Mini-Symposia Title:

Implantable Wireless System For Neural Recording and Brain Stimulation

Mini-Symposia Organizer Name & Affiliation:

Dr. Gabriel Gagnon-Turcotte[1] & Dr. Benoit Gosselin[2]:
[1]Research professional in the Department of Electrical and Computer Engineering at the Laval University, Québec, Canada.
gabriel.gagnon-turcotte.1@ulaval.ca
[2] Full professor in the Department of Electrical and Computer Engineering at Laval University, Québec, Canada.
benoit.Gosselin@gel.ulaval.ca

Mini-Symposia Speaker Name & Affiliation 1:

Dr. Gabriel Gagnon-Turcotte: Research professional in the Department of Electrical and Computer Engineering at the Laval University, Québec, Canada.
gabriel.gagnon-turcotte.1@ulaval.ca

Mini-Symposia Speaker Name & Affiliation 2:

Dr. Mohamad Sawan: Full professor in the Department of Electrical and Computer Engineering at the École Polytechnique De Montréal, Canada, and Chair Professor at Westlake University School of Engineering, Hangzhou City, China.
sawan@westlake.edu.cn

Mini-Symposia Speaker Name & Affiliation 3:

Dr. Pedram Mohseni: Full Professor in the Electrical Engineering and Computer Science Department at Case Western Reserve University, Cleveland, OH, USA.
pedram.mohseni@case.edu

Mini-Symposia Speaker Name & Affiliation 4:

Dr. Hossein Kassiri: Assistant Professor in the Department of Electrical Engineering and Computer Science at York University, Canada.
hossein@eecs.yorku.ca

Mini-Symposia Speaker Name & Affiliation 5:

Dr. Shahriar Mirabbasi: Professor in the Department of Electrical and Computer Engineering at the University of British Columbia, Canada.
shahriar@ece.ubc.ca

Theme:

- ○ 01. Biomedical Signal Processing
- ○ 02. Biomedical Imaging and Image Processing
- ○ 03. Micro/ Nano-bioengineering; Cellular/ Tissue Engineering &
- ○ 04. Computational Systems & Synthetic Biology; Multiscale modeling
- ○ 05. Cardiovascular and Respiratory Systems Engineering
- ○ 06. Neural and Rehabilitation Engineering
- ◉ 07. Biomedical Sensors and Wearable Systems
- ○ 08. Biorobotics and Biomechanics
- ○ 09. Therapeutic & Diagnostic Systems and Technologies
- ○ 10. Biomedical & Health Informatics
- ○ 11. Biomedical Engineering Education and Society
- ○ 12. Translational Engineering for Healthcare Innovation and Commercialization

Mini-Symposia Synopsis— Max 2000 Characters

Recent advancements in low-noise bio-amplifier circuits design, precise electrical and optical neural stimulation circuits, energy efficient digital/analog circuits, and hardware implementation of complex signal processing for in situ neural data analysis, have allowed the development of new miniature electronic microsystems for studying the brain. Such devices can interface with the brain and/or the nervous systems in both electrical and optical paradigms for stimulating neural circuitry, as well as for large-scale recording of the neuroelectrical activity. Some of these devices can also close-the-loop between the neural recording interface the stimulation circuitry, allowing novel studies and experiments that were not possible before.

The esteemed contributors to this Special Session on Implantable *Wireless System For Neural Recording and Brain Stimulation* will discuss their latest achievements in developing sensors, circuits, algorithms, and overall systems that have been validated for a wide range of applications in neurophysiology research involving wireless neural recording and brain stimulation.

A 0.13-µm CMOS Digital Neural Decoder IC for Closed-Loop Electrophysiology and Optogenetics

Gabriel Gagnon-Turcotte and Benoit Gosselin, Laval University, Québec, Canada.

Abstract— **We present a digital neural decoder integrated circuit (ND-IC) to detect, compress, and classify the neural signals on-the-fly without supervision. This IC is incorporated within a tiny electro-optic headstage for closed-loop (CL) optogenetics, allowing us to report one of the first *in vivo* results obtained in a CL experiment with a freely moving animal. The ND-IC processes neural activity data using 3 digital cores: 1) The *Detector core* detects and extracts the action potential (AP) of individual neurons utilizing an adaptive threshold, 2) the data *Compression core* compresses the detected AP using an efficient Symmlet-2 discrete wavelet transform (DWT) processor for decreasing the amount of data to be wirelessly transmitted, 3) the *Sorting core* sorts the compressed AP into separated clusters according to their wave shapes. Our headstage is using a new technique to close the loop between the neural data acquisition module and the optical stimulator using the AP classification and timing information. The headstage along with the ND-IC are validated *in vivo* in freely-moving CL experiments involving a mouse virally expressing ChR2-mCherry in inhibitory neurons of the prelimbic cortex.**

I. INTRODUCTION

Using optogenetics in parallel with multi-channel electrophysiology is a powerful experimental approach to track the brain microcircuits of live animal models [1]. A new paradigm that holds potential to accelerate development of new therapeutics against brain diseases consists of closing the loop between the optical stimulator and the neural sensing device. For this purpose, custom integrated circuits (IC) have been developed to establish a closed-loop (CL) proof-of-concept in live laboratory rats or mice. These first solutions use simplistic feedback action potential (AP) detection trigger [2], PID controller based on the local filed potential (LFP) energy [3], or power/area consuming AP-to-clusters triggers [1].

In this presentation, we report a digital neural decoder (ND-IC) that can detect, compress, and sort the neural signals over 10 channels in parallel without supervision, enabling a complex CL strategy, such as the wired approach introduced in [1]. We also report one of the first CL optogenetic results obtained with a freely moving animal. The 0.13-µm CMOS ND-IC is integrated inside a tiny wireless electro-optic headstage, beside a neural recording and optogenetic stimulator IC [4], which is demonstrated *in vivo* with a freely moving mouse.

This work was supported, in part, by the NSERC (Canada), the FRQNT (Quebec), the ReSMiQ (Quebec), the Weston Brain Institute, and the Canada Research Chair in Smart Biomedical Microsystems. G. Gagnon-Turcotte and B. Gosselin are with the ECE Dept. Université Laval, Quebec, QC G1V 0A6, Canada.

Figure 1: ND-IC (left), headstage (center) and packaged (right).

II. METHOD

The proposed electro-optic wireless headstage using the 0.13-µm CMOS ND-IC is presented in Fig. 1. The ND-IC provides real-time neural data decoding to establish a connection between a readout and a stimulator, and has three main cores:

1) The Detector core detects and extracts the AP of individual neurons. It uses an adaptive threshold based on real-time signal analysis performed through a feedback loop with a simplified implementation [5].
2) The Compression core is using a Symmlet-2 (Sym-2) Discrete wavelet transform (DWT)lifting scheme followed by dynamic coefficient discrimination using a sorting tree and dynamic coefficient re-quantization scheme for neural data compression [5]. Each AP waveform is compressed for saving power and bandwidth, and transmitted wirelessly along with the classification ID for live monitoring. Additionally, the data compression allows to operate the wireless transceiver in low-data rate mode, which extends the lifespan and increases the transmitting range.
3) The Classification core sorts the AP on-the-fly according to their wave shapes. For performing automatic classification, this core reuses a subset of the DWT coefficients from the compression core.

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Neural Recording Implants and the Challenges Ahead

Fereidoon Hashemi Noshahr, and Mohamad Sawan, *Fellow, IEEE*

***Abstract*— The recent growing progress in neuroscience research and achievements as well as the fabrication technology have increased the demand for neural interfacing system. Brain-machine interfaces (BMIs) have revealed to be the promising method for the diagnosing and treatment of neurological disorders and the restoration of sensory and motor function. Besides, a fundamental and vital part of a medical diagnostics system is the monitoring of the bio-potential signals. For this purpose, patients are generally connected to a massive bio-potential acquisition equipment. However, this bulky acquisition system limits the patients' daily routine on one hand and on the other hand makes it arduous, the diagnostics requiring long-term monitoring. One possible solution is to use neural recording implants. Due to high demand for them, they are in daily developing with the pace of technology growing. The neural recording implants as a part of BMI are capable of capturing the brain signals, amplify, digitize and transferring them outside the body by a transmitter. The main challenges in designing of such implants are minimizing the power consumption and chip area. However, the requirement for raising the number of the recording channels and utilizing the advanced technology make the new challenges ahead of researchers.**

I. Introduction

BMIs can serve people with different clinical disorders. For example, researchers have shown robotic limbs, speech synthesizers, and human neuroprosthetic control of computer cursors utilizing less than 256 electrodes. Incapacitation to record from large numbers of neurons has limited the development of BMI. The invasive techniques have been used by most BMI's. It is because, recording single action potentials from neurons in distributed, functionally-linked ensembles is necessary for the most accurate readout of neural activities. Therefore, increasing the spatial resolution and the number of electrodes are essential for developing BMI. The implementation of neural recording implant is multi-disciplinary as it involves the various scientific fields such as electronics, medical, materials, electrodes and system integration. Increasing the number of electrodes and consequently the number of channels (in the range of thousands) create new challenges for the neural recording in the various mentioned fields.

II. Method

Microelectrode technology is not appropriate for this large-scale recordings. Recently, Neuralink Company has built arrays of small and flexible electrode (3072 electrodes per array) which has enabled thousands of channel recording [1]. In the microelectronics field, large-scale recordings makes a lot of challenges in terms of decreasing the power consumption and chip area. Although utilizing the small and advanced technologies helps to mitigate the power consumption and chip area and to increase the bandwidth of the circuit, it causes other challenges, especially in the analog front-end due to short-channel effects of the MOS transistors. Short-channel effects in the MOS down-scaled technologies decrease the transconductance (g_m) of the transistor on one hand and on the other hand increase the gate leakage current, the flicker and thermal noise power of an MOS transistor. This makes challenges in design of the high gain and low noise neural amplifier.

Another problem of the large-scale recording is increasing the power consumption and data transferring. For example, assuming one thousand channels (as a normalized value) that the signal of each channel is sampled with a typical sampling frequency of 10 kS/s which is digitized with a 10-bit resolution ADC, generates the whole output data rate of 100 Mb/s. To transfer this vast amount of data to outside of the body, the recording implant consumes a lot of power especially in the transmitter. One solution is utilizing data compression techniques in analog or digital domain to eliminate the data redundancy. The compression technique should be simple so that its implementation be compact and low power. The research in neural signal compression techniques can improve the compression factor of the existing methods or even develop the new techniques. Also ultrawide-band (UWB) communications as a low-power wireless short-range technology are suitable choice for high data transferring [2]. They are capable of transmitting data rates of several tens of Mb/s with power consumption less than 1 mW.

Providing the power supply for large-scale neural recording implants is another challenge of researchers. They investigate the various methods of power transferring from outside the body as well as the power harvesting techniques. Inductive coupling in the literature is one of the safe and applicable approaches for power transferring. On the other hand, power harvesting from various energy sources is a hot topic among the research groups.

III. Results

Large-scale neural recording in the advanced technology makes new challenges ahead of the researcher in the near future. However, the emerging technologies in electrodes, materials and microelectronics as well as the circuit and system design techniques helps researcher to overcome these problems.

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Pedram Mohseni, Case Western Reserve University, Cleveland, OH, USA.

A Miniaturized Brain-Machine-Brain Interface (BMBI) for Restoration of Function after Brain Injury

Abstract— **To date, brain-machine interfaces (BMIs) have sought to interface the brain with the external world using intrinsic neuronal signals as input commands for controlling external devices, or device-generated electrical signals to mimic sensory inputs to the nervous system. A new generation of implantable neuroprostheses aims to combine neural recording, neural signal processing, and microstimulation functions for closed-loop neuromodulation. These devices extract and analyze information from the brain neural activity to trigger microstimulation or dynamically modulate stimulus parameters in real time, potentially enhancing the clinical efficacy of neuromodulation in alleviating pathologic symptoms or restoring lost sensory and motor functions in the disabled.**

This talk will present a miniaturized system for spike-triggered intracortical microstimulation (ICMS) as a novel, device-based, closed-loop neuromodulation approach for promoting functional recovery after traumatic brain injury (TBI). Our previous findings from experiments with ambulatory, brain-injured rats using a battery-powered, head-mounted microdevice will be discussed. Our current work on developing a Bluetooth Low Energy (BLE)-enabled microdevice for use with non-human primates will also be presented. This work has the potential to remarkably advance the neurorehabilitation field at the level of functional neurons and networks.

Fully-Implantable Optogenetic Neuro-Stimulators: A Design Review and A mm-Scale Directivity-Enhanced Example SoC

Tayebeh Yousefi, Mansour Taghadosi, Alireza Dabbaghian, Hossein Kassiri
Department of Electrical Engineering and Computer Science, York University, Canada

***Abstract*—In this talk, first, an analytical discussion on circuit- and system-level design considerations for the development of fully-implantable optogenetic stimulators will be presented. Next, the design, development, and experimental characterization of a mm-scale self-contained bidirectional optogenetic stimulator with enhanced light directivity will be presented.**

I. Introduction

Wireless mm-scale optogenetic neuro-stimulators have recently gained significant popularity as they offer knowledge about the underlying mechanisms of brain functions and dysfunctions for a freely-moving animal subject [1], [2]. However, due to the implantation of the μLED light source and its high driving current (typ. 1-10 mA), the risk of tissue overheating for these devices is significantly higher than tethered head-mounted counterparts. It has been shown repeatedly, (most recently in [3]) that tissue heating during optical stimulation suppresses neural firings and impacts the animal behavior (e.g., affecting locomotor activity). Recent studies also revealed the importance of precise control of stimulation pulse shape in avoiding tissue overheating [4]. This is particularly challenging as the threshold voltage of the μLEDs (typ. 2.7-3 V) leaves very small headroom for the operation of a current driver with a VDD that is already reduced to save power. The above motivate for devising system- and circuit-level methods for minimizing the electrical power consumption required to deliver a specific irradiance (i.e., optical power per area) with a precisely-controlled pulse shape to the target cells.

In this talk, first, we will discuss design considerations that must be taken into account in the development of a fully-implantable wireless optogenetic neuro-stimulator. The focus of the discussions will be mainly around design ideas for energy efficiency optimization at both system and circuit levels. Next, we will present a mm-scale two-channel fully-wireless and battery-less bidirectional neuro-recording opto-stimulation system-on-a-chip (SoC) that (a) utilizes printed μlenses for light directivity enhancement resulting in significant irradiance-to-power improvement, and (b) employs a novel arbitrary-waveform energy-efficient highly-linear μLED driver for the optical stimulation channels.

II. Methods

Figure 1 depicts the top-level block diagram of a wirelessly-powered multi-channel optical neurostimulator and the partial power loss at every major stage from the external electrical power supply to the optical power that is delivered to the targeted neurons. This includes the power that is lost (a) within the inductive link due to the link's power transfer efficiency (PTE), (b) in the integrated circuits designed for power management and driving of μLEDs, (c) in the process of μLED electrical to optical power conversion, and (d) due to the diverging nature of the light generated by μLEDs resulting in a significant part of the optical power being illuminated at non-target neurons.

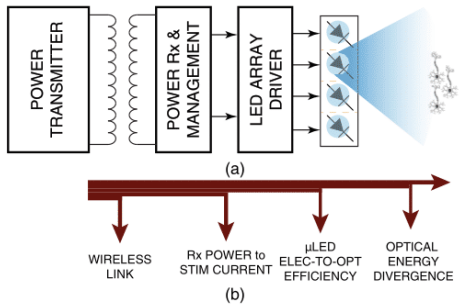

Fig. 1: (a) Top-level block diagram of an implantable optical stimulator with (b) major power losses indicated.

Among these, perhaps the most important energy loss happens due to the diverging light beams generated by the μLEDs. It results in a very small portion of the generated optical power to be delivered to the target cells and the majority of the power to be wasted. preventing such a loss not only helps with the overall energy efficiency of the implant, but also means smaller light intensity will be required from the μLEDs, hence, reducing the risk of tissue overheating by the implanted light source. Additionally, compared to external laser-based light sources, the diverging light of μLEDs has the disadvantage of poor spatial resolution. Therefore, enhancing the light beams directivity will improve the implant's performance in that aspect as well.

Toward achieving this goal, we have developed and characterized a mm-scale implantable wireless and battery-less optogenetic stimulator SoC. It integrates two recording and two stimulation channels, each equipped with a highly-linear energy-efficient μLED current driver, a two-stage neural amplification, and a dedicated SAR ADC. Two optical μlenses were designed, optimized, and inkjet printed on top of the system to enhance the light directivity, hence, the energy efficiency of the optical stimulation (>30×). The self-contained system is sized 6mm^3 and weighs 12.5mg. Complete experimental characterization and in-vitro measurement results will be and compared with the state of the art.

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A Signal-Dependent Sampling Technique for Recording and Processing Neural and Other Bio-Signals

E. Hadizadeh Hafshejani[1,2], M. Elmi[2], N. TaheriNejad[3], R. Rabbani[2],
Z. Azizi[2], A. Fotowat-Ahmady[2], and Shahriar Mirabbasi[1]

[1]University of British Columbia, [2]Sharif University of Technology, [3]TU Wien

Abstract— **In modern neural recording and/or stimulation devices (and in bio-signal recording devices, in general), bio-signals are almost always digitized to facilitate signal processing, data transfer, and storage/recording of the data. Thus, analog-to-digital converters (ADCs) are among the critical building blocks of the system and often the analog front-end and ADC consume a sizable portion of the power budget of the system. We present a signal-dependent sampling method for converting bio-signals to digital that can significantly reduce the required number of samples for representing the signal with a desired reconstruction accuracy. By reducing the number of required samples, the power consumption of subsequent signal processing, (wireless) data transfer, and/or data storage units will also be reduced and thus the overall system will become more power efficient. A proof-of-concept prototype system confirms the efficiency of the proposed technique in various application scenarios.**