Continuous-waveform constant-current isolated physiological stimulator

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We have developed an isolated continuous-waveform constant-current physiological stimulator that is powered and controlled by universal serial bus (USB) interface. The stimulator is composed of a custom printed circuit board (PCB), 16-MHz MSP430F2618 microcontroller with two integrated 12-bit digital to analog converters (DAC0, DAC1), high-speed H-Bridge, voltage-controlled current source (VCCS), isolated USB communication and power circuitry, two isolated transistor-transistor logic (TTL) inputs, and a serial 16 × 2 character liquid crystal display. The stimulators are designed to produce current stimuli in the range of ±15 mA indefinitely using a 20V source and to be used in *ex vivo* cardiac experiments, but they are suitable for use in a wide variety of research or student experiments that require precision control of continuous waveforms or synchronization with external events. The device was designed with customization in mind and has features that allow it to be integrated into current and future experimental setups. Dual TTL inputs allow replacement by two or more traditional stimulators in common experimental configurations. The MSP430 software is written in C++ and compiled with IAR Embedded Workbench 5.20.2. A control program written in C++ runs on a Windows personal computer and has a graphical user interface that allows the user to control all aspects of the device. © 2012 American Institute of Physics. [<http://dx.doi.org/10.1063/1.3700977>]

I. INTRODUCTION

Many cardiac electrophysiology studies require some form of electrical stimulation.¹ One class of stimulators is designed to create high current densities over large regions in order to study shock-induced transmembrane polarization,^{2,3} or if used as a defibrillator, to reset electrical activity in a sufficient amount of the myocardium over a period tens of ms in order to terminate arrhythmia and resume normal cardiac rhythm. These devices have compliance voltages (the maximum voltage they can produce) in the hundreds of volts (V), can deliver tens of amperes (A), and are effectively a simple switched capacitor discharge. These high power devices are designed to deliver their stimulus via electrodes with surface areas comparable to the surface area of the heart. More recent devices seek to terminate fibrillation by delivering arbitrary waveforms on the order of 1 A that are continually adjusted using feedback from the heart.⁴

The device described here is designed to be used in a large class of experiments that require point stimulation where the stimulus is delivered by at least one electrode with a diameter typically less than 1 mm. Most of the electrical resistance in these experiments is due to the small cross-section of tissue that surrounds the electrodes, termed access resistance. The access resistance is affected by electrode placement and condition of the heart. For example, the resistance across dog hearts measured through large electrodes interfaced to the heart with a conducting medium is approximately 50 Ω.⁵ A clinical study of permanently implanted pacemaker electrodes in humans reports average impedance measurements of 719 Ω

to 923 Ω depending on anatomical location.⁶ In our measurements a unipolar point platinum electrode 300 μm in diameter was placed on the left or right ventricle of the rabbit heart and an Ag-AgCl electrode 2 mm in diameter (model E252, In Vivo Metric) was located in the left ventricle chamber. In these experimental conditions, the resistance was measured to be 819 ± 71 Ω (4 hearts, 18 measurements) based on recordings using current (TCP305, Tektronix) and voltage (P5205, Tektronix) probes. In addition, the conductivity of the cardiac tissue at the electrode-tissue interface can change over time depending on the electrode material, current polarity, and net charge passed through this region. So in the design of our stimulator we assume a load to be 1 kΩ. Since our stimulator outputs a constant current, the assumed load is only used at design time to determine the compliance voltage to achieve the desired output range. The stimulator will output the desired current regardless of load resistance, provided the compliance voltage is sufficient.

We have previously reported the design of a stimulator that was capable of producing rectangular constant-current stimuli in the range of ±100 mA.⁷ Other custom stimulators have been reported that produce constant voltage and constant current for specific applications, such as Land *et al.*,⁸ Brasil *et al.*,⁹ and Cheever *et al.*,¹⁰ but none are suitable for our application. In our previous design, we successfully sought to overcome deficiencies in our commercial stimulators (Bloom), hereafter called legacy stimulators. The magnitude of the legacy stimulators is set by an analog control on the enclosure and the duration of the stimuli is controlled by

external transistor-transistor logic (TTL) pulses. Our previous design had limited duration rectangular pulses, relatively slow polarity switching times, limited waveform complexity, and detectable 25 kHz noise at the output due to the high-voltage dc-dc converter. The stimulators described here overcome these limitations.

The device described here is designed to deliver ± 15 mA indefinitely using a 20 V compliance voltage. The stimulator communicates with a host personal computer (PC) and receives all power through a universal serial bus (USB) connection and has at least 3000 V isolation between the stimulator and external inputs. There are several built-in protocols or user-defined continuous waveforms can be generated.

II. STIMULATOR DESIGN

A picture of the custom printed circuit board (PCB) is shown in Figure 1. Figure 2 shows the schematic of the stimulator. The stimulators have two BNC connectors that input external TTL pulses that are used in some modes. Each TTL input is connected through an 800 Ω current limiting resistor (R7,R4) to a Fairchild 4N25 phototransistor optocoupler (U5, U6). Each 4N25 is powered by the stimulator's isolated 3.3 V supply and has a base resistor of 42 k Ω (R8, R5) and emitter resistor of 28 k Ω (R9, R6). The inclusion of a base resistor lengthens the rise time, but significantly reduces the fall time as it allows charge to drain quickly from the base when the input signal goes low. Resistor sizes were chosen to minimize power usage and give approximately symmetric rise and fall times, measured to be 3.2 μ s and 4.2 μ s, respectively. Each emitter resistor is connected to a pair of digital

inputs on the MSP430 that are configured to trigger interrupts on rising and falling edges. When the input is low, the emitter resistor serves as a pull-down resistor, and when high presents a potential of approximately 3 V at the MSP430 pins, which is well above the maximum high input threshold voltage of 1.9 V, according to the datasheet. Unlike our previous design, there is no direct connection between the TTL input and the analog output circuitry and all stimuli are controlled by the MSP430.

The TTL inputs are multipurpose. While mimicking the behavior of the legacy stimulators they serve as simple on/off controls. In what we call *standard mode*, the user sets two current values of either polarity for channel A and channel B in the graphical user interface (GUI). In this mode, the GUI accepts currents and times in 100 μ A and 100 μ s increments, respectively. In other modes, described below, finer control is available. The stimulator outputs a rectangular current pulse of the given magnitudes for the durations of the pulse on the respective channels. In this mode, with the stimulators connected to a 1 k Ω load and set to 10.0 mA, we measure the delays from the onset and termination of an external TTL signal to reaching the requested current to be 7.0 μ s and 8.0 μ s, respectively. This total delay includes contributions from the optocoupler, MSP430 interrupt and software execution, DAC rise time, and VCCS rise time. This stimulator can directly replace two legacy stimulators in existing setups by using the two TTL inputs. Another disadvantage of the legacy stimulators is that, since they are not bipolar devices, they have a zener diode across their inputs, which provide an alternate path for the current of the second stimulator if it is set at the opposite polarity.

FIG. 1. Custom PCB. Shown with the four jumpers removed that connect the custom PCB to the USB power, CP2102, TTL inputs, and serial LCD, and stimulator output.

FIG. 2. Stimulator schematic.

The USB connection provides all power and communication with the PC. The USB input is connected to a Silicon Labs CP2102 USB to universal asynchronous receiver/transmitter (UART) bridge. The TX and RX signals from the CP2102 (not shown), along with its regulated 3.3 V and ground pins, are connected to a Fairchild FOD8012 bi-directional optocoupler (U7). The RX and TX signals on the other side of the FOD8012 are connected to one of the MSP430's UARTs. This configuration provides reliable 921 600 bits per second (bps) bi-directional communication and 3000 V isolation.

Our previous design made use of a 5 V to 200 V dc-dc converter that had a switching frequency of 25 kHz. While the rms value of the noise produced by these converters had negligible effect on our fluorescence imaging experiments, the signal was clearly visible when using electrodes, so we sought to eliminate it in the new design. The USB connection provides 5 V input to two 3 kV isolated Texas instruments DCH01 dc-dc converters with outputs of 5 V and 15 V (U9, U10). The converters come assembled on a small PCB in a SIP-7 package that contains some filtering components onboard. Used alone, we still measure noise at the switching frequency as well as at several MHz. To remove this noise, we make use of a cascaded LC filter. The first element is a ferrite bead rated with an impedance of 600 Ω at 100 MHz (L1, L3), and the second a 2.2 μ H inductor (L2, L4). In addition, the converters and filter elements sit on a filled ground plane on our PCB and are distant from the analog components. The unregulated 5 V output is regulated with a KFB33 3.3V LDO regulator (U8). The 5 V and 15 V outputs are connected in series to form a 20 V source for the VCCS. A maximum of 500 mA may

be drawn by a USB connected device. The stimulator draws 190 mA and 280 mA when idle and producing a sustained 15 mA stimulus, respectively. R11 provides a minimum load for the 15V converter as no current is drawn when the stimulator is not producing a pulse.

The VCCS is a classic, buffered, voltage-controlled current source configured with a Texas Instruments TLE2142 op-amp (U1), 2N2904 NPN transistor (Q1), and 82 Ω feedback resistor (R3) connected in series with the load. The MSP430's DAC1 uses the internal 1.5 V reference and is connected to the non-inverting input of the op-amp, and it provides control of the VCCS output. The feedback resistor drops 1.25 V at the maximum 15 mA current so most of the DAC's dynamic range is used. There is a 0.5 μ F capacitor (C1) connected in parallel with the load to reduce noise.

Our principal concern is that the stimulator has zero current output when it is set to zero. The legacy stimulators have a quiescent current of approximately a 25 μ A when not producing a pulse. In our previous design, we solved this problem by effectively disconnecting power from an op-amp when the stimulator was not producing a pulse. This technique is effective but precludes high-speed operation. The H-bridge prevents any current from being output when both sides are inactive, but in this scenario the inverting input is pulled to ground by the feedback resistor and the input offset, along with the small offset of DAC1, drives the op-amp output to the supply rail. This causes a current spike of several μ s to be generated the next time the H-bridge is activated as it takes time for the op-amp to recover. We solve this problem by connecting the MSP430's DAC0 to the inverting input through a small signal diode (D1). When the stimulator is inactive

(H-bridge off), DAC1 is set to 0 V and DAC1 is set to 0.68 V, which causes approximately 0.08 V to appear at the inverting input and drives the output to zero. When the stimulator is active, DAC0 is set to zero and the diode protects the low impedance output. A digital output along with a voltage divider could accomplish the same function, but we chose this method to reduce the component count and also take advantage of the MSP430's ability to simultaneously update both DACs.

In our previous design, we used a latching mechanical relay to change output polarity. The H-bridge circuit allows fast polarity switching. The H-bridge is constructed from two Fairchild FDS4559 chips that contain one P-type and one N-type MOSFET each (Q4, Q5, Q6, Q7). A Fairchild FDS9945 contains two N-type MOSFETs (Q2, Q3) and is used to switch the H-bridge. Q2 and Q3 have their source connected to ground and drain connected to a 2.2 k Ω resistor (R1,R2) which is connected to the 2N3904 (Q1) emitter. Their gate is connected directly to a digital output of the MSP430. According to the FDS9945 datasheet, the typical gate threshold voltage is 2.5 V, which is well below the MSP430's 3.3 V supply voltage. This allows the H-bridge to be switched directly with two MSP430 digital outputs.

Absolute current output accuracy is rarely important in our experiments. Typically, the minimum current needed for a 2 ms pulse to generate a sustained action potential, termed the threshold current, is first determined, and other stimulus parameters are some multiple of the threshold current. The feedback resistor, DAC non-linearity, and DAC quantization are the main contributors to errors in output current. After construction, we measure the output at regular intervals over the entire range with a multimeter (Mastertech M3900). We then do a least squares fit to a second order polynomial, which we have found gives the best results. As with any calibration method, the error and linearity characteristics of the device used to acquire the calibration data will be transferred to the device being calibrated. The three constants are stored in the MSP430's flash memory and retained indefinitely. The constants are retrieved along with the device ID by the PC application during initialization. This simple method provides acceptable accuracy for our experiments, but if absolute accuracy were to become important a look-up table, the MSP430's internal temperature sensor, and a larger sense resistor for smaller currents could be employed to reduce the output error.

III. VALIDATION AND TESTING

To verify that the output accuracy is not dependent on load, we tested load resistances of 0 Ω (connected to ammeter only), 500 Ω , 1 k Ω , 1.5 k Ω , and 2 k Ω . For each resistor we requested currents from 0.1 mA to 0.9 mA in 0.1 mA increments, then from 1.0 mA to 15.0 mA in 2.0 mA increments. For 0.1 mA the output error is as high as 8% due mostly to DAC quantization and offset. From 0.6 mA to 15.0 mA the measured output current is within 1% of the requested current for all resistors. The exceptions are the currents that cannot be delivered due to the 20 V compliance voltage.

To quantify the output noise, we measured currents of 1.0 mA, 5.0 mA, and 10.0 mA through a 1 k Ω resistor with

FIG. 3. 1 Hz-50 kHz noise spectra. Measurements were taken across a 1 k Ω load resistor with the stimulator set at constant currents of 1.0 mA, 5.0 mA, and 10.0 mA using a Hewlett Packard 3562A signal analyzer. The SNRs over the full bandwidth are 60 dB, 72 dB, and 75 dB, respectively.

a Hewlett Packard 3562A 50 kHz signal analyzer. Figure 3 shows the spectra. The harmonics of the switching regulators are clearly visible but are of very low amplitude. The signal-to-noise ratio (SNR) of the three currents is 60 dB, 72 dB, and 75 dB, respectively. With the stimulator set to 0.0 mA, the noise over the 50 kHz bandwidth is 1.2×10^{-7} V/ $\sqrt{\text{Hz}}$. These noise levels are satisfactory for our optical fluorescence or electrode measurements.

Standard mode was described earlier. *Autonomous mode* allows the user to specify period, duration, and amplitude of a rectangular pulse sequence in the GUI and does not require external TTL inputs, although there is an option to use one of them to trigger a sequence.

A novel built-in protocol is *S1-Sine Mode*, which allows the user to specify a series of S1 pulses to condition the heart, a delay, followed by a sinusoidal waveform of specified frequency, starting phase, offset, amplitude, and total duration. Figure 4(a) shows an example of *S1-Sine Mode*. The primary

FIG. 4. Stimulator output. Voltage measured across a 1 k Ω resistor with a Tektronix TDS 1212B oscilloscope. (A) (Upper trace) S1-Sine mode example. Three 3.0 mA S1 pulses of 10.0 ms duration and period 50.0 ms, followed by a 25.0 ms delay, followed by a 300.0 ms duration 50 Hz sine stimulus of amplitude 8.0 mA with a -4.0 mA offset and 270° starting phase. (B) (Lower trace) Streaming mode example. A damped sine wave specified by 5000 currents loaded from a text file in the GUI. Values are updated every 175 μs . This trace was recorded at 100 ms per division and overlaid to make efficient use of the figure.

FIG. 5. Induction of Arrhythmia in a Rabbit Heart using *S1-sine mode*. Electrogram was recorded using two Ag-AgCl pellet electrodes (EP8, Word Precision Instruments) placed on opposite sides of the heart. Six 1.0 mA S1's of 2.0 ms duration and 300.0 ms period followed by a 300.0 ms delay precede a sine wave with 4 mA amplitude, 90 ms period, 0° offset, 0.0 mA offset, and 2.0 s total duration.

purpose of this mode is to initiate a cardiac arrhythmia. We are unaware of another published device that includes this functionality. Figure 5 illustrates the recording of arrhythmia induction in a rabbit heart. The unipolar electrode was located on the epicardial surface of the left ventricle. It is seen that during the first two seconds of arrhythmia it has polymorphic structure with variable amplitude and period. Thereafter, the arrhythmia spontaneously converts to a sustained monomorphic tachycardia.

Streaming Mode is the most innovative mode and allows the user to load a text file containing an arbitrary number of currents that specifies a custom waveform or sequence from within the GUI. The frequency with which to update the output with each successive entry is also specified by the user. Update frequencies up to 10 kHz are supported which allow any waveform of physiological interest to be generated. The length of the sequences is only limited by the memory of the PC. Figure 4(b) shows a damped sine wave generated by specifying 5000 currents that are updated every 175 μ s.

The MSP430 uses the 16 MHz crystal as input to its 16-bit Timer A. During the initialization of *Streaming Mode*, the number of 16 MHz cycles between updates, along with the total number of entries in the entire sequence, is passed to the MSP430. The MSP430 creates two 2-kB (1000 entry) buffers in RAM and the PC control program sends waveform information over the USB connection as needed. Before the sequence begins, the PC sends the first 2000 entries, which fill both buffers. Timer A is configured to trigger an Interrupt Service Routine (ISR) at the update frequency. The series begins with a software command or can be triggered by one of the TTL inputs. Of the two buffers, one is the active buffer and is used by the ISR to update the output each time it is called. When the ISR reaches the end of one buffer, it switches to the next buffer and sends a message to the PC that requests another 1000 entries, which are copied to the non-active buffer as they are received. Another ISR could be used to read incoming data from the UART, but this would lead to a small jitter in the update frequency, so incoming data are read and copied to the non-active buffer in the main body of the program. The performance of the MSP430 and USB interface is sufficient to allow update frequencies up to 10 kHz.

The scheme used to stream data to the stimulator is optimized to minimize the processing load placed on the MSP430 as well as the amount of data sent. For each entry in a sequence the stimulator needs the 12-bit DAC setting and the state of the bridge, which can be high, low, or off. Additionally, in order to allow the user to terminate the sequence before it reaches the end, the MSP430 needs to be able to recognize an escape command in the datastream. Each entry is encoded in a 16-bit value. The lower 12 bits (bits 0 to 11) of this give the DAC setting, bits 12 and 13 represent the bridge state, and bit 14 is used to indicate if the sequence should terminate immediately. The ISR recognizes an output setting of zero and will set DAC0 and DAC1, as described earlier.

IV. DISCUSSION

The total cost in parts, including the custom PCBs, is approximately \$220, making this stimulator an attractive device for use in either research or student labs. Breakout boards are used for the MSP430 (Olimex, MSP430-H2618) and CP2102 (Sparkfun, BOB-00198) due to their small pitch packages. All other components are no smaller than SOIC or 0805 packages, which can be soldered by students/novices using an inexpensive soldering station. Stimulators from a prominent commercial vendor range from approximately \$1000 for simple devices similar to our legacy stimulators to over \$9000 for devices that can provide isolation and user-defined continuous waveforms comparable to our device. Commercial stimulators are also not well suited for customization. This does not imply that the stimulators described here are equivalent to, or are suitable replacements for, any particular commercial stimulator. Commercial stimulators may have desired features that our stimulators lack; however, the comparison is useful to put the cost and functionality into context.

Our designs have not been certified by a professional engineer, and we have not attempted to identify all possible failure modes. Our device is not intended for use on humans. The MSP430 and Windows programs, complete parts list, and information required to reproduce the PCB will be provided upon request.

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