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Design of a Configurable 16-Electrode Sense and Stimulation Neuromodulation System

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***Abstract*— Electrical sensing and stimulation of nervous system activity is a valuable tool to investigate neural activity both in vivo and in vitro. A general system capable of supporting users across a variety of use cases would be valuable for the field of neuroscience. We propose a new system capable of supporting a variety of experimental cases including low and high impedance electrodes with stimulation amplitudes up to multiple mA. The system is designed to support sampling frequencies up to 26 kHz and to maximize stimulation flexibility with an electrically isolated system.**

I. Introduction

Electrical sense and stimulation systems hold an important role in the investigation of the nervous system and in the treatment of neurological diseases. Sensing the electric field produced by neurons provides a measure of collective neural behavior in the region being probed with time resolutions as short as microseconds [1, 2]. Delivering an electrical stimulation pulse manipulates neural behavior by forcing activation of nerves in response to the signal [3]. The combination of both sense and stimulation provides a powerful tool for both the investigation of the behavior of nerves and the treatment of neurological diseases [4, 5]. Because this method of investigation is appropriate for therapeutic applications, it also provides meaningful translatability from research to application.

The questions in need of investigation in the neuromodulation space are many and varied. In some cases the electrodes used are relatively large with impedances on the order of 1 kΩ [6]. Other potential systems of interest involve electrodes with impedances in the range of 100 kΩ [7]. An ideal general-purpose sense and stimulation system would support a wide range of these impedances for sensing and provide a meaningful stimulation capability while being commercially viable. In addition, a general-purpose system would be capable of amplifying the signals of interest that are assessed with these types of electrodes. A microelectrode with high impedance is typically used to assess single or multi-neuron behavior. These signals have frequency content up to roughly 10 kilohertz and should consequently be sampled at rates roughly equal to 20 kHz. Macro-electrodes with lower impedance typically assess local field potentials which are representative of the electrical activity of thousands of neurons. The frequency content of this type of signal ranges from close to DC up to roughly 200 Hz. For both types of electrodes the amplitudes recorded are typically less than 1 mV.

Stimulation amplitudes to support investigations range between μAs and mAs. This requires the stimulator to support output voltage ranges sufficient to supply an appropriate stimulation level to a 100kΩ electrode and a 1kΩ electrode.

Prior reported sense and stimulation systems have focused on a variety of problems including wireless operation [8], large channel count [9], and operation in an implantable device [10]. Each of these solutions have benefits for the use case they are designed for; however, none are appropriate for the general neuroscience research user.

To address these needs, a system consisting of off the shelf components has been designed. The sense and stimulation circuitry are powered by batteries to support electrical isolation. System allocation supports physical separation of the Intan board from the remaining electronics to limit the weight of electronics mounted to the head of a behaving animal. System design requirements included minimization of weight, electrical isolation, configurability, and simplicity of use for the general neuroscience research user.

II. Methods

An adaptable, low-cost system to support sense and stimulation studies in animals was developed using commercially available components. The system, shown in Fig. 1, makes use of a laptop for the user interface that provides input to a serial peripheral interface (SPI) controller. Signals from the controller are transmitted through an isolation power supply system that is externally powered by a battery. Isolated SPI commands and power supplies drive an RHS 2116 sense and stimulation IC which in turn creates stimulation pulses and samples the signal on electrodes for the neural signal. The components in the system include a laptop, a Xilinx FPGA, an Analog Devices isolating DC/DC

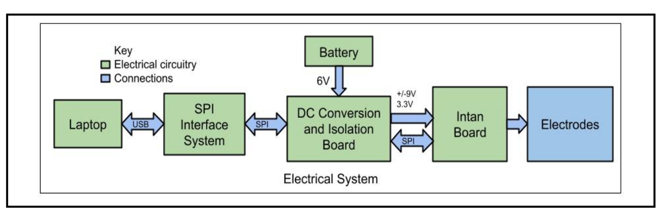

Figure 1. Electrical sense and stimulation system design. The configuration supports isolation of power from the test subject for enhanced safety and supports highly flexible system operation through configuration of commands at the PC level. High data throughput consisting of 16-bit sensed signals is supported through the wired SPI interface

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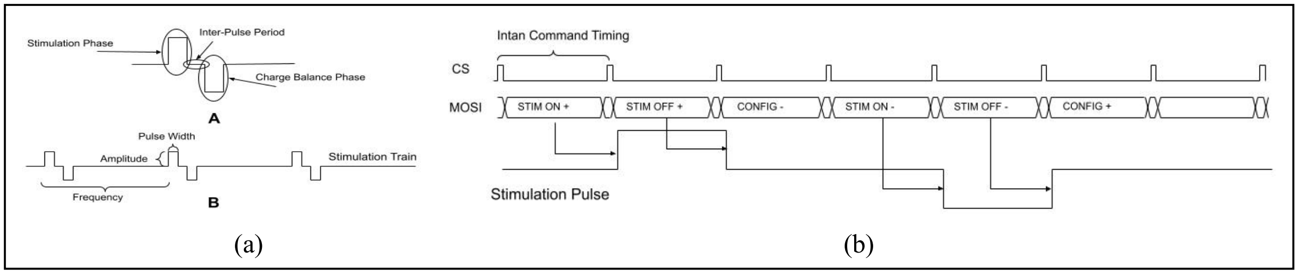

Figure 2. (a) Stimulation terminology defintion. Note pulse width describes the width of only one section of the simulation pulse. Image A describes the terms used to describe the phases of a stimulation pulse and image B describes terms for the repeating components of the wave.. (b) Command construction of a stimulation pulse using the RHS 2116. Minimum stimulation pulse width is determined by the frequency of the CS line

power converter ADP 1031, and an Intan RHS 2116 [11] along with various support components.

One significant design constraint for this system is the timing requirement for the RHS 2116 chip. Stimulation pulse generation with this component requires that each part of a stimulation pulse make use of one command. For instance, a basic pulse such as that shown in Fig. 2 requires six commands; STIM ON +, STIM OFF +, CONFIG -, STIM ON -, STIM OFF -, and CONFIG +. The pulse width of the stimulation signal is consequently set by the speed at which the system transmits each command. In addition, the timing of each change is driven by the chip select (CS) line, meaning that for a system to maintain desired timing it is necessary for the CS line to have a fixed frequency. This is a highly unusual design constraint for a SPI interface and severely limits design options. Given the need for a component that is capable of both sensing and stimulation functions and low weight, the complexity required to appropriately use the RHS 2116 was accepted.

To support the command timing design constraints, the digital interface was implemented to support maximum stimulation configuration flexibility and full utilization of all 16 sense amplifiers. A typical stimulation waveform is shown in Fig 2 (a) along with terminology used in to describe portions of the wave. This type of waveform can be created with the RHS 2116 and for this application a 24-word command structure was selected to balance sampling timing with stimulation and safety considerations. Within the command structure, the 24 words include the following: 16 CONVERT commands, 2 STIM ON commands, 2 CONFIG commands, 2 STIM OFF commands, and 2 commands for system checks. Each CONVERT command forces a sample on an individual sense amplifier, so to sample all 16 electrodes requires 16 commands. A full stimulation pulse requires 6 commands, as seen in Fig. 2 (b), and some system checks are necessary as a safety precaution for proper system functioning. Within the command structure, the STIM commands can be distributed among the CONVERT commands to vary the pulse width of the stimulation signal. The frequency of stimulation can be set by adjusting how often a command structure with STIM commands is executed. Finally, using consistent command structure sizes with a fixed slot for each CONVERT command ensures that the timing between each sample on a given sense amplifier is consistent.

The sampling rate of the sense amplifiers is dependent on the rate of the CS line and the number of words between conversion commands. A 24-word command structure results in a sampling rate for each sense amplifier of:

$$Sample\ Rate = \frac{f_{CS}}{24}. \quad (1)$$

where f_{CS} is the frequency of the CS line.

Assuming a 20 MHz SPI clock and knowing that each RHS 2116 command is 32-bits, this results in a sense sampling rate of approximately 26 kS/s. The minimum stimulation pulse width using this configuration would be 3.2 µs, the time for execution of two commands: STIM ON and STIM OFF.

If faster sampling rates are needed, the system can be configured to use a command structure smaller than 24 words. Doing this would require either no stimulation pulses or sampling fewer than all 16 sense amplifiers.

A SPI interface design incorporating an FPGA based on the design described in [12,13] was chosen to achieve a SPI interface with a fixed frequency CS line. The SPI interface must be capable of the following: operating at the maximum allowable SPI clock rate, providing a fixed frequency CS line, supporting configuration of stimulation and sense settings via a laptop, and handling a continuous stream of sense data from the RHS 2116. To support these requirements, the FPGA data handling architecture shown in Fig. 3 was implemented. This architecture uses a USB communication channel to interface between the systems and parses the commands from the host into debugging lines, register bridges, and data transfer lines.

The configuration supports two modes of operation with SPI data from two different sources. The first mode performs short tests such as an impedance or stimulation amplitude test. The second mode is designed for performing long term sense and stimulation runs. For tests of short duration, the timing accuracy can be relaxed and consequently commands from the host are transmitted directly through the FPGA to the SPI interface. Longer duration runs necessitate consistent timing accuracy. Consequently, commands issued using this mode are first loaded into an internal DDR3 memory segment Buffer A, shown in Fig. 3(b). This memory segment is accessed by the DDR controller when the system runs and each command is loaded into the DDR3 User Interface Buffer A prior to being transmitted on the SPI MOSI line. When the system receives return data on the MISO line, each word is recorded in the Buffer B which interfaces through the DDR3 user interface. This data is transferred through the

DDR controller to Buffer B in the DDR3 internal 1GB memory. Finally, the MISO data is transferred to the host computer through the pipe out interface for review, display, and analysis.

The FPGA SPI interface system provides consistent timing on the CS lines and the interface with the host supports stimulation flexibility and ongoing access to data from the sense amplifiers. To fully support the RHS 2116 operation with moving animals it is also necessary to provide three isolated voltage supplies and isolated communication lines. The power supplies support the core logic with a 3.3V supply and a plus and minus power supply for the stimulation circuitry. To simplify the system design for users and ensure the power supply is isolated from earth ground, the ADP 1031 was selected to generate these voltages. The component can be operated with a range of input voltages commonly available in rechargeable batteries. The micropower unit consists of an isolated flyback dc-to-dc regulator that generates the positive stimulation voltage, an inverting dc-to-dc regulator that generates the negative stimulation voltage, and a buck dc-to-dc regulator capable of supporting the 3.3V core supply all of which are current limited for safety. The component also provides an isolated SPI interface that supports the communication protocol of interest. The specified SPI clock rate supported by the component is slightly less than the maximum supported by the RHS 2116; however, the indicated clock rate still results in an acceptable sample rate of 21 kS/s and the isolation and power supply generation are important for the overall design.

To support studies with freely behaving animals and simplify the user interface, a power board was designed which configures the ADP 1031 to provide +/-7 V supplies to the positive and negative stimulation supplies and to provide 3.3 V for the core supply. The design is also configured to use the SPI isolation capability to fully isolate the sense and stimulation chip from external power.

The commercially available chip RHS 2116 from Intan was chosen to meet the system needs of weight, sensing, and stimulation. System design assessed possible electrode configurations and stimulation amplitudes to ensure maximal flexibility in the design. The interface supports a range of stimulation configurations including monopolar, bipolar, and tripolar stimulation. A minimum stimulation amplitude of 10 nA and a maximum stimulation amplitude of 2.55 mA can be produced by the chip. The stimulation supply voltage of +/- 7 V limits the maximum current that can be driven through a given electrode impedance. To ensure maximal operational longevity, the RHS 2116 should be powered using +/- 7 V supplies. An example electrode of interest for this system is described in [14]. A basic stimulation pulse such as that shown in Fig. 2 would be limited to 350 μA for a 20kΩ impedance electrodes with these power supplies. To extend the possible range of amplitudes with this system, the design allows for the stimulation pulse to be adjusted such that the second phase of the pulse has half the amplitude and twice the pulse width, resulting in a maximum amplitude for the stimulation phase of the pulse of 460 μA. This methodology can be extended to maximize the possible stimulation amplitudes given the power supply.

On the sensing side, the RHS 2116 includes 16 amplifiers capable of sensing neural signals at frequencies exceeding 20 kHz and maintains an input impedance of more than 1 MΩ over the frequencies of interest. The amplifiers provide a fixed gain of 192 V/V with a 16-bit ADC output, resulting in an LSB step size of 0.195 μV. In addition, the input referred noise of the chip is 2.4 μVrms over this bandwidth, providing more than sufficient signal-to-noise ratio for measuring the signals of interest.

III. RESULTS

The DC conversion and isolation board was configured to provide an isolated SPI signal and to generate 3.3 V and +/-7 V output supplies when powered by a 6 V battery. Because the sampling rate and the minimum stimulation pulse width for the RHS 2116 chip are set in the system by the frequency at which commands are sent through the SPI bus, the

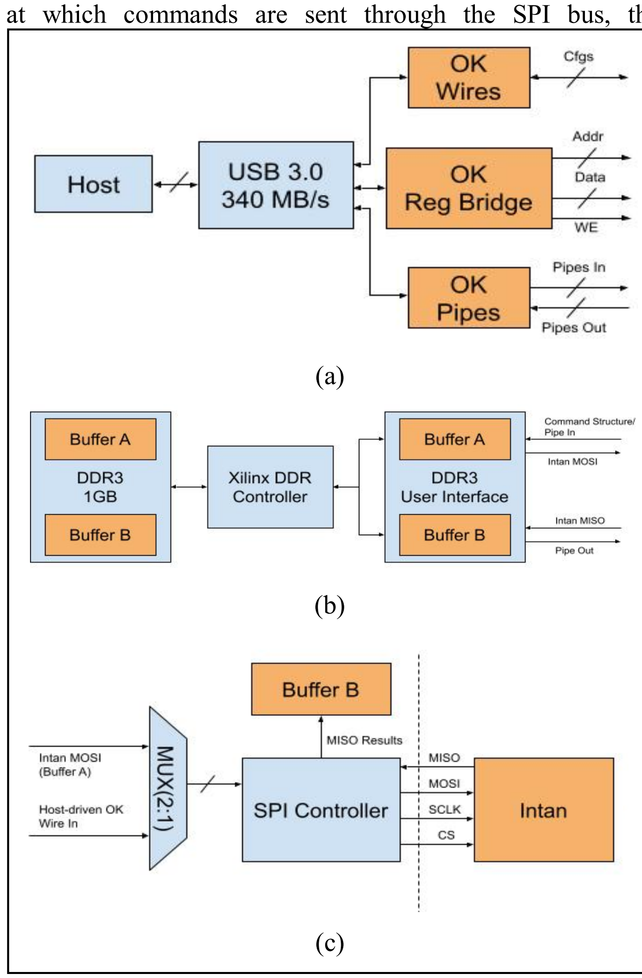

Figure 3. A block diagram overview of the FPGA design. (a) Host communication to and from the FPGA uses an application programming interface (API) that enables SPI controller configuration, RHS 2116 command configuration, and high-speed data streaming. (b) Memory configuration in the FPGA. The command structure is sent through the user interface to Buffer A memory using the DDR controller. MISO data from Intan is sent through the user interface to Buffer B memory via the DDR controller and provided through the user interface to the Host. (c) MOSI commands are submitted to the FPGA's internal SPI controller and transmitted to the Intan chip. The MUX enables the host to switch between timing agnostic Intan setup commands and timing critical repeated commands. MISO data from the RHS 2116 chip is routed to Buffer B for later download to the host.

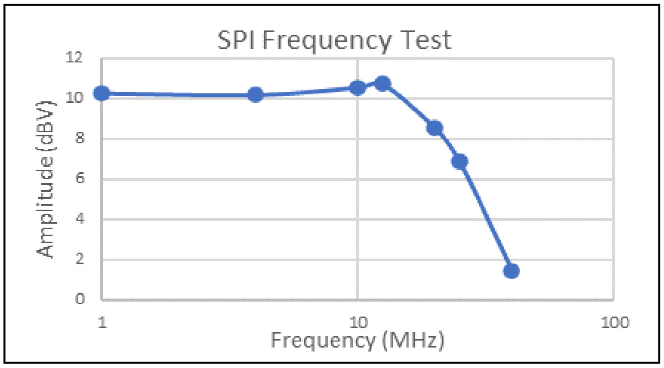

Figure 4. SPI isolation circuitry speed characterization

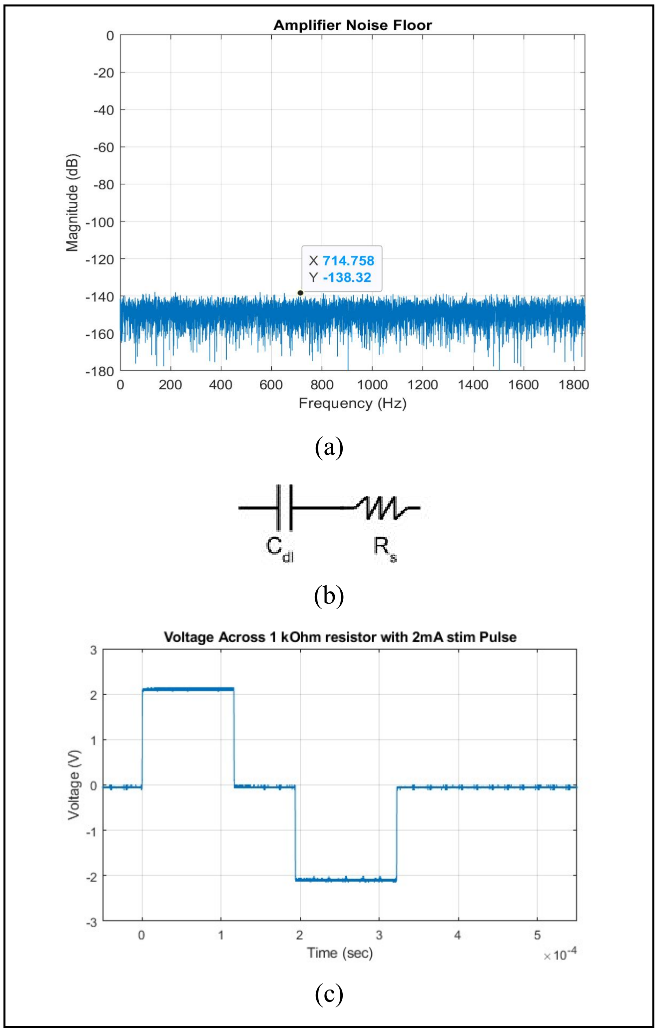

Figure 5. (a) Noise floor of the amplifier when powered with the isolation board . (b) Electrical model used to represent electrodes and (c) stimulation signal produced through electrical load.

maximum frequency of operation supported by the isolation board was characterized. The measurements were performed using a SPI communication signal transmitted through the ADP 1031 and the amplitude of the output signal was measured using an oscilloscope. The results of the test are shown in Fig 4 and indicate that operation can be maintained for SPI clocks up to 20 MHz. This is slightly higher than indicated by the ADP datasheet and slightly less than the maximum frequency supported by the RHS 2116 of 25 MHz. The SPI rate effectively limits the maximum system sampling frequency to approximately 26 kHz when using a 24-word command structure.

The power supplies need to support a current draw of at least 30 mA and limit the noise injected in the system. Each power supply was characterized for variation under load and for switching noise. All power supplies displayed roughly 20 mVpp of amplitude noise regardless of load condition. Additionally, the frequency content of the power supply noise was relatively flat in the frequency band of interest.

To ensure the use of the power isolation unit was appropriate for the RHS 2116, the system operation was characterized. When the RHS 2116 was powered by the ADP 1031 the noise floor of sense amplifiers and the stimulation output were assessed using power supplied by the DC conversion and isolation board. The SPI signal was provided through the isolation circuitry and data was captured. Initial characterization was performed at a command frequency of 1.8 kHz.

The noise floor on the sense amplifier was characterized in this configuration to assess the impact of power supply noise on the amplifier and ensure system operation matches expectations. To capture the internal noise floor of the amplifiers, the electrode input of the sense amplifier was shorted to the common reference node and the output signal was measured. The noise floor for the sense amplifiers in this system is shown in Fig 5 (a). As can be seen, the noise floor is roughly 130 nV/rt(Hz) across frequencies, which is consistent with the Intan specification of 2.4 µVrms and indicates no spectral skew is present. This is sufficient for monitoring neurological signals [2] and demonstrates the suitability of the system design for its intended use.

The operation of the stimulation circuitry was assessed using a simplified electrical circuit to represent electrodes. This model, shown in Fig 5b, was configured to represent a macro electrode with a capacitance of 1 µF and a resistance of 1kΩ. A 2 mA stimulation pulse was driven through the load between electrode E0 and the reference electrode. This resulted in the stimulation wave shown in Fig. 5c.

IV. DISCUSSION

Previous solutions such as [15] have focused on wireless implementations, been limited to only stimulation [16] or sensing [17] capabilities, or have required custom components [8]-[10]. These solutions have a variety of challenges for the average user including data throughput limitations with wireless implementations, sensing limitations, and part availability challenges. A commercial system exists to support some of the functionality enabled by this design [18]; however, the stimulation configurations available are limited. The design presented here provides a flexible platform suitable for future expansion to support a variety of stimulation waveforms.

Overall, the work presented here supports continuous data acquisition with sense and stimulation of a free-moving animal. The system is composed of a laptop running control software, an FPGA providing consistently timed SPI commands, a dc-to-dc power conversion board, a battery, and an Intan sense and stimulation chip. This system is capable of creating consistently timed sense and stimulation commands to ensure appropriate operation of the RHS 2116 module using commercially available components. In addition, the power supply solution isolates the communication and power lines. The communication framework balances sensing sample rate and stimulation needs to provide a flexible interface capable of support for a variety of neuroscience applications where continuous data acquisition and long run times for a free moving animal are required.

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