An Optogenetic Platform for Freely Moving Animal Applications

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1 OBJECTIVES

In this work, the main objective was to develop a closed-loop optogenetic platform capable of performing electrical recording and optical stimulation in a closed loop manner. The system is based on an ARM Cortex M4 Microcontroller Unit (MCU). The MCU is responsible for controlling the system and, processing and storing the recorded data. Placing an MCU as a processing unit significantly increases the flexibility of the system, as it allows several algorithms and software architectures to be implemented; this makes the system suitable for most optogenetic based applications. As presented by Ramezani et al., a custom Application Specific Integrated Circuit (ASIC) is responsible for recording the neural activity and delivering the optical stimulus. The recorded and stimulation data are stored on a micro-SD card. The system is powered by a 155 mAh Lithium-Polymer (LiPo) battery. Figure 1 illustrates a conceptual model of the system.

2 METHODS

The system comprises of two main blocks: 1) the head-stage unit and 2) the embedded control unit. The head-stage unit contains a neural interface ASIC responsible for recording neural activity and delivering optical stimulus. The ASIC is used in order for the capabilities of the system to be demonstrated. It requires a 5 V and a 3.3 V supply, which are provided by the embedded control unit. The data communication between the two units is established through a Serial Peripheral Interface (SPI) link. This makes the system capable of interfacing with any custom or commercial ASIC, provided that an SPI link exists on the ASIC to be used. The head-stage unit contains a microcontroller unit, a micro-SD card header and a Power Management Unit (PMU). The system is powered by a 3.7 V LiPo battery. Figure 2 represents the proposed system in the form of a block diagram.

2.1 Neural Interface ASIC

A detailed description of the neural interface ASIC is given by Ramezani et al. It consists of three main blocks: a) digital controller for external communication, interpreting and executing commands; b) neural recording system for amplifying, filtering, and digitising biopotentials; and c) optical stimulation system for generating, sequencing and driving µLEDs providing the systems with optogenetic neural stimulation capabilities.

For covering the power necessities of the system, two power domains have been used: 3.3V (using native devices) and 5V (using thick oxide devices). The 3.3V supply is used in order for all the electronics, apart from the optical stimulation output stage, to be powered. The 5V supply is required to power the blue µLEDs, due to their threshold voltage being significantly higher compared to conventional ones.

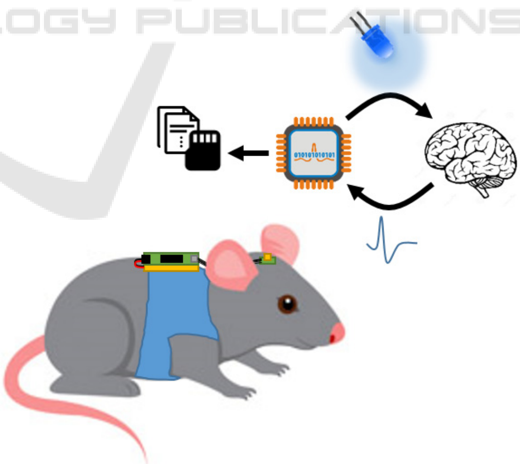

Figure 1: Conceptual model of the proposed system.

2.1.1 Digital Control

The digital controller is responsible for providing the following functions: 1) SPI communication interface with external processing and control units; 2) a Finite State Machine (FSM) with defined instructions, which allow the control of the µLED driving circuits,

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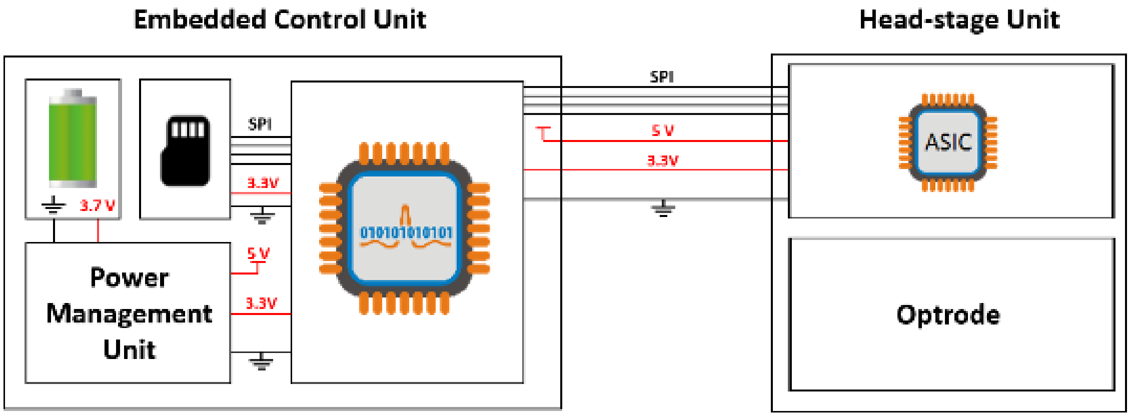

Figure 2: Block diagram representation of the proposed system. On the left the Embedded Control Unit, containing an MCU, a PMU, a µSD card and a battery. On the right the Head-stage Unit, containing the neural interface ASIC and an optrode. A 5V and 3.3 V supply are provided to the Head-stage Unit, and biderectional data communication is achieved via an SPI link.

as well as the configuration and control of the acquisition data from the recording circuits.

2.1.2 Neural Recording

The LFP recording sub-system is comprised of four recording channels, a shared Analog-to-Digital Converter (ADC) and corresponding control logic. Each recording channel consists of a low noise Front-End Amplifier (FEA) to couple to an electrode and provide low-noise amplification. It also consists of a 2nd amplification stage, allowing further amplification for low noise requirements. As mentioned previously, the ADC is shared between multiple recording channels, which raises the requirement of a buffer with sufficient drive strength, in order for the settling error and crosstalk between multiplexing to be reduced.

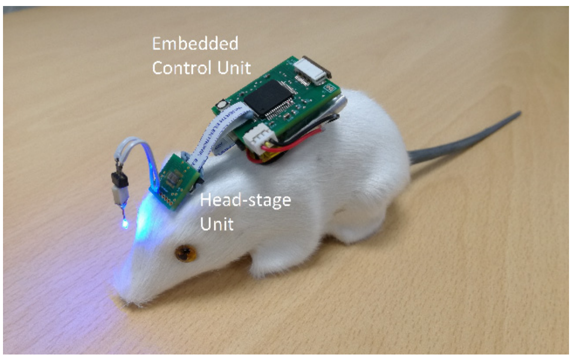

Figure 3: Physical representation of the proposed system. The system comprises of the head-stage and control units. A CREE Light Emitting Diode (LED) has been used for demonstrating the optical stimulation capabilities of the system. The LED was turned on through one of the addressable optical drivers in the ASIC.

2.1.3 Optical Stimulation

The system proposed in [6] allows up to six optical stimulation sites. Control of the light intensity can be achieved via a voltage DAC which is then converted to a current via a transconductance amplifier. Intensity can be controlled via both pulse width modulation and intensity control.

2.2 Microcontroller Unit (MCU)

The MCU used in the system is part of the Kinetis K22F family. It was selected due to its low power consumption and Digital Signal Processing (DSP) capabilities. The DSP block enhances the computational performance of the system allowing it to accommodate algorithms of various complexities. It is also responsible for acquiring the digitised data from the ASIC, performing some computation according to the selected algorithm and controlling the optical stimulation system within the ASIC. The control of the ASIC is achieved through a custom Finite State Machine (FSM) based software structure implemented on the microcontroller.

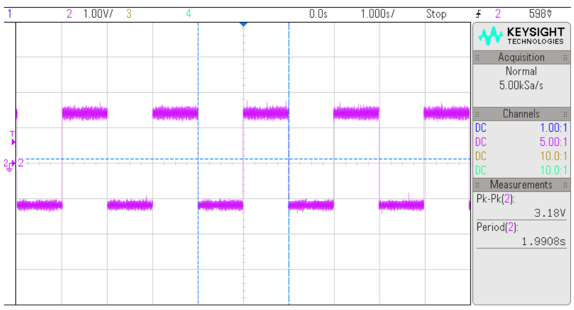

Figure 4: Output voltage of the optical stimulation circuit (1 second on – 1 second off period).

2.3 Data Logging

The recorded data, along with information about the stimulation commands and the algorithm, are stored in a 1 GB micro SD card. The data is stored to the SD card though an SPI link. The size of the SD card was selected to specifically accommodate enough memory space for a 24 hour continuous recording. However, depending on the application and power needs, any alternative memory size could be used.

2.4 Power Management Unit (PMU)

The PMU provides the whole system with 3.3 V and 5 V supply voltages. This is achieved by first regulating the 3.7 V - provided by a 155 mAh LiPo battery – down to 3.3 V. The 3.3V are then boosted up to 5 V, offering enough voltage for the optical stimulation system. A commercial boost converter IC was used in order for the 5 V source to be generated.

3 RESULTS

The funcionality of the system was evaluated through a series of bench top experiments. Both the stimulation and recording capabilities of the system were assessed.

3.1 Optical Stimulation

For testing the stimulation circuitry, a CREE LED was introduced to the output of one of the LED optical stimulation sites. Two main pulsing sequences were applied with variations on the intensity level and duty cycle of the pulse. The first one was a fixed intensity and fixed duty cycle (1 s ON, 1 s OFF). As shown in figure 3, the LED could be successully turned on. The same stimulation pattern was tested for different duty cycles. Figure 4 represents the voltage at the output of the optical stimulation circuit.

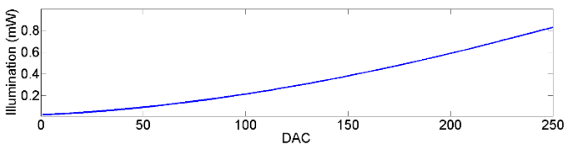

Figure 5: Measured response of LED across output range of DAC value showing the range of illumination power.

The ability of the optical driver to define different light intensities by controling the output of voltage DAC was also tested. For an increasing DAC value, the current at the output of the stimulation circuit and the intensity of the LED were increasing accordingly. Optical measurements we performed by placing the LED inside and integrating sphere. The measured results are shown in Figure 5. An optical stimulus of up to 0.8 mW can be illuminated.

3.2 Electrical Recording

In order for the recording of the system to be tested, pre-recorded LFP data were introduced inside some saline solution with the use of a signal generator. The signal signal was captured from the solution using an electrode from a Neuronexus probe. Part of the results (20 seconds) is shown in figure 6.

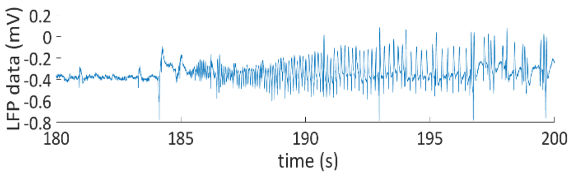

Figure 6: Pre-recorded seizure data were introduce in the saline with the use of a signal generator. The signal was recorded by the Neural ASIC and stored in the SD card. The figure illustrates part of (20 seconds) the 3-hour continuous recording. The system was powered off a LiPo battery.

4 DISCUSSION

As presented in the results section, the system successfully managed to produce stimulation patterns of various on/off periods and LED light intensities. The system also managed to record seizure-like data and store the recorded data on the µSD card. For the whole duration the system was powered off a 3.7 V LiPo battery.

REFERENCES

Reza Ramezani, Yan Liu, Fahimeh Dekhoda, Ahmed Soltan, Dorian Haci, Hubin Zhao, Dimitrios Firfilionis, Timothy G. Constantinou, Patrick Degenaar, 2018, “On-probe Neural Interface ASIC for Combined Electrical Recording and Optogenetic Stimulation”, *IEEE Transactions on Biomedical Circuits and Systems*.