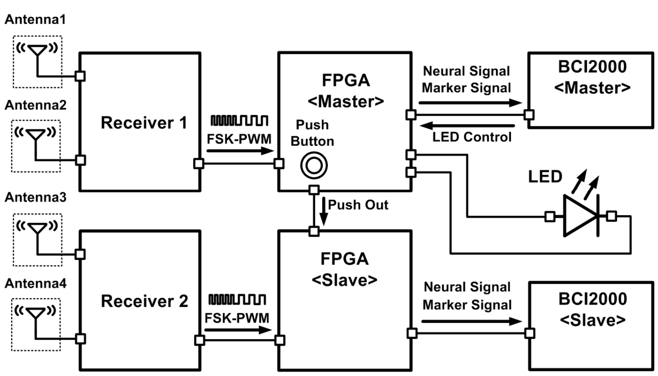


Fig. 2. Synchronization between two WINeR receivers each of which has two antennas. The optical signal helps with synchronization of the video stream.

the stronger signal will be connected to the mixer, which down-converts the RF signal to the baseband (41/59 MHz) before demodulating the FSK signal. The amplified and filtered FSK signal is fed into an FPGA, which demodulates it in the digital domain and recover the PWM signal.

The WINeR Tx has poor frequency stability due to the absence of frequency stabilization components, such as phase-locked loops (PLL) or crystals, due to power and size constraints. As a result, the Tx frequency varies because of temperature, supply voltage, and antenna loading variations. Hence, the Rx VCO frequency cannot be fixed. The automatic frequency control (AFC) function has been implemented on the Rx side to solve this issue. Following time to digital conversion (TDC), the AFC block averages the IF FSK periods in the digital domain. The AFC tries to match the averaged TDC value to a reference period by changing the VCO control voltage. In practice, the AFC changes the VCO frequency until the down converted FSK signal is centered at 50 MHz. In this way, the Rx VCO can track the changes in the carrier frequency by moving the down converted FSK towards a predefined value.

The digitized data is buffered in a 1 Mbit SDRAM to handle data transfer delays and transferred to PC through a USB port. The BCI2000, which is a general-purpose open- source software for brain-computer interfacing (BCI) research applications, runs on the PC to show the received neural signals on the screen and save them in the hard disk in real time [4]. The BCI2000 consists of four modules that operate together as shown in Fig. 1b. We have modified the source module to continuously receive the WINeR neural signal raw data from the USB port. Fig. 1c shows the flowchart of the data acquisition algorithm in the source module. An important task by this module is to detect the marker that indicates the first channel and time division multiplex the incoming data into 32 individual traces [3].

III. Multiple Receiver Synchronization Architecture

Behavioral animal experiments often require large experimental arenas, such as running tracks, which should be reliably covered by the wireless neural recording system with no blind spots to maintain data stream from the animal subject(s). To address this problem, we adopted a multiple-antenna and multiple-Rx solution. Fig. 2 shows the operating diagram of the multi-Ant/Rx solution. When two receivers record the same neural signal from an animal, the data needs to be synchronized by indicating the same marker signals in both recorded data streams. For this purpose, a predefined marker signal is generated in the master FPGA when a push button is pressed. This marker signal is transferred to the

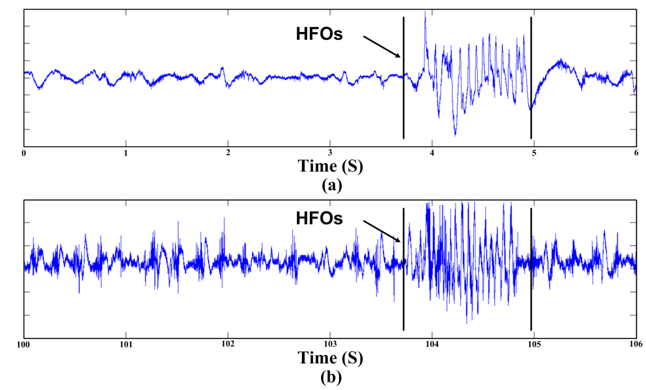


Fig. 3. Epilepsy detection by LFP recording from (a) Hard-wired system and (b) WINeR-6.

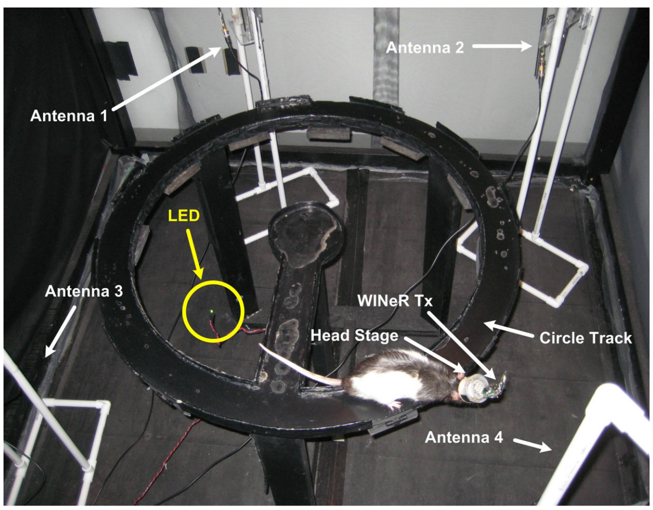


Fig. 4. Animal Experiment Set-up.

Fig. 5. Detection of the optical marker on the video streaming data.

master BCI2000, and easily distinguished from the neural signals. The same marker signal is generated in the slave FPGA board at the same time and sent to the slave BCI2000.

In behavioral experiments, it is also important to synchronize the video streaming data to the neural recording data. For this purpose, an LED is driven by the master FPGA, which turns on when the master BCI2000 starts recording neural signals. The LED turns off when the BCI2000 stops recording or when the push button is pressed. With the marker signals in the BCI2000 neural recordings and the optical signal in the video recording, all data can be synchronized by the offline processor. Although, Fig. 3 only shows two Rx and four antennas, the number of slave Rx can be easily increased in the WINeR system architecture depending on the required wireless coverage area.

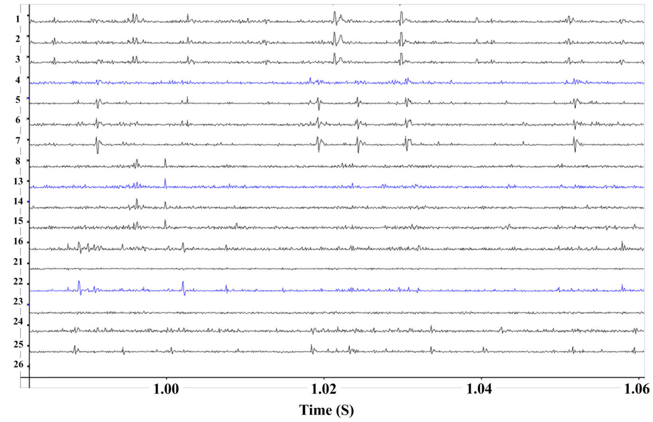


Fig. 6. The selected channel's neural recording in BCI2000.

IV. *IN VIVO* EXPERIMENTS

Two different animal experiments are presented here using the complete WINeR-6 system. They were conducted in compliance with and approval from the Institutional Animal Care and Use Committee's (IACUC) at the Georgia Institute of Technology and Emory University.

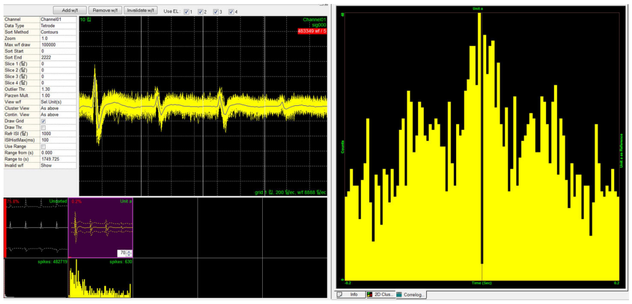
A. Wideband neural recording for seizure detection

We used the WINeR-6 system with the AFE bandwidth adjusted at 1 Hz - 8 kHz to record from a male Sprague-Dawley rat, injected with tetanus toxin (TT) in dorsal hippocampus. A 16-channel (2×8) multi electrode array (MEA) was also implanted with one row in the CA3 and the other in CA1. High frequency oscillations (HFO), which are considered emerging biomarkers for epileptic seizures, were recorded with the WINeR-6 system and compared with recordings from a custom hardwired system with commercial components, described in [5]. The hard-wired system bandwidth was set to 1 - 500 Hz for local field potentials (LFP). Fig. 3 compares the recorded neural waveforms at different times. Because of its wide bandwidth, the WINeR recording shows both HFO and LFP recordings.

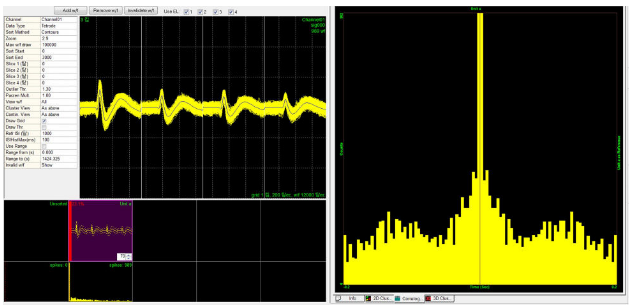
B. Single unit recording for behavioral experiments

A behavioral experiment was conducted on a Long-Evans rat that was implanted with 128 electrodes in the hippocampus region, which connected to four 36-pin male Omnetics micro connectors (Omnetics, Minneapolis, MN). In each connector, 4 pins are used for referencing (ground), and 32 are connected to eight tetrodes. The WINeR-6 AFE bandwidth for this experiment was adjusted at 400 Hz - 8 kHz with a total gain of 8000 to record single-unit activities (SUA). The test was done in a circular track with an outer diameter of 91.4 cm and track width of 7.6 cm, as shown in Fig. 4. During the test, the rat completed 40 laps on the track, while neural activities and a video stream were being recorded. For the comparison, the neural signal was recorded with an open-source hardwired recording setup (NSpike) [6]. Four antennas from two WINeR-6 receivers (see Fig. 2) were mounted on PVC stands and equally spaced around the track.

A video camera was mounted above the track to record the rat position on the track. Fig. 5 shows two sample frames of the video recording. The left figure shows the rat with the LED light off, meaning that no neural signal was being



(a)



(b)

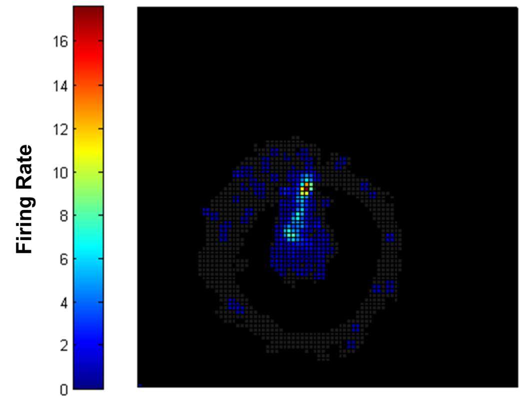
Fig. 7. Spike classification of Tetrode 5 from (a) WINeR-6 and (b) NSpike systems via using Plexon Offline Sorter.

recorded. The right figure, however, shows the LED on when the BCI2000 saves the data.

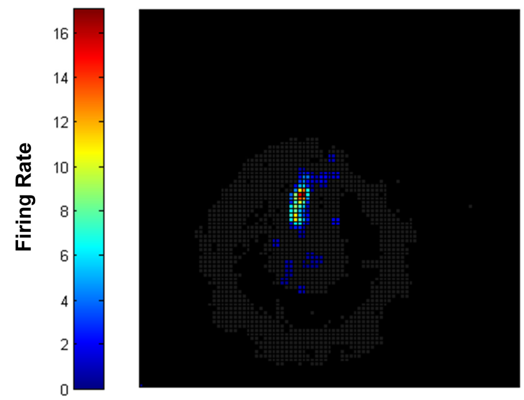
Fig. 6 shows the selected neural recording channels in the time domain on the BCI2000 visualization output. Spike classifications were conducted using Plexon Offline Sorter 2.0 software. Fig. 7a shows a classified unit from WINeR-6, and Fig. 7b shows the same unit from the open-source hard-wired recording set-up, called NSpike [5]. After classifying the SUAs, the spike firing location can be identified on the circular track by synchronizing the timing of the spike firing activities with the rat location from the video data. A collection of these spike firing locations is called a place field. Fig. 8 shows the place-cell field plots. Brighter color indicates higher firing rate of the classified unit cell. Most of the spike firing is observed in one specific location. Therefore, we can conclude that the classified SUA is related to memory of that specific location. The place field of WINeR-6 is similar to that of the hard-wired recording (gold standard) in terms of place-cell concentration and firing rate, which can prove the functionality and usability of this system in realistic behavioral neuroscience experiments as a substitute for the hardwired setups.

V. Conclusion

This paper presents a complete multi-receiver and multi-antenna wireless neural recording system, which uses a miniature sized 32-channel wireless implantable neural recording transmitter (WINeR-6), mounted on awake freely behaving small animal headstage. We successfully recorded HFOs, which are related to epileptic seizure activities, as well as place field maps by synchronizing classified SUAs with video recordings from a rat that completed 40 laps in a circular track. In both experiments, the wirelessly recorded



(a)



(b)

Fig. 8. Comparison between place fields resulted from (a) WINeR-6 and (b) NSpike wireless and hardwired recordings, respectively.

neural signals matched similar recordings from commercial hardwired counterparts. Neuroscientists can now begin eliminating cables from their experimental setups and continue acquiring high density and meaningful neural signals using multichannel wireless neural recording systems, such as the one presented here (WINeR-6).

VI. Acknowledgements

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