Development of an Electrophysiological Instrument for Universal Clamp Testing

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***Abstract*—The purpose of this study is to design a mixed-signal device capable of producing an output signal modeling a neuronal action potential. While targeting generalized lab use for education, the neuron emulator has been designed and tested with a versatile voltage, current, and patch clamp - the Universal Clamp. Results from this testing have been reported and used to improve performance.**

I. Introduction

Ionic currents producing the neuronal action potential can be assessed using a negative feedback circuit using two electrodes, this technique now known as the voltage clamp. This method gave way to allow future developments in the understanding of the diffusion of ions across their respective electrochemical gradients [1, 2]. However, smaller neurons, found in embedded tissue are susceptible to mechanical damage due to the use of two electrodes. A single electrode setting, introduced by E. Neher and B. Sakmann called the patch clamp, was made possible by time-multiplexing the voltage measurement with the current injection [3]. Another advantage of using a single electrode patch clamp is to allow the study of multiple ionic current channels [4].

This study is to design a device that will possess both the active and passive electrical properties of a biological neuron. This mixed-signal neuron emulator provides an educational and experimental platform. For evaluation of performance, a customized prototype voltage clamp, namely the Universal Clamp, was used. The Universal Clamp is an electrophysiological instrument capable of performing clamp techniques such as voltage clamp, current clamp, dynamic clamp, and patch clamp in one single integrated unit, while providing full digital feedback control to a digital signal processor (BF548, Analog Devices, Norwood, MA). When the neuron emulator input exceeds a preset threshold value, a train of impulses is generated, representing action potentials within a magnitude of +/- 1 volt as the result of the switching capacitors of a membrane modeled circuit. A microprocessor (PIC18F4525, Microchip Technology, Chandler, AZ) operating with firmware written in the C programming language is the main controlling component of this design project.

II. Methods

A. Modeling of the Neuronal Membrane

Initial modeling of action potentials was done in the simulation environment, MultiSim, shown in Figure 1. The cell membrane circuit consists of three parts: resting potential, resistance potential, and firing action potential. The PIC18F4525 was used to generate clock signals of opposing magnitudes with bidirectional I/O ports (pins labeled RC0, RC1, and RC2). These signals operate three voltage-controlled analog switches (MC14016). When RC0 = 1, RC1 = RC2 = 0; the circuit is producing action potentials by switching of the action potential RC circuit in series with the membrane RC circuit. Using a multitude of RC circuits has two advantages: First, the output waveform can be represented in a more realistic fashion to model a neuronal action potential. Second, the RC circuits can represent different ionic channels, providing a more detailed electrophysiological instrument. An important feature of the neuron emulator, as the action potentials are being fired, the current being discharged from the capacitors is limited by the analog switching [5]. This design allows the use of single-electrode settings.

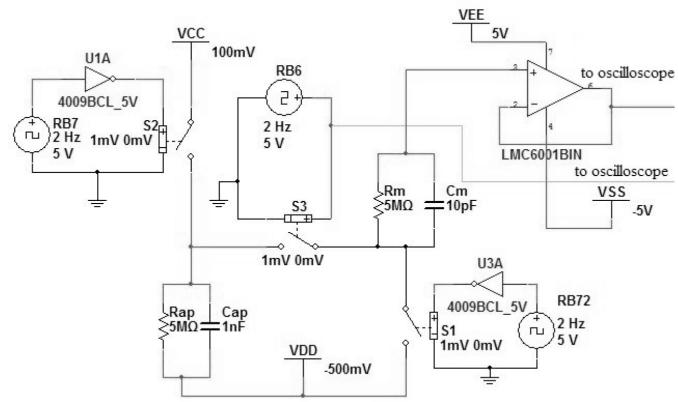

Figure 1. Cell membrane circuit modeled using SPICE based circuit simulation environment MultiSim.

B. Signal Acquisition

The RC membrane circuits are fed into a voltage follower (LMC6001), an ultra-low input current op-amp maintaining a high input impedance, high precision, and high immunity to noise. Preliminary results, as reflected in Figure 2, demonstrate a high level of noise in the output of the voltage follower and contained unwanted artifacts on the falling edge of the clock signals from the microprocessor. Significant performance improvements were made by placing electrolytic capacitors to serve as a virtual ground in the resting membrane circuit. Using bypass capacitors where components received direct power from a source improved the signal-to-noise ratio (SNR) significantly. The signal sent from the follower was then amplified using a summing circuit with a DC bias to meet the A/D voltage range specifications of the

PIC18F4525 [6]. The output of the processor is then sent to a digital-to-analog converter (DAC0800) where it serves as a testing point.

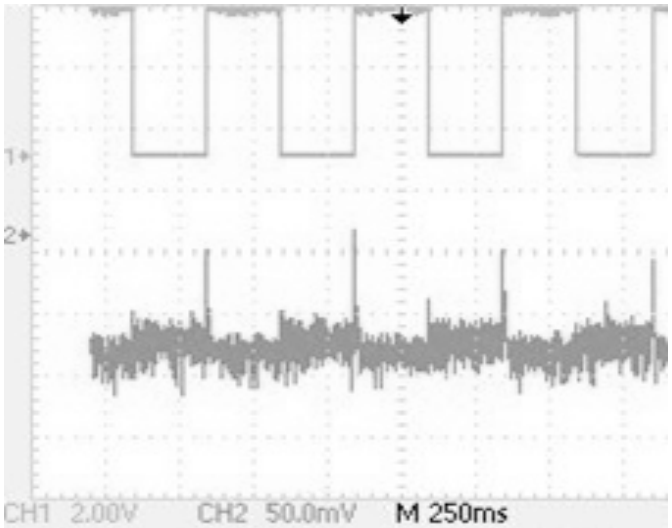

Figure 2. Preliminary results captured from neuron emulator circuitry. Channel 1 presents the clock signals generated from microprocessor corresponding to neuron firing. Channel 2 displays the output action potential waveform containing artifacts and high levels of noise.

III. RESULTS

A mixed-signal neuron emulator that generates the desired action potentials has been made glitch-free with low-noise, viewed on a digital oscilloscope, shown in Figure 3. While the output range can be customized easily with current architecture, the device has been configured to meet +/- 1 volt input range of a device under development, the Universal Clamp. The first functional prototype has been developed and demonstrated. Figure 4 illustrates results collected during testing in conjunction with the Universal Clamp.

IV. DISCUSSION

This study examines the design of a mixed-signal device capable of emulating the ionic potentials of a neuron. The small, portable device has been the main testing unit during development of the Universal Clamp. This neuron emulator can be developed into a commercial product for educational purposes due to its inexpensive cost, as well serve as a testing unit for other neurophysiological instruments. This device has strong potential in the field of electrophysiology because currently there is no product like it on the market. Future work in the development of the neuron emulator includes designing a professionally manufactured printed circuit board simplifying commercial production.

ACKNOWLEDGMENT

This study was supported in part by a grant from the National Institutes of Health (2R44NS048682-02A1, PI: Sun).

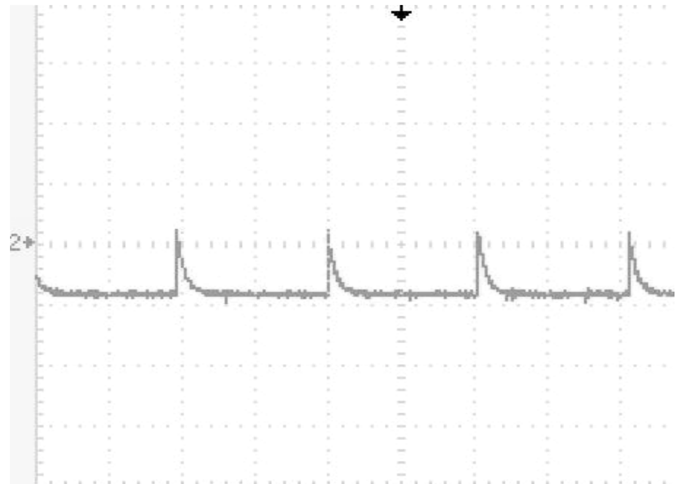

Figure 3. Action potentials generated from the neuron emulator, seen at the D/A. Testing of the device was performed to ensure functionality.

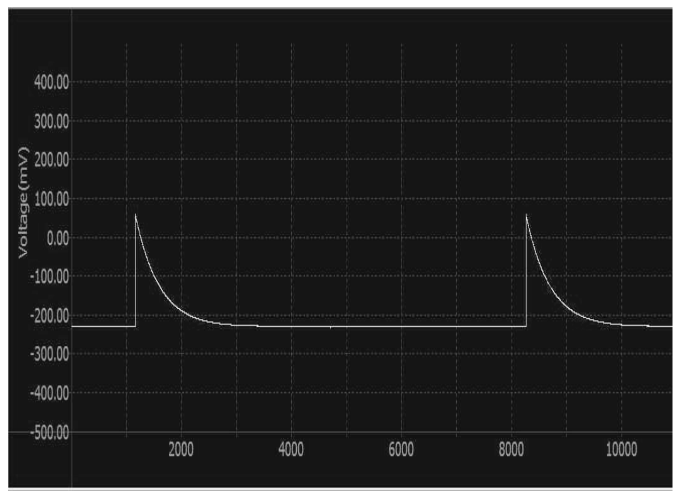

Figure 4. Software testing performed by the Universal Clamp, demonstrationing the neuron emulator has the capability of being computer interfaced.

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