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In Vivo Testing of A Low Noise 32-Channel Wireless Neural Recording System

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***Abstract*—We present a 32-channel wireless implantable neural recording system-on-a-chip (SoC) that operates based on time division multiplexing (TDM) of pulse width modulated (PWM) samples with minimal substrate noise and interference. We have utilized analog-to-time conversion (ATC) on the transmitter and time-to-digital conversion (TDC) on the receiver to reduce the size and power consumption of the implantable unit by moving the digitization circuitry to the external unit. We have managed the TDM switching times such that no switching occurs during sensitive sampling onsets. The chip has been implemented in the AMI 0.5-µm standard CMOS process, occupying 3.3 × 3.0 mm^2 and consuming 5.6 mW at ±1.5 V when all channels are active. The measured input referred noise for the entire system, including the receiver at 1 m distance, is only 4.9 µV$_{rms}$ from 1 Hz~10 kHz. Finally, in vivo testing results on rats have been presented to validate the full functionality of the system.**

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. The majority of the ongoing research is conducted on animal models and its accelerating pace has created a considerable demand for microsystems that can simultaneously record neural signals from a large number of electrodes in awake behaving animals [1]. For decades, researchers have been using racks of bulky data acquisition systems, connected to electrodes through a bundle of thin wires and a preamplifier headstage. Wires are wideband and easy to use. However, they can potentially bias the animal behavior, and add noise and motion artifacts to the recorded neural signals. Neuroscientists are interested in replacing the wire bundles with a wireless link and continue recording and processing the "entire" neural signals in their high performance computing clusters without losing any piece of the acquired information [2].

On the other hand, the majority of ongoing neural interfacing research has been focused on transferring some sort of limited processing capability to the implantable front-end to limit the required wireless bandwidth at the cost of losing part of the neural information and complicating the implantable unit [3].

We have developed a novel architecture that would directly tackle the bandwidth problem throughout the system, while transferring the complexities from the implantable unit, where size and power are extremely limited, to the external unit. This architecture also provides a high level of flexibility, allowing the user to form a tradeoff among bandwidth, sampling rate, dynamic range, and resolution of the system depending on the type of the neural signals and the number of active channels.

In this paper, we present a 32-channel wireless implantable neural recording (WINeR) system-on-a-chip (SoC) that time division multiplexes (TDM) a pulse width modulated (PWM) sample from every channel, while eliminating the need for large off-chip components, digital buffers, and particularly, the high frequency on-chip clock. This would greatly reduce the overall system noise and lower the complexity and power dissipation on the transmitter unit. Next section describes the architecture and circuit details of the transmitter and receiver units. Section III includes bench-top measurement results and detailed specifications. Section IV describes *in vivo* testing results on rats.

II. Sysem Architecture

The present WINeR system consists of a 32-ch transmitter ASIC (Tx) and a custom designed receiver using off-the-shelf components (Rx). Block diagram and top view of the system as well as the transmitter chip micrograph and floor plan are shown in Figs. 1a and 1b, respectively.

A. 32-Channel WINeR Transmitter SoC

1) Front end amplifier: The analog front-end of the WINeR ASIC consists of an array of 32 two-stage capacitively coupled low noise amplifiers (LNA), shown in Fig. 1a, which have built-in bandpass filtering capability to amplify the neural signals in the desired frequency range of 0.1 Hz to 10 kHz. The 1st stage is fully differential with fixed 40 dB gain and common-mode feedback. It dissipates 16.4 µA from a ±1.5 V supply. The 2nd stage is a differential to single-ended amplifier with 1-bit adjustable gain (27/37 dB) and draws 8.1 µA. The low-cutoff of the LNA stage is continuously tunable, and the high-cutoff is 4-bit programmable [4].

2) Pulse width modulator (PWM): The amplifier outputs are combined with four internal monitoring signals (V_{DD}, V_{SS}, bandgap reference V_{BG}, and a temperature dependent voltage V_T) and fed into the PWM block that consists of 36 rail-to-rail comparators. They are enabled one at a time by circulating a "1" in a circular shift register (CSR), converting the conditioned analog signals into pulses by comparing them with the output of a precision triangular waveform generator (TWG), shown in Fig. 1a. During each comparison, the substrate is entirely quiet and there is no digital transition anywhere on the chip, reducing the substrate noise and dynamic power dissipation. In addition to acting as feedbacks from the implant, the monitoring signals provide a unique pattern that can be used to indicate the beginning of each TDM packet on the receiver side (Rx).

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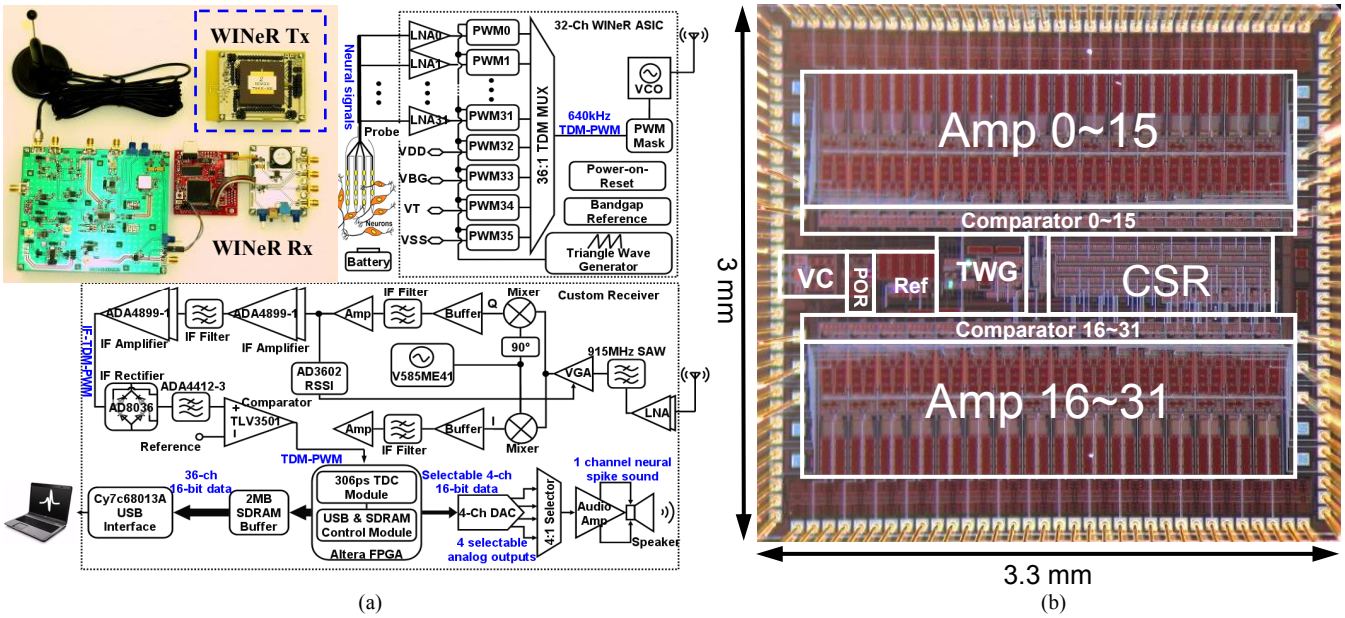

(a) (b)

Fig. 1. (a) 32-channel WINeR block diagram and top view photograph, (b) WINeR ASIC die microphotograph in AMI 0.5-µm CMOS process.

3) Time division multiplexer (TDM): This block consists of a 36-bit CSR running a 36:1 multiplexer (MUX). The CSR receives a time base from the TWG block as its clock. At the global reset, the CSR is loaded with 36-bit binary '10…00'. When the system is running, the single "1" circulates in the CSR and connects one out of 36 comparator PWM pulses to the MUX output. The resulting signal is a TDM-PWM signal, which is buffered and fed into the VCO after being trimmed and synchronized. This architecture significantly facilitates the extension of the WINeR system to 64 or 128 channels without requiring a large number of additional circuits.

4) Programmable triangular waveform generator (TWG): This is the heart of the clockless WINeR ASIC, and directly affects the noise, accuracy, and resolution of the system. Precision TWG consists of a binary weighted, high voltage compliance, large output impedance complementary current source/sink (CCSS) pair, which linearly charges/discharges a C_S = 6 pF capacitor [5]. A detailed description of the CCSS circuit, which utilizes MOSFETs in deep triode region, can be found in [6]. The current source/sink can each be digitally programmed in 16 steps. Controlling both charging and discharging not only mitigate substrate charge injection but also provides programmability over the sampling rate in a wide range. A window detector limits the TWG output and generates the switching signals for the CCSS, CSR, and TDM blocks. The lower and upper limits of the triangular waveform, V_{low} and V_{high}, can be either generated internally (V_{SS} + 0.1 V and V_{DD} − 0.1 V) or adjusted externally based on the dynamic range of the amplified neural signals [5].

5) Pulse trimming and synchronization (PTS): This block is responsible for limiting the TDM-PWM signal to either rising or falling ramps of the triangular wave by masking the other side. The PTS also synchronizes all the PWM pulses at their falling edge, improving the WINeR system accuracy and facilitating data recovery on the Rx. Another function of the PTS block is enforcing minimum and maximum widths of the PWM pulses, which can reduce the required wireless link bandwidth and improve the system resolution by avoiding too narrow pulse widths [5].

6) Voltage controlled oscillator (VCO): Trimmed PWM-TDM signal drives a hybrid LC-VCO, which has an off-chip surface mount (SMD) inductor. The VCO can operate in two modes: I. Wideband FSK when the varactor input is driven, II. Wideband OOK when the VCO enable input is driven.

B. Custom WINeR Receiver

On the Rx side, the FSK-TDM-PWM carrier is amplified and filtered by a wideband custom designed receiver RF front-end, shown in Fig. 1a [7]. A mixer down converts the received carrier to IF band, which is power stabilized by an AGC block within ±0.5 dB. The IF-TDM-PWM is rectified and low pass filtered with selectable bandwidths of 9/18/36 MHz to recover the baseband TDM-PWM. The edges of this signal are further sharpened by a high speed comparator. An FPGA-based time-to-digital converter (TDC) with 0.3 ns resolution converts the TDM-PWM into a series of 16-bit digitized samples. This data is then buffered through a 2 MB SDRAM, and sent to a PC via USB 2.0 for further processing and visualization. Rx also has an analog block, using which the user can select 4 out of 32 channels and convert them to analog neural signals. These 4 channels can be monitored in real time on an oscilloscope independent of the PC. One of these signals is audio amplified to drive a speaker for the user to hear the "sound" of neurons.

III. Measurement Results

The 32-ch WINeR ASIC, shown in Fig. 1b, was fabricated in the AMI 0.5-µm 3M2P standard CMOS process, and measures 3.3 × 3 mm^2. When all recording channels are active, it consumes ~5.6 mW from ±1.5 V supplies.

The 1st and 2nd stages of the LNA block had a measured gain of 40 dB and 27.7/37.1 dB, respectively. The low-cutoff

is continuously tunable in 0.1 Hz ~ 1 kHz range, while the high-cutoff was 4-bit programmable from 0.7 to 10 kHz. This topology provides 1% total harmonic distortion (THD) at 17.4 mV input for the 1st stage. The fully differential design leads to 65 dB PSRR and 139 dB CMRR with 3.9 μV_{rms} input referred noise in 10 Hz ~ 10 kHz range. Thanks to the capacitive coupling, the amplifiers are robust against input baseline variations and random 1st stage offset. The crosstalk for the entire system was smaller than -33 dB.

The CCSS has maximum current source/sink equal to 34.6/123.3 µA, and provides voltage compliance in -1.4 V to +1.4 V range. Measurements showed that the TWG operates as expected and the triangular wave can vary from 0 to ±1.4 V. For the maximum output swing, the WINeR sampling rate could be adjusted in 225 steps from 58 kHz to 660 kHz.

The functionality of the entire WINeR system was bench-top tested using 3 function generators creating a 30 Hz cardiac signal, 80 Hz triangular waveform and 100 Hz sine wave, which were all attenuated and voltage divided to generate 4 equally spaced amplitude levels below 1 mV. Eight out of 12 different signals were given to 3 channels each (a total of 24 inputs), and the other 4 signals were given to 2 channels each (the rest of 8 inputs). These signals were amplified and filtered by the LNA block at 67.7 dB and 0.1 Hz ~ 10 kHz, respectively. The TWG output signal was adjusted at ±1.4 V and 640 kHz, which indicates the overall sampling rate of the WINeR system. The PWM block compared the 32 LNA outputs and 4 monitoring signals with the TWG output. The MUX organized the resulting PWM samples into frames of 36 pulses. TDM-PWM signal was further masked by the PTS at the TWG falling ramp. This signal drove the on-chip MOS varactor of the hybrid LC-VCO, running at 898/926 MHz in the FSK mode. We used a 16 nH off-chip SMD inductor for the VCO with reasonable dimensions of 1.75 × 1.09 × 0.86 mm^3 and Q = 77 at 900 MHz (0603HQ-16NX_L_, CoilCraft, Cary, IL).

The transmitted FSK-TDM-PWM carrier was picked up at ~1 m from the WINeR ASIC by the custom designed Rx. The Rx amplified and down converted the FSK signal to 42/70 MHz IF-TDM-PWM, and further rectified and filtered it to a baseband TDM-PWM signal with 18 MHz bandwidth. It was then translated to TTL levels, and sent to the FPGA-based TDC for digitization. The 16-bit digitized samples were buffered in SDRAM and sent to a PC through its USB port. On the PC, we ran a custom developed Visual C++ GUI to record, demultiplex, and demonstrate the received waveforms in real-time, which are shown in Fig. 2. In this experiment, each of these waveforms has been sampled at 640 kHz/36 = 17.8 kHz. However, this rate can be simply changed by programming the TWG through CCSS and the TW amplitude. Table I shows a summary of the 32-ch WINeR system ASIC transmitter specifications.

We measured the input referred noise of the entire 32-ch WINeR system by grounding all channels and conducting fast Fourier analysis on the recorded signals from three channels (Ch4, 14, and 24) in 1 s at 1 m distance. The input referred noise spectrum density had a noise corner at ~10 kHz. Integration of those curves from 1 Hz to 8.8 kHz resulted in an input referred noise voltage of ~4.9 μV_{rms}.

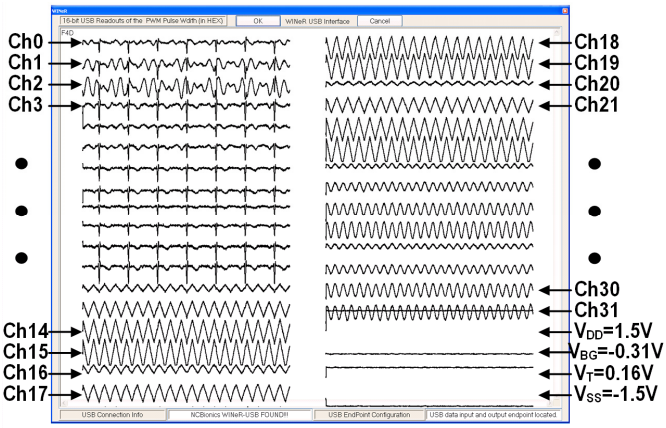

Fig. 2. Screen shot of the WINeR custom GUI showing simultaneously recorded waveforms of 32 + 4 wireless channels at ~1 m distance.

TABLE I
SUMMARY OF WINER TRANSMITTER ASIC SPECIFICATIONS

Parameter	Value
Number of channels	32 recording + 4 monitoring
LNA gain (dB)	67.7 and 77.1
LNA CMRR and PSRR (dB)	139 and 65
LNA input referred noise (µVrms)	3.9
LNA low cutoff (Hz)	0.01 ~ 1000 (continuous)
LNA high cutoff (kHz)	0.7 ~ 10 (in 16 levels)
Sampling rate (kHz)	58 ~ 660
FSK carrier frequency (MHz)	898 / 926
Entire system input referred noise (µVrms)	4.9 @ 1 m distance
Total power dissipation (mW)	5.6
Power supply (V)	±1.5
Technology	0.5-µm 3M2P CMOS
Die size (mm)	3.3 × 3

IV. *IN VIVO* EXPERIMENTS

We tested the 32-ch WINeR system in an electro-physiology lab on an awake freely moving adult male Sprague-Dawley rat, as shown in Fig. 3. This rat had 20 electrodes chronically implanted in the basolateral amygdala and infralimbic cortex area of its brain. The electrodes were connected to two 10-pin Omnetcis male microconnectors (A11365-001, Omnetics Connector Co., Minneapolis, MN). These connectors were fixed on the skull with metal screws and dental acrylic. Each connector had 10 pins, 2 of which were used as reference (ground) electrodes, and the other 8 were for recording. On the WINeR headstage, the LNAs were set to 600 Hz ~ 6 kHz bandwidth (rejecting local field potentials), 77.1 dB gain, and system sampling rate was adjusted to 640 kSps. The distance between the Tx headstage and the Rx antenna was ~0.5 m on average.

Real-time WINeR GUI screenshot for a recording length of ~1.1 s is shown in Fig. 4. In this experiment, 16 channels out of 32 were left open, because the rat only had 16 recording electrodes. The open channels are indicated by "X" in the GUI screenshot. The last 4 traces on the lower right are the monitoring channels. The wirelessly recorded traces on some of the channels showed that the WINeR system was able to successfully record neural spikes. Two of the recording channels (Ch6 and Ch25) carried neural signals as high as 200~300 μV_{P-P}. Some other channels (Ch26 and

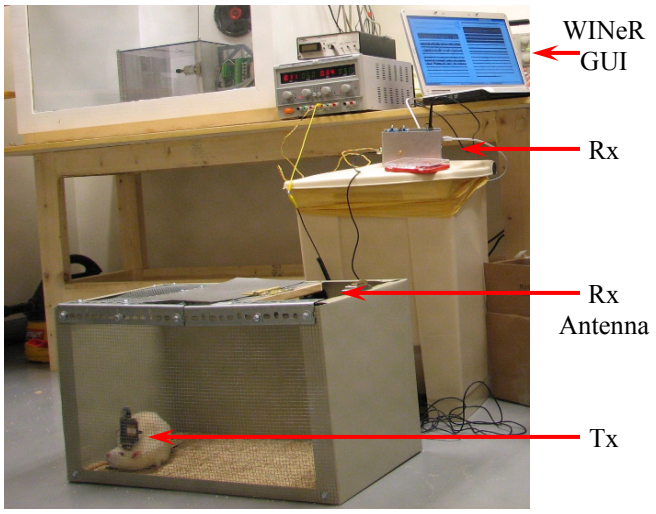

Fig. 3. *In-vivo* experimental setup of 16-ch recording using the WINeR system on a freely moving adult male Sprague-Dawley rat in a metal cage with less than 0.7 m separation between Tx headstage and Rx antenna.

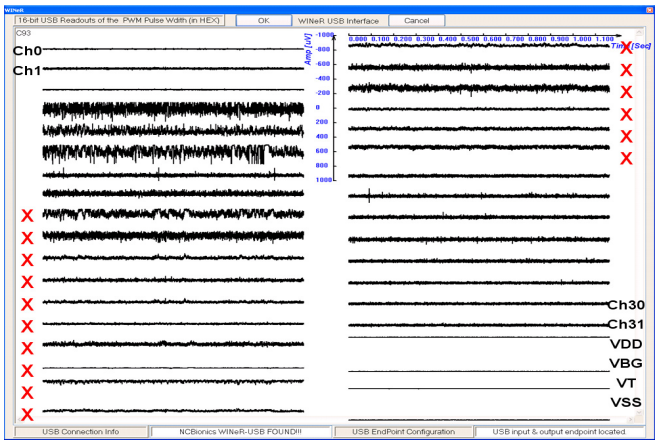

Fig. 4. Real-time WINeR GUI screenshot during *in vivo* recording from awake freely moving rat using WINeR system (**X** are open channels).

Ch27) showed neural signals at ~100 μV_{P-P}, and the rest of the recording channels had signals with amplitudes less than 100 μV_{P-P}. For the open channels, most of them were restive around "0" volts, and a few channels had large noise on them, which could be resulted from oscillation.

To extract more information, 24 s of recorded raw data from 4 channels that carried the largest neural signals were fed into two commercial neural signal processing software, NeuroExplorer and Plexon Offline Spike Sorter, for offline signal processing. The high resolution raw data and classified spike activities using principle-component-analysis (PCA) are plotted in Fig. 5. Background noise in the *in vivo* testing results was in the range of ~50 μV_{P-P}, or ~9 μV_{rms}.

V. Conclusion

This paper presents a flexible 32-channel wireless implantable neural recording system based on time division multiplexing of pulse width modulated signals. We reduce the substrate noise using a novel TWG block that eliminates the on-chip high frequency clock. Measurement results proved functionality of the system by wirelessly recording 32 channels simultaneously at 640 kSample/s at 1 m distance

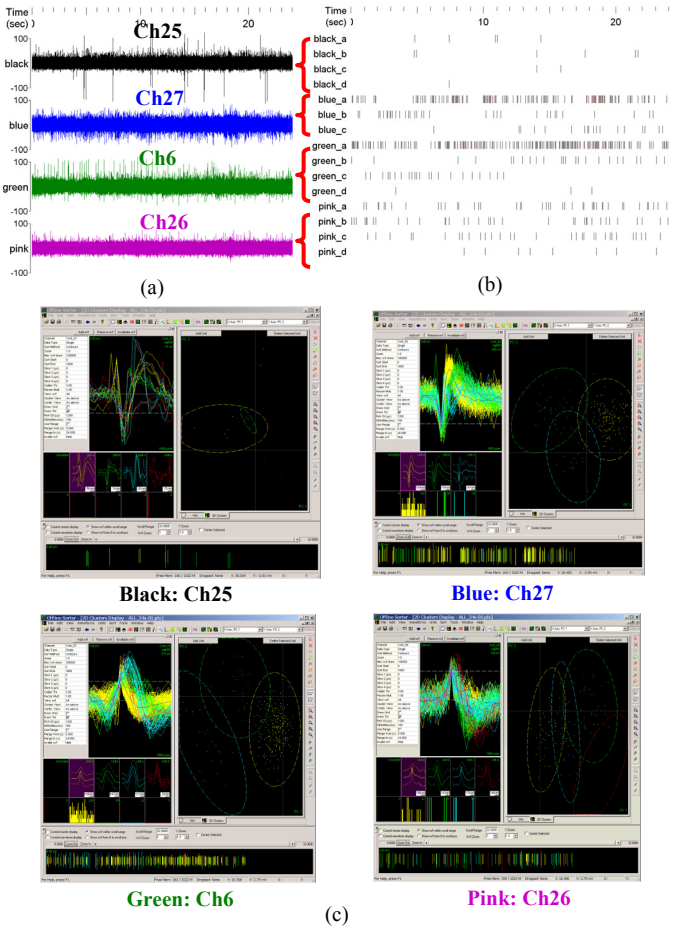

Fig. 5. Offline processing of the recorded data for the 4 channels carrying large neural signals (Black:Ch25, Blue:Ch27, Green:Ch6, Pink:Ch26) (a) NeuroExplorer high resolution raw data (b) NeuroExplorer classified spike data (c) Plexon Offline Spike Sorter screenshots for each channel.

with more than 8 bits of resolution [8]. This is equivalent to a bandwidth of 5.12 Mb/s throughout the WINeR system.

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