Modular Optoelectronic System for Wireless, Programmable Neuromodulation During Free Behavior

Modular Optoelectronic System for Wireless, Programmable Neuromodulation During Free Behavior

S. Orguc[1†], J. Sands[1†], A. Sahasrabudhe [1], P. Anikeeva[1], and A.P. Chandrakasan[1]

***Abstract*— This work presents a modular, light-weight headborne neuromodulation platform that achieves low-power wireless neuromodulation and allows real-time programmability of the stimulation parameters such as the frequency, duty cycle, and intensity. This platform is comprised of two parts: the main device and the optional intensity module. The main device is functional independently, however, the intensity control module can be introduced on demand. The stimulation is achieved through the use of energy-efficient μLEDs directly integrated in the custom-drawn fiber-based probes. Our platform can control up to 4 devices simultaneously and each device can control multiple LEDs in a given subject. Our hardware uses off-the-shelf components and has a plug and play structure, which allows for fast turn-over time and eliminates the need for complex surgeries. The rechargeable, battery-powered wireless platform uses Bluetooth Low Energy (BLE) and is capable of providing stable power and communication regardless of orientation. This presents a potential advantage over the battery-free, fully implantable systems that rely on wireless power transfer, which is typically direction-dependent, requires sophisticated implantation surgeries, and demands complex custom-built experimental apparatuses. Although the battery life is limited to several hours, this is sufficient to complete the majority of behavioral neuroscience experiments. Our platform consumes an average power of 0.5 mW, has a battery life of 12 hours.**

I. INTRODUCTION

Optogenetics is a technique that uses visible light illumination stimulation to activate or inhibit neurons genetically-modified to express light-sensitive proteins from microbial rhodopsin family [1]. It offers light-sensitive opsin proteins to the region of interest and provide advantages such as cell type specificity, millisecond temporal precision, and rapid reversibility [2]. Furthermore, compared to the electrical stimulation methods, it causes negligible electrical perturbation to the environment; which enables simultaneous electrical recording while stimulating a region of interest [2], [3]. The stimulation of the targeted neurons can be achieved using lasers, LED-coupled optical fibers or wireless μLEDs.

Wireless neuromodulation devices deliver the illumination using μLEDs. They are power-efficient, low-cost and suitable for tether free operation in behaving subjects [4]–[6]. The latter is an advantage over the wired setups, which are prone to binding/breaking over time and limit the behavior of the research subjects while also introducing additional confounds and behavioral artifacts. One challenge in using μLEDs is the significant portion of the radiation power being lost. Hence, they must be driven from high power to output minimum required light intensity (1 mW/mm^2 for channelrhodopsin 2, ChR2, mediated excitation, 7 mW/mm^2 for halorhodopsin mediated inhibition) [7].

In most LED-based wireless applications, the high power required to drive the LEDs presents a bottleneck to reducing the power consumption. Battery-powered operation becomes inconvenient especially when fully-implantable design is required or if the system needs to operate for extended periods. As an alternative, researchers have explored different ways to achieve wireless transfer using methods such as ultrasonic power, magnetic resonant coupling and resonant RF power link [6], [8], [9]. Even though these methods allow indefinite operation time, they usually require sophisticated setups with precision tuning . Furthermore, the received power in most cases is orientation-dependent, causing variations in the supply voltage, thus the illumination intensity. There is one example that presents omni-directional, relatively stable power transfer through the use of magnetic coupling [8]. However, the system requires complex antenna setups in multiple locations and needs to be aligned at each experiment, which is potentially impractical for frequent use.

To address these challenges, we propose a battery-operated, low-power, modular neuromodulation system that is capable of 12 hours of stimulation, which is sufficient for many neuroscience experiments. It is a plug and play platform that consists of commercially available electronics. An optional intensity module can be introduced to precisely control intensity. Stimulation parameters such as frequency, duty cycle, intensity, and rise/fall time can be updated in real-time. Multiple LEDs can be driven by one device and multiple devices can be controlled simultaneously. Even though it is battery-powered, the system weighs only 2.2 g, which is suitable for working with small experimental models such as mice.

II. METHODS

A. System Overview

Figure 1 shows an overview of the system. The modular headborne neuromodulation platform is comprised of two

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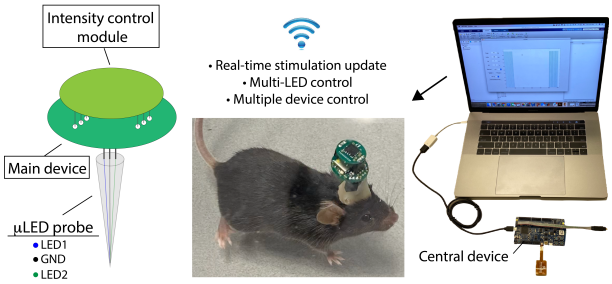

Fig. 1. The overview of the system showing the neuromodulation platform, the fiber-based probe that carries the μLEDs as well as the system setup. The headborne system can connect to the central device to achieve real-time stimulation update, multiple LED and multi-device control.

parts: the main device and the intensity control module. The main device achieves low-power neuromodulation through optical stimulation of μLEDs and is fully functional on its own. The main device can be mounted to the fiber-based, implanted probe using a 3 pin header connector. It achieves two channel stimulation. The system provides real-time updating of the stimulation parameters and can perform neuromodulation in 4 mice simultaneously. The intensity module is optional, and can be mounted on the main device through pin headers. It allows the user to adjust the rise/fall time of the stimulation as well as the maximum intensity.

Fibers and Implantation: The fiber-based neural probe carries two μLEDs - one blue (LED1) and one green (LED2) for optical stimulation.

Thy1-ChR2-YFP transgenic mice were used to test the neuromodulation platform. The probe was implanted in a deep brain structure called the ventral tegmental area (VTA). The surgical procedure for probe implantation is achieved through standard craniotomy and the device is affixed to the skull using dental cement.

Experimental Setup: Figure 1 also shows the system setup. Once the mouse recovers from the surgery, it is ready for the neuromodulation experiment. For this purpose, we simply connect our platform to the header pins of the fiber and put the power jumper on the main device to connect the battery to the supply of the system. Once powered, it is ready to connect to the central device, which is connected to the computer through a USB. The user can start neuromodulation by setting and sending stimulation parameters through the custom designed user interface developed in MATLAB.

B. Device Design

1) The Neuromodulation Device: Figure 2 shows the circuit details of the neuromodulation platform. The main PCB carries the wireless microcontroller and the programming interface on the top side and the battery on the bottom side. The microcontroller is MDBT42V package from Raytac and has the Nordic nRF52832 chip on it. The MDBT42V

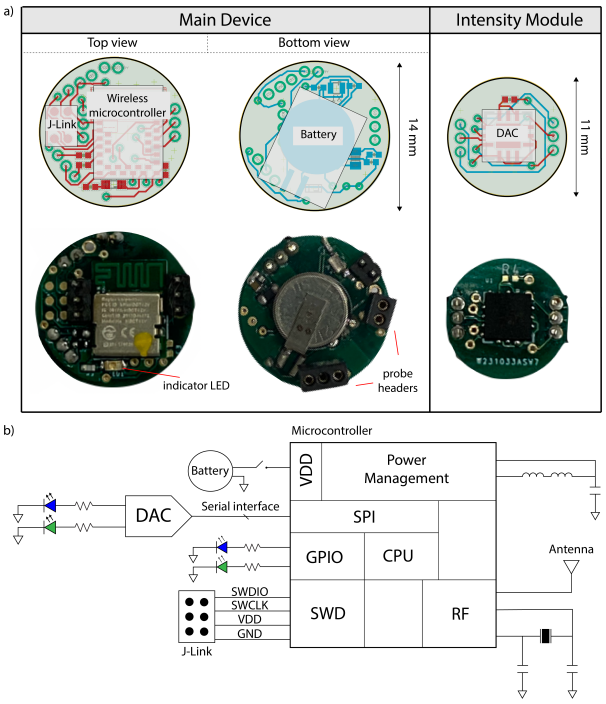

Fig. 2. The PCB design details of the main device and the intensity control module. a) The PCB board footprint as well as the actual pictures of the built prototypes. b) The circuit diagram of the overall neuromodulation system.

package comes with the on-chip PCB antenna. In order to program the device, we use the J-Link interface through a 6-pin needle connector. Both the microcontroller as well as the J-Link interface have miniaturized footprints to save PCB area. The battery is a rechargeable lithium ion battery (MS621FE) and can be easily recharged from a DC source. Overall the main PCB is 14 mm in diameter and weighs 2.2 g. The intensity control module is a smaller PCB that is 11 mm in diameter and weighs 1g. It only carries an 8-bit digital-to-analog-converter (DAC) and is connected to the main device through male headers. The DAC is programmed through the serial interface. The required pins to program the DAC are: VDD, GND, CS, DIN, SCLK and DOUT.

Figure 2.b shows the schematics of the neuromodulation platform. In the absence of the intensity module, the system uses the two GPIO pins to control the LEDs from maximum intensity level. On the other hand, in the presence of the intensity module, the DAC output connects to the LEDs. Different header pins are used to connect the probe to either to the main device or to the output of the intensity control module. In addition to the main components, the PCB has the 32 kHz crystal oscillator and several inductors for power management. The J-Link programming interface is connected to a two-pin serial-wire-debug (SWD) interface. Furthermore, the battery is connected to VDD of the system using a jumper when needed. The code to program the device was written in Arduino IDE.

2) The Central Device: The central device is nRF52840 Development Kit. The kit is used to load the Arduino code to

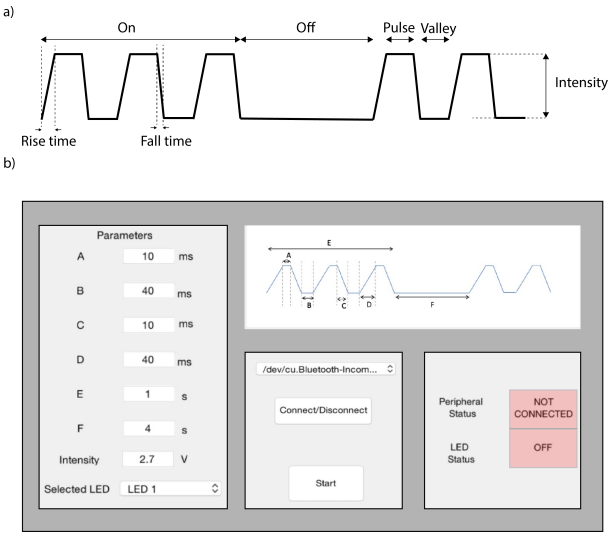

Fig. 3. a) The explanation of the stimulation parameters from a sample waveform. b) the developed GUI to set the parameters and to communicate with the platform.

the neuromodulation device using the 6-pin needle connector as well as to communicate with it to update the stimulation parameters. The central device can control up to 4 peripheral devices at the same time. The program running on the central device was written in Segger Embedded Studio.

C. Functionalities

The flexibility of the system comes into play not only in the modularity of its hardware but also in the tunability of its software. The software allows the user to choose the LED they intend to control. For instance, the user could select the blue LED to activate the ChR2-expressing neurons or the green LED to silence the halorhodopsin expressing neurons. Furthermore, the user has control over the stimulation parameters including the pulse rise/fall time, maximum intensity, and duty cycle as well as the on and off times.

These selections are all passed to the system using the graphical user interface (GUI) developed in MATLAB. Beyond allowing users to communicate these changes in real time, the system can turn off real-time adjustment to save battery and can give users feedback on the current state of the system. A preview of the user interface as well as the explanatory pulse waveform are shown in Figure 3.

III. RESULTS AND DISCUSSIONS

The electrical and optical characterization experiments except for the intensity control experiments were performed using the following pulse parameters: pulse: 10ms, valley: 40ms, on: 1s, off: 4s, rise/fall time: 1ms, intensity: 100%.

Figure 4.a shows the current consumption of the system for different phases of operation. As can be seen, when the

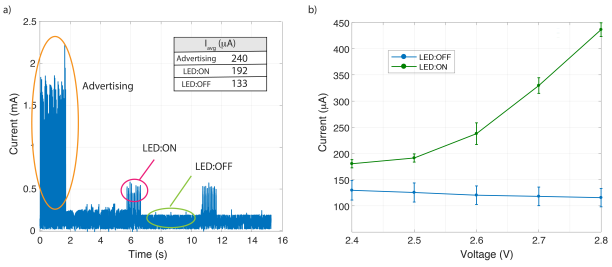

Fig. 4. a) The current waveform when the system is operating at 2.8 V. The average current at each region is labeled. b) The scaling of current consumption for ON/OFF state of the LED with changing supply voltage.

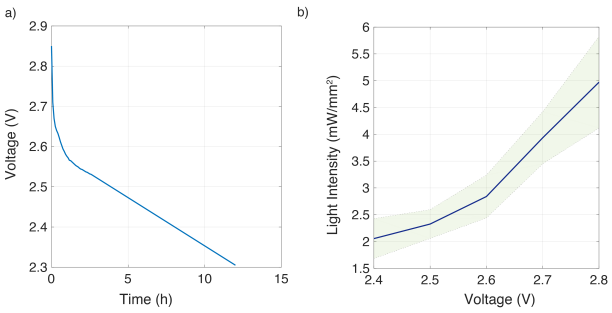

Fig. 5. a) The battery performance measured over 12 hours. b) The light intensity of the μLEDs at different voltage levels measured from 6 fiber samples. A series resistor is used to limit the current into the μLED.

LED is on with the default set of parameters from 2.8 V, the average current consumption is 192 μA. Figure 4.b shows the effect of the voltage scaling on the ON/OFF current consumption. As expected, μLED requires more current at higher voltages. The OFF power is almost the same for the voltage range we are interested in.

Figure 5.a shows the battery measurement. When the system is initiated with the default parameters using a fully-charged battery, it is able to operate 12 hours. The LED turns off around 2.3 V. Figure 5.b shows the change in the light intensity with the change in voltage. At 2.8 V, the μLEDs have a mean light intensity of 4.97 mW/mm^2. Note that even the lowest light intensity levels are above the threshold for effective optical modulation of neural activities.

Figure 6 shows the intensity control in real-time. As can be seen, the DAC can be programmed to provide a range of voltages. Since the LED turns off at 2.3 V, we chose that as our minimum voltage. The rise/fall time has been programmed to range between 1-10 ms. In the presence of the DAC, using the following parameters: pulse: 10ms, valley: 40ms, on: 1s, off: 4s, rise/fall time: 5ms, intensity: 100%; the LED:ON mode current consumption becomes 890 μA and the LED:OFF mode takes 189 μA. The DAC can be programmed to provide frequencies up to 10 kHz. The additional current consumption during the ON mode mostly comes from the SPI communication.

To test the ability of the platform to control neural activity in vivo, we implanted the modules along with the integrated

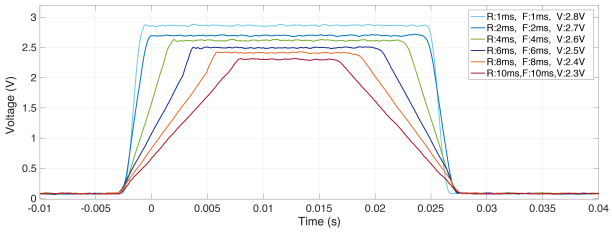

Fig. 6. Demonstration of the intensity control. Rise time (R), fall time(F), and intensity (V) can be configured using the DAC output.

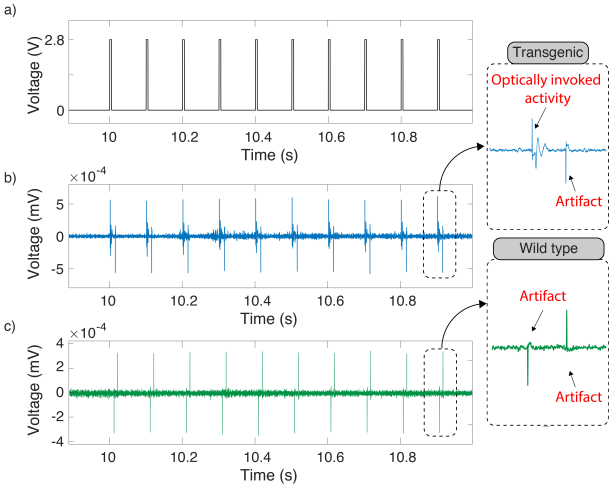

Fig. 7. In vivo evaluation: a) Stimulation waveform used. b) The voltage output from the transgenic mouse after stimulation. Optically invoked activity is visible. c) The voltage output from the wild type mouse. No spikes observed, only artifacts are visible.

recording electrodes. Transgenic Thy1-ChR2 mice broadly expressing ChR2 in excitatory neurons throughout the brain were used as the test group and wild type mice were used as the controls. The wild type mice were not injected with any virus unlike the transgenic ones. Hence, no optically evoked activity was expected in the wild type mice lacking opsin expression. As shown from Figures 7.b and 7.c, after the stimulation pulse is applied, optically evoked spikes can be detected in Thy1-ChR2 mice, where as only artifacts are observed in the wild type mice.

Table I summarizes the system performance and compares it with state-of-the-art wireless optoelectronic platforms employing μLEDs. Our platform requires significantly lower stimulation power, while achieving sufficient stimulation intensities. The system also integrates a precise intensity control, which is either not available [6] or has not been characterized extensively in the previous studies [2], [8]. The work presented in [8] is the most miniaturized, fully-implantable system that achieves intensity control. However, it is limited to program states that are preloaded onto the implant before the implantation surgery and hence does not allow real-time control on key stimulation parameters. In contrast, our platform allows for fine-tuning of parameters and states, even during the stimulation process. Compared to [2], the key advantage of the platform is that the weight

TABLE I

BENCHMARKING OF THE WIRELESS μLED-BASED NEURAL INTERFACE SYSTEMS.

		This work	**[6]**	**[8]**	**[2]**	**[10]**
General	Volume (cm^3)	0.98	1	0.1	6	0.92
	Weight (g)	2.17	2	0.075	5.5	1.6
	V_{DD}	2.8	5.5	2.5-3.5	3.3	3.3
	Battery	✓	x	x	✓	✓
	Recording	x	x	x	✓	x
Stimulation	# of channels	2	16	4	4	1
	Power (mW)	0.5	2000	NA	NA	NA
	Stim. current/channel (mA)	0.45	NA	0.85-1.1	5-30	5-21
	Intensity control	✓	x	✓	✓	✓
	Light intensity (mW/mm^2)	2-5	NA	NA	4-12	27
	Battery lifetime ($hours$)	12	∞	∞	NA	NA

of the modules remains within the acceptable threshold for behavioral experiments using smaller animals.

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